

1249

CONSIDERABLE PROPORTION OF *LEISHMANIA BRAZILIENSIS* RRNA MOLECULES ARE POLYADENYLATED

Marlene Jara Portocarreo, Jorge Arevalo

Instituto de Medicina Tropical Alexander von Humboldt, Lima, Peru

Leishmania parasites are ancestral eukaryotes with unusual characteristics like polycistronic transcription and RNA trans-splicing. Like other eukaryotes, their rRNA ribosomal genes are tandemly repeated and transcribed by RNA polymerase I. Unlike other eukaryotes, *Leishmania* ribosomes have rRNA molecules of 18S, 5.8S, and 28S, with the latter one being split into six rRNAs (α , γ , β , δ , ζ and ϵ). The polyadenylation is a post-transcriptional process well known for mRNA but scarcely reported for rRNA. Our previous work on *L. braziliensis* and *L. donovani* demonstrated that at least the rRNA 28S ϵ undergo the polyadenylation process and that its relative abundance varies in *Leishmania* promastigote and amastigote stages. To determine if all rRNA gene subunits are subjected to polyadenylation, we evaluated the 18S rRNA, 5.8S rRNA and all the subunits homolog to 28S rRNA at stationary and logarithmic phase promastigotes of the *L. braziliensis* strain MHOM/BR/75/M2904. We found that all the rRNA subunits were polyadenylated. Moreover, we quantified the absolute amount of polyadenylated and non-polyadenylated rRNA of the sub-units 18S, 5.8S and 28S α by Reverse Transcription-Real time quantitative PCR. In the logarithmic promastigotes, the percentage of polyadenylated rRNA 18S, rRNA 5.8S and rRNA 28S α were 0.378 ± 0.02 (mean \pm standard deviation), 4.55 ± 0.43 and 13.86 ± 0.95 , respectively. The stationary promastigotes had higher percentages of polyadenylated rRNA 18S (0.704 ± 0.29 , $P=0.064$) and rRNA 5.8S (5.69 ± 0.28 , $P=0.045$) than the logarithmic promastigotes, whereas the 28S α did not show any significant differences between log and stationary promastigotes. These findings confirm a remarkable fact of *Leishmania* rRNA gene expression (also present in *L. amazonensis*, data not shown) and it is related to the parasite growth. The biological role of this phenomenon remains unknown but its wide conservation in the genus *Leishmania* indicates it is an important one.

1250

PHENOTYPIC CHARACTERISTICS OF ACUTE CHAGASIC MYOCARDITIS AMONG C57 AND BALB/C MICE

Andrés F. Henao-Martínez, Anne H. Agler, Timothy A. McKinsey, David A. Schwartz, Ivana V. Yang

University of Colorado Denver, Aurora, CO, United States

Chagasic disease is a notable neglected tropical disease with high morbidity in Latin America and among immigrants to the US. The primary mechanism of mortality is cardiomyopathy and sudden death. Acute chagasic myocarditis is consistently found in acute infections but little is known about its contribution to chronic forms of cardiomyopathy and what host factors play a role in acute myocarditis. The aim of this study was to phenotypically characterize two strains of mice with differential susceptibility to acute chagasic infection and correlate strain phenotypes with heart tissue gene expression. Laboratory mouse Tula strain of *Trypanosoma cruzi* was grown in 3T3 fibroblast cell culture and tissue-derived trypomastigotes (TCT) were harvested from supernatant. C57 and Balb/c mice were injected intraperitoneally with 0 or 150-200 TCT. Weekly, mice were weighed and parasitemia was monitored via retro-orbital blood sample. At 4 weeks Brain natriuretic peptide (BNP) and Troponin were measured in plasma and echocardiograms were obtained. 4-week mortality was 56.3% and 12.5% for Balb/c and C57 ($p=0.009$), respectively. Infected Balb/c mice lost more weight than infected C57 mice ($p=0.018$). Parasitemia peaked at 2 weeks, but was not significantly different between strains due to high variation in counts: $500,781 \pm 866,464$ (Balb/c) vs. $140,625 \pm 280,606$ (C57) parasites/ml ($p=0.12$). For infected mice, BNP and troponin levels were not significantly different between strains, but BNP differed from uninfected mice. Echocardiograms demonstrated differences in heart rate in BALB/c vs. C57 mice: 413 vs.

476 bpm, ($p=0.0001$) and stroke volume: 31.9 ± 9.3 vs. 39.2 ± 5.5 μ l ($p=0.03$); therefore in cardiac output: 13.1 ± 3.5 vs. 18.7 ± 3.2 μ l/min ($p=0.002$). There are relevant susceptibility and hemodynamic differences between these strains of mice during acute chagasic infection. Further characterizations of heart tissue histopathology, immunohistochemistry and gene expression will investigate possible host factor determinants for acute chagasic myocarditis.

1250A

QUANTITATIVE KDNA ASSESSMENT DURING TREATMENT OF MUCOSAL LEISHMANIASIS AS A POTENTIAL BIOMARKER OF OUTCOMEMarlene Jara¹, Braulio M. Valencia¹, Milena Alba¹, Vanessa Adauí¹, Jorge Arevalo¹, Alejandro Llanos-Cuentas¹, Andrea K. Boggild²¹Universidad Peruana Cayetano Heredia, Lima, Peru, ²University of Toronto, Toronto, ON, Canada

Mucosal leishmaniasis (ML) is a disfiguring manifestation of infection with *Leishmania* (*Viannia*) spp. As there is no known biomarker of treatment outcome in ML, we evaluated the concentration of kinetoplast minicircle DNA (kDNA) by cytology brush quantitative PCR before, during, and after treatment of ML in Peruvian patients. ML lesions were sampled by cytology brushes for quantitative PCR at enrolment, days 14 and 21_28 of therapy, and 3-, 6-, or 12-mos after treatment. Parasite concentration in tissue was correlated to demographic, clinical, and parasitologic factors. Twenty patients completed follow-up: 12 men and 8 women, with median age of 37 yrs (range 18_78 yrs). Fifteen patients were treated with sodium stibogluconate, and 5 with amphotericin B. Cure was achieved in 17 patients, while 2 patients failed multiple courses of therapy. Clinical outcome is unknown in 1 patient. Mean parasite load (PL) at enrolment was $85,614.8 \pm 60,427.3$ parasites per μ g of tissue DNA (par/ μ g tDNA). Three patterns of quantifiable kDNA during therapy and follow-up emerged: pattern 1 (N=10) was characterized by a mean PL of $170,867 \pm 117,482.6$ at enrolment, with sequential decline in PL during and after therapy until kDNA was undetectable. Pattern 2 (N=4) was characterized by mean PL of 566.4 ± 306.4 at enrolment, with clearance of detectable kDNA by D14 of treatment, followed by an increased PL by D21-28 of treatment to 80.4 ± 32.1 par/ μ g tDNA. Pattern 3 (N=6) was characterized by mean PL of 226.7 ± 116.1 at enrolment, with clearance of detectable kDNA during treatment, followed by increased PL by 6-mos follow-up to 36.6 ± 13.1 par/ μ g tDNA. Both patients who failed treatment demonstrated Pattern 1. Patterns 2 and 3 were associated with granulomatous inflammation ($p=0.02$). Younger age (33.5 vs. 64 yrs, $p=0.10$) and shorter ML duration (20.5 vs. 48 mos, $p=0.11$) are potentially correlated to sequential clearance (pattern 1). Baseline PL, sex, exposure duration, lesion number, and ML location were not correlated to pattern of PL. We have demonstrated that the concentration of parasite kDNA in ML can be quantified by cytology brush sampling and quantitative PCR during and after treatment. Interim analysis demonstrates 3 distinct patterns of PL during and after treatment, which warrant further investigation. Granulomatous inflammation may predict rebound of PL during or after treatment, though the clinical significance of this rebound is presently unknown.

1251

COMPARISON OF TWO COMBINATION PARASITE LACTATE DEHYDROGENASE-BASED RAPID TESTS FOR THE DIAGNOSIS OF MALARIA DUE TO *PLASMODIUM KNOWLESI* AND OTHER *PLASMODIUM* SPECIES IN SABAH, MALAYSIAMatthew J. Grigg¹, T. William¹, B. E. Barber¹, U. Parameswaran¹, T. W. Yeo², N. M. Anstey²¹Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia, ²Menzies School of Health Research and Charles Darwin University, Darwin, Australia
Plasmodium knowlesi human infection has been reported throughout South-East Asia, and is the most common cause of severe malaria in parts

of Borneo. Microscopic misdiagnosis is common, and may impact prompt initiation of treatment shown to improve mortality outcomes. Previous studies have shown cross-reactivity of *P. knowlesi* with parasite lactate dehydrogenase monoclonal antibodies used to detect *P. falciparum* and *P. vivax*. Our initial evaluation of rapid diagnostic tests (RDTs) has not demonstrated sufficient sensitivity for *P. knowlesi*, and no specific antibody for *P. knowlesi* has been developed. At both tertiary and district referral sites in Sabah, Malaysia, we prospectively evaluated two combination RDTs for the diagnosis of uncomplicated and severe malaria. Firstly with a pan-*Plasmodium* parasite lactate dehydrogenase (pan-pLDH) and *P. falciparum* specific parasite lactate dehydrogenase (PfLDH) RDT (Optimal-IT). Secondly with a non-*P. falciparum* pan-parasite lactate dehydrogenase (VOM), and *P. falciparum* histidine-rich protein-2 (HRP2) RDT (Carestart). Among 250 patients hospitalised with PCR-confirmed *P. knowlesi*, *P. falciparum* and *P. vivax* monoinfection, the pre-treatment sensitivity of the pan-pLDH test for each species was 36% (49/137; 95% confidence interval [CI] 28 to 44%), 75% (63/84; CI 64 to 84), and 83% (24/29; CI 64 to 94) respectively. The PfLDH test sensitivities were 33% (45/137; CI 25 to 41), 77% (65/84; CI 67 to 86) and 14% (4/29; CI 4 to 32) respectively. The VOM component was the most sensitive test for both uncomplicated (44%; 60/137; CI 35 to 53) and severe (79%; 15/19; CI 54 to 94) *P. knowlesi* malaria but remained clinically insufficient. More sensitive RDTs or alternative molecular diagnostic tools are needed in areas of *P. knowlesi* endemicity.

1252

COMPARATIVE ANALYSIS OF MALARIA INFECTIONS BY NESTED PCR USING A POOLING STRATEGY ON DRIED BLOOD SPOTS AND PLACENTAL HISTOLOGY IN MICROSCOPY-NEGATIVE MALAWIAN WOMEN ON IPTP

Zhiyong Zhou¹, Julie R. Gutman¹, Dyson Mwandama², Doreen Ali³, Don Mathanga², Jacek Skarbinski¹, Ya Ping Shi¹

¹Centers for Disease Control and Prevention, Atlanta, GA, United States, ²University of Malawi College of Medicine, Blantyre, Malawi, ³National Malaria Control Program, Ministry of Health, Lilongwe, Malawi

Malaria infection in pregnant women on intermittent preventive treatment in pregnancy (IPTp) often presents low parasite densities at delivery and this poses a great diagnostic challenge. In this study, a nested polymerase chain reaction (nPCR) assay for the 18S rRNA gene of *Plasmodium falciparum* was conducted to detect malaria infection in microscopy-negative pregnant women at delivery from an IPTp effectiveness study conducted in Malawi. A sample pooling strategy was developed for screening malaria infection using dried blood spots samples (DBSs) collected from placenta or periphery at delivery. Considering a known malaria prevalence of 7.6% by microscopy in pregnant women at delivery, histologic results were used to stratify the 619 available microscopy-negative samples into sample pools. Each sample pool contained 4 DBSs from histology-positive samples or 10 DBSs from histology-negative samples prior to DNA extraction for first round of nPCR screening. For those nPCR-positive pools, DBSs were then individually extracted and a second round of nPCR assay was performed. Overall, of 619 microscopy-negative DBSs, 179 (28.9%) were positive by histology and 52 (8.4%) were positive by nPCR. Among the histology-positive samples, 39 (21.8%) had active infection (acute and chronic) and 140 (78.2%) had past infection. Using the histology results as a reference, 71.8% women were nPCR-positive in the active infection group, 7.1% were nPCR-positive in the past infection group, and 3.2% were nPCR-positive in histology-negative group. In conclusion, histology diagnosis detected more malaria infection, but nPCR combined with a proper sample pooling strategy is still a practical and sensitive method to detect low density, active malaria infection at delivery. This study has demonstrated that nPCR can be a useful tool to detect submicroscopic malaria infection in pregnant women at delivery when histology diagnosis is not available.

1253

NATIONALLY REPRESENTATIVE SURVEYS OF MALARIA DIAGNOSTIC CAPACITY IN THE PUBLIC SECTOR: FINDINGS FROM GHANA AND BENIN

Joseph Keating¹, Tim Finn¹, Luis Benavente², Chris Petrucci², Nicole Whitehurst², Thomas Eisele¹, Gilbert Dery³, Ekow Biney⁴, Benjamin Fayomi⁵, Joshua O. Yukich¹

¹Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, United States, ²Medical Care Development International, Silver Spring, MD, United States, ³DERMED Consult LLC, Tamale, Ghana, ⁴Ghana Health Services, Accra, Ghana, ⁵Institut d'Sciences Biomedicales Appliquees (ISBA), Cotonou, Benin

In many African settings, malaria cases are treated presumptively. The absence of parasitological confirmation of malaria infection can lead to overtreatment of febrile illness with anti-malarial drugs, or the missing of other potentially fatal conditions. The development of rapid diagnostic tests for malaria (RDTs) combined with the scale up of Artemisinin Combination Therapies (ACTs) has led to increasing pressure to scale up parasitological diagnosis. In order to assess the availability, quality and accuracy of malaria diagnosis in Ghana and Benin, nationally representative health facility surveys were conducted in publicly supported health facilities in both countries. Results indicate that diagnostics are performed accurately a majority of the time when they are applied. The sensitivity and specificity of microscopy compared to expert readings was approximately 80% across all sampled facilities on the day of the survey. Furthermore, all observed RDTs in Ghana were interpreted correctly based on a surveyor's re-interpretation. These results appear significantly better than historic literature on malaria diagnosis with microscopy in many African locations. In Ghana, in the majority of cases, clinicians gave or prescribed drugs in line with test results. While this result is promising, it only reflects practice among patients where a test result was received. Many patients were diagnosed with malaria clinically (i.e. in the absence of any test results). While few of the patients with negative test results received a malaria diagnosis, only half of all fever patients were referred for a malaria test. Despite the overall appearance of the acceptance of testing and the agreement of clinical prescribing practice with laboratory results, approximately 30% of patients who received negative test results still received anti-malarial drugs.

1254

MAGNETIC DETECTION OF HEMOZOIN SURPASSES GOLD STANDARDS OF MALARIA DIAGNOSIS AND RIVALS SENSITIVITY OF MOLECULAR BASED METHODS

John R. Lewandowski¹, William C. Condit¹, Robert J. Deissler¹, Richard F. Bihary¹, Mark R. Lewandowski¹, Jason E. Jones¹, D'Arbra R. Blankenship¹, Melinda J. Zikursh¹, Arsene Ratsimbasa², Moses J. Bockarie¹, Peter A. Zimmerman¹, Robert W. Brown¹, Brian T. Grimberg¹

¹Case Western Reserve University, Cleveland, OH, United States, ²National Malaria Control Programme, Antananarivo, Madagascar

Malaria parasites digest hemoglobin and in the process release cationic alpha-hematin, which is toxic to the red blood cell (RBC) and developing parasite. The developing parasite polymerizes this substance into chemically inert crystals known as hemozoin. Here we have exploited the paramagnetic properties of hemozoin to develop magneto-optical diagnosis (MOD) of malaria. When mixed with water, parasitized RBCs swell, burst open and release hemozoin into solution. Exposure of this lysate to an alternating magnetic field periodically aligns the hemozoin crystals so they block the transmission of light through the solution in proportion to parasitemia. When testing MOD on 291 samples from a malaria-endemic area we detected as few as 39 parasitized cells/ μ L from patients in less than 1 minute with an overall accuracy of 93% compared to PCR based detection methods. Additionally, a subset of these patient samples were also compared to RDT (CareStart HRP2/pLDH (Pf/PAN)

COMBO) based detection methods which showed only 29% accuracy when compared to PCR results. Further studies of cultured parasites showed even lower detection of <1 parasitized cells/μL. This device provides a rapid, robust, and inexpensive diagnosis of malaria which is an improvement over microscopic and RDT based diagnosis and allows for screenings on a population-based scale which is in line with the goals of global malaria elimination.

1255

SCALING-UP MALARIA RAPID DIAGNOSTIC TESTS AND ARTEMISININ-BASED COMBINATION THERAPY INTO INTEGRATED COMMUNITY CASE MANAGEMENT SITES: RESULTS FROM TWO REMOTE AND LOW-RESOURCE SETTINGS IN THE DEMOCRATIC REPUBLIC OF CONGO

John Otshudiema¹, Narcisse Embeke², Filiberto Hernandez³, Jose Tchofa¹, Clarisse Mbo Modiri⁴, François-Xavier Mwema⁴

¹United States Agency for International Development, Kinshasa, Democratic Republic of the Congo, ²Management Sciences for Health, Kinshasa, Democratic Republic of the Congo, ³Centers for Disease Control and Prevention, Kinshasa, Democratic Republic of the Congo, ⁴National Malaria Control Program, Kinshasa, Democratic Republic of the Congo

Integrated Case Management of Childhood Illness (iCCM) improves access to prompt, accurate diagnosis and effective treatment of malaria for populations with limited access to health facilities. In the Democratic Republic of Congo (DRC), a pilot study in 2008-2009 demonstrated the feasibility and the acceptability of integrated use of rapid diagnostic tests (RDTs) for malaria and artemisinin-based combination therapy (ACT) in remote villages by community health workers (CHWs). Scaling-up of the newly adopted strategy began in 2012, reaching currently 129 iCCM sites. This abstract reports the results of the scaling-up in two targeted sites in order to improve their implementation. Patients' forms filed by CHWs from two targeted iCCM sites in Kanda-Kanda health zone were reviewed to assess their adherence to the new malaria treatment guidelines. From July 2012 through March 2013, 644 sick children under five years were managed by CHWs, out of which 432 (67%) were complaining of fever for less than two days without signs of danger. RDTs were performed on 181 (42% of those with fever) children. The remaining uncomplicated cases were treated presumptively with ACTs. CHWs referred 12 severe cases to health facilities for proper case management. Among those tested, 169 (93%) had a positive RDT of which 166 (98%) were treated with ACTs. However, 11 of the 12 patients with negative RDTs were treated also with ACTs. Among those confirmed uncomplicated RDT-positive cases treated with ACTs, 68% were treated within 48 hours of the onset of fever. iCCM has the potential to improve access to prompt, effective management of uncomplicated malaria in remote, low resource settings but challenges remain to improve CHW use of RDTs for diagnosis and adherence to test results.

1256

USING OUTCOME-DRIVEN INNOVATION THEORY TO CLARIFY TARGET PRODUCT PROFILES FOR NEXT-GENERATION MALARIA DIAGNOSTICS

Kathleen Tietje, Christine Clerk, Kenneth Hawkins, Sarah McGray, Paul LaBarre

PATH, Seattle, WA, United States

Diagnostic tools used to reduce the burden of malaria in the control phase are less effective in regions undergoing programmatic reorientation toward malaria elimination. Next generation diagnostics for malaria elimination will need to be more accurate than microscopy and existing rapid diagnostic tests to detect the reservoirs of low-density, asymptomatic infections that perpetuate disease transmission. In addition, new diagnostics will need to be user friendly, field deployable, and capable of high throughput at low cost. Despite ongoing progress in several diagnostic development programs, the technical and market requirements

for elimination phase diagnostics remain ambiguous, and therefore developers lack the incentive necessary to bring new technologies to market. To address the need for detailed target product profiles (TPPs) for elimination-specific diagnostics, PATH's project DIAMETER (diagnostics for malaria elimination toward eradication) team has identified a comprehensive list of outcome-based use-scenarios that are critical to the elimination context. Through a review of the literature and stakeholder interviews, we capture the essential system components, performance criteria, and market requirements that define success for malaria elimination stakeholders including health workers, global and national policymakers, and public and private health providers. Our findings will inform recommendations and TPPs to provide clear guidance ensuring the most efficient new diagnostic innovations are accelerated to market to support elimination campaigns.

1257

HIGHLY SENSITIVE RNA-BASED PARALLEL DETECTION OF *PLASMODIUM FALCIPARUM* AND *P. VIVAX* ASEQUAL STAGES AND GAMETOCYTES

Ingrid Felger¹, Rahel Wampfler¹, Felistas Mwingira¹, Sarah Javati², Leanne Robinson², Inoni Betuela², Peter Siba², Hans-Peter Beck¹, Ivo Mueller³

¹Swiss Tropical and Public Health Institute, Basel, Switzerland, ²Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea, ³Walter and Eliza Hall Institute, Parkville, Australia

For studies requiring highly sensitive and simultaneous quantification of sexual and asexual stages of *Plasmodium falciparum* and *P. vivax*, 18S rRNA transcript-based detection saves efforts or costs. RNA-based positivity is considerably higher than other methods. For simultaneous highly sensitive quantification of both blood stages and gametocytes in an area of equally high prevalence of both *Plasmodium* species, we have compared and optimized different strategies for field and laboratory procedures in a cross sectional survey in 315 5-9 yr old children from Papua New Guinea. qRT-PCR was performed for gametocyte markers pfs25 and pvs25, *Plasmodium* species prevalence was determined by targeting both, 18S rRNA genes and transcripts. RNA-based parasite detection resulted in a *P. falciparum* positivity of 24%; of these 41% carried gametocytes. *P. vivax* positivity was 34%, with 36.4% of these carrying gametocytes. Sensitivity of DNA-based parasite detection was substantially lower with 14.1% for *P. falciparum* and 19.6% for *P. vivax*. Using the lower DNA-based prevalence of asexual stages as a denominator increased the percentage of gametocyte-positive infections to 59.1% for *P. falciparum* and 53.1% for *P. vivax*. Because of its easy measurability in host blood the prevalence of gametocyte carriage can be used to assess the effects of malaria interventions on transmission intensity. With optimized field procedures RNA-based assays were feasible in remote settings. This approach provides in parallel a highly sensitive measure for asexual stage prevalence.

1258

TOWARDS THE DEVELOPMENT OF SALIVA-BASED MALARIA DIAGNOSTICS: MASS SPECTROMETRY BASED IDENTIFICATION OF GAMETOCYTE PROTEINS IN HUMAN SALIVA

Dingyin Tao¹, Jonas G. King¹, Ceereena Ubaida Mohien², William John Moss¹, Sungano Mharakurwa³, Isabelle Morlais⁴, David R. Graham², Rhoel R. Dinglasan¹

¹Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, ²Johns Hopkins School of Medicine, Baltimore, MD, United States, ³The Malaria Institute at Macha, Choma, Zambia, ⁴Laboratoire de Recherche sur le Paludisme, Yaoundé, Cameroon

Robust and highly sensitive saliva-based malaria diagnostics, especially for asymptomatic carriage of *Plasmodium falciparum* gametocytes (the only mosquito-transmissible stage), are an important research priority towards the eradication of malaria. Here, we detail our plan to develop such

diagnostics and present data from our baseline proteomic analyses and initial field trials. We first built a comprehensive Mass Spectrometry (MS) workflow to establish updated proteome databases for (a) the human red blood cell, (b) human saliva and (c) *P. falciparum* gametocytes. Using this new baseline information, we developed an optimized MS protocol for determining the limit of sensitivity of gametocyte protein identification in human saliva by spiking extracted proteins from 20-200 gametocytes into 1 μ L of healthy human saliva. However, the high abundance of salivary amylases, proline-rich proteins and statherin interfered with MS data-dependent scan mode and the identification of low abundance proteins was difficult. To overcome this limitation, we used peptide ligand library technology (PLLT) to "balance" protein concentrations, which can improve the gametocyte protein detection limit in spiked human saliva by 5 to 10 folds. In collaboration with clinicians in Cameroon, we then used our optimized protocol to analyze both blinded and unblinded saliva to identify candidate biomarkers for asexual and gametocyte stages of *Plasmodium*. Multi-Reaction Monitoring (MRM) will be used in ongoing experiments to validate these candidate biomarkers in individual human saliva samples. We anticipate that the confident, reproducible identification of gametocyte-specific proteins from saliva will compel the production of high-affinity rabbit polyclonal antibodies against the targeted proteins. These antibodies, once validated further by Western blot and Immunofluorescence assays, can then form the basis for the development of prototype gametocyte-specific saliva rapid diagnostic tests.

1259

USE OF MALARIA RAPID DIAGNOSTIC TEST RESULTS AMONG COMMUNITY MEDICINE DISTRIBUTORS IN RURAL UGANDAN COMMUNITIES: IMPACT ON APPROPRIATE TREATMENT

Richard Ndyomugenyi¹, Pascal Magnussen², Sham Lal³, Kristian S. Hansen³, Clare Chandler³, Sian E. Clarke³

¹Ministry of Health, Kampala, Uganda, ²University of Copenhagen, Copenhagen, Denmark, ³London School of Hygiene & Tropical Medicine, London, United Kingdom

WHO recommends universal access to malaria diagnostics, and malaria rapid diagnostic test (mRDT) is the only feasible test at community level. Evidence regarding adherence to mRDT results by community medicine distributors (CMDs) and feasibility for use in community case management (CCM) remains limited. We assessed adherence to mRDT results by CMDs in rural Uganda, to provide information that could guide mRDT-based CCM to avoid overuse of artemisinin-based combination therapy (ACTs). A cluster-randomised trial was undertaken to examine the impact and cost-effectiveness of mRDT use by CMDs on the proportion of children receiving appropriate ACT treatment (consistent with parasitological status defined by microscopy on a research slide) in two areas with differing malaria transmission. In each setting, communities were randomised to one of two arms: ACT treatment following mRDT testing (intervention arm) was compared with presumptive treatment (control arm). Data on diagnosis and treatment were recorded by CMDs in treatment registers. Household follow-up interviews and focus group discussions were conducted with CMDs and caretakers of under-five children. Adherence to mRDT results by CMDs exceeded 85% in both transmission settings. In the high transmission area, only 44% of children seen by CMDs in the mRDT arm compared with 99% of patients in the presumptive arm were treated with an ACT, reducing ACT treatment by 55%. Similarly, in the low transmission area, less than 10% of children in the mRDT arm overall were treated with an ACT compared with 94% in the presumptive arm, reducing ACT prescription by 87%. Analysis of whether this treatment was appropriate treatment (in line with microscopy on a research blood slide) is ongoing, and will be presented. In conclusion, training CMDs in use of mRDT in the context of CMM is feasible. CMDs performed well and adhered to malaria treatment guidelines thus improving rational use of ACTs.

1260

A CLUSTER RANDOMIZED TRIAL INTRODUCING RAPID DIAGNOSTIC TESTS INTO REGISTERED DRUG SHOPS IN UGANDA: IMPACT ON APPROPRIATE TREATMENT OF MALARIA

Anthony K. Mbonye¹, Pascal Magnussen², Sham Lal³, Kristian S. Hansen³, Bonnie Cundill³, Clare Chandler³, Sian E. Clarke³

¹Ministry of Health, Kampala, Uganda, ²University of Copenhagen, Copenhagen, Denmark, ³London School of Hygiene & Tropical Medicine, London, United Kingdom

WHO recommends universal access to malaria diagnosis, encompassing all treatment providers, including the private sector. Diagnosis reduces inappropriate treatment practices, such as overdiagnosis of malaria and overtreatment with antimalarial drugs. Rapid diagnostic tests (mRDTs) may provide a simple means of confirming malaria diagnosis in drug shops. As yet, there is little evidence of the impact of diagnostic testing on antimalarial drug sales and referral practices by drug shops in Africa. A cluster-randomised trial to evaluate the impact and cost-effectiveness of using mRDTs, compared with presumptive treatment, has been conducted in registered drug shops in Mukono District, Uganda since October 2010. The trial aimed to evaluate the impact of mRDT testing on the proportion of drug shop clients who receive appropriate ACT treatment (consistent with parasitological status defined by microscopy on a research slide). A total of 65 drug shops were randomised to receive training either in use of mRDTs or presumptive diagnosis of malaria. All drug shop vendors (DSVs) were trained on the national malaria treatment guidelines, use of rectal artesunate pre-referral treatment, and when to refer. Supporting interventions included activities to raise community awareness emphasising that not all fevers are malaria and to test blood before receiving or purchasing an ACT. DSVs received close support supervision for first 2 months of implementation. Introduction of mRDTs in drug shops was acceptable to DSVs, the community and health staff. Adherence to mRDT results by DSVs was high with 92% of treatment decisions being consistent with mRDT test results, reducing sales of ACTs by approximately 40%, compared to drug shops in the control arm (presumptive diagnosis). Overall, appropriate treatment in drug shops using mRDTs was significantly higher than in drug shops using presumptive diagnosis (70.1% versus 33.5%, $P=0.0001$). In conclusion, introducing mRDTs in drug shops was feasible and acceptable; and had a substantial impact on appropriate treatment of malaria.

1261

BURDEN OF MALARIA IN HIV POSITIVE PERSONS IN A MALARIA ENDEMIC AREA

Catherine O. Falade, Bukola Adesina-Adewole, Olusegun Ademowo, Isaac Folorunso Adewole

University of Ibadan, Ibadan, Nigeria

In endemic areas, malaria is usually diagnosed presumptively despite the WHO recommendation that malaria diagnosis be parasite based. HIV increases susceptibility to malaria with the result that HIV +ve persons are treated for presumed malaria very frequently. In a cross-sectional study, 2082 people living with HIV (PLWHIV) were evaluated for presence of malaria parasite by expert malaria microscopy of Giemsa stained thick blood film over a one year period. Study population was drawn from the HARVARD partnered President's Emergency Plan for AIDS Relief (PEPFAR) funded APIN adult ARV outpatient clinic, University College Hospital, Ibadan in south-western Nigeria were malaria transmission is intense. The mean age of enrollees was 36.7 ± 9.1 years (range 16-70). 81.5% (1696/2082) were female. The prevalence of malaria *parasitemia* was 15.8% (329/2082). Female PLWHIV was significantly more likely to be parasitemic than her male counterpart (13.9% versus 1.9% $p<0.0001$). The higher the level of education the less likely it is for patent *parasitemia*. Almost half (49.2%; 1024/2082) of the study population had one symptom or another at enrolment. The 5 most common symptoms were

Fever (70.1%), headache (63.2%), loss of appetite (44.3%), abdominal pains (32.1%), chills and rigors (22.3%) and vomiting (22.3%). Vomiting was the only symptom significantly associated with patent *parasitemia*. Temperature >37.4°C was not significantly associated with malaria *parasitemia*. 43.9% had received antimalarial drugs in the preceding three months. 251 (12.1%) reported three or more attacks of presumptively diagnosed and treated malaria in the same time frame. Thirty five (35/251; 13.9%) of these claimed to have had 6 to 10 episodes each. Drug use history in the two weeks before enrolment include antibacterial agent (15.6%), antimalarial drugs (34%) with 9% haven taken chloroquine, 12% had ACT and 12.2% sulfadoxine-pyrimethamine. 316 (15.2%) of the PLWHIV believed that they had malaria more frequently and each attack was more severe before their HIV status changed. In conclusion, malaria *parasitemia* is less frequent than earlier believed and parasite - based diagnosis will reduce over treatment with antimalarial drugs.

1262

RAPID DIAGNOSTIC TEST (RDT) PERFORMANCE OF THE MALARIA GOLD MINING PROGRAM IN SURINAME: COMPARING THE PERFORMANCE OF TWO RDT'S

Deborah Stijnberg, Hedley Cairo

Ministry of Health, Paramaribo, Suriname

Good Rapid Diagnostic Test (RDT) performance is at the cornerstone of the malaria diagnoses in Suriname. This because malaria infections occur mainly among persons (ca. 15,000) engaged in small-scale gold mining and related activities. Because this mining areas are remote diagnoses is primarily done by RDT either in the goldmines or in the city, in the gold miners' neighborhood, at the Tourtonne laboratory where testing occurs. End of 2011 the RDT test used switch from Binax to the use of Care Start. To assess the difference in performance of these tests from both test 82 RDT results were compared with microscopical examination by Tourtonne Laboratory (TL). Data was collected from may 2012 till April 2013. The 82 Binax results, compared with microscopy, gave a sensitivity of 76.5% compared to 94.19% for CareStart. The specificity was for both Care Start and Binax 96.9%. A PPV of respectively 86.7% and 88.9% was calculated for Binax and Care Start. Not wanting to miss positive cases the false negative rate found was 6.3% for Binax compared to 1.6% for Care Start with *Plasmodium vivax* being the species being missed in both cases. Looking at the performance of the CareStart RDT test in regards to the sensitivity, specificity, PPV and the false negative rate, the Care Start has proven in the Surinamese setting to give a much better performance than the Binax. In this regard the switch from the use of Binax to Care Start was a justified and wise choice.

1263

NEW PULSE ASSAYS THAT MIMIC *IN VIVO* EXPOSURE REVEAL DIFFERENCES IN SENSITIVITY OF *PLASMODIUM FALCIPARUM* TO ARTEMISININ

Stanley C. Xie, Nectarios Klonis, Con Dogovski, James McCaw, Maria P. Crespo-Ortiz, Sophie Zaloumis, Julie A. Simpson, Leann Tilley

University of Melbourne, Melbourne, Australia

Artemisinins (ARTs) are the most effective class of antimalarials against *Plasmodium falciparum*. However, ART resistance has emerged in regions along the Cambodia-Thailand border and many patients in that area experience delayed clearance of blood parasites. Frustratingly, the parasites isolated from those patients do not always show reduced ART sensitivity in standard 3-day *in vitro* assays. Since ART antimalarials have short *in vivo* half-lives of 1 to 2 hours, we have applied short drug pulses to parasites in an effort to better mimic *in vivo* conditions. We hypothesised that short drug pulses may reveal stage and strain-dependent differences in drug sensitivity that are not apparent in standard 3-day assays. We have examined and compared the two laboratory strains D10 and 7G8. In standard 3-day assays, D10 has 2-3 fold higher ART IC₅₀ values than 7G8

parasites. In pulse assays, tightly synchronised parasites were subjected to 4 h drug pulses at different stages throughout the intraerythrocytic asexual life cycle. Parasite viability following drug exposure was monitored in the cycle following the drug pulse by flow cytometry using the nucleotide-binding dye, Syto61. Under these conditions, the 7G8 strain exhibited up to 100 fold higher ART sensitivity than D10 parasites. Furthermore, parasites treated with 4 h drug pulses showed significant stage-dependent differences in drug sensitivity. Very early rings (less than 6 h post invasion) were very sensitive to ART. Apart from this very early stage, most of ring stage parasites (mid-ring to late-ring) were relatively insensitive to ART compared to trophozoites and schizonts. We have applied pulse assays to field isolates from the Pailin region in Cambodia that exhibit similar ART IC₅₀ values in standard 3-day assays. Our results show that pulse assays can reveal large differences in sensitivity of field strains to ARTs that are not evident in standard assays, which may be clinically relevant.

1264

STATUS OF CHLOROQUINE RESISTANT HAPLOTYPES IN *PLASMODIUM FALCIPARUM* PARASITE POPULATIONS COLLECTED IN POST-EARTHQUAKE HAITI

Lindsay C. Morton¹, Sheila Akinyi¹, Curtis Huber¹, Meredith McMorro¹, Michelle Chang¹, David Townes¹, Jacques Boncy², Roland Oscar³, Venkatachalam Udhayakumar¹, John W. Barnwell¹

¹Centers for Disease Control and Prevention, Atlanta, GA, United States, ²National Public Health Laboratory, Ministry of Public Health and Population, Port-au-Prince, Haiti, ³National Malaria Control Program, Ministry of Public Health and Population, Port-au-Prince, Haiti

Haiti is located on the island of Hispaniola, the last remaining Caribbean island with endemic malaria. In Haiti, chloroquine (CQ) remains the first-line treatment for malaria. Given the challenges of conducting *in vivo* drug efficacy trials in low endemic settings such as Haiti, molecular surveillance for chloroquine resistance markers in the *pfcr* gene is useful to identify emergence of resistant alleles in the population. After the January 2010 earthquake, enhanced malaria surveillance was rapidly instituted to monitor for CQ resistance and contain the spread of disease. In this study, 349 bloodspots were collected from suspected malaria cases mostly in areas in and around Port-au-Prince from March through July of 2010. We investigated the CQ resistant *pfcr* markers for 121 *Plasmodium falciparum* PCR-positive samples. DNA sequencing of the *pfcr* gene covering codons 72-76 was performed on PCR amplified samples. Among a total of 110 samples able to be sequenced, 108 samples were wild-type (CQ sensitive, CVMNK) while only two samples were of a resistant haplotype (CVIET). To determine if these resistant parasite alleles were imported from other endemic countries we conducted a population structure analysis using seven neutral microsatellite markers. This analysis revealed that one of the CQ resistant samples had a neutral multi-locus genotype distinct from all other Haitian samples. We were unable to amplify the other resistant parasite sample for the neutral markers. Cluster analysis of neutral microsatellite data using Structure v2.3 revealed population sub-structure with at least five distinct clusters among the CQ sensitive parasites. Furthermore, genotypes of the CQ sensitive parasites were unique to Haiti when compared to the genotypes of parasites collected in Honduras, Nicaragua, and a number of South American countries. These findings suggest a nonexistent or a very low level of CQ resistant alleles in Haiti, supporting current recommendations to use CQ as first-line treatment, while emphasizing a need for continued molecular monitoring for the emergence of antimalarial resistant parasite populations.

1265

GENETICALLY DISSECTING THE *PLASMODIUM FALCIPARUM* CHLOROQUINE RESISTANCE TRANSPORTER: EVALUATING FUNCTION AND EVOLUTION OF ANTIMALARIAL DRUG RESISTANCE

Stanislaw J. Gabryszewski¹, Andrew H. Lee¹, Satish K. Dhingra², J. Koji Lum², David A. Fidock¹

¹Department of Microbiology and Immunology, Columbia University College of Physicians and Surgeons, New York, NY, United States,

²Department of Biological Sciences, Binghamton University, Binghamton, NY, United States

As few as four amino acid changes in the *Plasmodium falciparum* Chloroquine Resistance Transporter (PfCRT) are required to mediate malaria parasite resistance to chloroquine (CQ). An example is the Ecu1110 parasite (Ecuador) whose *pfcr*t allele is comprised of K76T, A220S, N326D, and I356L, the necessary determinant being K76T. However, in its evolution, *pfcr*t has accrued additional mutations likely to balance the requirements of enhanced drug resistance and overall parasite fitness. The current understanding of these mutations only depicts the binary states of CQ resistance and CQ sensitivity, however the contribution of each mutation in parasite fitness and drug susceptibility is unknown. Additionally, the order in which these mutations appeared is likely nonrandom, given the rarity of the emergence of CQ resistance. Using Zinc-Finger Nuclease (ZFN) technology as a tool for reverse genetics, we have edited *pfcr*t to recreate the possible evolutionary trajectory of the Ecu1110 *pfcr*t in its transition from CQ sensitive to CQ resistant. We have also investigated additional mutations to recreate the evolutionary path that parasites from Papua New Guinea might have taken as CQ was introduced in the 1950s, leveraging recent genotyping studies of old archived samples. In regenerating historical *pfcr*t loci, our goal is to narrow the possibilities of evolutionary trajectories *pfcr*t has taken to achieve CQ resistance in order to get a clearer understanding of the contributions of not only each mutation but also of each domain of PfCRT in both fitness and function. To further this, we are also using this technology to introduce novel mutations in the vacuolar loop of PfCRT, suspected to be involved in redox sensing, in order to interrogate its native function. Our studies provide further insight into the evolution of *pfcr*t-mediated CQ resistance in the context of fitness constraints, and suggest a role for this protein in maintaining solute homeostasis in the digestive vacuole.

1266

FIELD VALIDATION OF CANDIDATE MOLECULAR MARKERS OF ARTEMISININ RESISTANCE IN MYANMAR

Christian P. Larsen¹, Meera Venkatesan¹, Christopher G. Jacob¹, Matthew Adams¹, Hsu H. Mon¹, Kay Thwe Han², Myat Htut Nyung², Shannon L. Takala-Harrison¹, Jeffery J. Smith¹, Myaing M. Nyunt³, Pascal Ringwald⁴, Myat P. Kyaw², Christopher V. Plowe¹

¹Howard Hughes Medical Institute/University of Maryland School of Medicine, Baltimore, MD, United States, ²Department of Medical Research (Lower Myanmar), Yangon, Myanmar, ³Department of International Health, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, United States, ⁴Drug Resistance and Containment Unit, Global Malaria Programme, World Health Organization, Geneva, Switzerland

The emergence and spread of artemisinin-resistant *Plasmodium falciparum* in Southeast Asia threatens malaria control efforts worldwide. Molecular markers of artemisinin resistance, which can be easily assayed at minimal cost, will be critical for directing surveillance and containment. A recent genome-wide association study using samples from Bangladesh, Thailand, and Cambodia identified two SNPs (MAL13-1718319 "MAL13" and MAL10-688956 "MAL10") strongly associated with delayed parasite clearance after treatment with artesunate. To validate the use of these target SNPs as potential markers of resistance, we analyzed dried blood spots obtained during a 2010 WHO Dihydroartemisin-piperazine

Therapeutic Efficacy Survey in Thanbyuzayat, Myanmar for the presence of artemisinin resistance-associated candidate SNPs. DNA was extracted from 68 dried blood spots collected prior to treatment and genotyped for the SNPs on MAL10 and MAL13 using pyrosequencing. Data were corrected using a standard curve to best estimate true ratios of sensitive to resistant genotypes for each sample. Preliminary results are as follows. For MAL10, of 66 samples successfully extracted, 21 (32%) samples contained parasites with the resistant allele, of which 18 samples (27%) were pure resistant and 3 (5%) contained both sensitive and resistant alleles. 45 samples (68%) had only sensitive MAL10 alleles present. All samples had the sensitive allele at MAL13, suggesting that the resistant allele is absent or present at very low levels in the population. Using *parasitemia* on day 3 as a surrogate for delayed parasite clearance, we analyzed the association of the MAL10 resistant allele with this phenotype. 38% (8/21) samples with resistant MAL10 had *parasitemia* on day 3, while 11% (5/45) of sensitive samples had day 3 *parasitemia*. Logistic regression indicated that the resistant MAL10 genotype was a significant predictor of *parasitemia* on day 3 (Odds ratio 4.92, $p=0.015$). When adjusting for log-transformed day 0 *parasitemia* in the model, the MAL10 resistant SNP became a marginally significant predictor of day 3 *parasitemia* (Odds ratio 3.90, $p=0.08$). MAL10 may be a valuable marker of delayed parasite clearance and should be investigated further to validate its predictive capability.

1267

HIGH PREVALENCE OF DHFR AND DHPS RESISTANCE HAPLOTYPES FIVE YEARS AFTER REMOVAL OF SULFADOXINE-PYRIMETHAMINE AS THE FIRST-LINE TREATMENT FOR UNCOMPLICATED MALARIA IN MALAWI

Elena M. Artimovich¹, Miriam K. Laufer², Kristan Schneider³, Terrie E. Taylor⁴, James G. Kublin⁵, Fraction K. Dzinjalama⁶, Ananias A. Escalante⁷, Shannon Takala-Harrison¹, Christopher V. Plowe¹

¹HHMI/Center for Vaccine Development, University of Maryland, Baltimore, MD, United States, ²University of Maryland, Baltimore, MD, United States,

³Department of MPI, University of Mittweida, Mittweida, Germany,

⁴University of Blantyre Malaria Project, University of Malawi College of Medicine, Blantyre, Malawi, ⁵Fred Hutchinson Cancer Research Center, Seattle, WA, United States, ⁶Department of Pharmacy, University of Malawi College of Medicine, Blantyre, Malawi, ⁷School of Life Sciences, Arizona State University, Tempe, AZ, United States

Less than a decade after the replacement of chloroquine with sulfadoxine-pyrimethamine (SP) as the first-line treatment for uncomplicated *Plasmodium falciparum* malaria in Malawi, chloroquine-sensitive parasites re-expanded in the population, to the point of renewed chloroquine clinical efficacy. Decreasing clinical efficacy due to spreading resistance mutations in dihydrofolate reductase (dhfr) and dihydropteroate synthase (dhps) caused SP to be replaced by an artemisinin-based combination therapy in 2007. Whether SP resistance in Malawi will decline in the absence of drug pressure remains unknown. Here, we report the maintenance of a high prevalence of SP resistant haplotypes five years after the removal of SP as the first-line treatment of uncomplicated malaria in Malawi. Resistance loci at dhfr codons 51, 59, 108, and dhps codons 437, 540, 581 were genotyped from 689 infections from 1999-2001 and 893 infections from 2012. Haplotype prevalence was estimated for both time points. SP-sensitive parasite haplotypes were not found at either time point. The prevalence of dhfr 51I/59R/108N triple mutants and dhfr 51I/108N double mutants did not change significantly between time points (85%-88%, $p=0.29$ and 4%-7%, $p=0.06$, respectively), although a decrease in dhfr 59R/108N double mutants did occur (38%-0%, $p<0.001$). An increase in the prevalence of dhps 437G/540E double mutants (84%-96%, $p<0.001$) and dhps 437G/540E/581G (0%-4%, $p<0.001$) was observed. The prevalence of dhps A437/K540 SP-sensitive parasites decreased from 7%-1% ($p<0.001$). These results suggest that although some SP-resistant haplotypes did decrease in prevalence the removal of SP as the first-line treatment of uncomplicated malaria was not sufficient to effect a return of SP-sensitive parasites. Possible explanations for these

findings include minimal fitness cost of resistant haplotypes in the absence of strong SP-drug pressure, sustained selection by the prophylactic use of SP in pregnancy and trimethoprim-sulfamethoxazole in HIV+ individuals, and/or the fixation of dhfr 108N.

1268

DIHYDROPTEROATE SYNTHASE 581 MUTATION IS ASSOCIATED WITH PARASITEMIA AT DELIVERY IN WOMEN WHO RECEIVED INTERMITTENT PREVENTIVE TREATMENT WITH SULFADOXINE-PYRIMETHAMINE

Julie Gutman¹, Zhiyong Zhou¹, Dyson Mwandama², Ryan E. Wiegand¹, Doreen Ali³, Don P. Mathanga⁴, Jacek Skarbinski¹

¹Centers for Disease Control and Prevention, Atlanta, GA, United States, ²Malaria Alert Center, University of Malawi College of Medicine, Blantyre, Malawi, ³National Malaria Control Program, Lilongwe, Malawi, ⁴Malaria Alert Center, University of Malawi College of Medicine and Department of Community Health, College of Medicine, Blantyre, Malawi

Intermittent preventive treatment in pregnancy (IPTp) with sulphadoxine-pyrimethamine (SP) is recommended for the control of malaria in pregnancy. Parasite resistance due to mutations in *Plasmodium falciparum* dihydrofolate reductase (*Pfdhfr*) and dihydropteroate synthase (*Pfdhps*) threatens its effectiveness. The *Pfdhps*581G mutation has been associated with increased placental inflammation among women receiving IPTp-SP. HIV-uninfected women with a singleton pregnancy were enrolled at delivery. Peripheral blood and placental samples were collected. Birth weight and gestational age (assessed by Ballard exam) were recorded. Nested polymerase chain reaction (nPCR) for 18S rRNA gene was done for detection of malaria; positive samples were sequenced to determine genotype at *dhfr* and *dhps* loci. We estimated a density of 20 parasites/ μ l for PCR positive, smear negative samples. PCR was positive in 91 of 710 samples. Genotype data for *dhps*581 were obtained for 81 samples. Of these, 10 were mutant (14%) and 71 were wild type (WT). With the exception of three samples that were not amplified at *dhfr*108, all mutant samples were mutated at *dhfr* codons 51, 59, 108 and *dhps* codons 437 and 540. All samples with *dhps*581G and 69% WT samples were from women who had two doses of IPTp-SP. The *dhps*581G mutation was associated with a positive smear (maternal peripheral, placental, or cord) at delivery (adjusted prevalence ratio (aPR) 3.0, 95% CI 2.0-4.4), even after adjusting for timing of last SP dose. *Pfdhps*581G was associated with increased parasite densities in both maternal peripheral (267 parasites/ μ l, 95% CI 67-1055 for mutant vs. 39 parasites/ μ l, 95% CI 28-54 for WT, $p=0.0002$) and placental (112 parasites/ μ l, 95% CI 43-290 for mutant vs. 36 parasites/ μ l, 95% CI 27-50 for WT, $p=0.01$) samples. The presence of *dhps*581G was not associated with an increased risk of maternal anemia (aPR 0.55, 95% CI 0.21-1.44), histologically-confirmed placental malaria (aPR 0.90, 95% CI 0.59-1.38), a composite outcome of LBW, preterm delivery, or small for gestational age (aPR 1.48, 95% CI 0.73-2.98), or a significant change in mean birth weight ($p=0.77$). The *dhps*581G mutation, when present in addition to the quintuple *dhps*/*dhfr* mutant, is associated with increased maternal peripheral and placental parasite densities among SP recipients. Monitoring the prevalence of *dhps*581G is critical in areas where IPTp-SP is used.

1269

SELECTION OF CYTOTOXIC RESISTANCE TO A REVERSED CHLOROQUINE COMPOUND IN *PLASMODIUM FALCIPARUM*

Melissa Forbush¹, Steven Burgess², Daniel A. Daley³, Marco Morelli¹, John C. Tan⁴, Philip J. Rosenthal⁵, David H. Peyton⁶, Roland A. Cooper¹

¹Dominican University of California, San Rafael, CA, United States, ²DesignMedix, Inc., Portland, OR, United States, ³Old Dominion University, Norfolk, VA, United States, ⁴University of Notre Dame, Notre Dame, IN, United States, ⁵University of California San Francisco, San Francisco, CA, United States, ⁶Portland State University, Portland, OR, United States

Antimalarial "reversed chloroquines" are comprised of a chloroquine-like moiety and a resistance reversal-like moiety, and show excellent potency against multi-drug resistant strains of *Plasmodium falciparum*. The dipyrindyl analog DM1157 is highly potent against chloroquine-resistant parasites *in vitro* and *ex vivo*. It also showed good oral availability and was curative in 9/10 *P. berghei*-infected mice at doses equimolar to those at which chloroquine is effective. Like chloroquine, DM1157 inhibited beta-hematin formation *in vitro* and hemozoin formation in the parasite. While DM1157 may share a similar mechanism of action to chloroquine, it is not affected by the same *pfcr* mutations that cause resistance to chloroquine, most significantly the K76T polymorphism. The potential for resistance to reversed chloroquines is unknown, thus we are attempting *in vitro* DM1157 resistance selection in the Dd2 line of *P. falciparum* using 24 hour on-off selection with incrementally increasing concentrations of the compound. Following drug removal, parasites are allowed to recover to 3% parasitemia before the next round of selection. After 48 rounds of selection, parasites showed a 2-3 fold increase in the DM1157 IC₅₀, and a 2 fold increase in the chloroquine IC₅₀, and negative cross-resistance with mefloquine. Continued selection has not resulted in further increases in IC₅₀; rather a 4 fold increase in the LD₅₀ emerged after 69 rounds of selection, indicating resistance to cytotoxic effects of the drug. The resistant parasites also showed a slow-growth phenotype. The results suggest that cytotoxic resistance to DM1157 comes at a cost of fitness, seen as slower rates of culture expansion. Parasite cloning and preparation for whole genome analysis is currently underway in order to identify the genetic determinants of resistance and parasite fitness.

1270

EVALUATION OF COARTEM TREATMENT FAILURES IN WEST AFRICA

Daouda Ndiaye¹, Ousmane A. Koita², Davis Nwakanma³, Baba Dieye¹, Yaya D. Ndiaye¹, Lansana Sangare², Fatou Joo³, Clarissa Valim⁴, Sarah K. Volkman⁴, Dyann F. Wirth⁴, Donald J. Krogstad⁵

¹University Cheikh Anta Diop, Dakar, Senegal, ²University of Science, Technologies and Techniques, Bamako, Mali, ³Medical Research Council Unit, Fajara, Gambia, ⁴Harvard School of Public Health, Boston, MA, United States, ⁵Tulane University Health Sciences Center, New Orleans, LA, United States

Because of concern about potential resistance (prolonged parasite clearance times) in Southeast Asia and the potential for artemisinin resistance, we have examined the effectiveness of Coartem for the treatment of uncomplicated *Plasmodium falciparum* malaria in three communities in West Africa (Gambissara in The Gambia, Dioro in Mali and Thiès in Senegal). These studies have enrolled participants 2-15 years of age with 2,000 to 199,999 asexual parasites per μ l of blood who had no evidence of severe or complicated malaria and no medical problems which required treatment other than malaria. Primary endpoints for this study include asexual parasite counts <25% of baseline by day 3, clearance of all asexual parasites by day 7 and the lack of recurrent infection between days 8 and 42. Secondary endpoints include asexual parasite clearance times, *ex vivo* determinations of susceptibility/resistance to antimalarials such as the artemisinins and their derivatives, amodiaquine, chloroquine, quinine and pyrimethamine; testing for drug resistance markers and for presumptively

neutral markers (barcode assays). These studies have now enrolled 171 subjects with uncomplicated *P. falciparum* malaria, who have been treated with Coartem and followed for recurrent infection or other evidence of treatment failure. Of the 171 subjects enrolled, 8 have been lost to follow-up and 13 have developed recurrent infection between days 8 and 42, although there have been no early treatment failures (on or before day 7). Twelve of 13 subjects with recurrent infections had parasites at the time of recurrence with different genetic markers. The thirteenth subject had parasites with similar markers at the times of diagnosis and recurrence and delayed parasite clearance on day 3. That patient was therefore classified as having antimalarial resistance. Apart from that subject, the results obtained thus far provide no evidence for artemisinin or Coartem resistance at the community level in The Gambia, Mali or Senegal.

1271

SELECTION OF *PLASMODIUM FALCIPARUM* RESISTANCE TO ANTIMALARIAL ACRIDONES

Stephanie J. Huez¹, Daniel A. Daley², Stephanie A. Rasmussen¹, Yuxin Li³, Rosie Dodean³, John C. Tan⁴, Michael K. Riscoe⁵, Jane X. Kelly³, Roland A. Cooper¹

¹Dominican University of California, San Rafael, CA, United States, ²Old Dominion University, Norfolk, VA, United States, ³Portland State University, Portland, OR, United States, ⁴University of Notre Dame, Notre Dame, IN, United States, ⁵Veterans Affairs Medical Center, Portland, OR, United States

The need for potent antimalarials to prevent the emergence of drug resistant *Plasmodium falciparum* is urgent. Discovery of novel acridone chemotypes has shown promise for a new antimalarial drug treatment. Dual-function acridones (chemotype II) are N10 substituted, which targets the molecule to the parasite digestive vacuole where they inhibit hemozoin formation and synergize potency of other antimalarials such as quinine and piperazine. However, the molecular target(s) of broad-spectrum (chemotype I) acridones with efficacy against both liver and blood stage malaria are unknown. Therefore, selection of acridone resistance may lead to identification of a molecular target and the mechanism of action. Using the Dd2 line and the chemotype I compound, T13, we selected stable acridone resistance by using multiple rounds of incremental, 24 hour on-off selection, followed by continuous pressure up to three times the IC₅₀ value. Parasites not exposed to the initial on-off pressure have failed to develop resistance while under continuous T13 selection, thus far. A similar strategy with the chemotype II acridone, T16.5, has failed to produce resistance. Control parasites showed an T13 IC₅₀ value of ~18 nM, while clonal resistant parasite lines showed an average IC₅₀ of 670 nM. Cross-resistance was seen with other chemotype I acridones, but not chemotype II acridones, indicating the importance of the N10 substitution in avoiding the resistance mechanism. Only slight cross-resistance to atovaquone was seen in T13-resistant parasites. This suggests that T13 may target a unique component of the mitochondrial electron transport chain from atovaquone, which specifically inhibits ubiquinone binding to the Q_o site of the cytochrome bc1 complex. T13-resistant parasites are being prepared for whole genome sequencing to identify the target molecule(s) of acridone resistance.

1272

ARTEMETHER-LUMEFANTRINE, ARTESUNATE+AMODIAQUINE AND DIHYDROARTEMISININ-PIPERAQUINE FOR TREATING UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA IN UNDER-FIVE NIGERIAN CHILDREN: A RANDOMIZED CONTROLLED TRIAL

Martin M. Meremikwu¹, Friday Odey¹, Sarah Donegan², Chioma Oringanje³, Angela Oyo-Ita⁴, Iwasam Elemi⁴, Vivian Asiegbu³, Emmanuel Ezedinachi³, Paul Garner², Umberto D'Alessandro⁵

¹Department of Paediatrics, University of Calabar Teaching Hospital, Calabar, Nigeria, ²Liverpool School of Tropical Medicine, Liverpool, United Kingdom, ³Institute of Tropical Diseases Research and Prevention, University of Calabar Teaching Hospital, Calabar, Nigeria, ⁴Department of Community Medicine, University of Calabar Teaching Hospital, Calabar, Nigeria, ⁵Institute of Tropical Medicine, Antwerp, Belgium

Plasmodium falciparum is responsible for over 90% of malaria infections in Nigeria, and accounts for 30% of under-five deaths. Uncomplicated malaria in under-five children could rapidly deteriorate to severe fatal malaria if treatment is delayed or ineffective. This paper reports the findings from Afokang, one of two Nigerian sites in a multi-centre African study of the efficacy and safety of three artemisinin-based combination treatment regimens in under-five children. Trial design was open-label, parallel group randomized controlled trial. Children aged 6-59 months with uncomplicated malaria that fulfilled eligibility criteria were randomized to receive arthemether lumefantrine (AL), artesunate + amodiaquine (ASAQ) or dihydroartemisinin-piperazine (DHAPQ). Participants were actively followed up for 28 days and then passively for 6 months. PCR was performed to distinguish recrudescence parasitaemia from new infections. Intention to treat and per protocol analysis were performed for primary outcomes assessed by D28. A total of 92, 92 and 77 eligible children were randomized to AL, ASAQ and DHAPQ groups respectively. The unadjusted D28 cure rates for AL, ASAQ and DHAPQ were 96.6% (84/87), 94.0% (78/83) and 93.1% (67/72) respectively; with PCR-adjusted D28 cure of 97.7% (84/86) for AL, and 100% for both ASAQ (80/80) and DHAPQ (70/70). Unadjusted D63 cure rates for AL, ASAQ and DHAPQ were 93.1% (81/87), 92.8% (77/83) and 93.1% (67/72) respectively; with PCR-adjusted D63 cure of 98.8% (83/84) for AL and 100% for both ASAQ (80/80) and DHAPQ (70/70). The PCR-adjusted D28 cure rate of DHAPQ was not statistically significantly different from those of AL (OR: 0.24; 95% CI 0.00,13.25) and ASAQ (OR: 1.14 ; 95% CI 0.01,200.69). As these cure rates exceed 95%, all drugs tested meet the WHO criteria for an effective ACT. Serious adverse events were few (n=4); all four in the ASAQ group but not related to drug effects. These results confirm the appropriateness of continued use of AL and ASAQ in this locality, and have programmatic implications for wider use of DHAPQ in the country.

1273

CHARACTERIZATION OF THE BC1 QI SITE AS A NOVEL ANTIMALARIAL TARGET

Allison M. Stickle¹, Joanne Morrisey², Mariana Justino de Almeida³, Aaron Nilsen¹, Michael Mather², Akhil Vaidya², David A. Fidock³, Dennis E. Kyle⁴, Jeremy Burrows⁵, Michael K. Riscoe¹

¹Oregon Health and Science University, Portland, OR, United States, ²Drexel University College of Medicine, Department of Microbiology and Immunology, Philadelphia, PA, United States, ³Columbia University Medical Center, Department of Microbiology and Immunology, New York, NY, United States, ⁴University of South Florida, Tampa, FL, United States, ⁵Medicines for Malaria Venture, Geneva, Switzerland

Malaria is a tropical disease that exerts a staggering impact on health and economic productivity, due in part to the emergence of *Plasmodium* drug resistance. To counter the spread of drug resistance, the identification of novel antimalarial targets, especially those that are vital and conserved throughout the *Plasmodium* life cycle, has become a major focus of drug

development. Here, we introduce a subset of endochin-like quinolones (ELQs) that appear to inhibit the reductive (Q_i) site of the mitochondrial cytochrome *bc*₁ complex. The Q_i site represents a previously unreported antimalarial target that is unaffected by atovaquone resistance mutations at the *bc*₁ oxidative (Q_o) site, and is compatible with high potency, broad-stage antimalarial activity. Preclinical candidate ELQ-300 was used to generate resistant parasites under incremental drug pressure. Isolated clones were 10-20 fold less sensitive to ELQ-300, and contained a point mutation in the mitochondrially encoded cytochrome *b* gene. This mutation (resulting in Ile to Leu change at position 22) maps close to the cytochrome *bc*₁ Q_i site and has not been observed in any other malaria parasite resistant to cytochrome *bc*₁ complex inhibitors. Screens against the ELQ-300 resistant "D1" clone were used to identify additional potentially Q_i-selective ELQs and to pinpoint chemical features that contribute to Q_i targeting. The strongest evidence for Q_i site activity was found for ELQs with bulky chemical groups at the 6-position. Many of these sterically hindered ELQs were 100-1000 fold less potent against the D1 clone. Conversely, D1 cross-resistance was completely absent in ELQs containing small 6-position groups such as fluorine or hydrogen. ELQs containing these smaller groups retained full potency against both ELQ-300 and atovaquone resistant parasites, suggesting that a subset of ELQs are capable of circumventing ELQ-300 resistance at the Q_i site. These results provide compelling evidence that subtle structural features of the *bc*₁ complex influence targeting and selectivity by quinolones.

1274

IMPACT OF ARTEMISININ BASED COMBINATION THERAPY (ACTS) REPEATED TREATMENT ON THE PREVALENCE OF *PLASMODIUM FALCIPARUM* DRUG RESISTANCE MOLECULAR MARKERS (*PF CRT* AND *PFMDR1*)

Aliou Traore, Demba Dembele, Bakary Sidibe, Sekou Toure, Sekou Koumare, Amadou Togo, Sanogo Kassim, Doumbo Ogobara, Abdoulaye Djimde

Malaria Research and Training Center, Bamako, Mali

ACTs are currently used as the malaria first-line treatment in most endemic countries. The aim of this study was to assess the impact of repeated treatment with AS + AQ and AR-L on *Pf crt* and *Pfmdr1*, in a 3 years randomized clinical trial in Bougoula (Mali). We use WHO 28-day standard in-vivo protocol. Overall 521 blood spotted filter papers were analyzed; mutations frequencies on *Pf crt* and *Pfmdr1* genes were compared before and after intervention. In the AS + AQ arm we observed a base line frequency of 41.6% against 77.1% for *Pfmdr1*-86Y during the first episode and > 93% in the second, third and fourth episodes of malaria. For the *Pf crt*76T gene we observe a baseline frequency of 58.9% against 88% during the first episodes and > 93% in the next episodes. For the AR-L arm's, we obtained a baseline frequency of 41.6% against 6.2%, 18.2%, 7.1% and 0% on *Pfmdr1*86Y gene for episodes 1, 2, 3 and 5 respectively. Concerning *Pf crt*76T gene the base line frequency was 58.9% against 59.1%, 75% and 88.8% for episodes 1, 2 and 3 respectively. This study demonstrate that there is a significant increase in *Pfmdr*-86Y, and *Pf crt*-76T mutants after treatment with AS + AQ and a significant decrease of *Pfmdr1* mutations after treatment with AR-L. Despite the presence of artemisinin, the CTAs select the molecular markers of resistance to the partner molecule.

1275

EVALUATION OF DIAGNOSTIC PLATFORMS FOR G6PD DEFICIENCY INCLUDING TWO QUANTITATIVE TESTS, THE FLUORESCENT SPOT TEST, A POINT-OF-CARE TEST AND A CYTOCHEMICAL STAINING-BASED ASSAY

Nicole LaRue¹, Maria Kahn¹, Michael Kalnoky², Brandon T. Leader¹, Pooja Bansil¹, Sarah McGray¹, Gonzalo J. Domingo¹

¹PATH, Seattle, WA, United States, ²Tsuga Analytics, Seattle, WA, United States

A key barrier to achieving elimination of malaria caused by *Plasmodium vivax* infection is effective treatment. There is currently only one class of drugs, 8-aminoquinolines, which can entirely clear the parasite from a patient (radical cure). Unfortunately, patients with a common human trait, glucose-6-phosphate dehydrogenase (G6PD) deficiency, are at high risk of experiencing severe adverse side effects with this class of drugs. Point-of-care G6PD tests are needed to promote safe access to these drugs for patients with malaria. PATH is working with national malaria programs, manufacturers, and other key stakeholders to accelerate development and introduction of point-of-care G6PD tests where they are most needed. As part of this initiative, we evaluated different assays and platforms for determining the G6PD status of a patient. We compared the performance of a lateral flow-based G6PD test, a fluorescent spot test, and two quantitative tests for G6PD deficiency. We provide sensitivity and specificity performance data for these tests and highlight discordant test results. Discordant test results are discussed in the context of sequencing data. Additionally, we show the utility of a cytochemical staining-based assay for determination of G6PD status in addition to identification of females with heterozygous traits for G6PD.

1276

MASS DRUG ADMINISTRATION FOR THE CONTROL AND ELIMINATION OF *PLASMODIUM VIVAX* MALARIA: AN ECOLOGICAL STUDY FROM JIANGSU PROVINCE, CHINA

Michelle S. Hsiang¹, Jimmie Hwang², Amy R. Tao¹, Yaobao Liu³, Adam Bennett⁴, G. Dennis Shanks⁵, Jun Cao³, S. Patrick Kachur², Richard G. Feachem¹, Roly Gosling¹, Qi Gao³

¹University of California San Francisco, San Francisco, CA, United States,

²Centers for Disease Control and Prevention, Atlanta, GA, United States,

³Jiangsu Institute of Parasitic Diseases, Wuxi, China, ⁴Tulane University,

New Orleans, LA, United States, ⁵Australian Army Institute, Brisbane, Australia

Recent progress in malaria control has caused renewed interest in mass drug administration (MDA) as a potential elimination strategy but the evidence base is limited. China has extensive experience with MDA but it is not well documented. We conducted an ecological study to describe the use of MDA for the control and elimination of *Plasmodium vivax* in Jiangsu Province and explore the impact of MDA on malaria incidence. We focused on two periods: 1973–1983 when malaria burden was high and MDA administered to entire counties, and 2000–2009, when malaria burden was low and a targeted approach was used in two counties. We collected all available data about the strategies implemented, MDA coverage, co-interventions, incidence, and adverse events. From 1973–1983, MDA with pyrimethamine and primaquine was used on a large scale, with annual peak coverage reaching almost 30 million people (50% of the population). Joinpoint analyses identified declines in annual incidence, -56.7% (95% CI -75.5 to -23.7%) from 1973–1976 and -12.4% (95% CI -24.7 to 2.0%) from 1976–1983. Population average negative binomial models identified a relationship between higher MDA coverage and lower monthly incidence from 1973–1976, IRR 0.98 (95% CI 0.97 to 1.00), while co-interventions, rainfall, and GDP were not associated. From 2000–2009, MDA using chloroquine and primaquine was targeted to villages and/or individuals residing near passively detected index cases (median 0.04% population coverage) and incidence declined (annual change -43.7 to -14.0%). Safety data were not collected systematically but there were rare reports of

serious but non-fatal events. In Jiangsu Province, China, large scale MDA was associated with declines in high *P. vivax* malaria transmission and a targeted approach likely contributed to interruption of transmission. MDA should be considered a key strategy for malaria control and elimination.

1277

A SAFETY MONITORING TOOL FOR PRIMAQUINE USE TO REDUCE TRANSMISSION OF *PLASMODIUM FALCIPARUM*

Eugenie Poirot¹, Jimmie Hwang², Joelle Brown¹, Roly Gosling¹

¹Global Health Group, University of California, San Francisco, CA, United States, ²Malaria Branch, Centers for Disease Control and Prevention, Atlanta, GA, United States

In 2012, the World Health Organization published new guidelines recommending the addition of a lower single dose of primaquine (PQ) (0.25 mg base/kg) than previously recommended as gametocytocidal treatment for *falciparum* malaria in areas threatened by artemisinin resistance and in settings targeting elimination. However, concerns over the small but real risks of drug-related hemolysis associated with the administration of PQ, especially in glucose-6-phosphate dehydrogenase (G6PD) deficient individuals, have restricted its widespread use. In response, this study was designed to support the safe roll-out of low dose PQ through safety monitoring for the treatment of *Plasmodium falciparum* infections to reduce transmission. We developed a tool offering enhanced monitoring to evaluate the safety and tolerability of PQ use in malaria endemic settings. The tool can assist programs to either establish a passive reporting system for adverse events related to low dose PQ therapy or a protocol for enhanced monitoring that actively tracks hematologic response. Confirmed, uncomplicated *falciparum* malaria cases prescribed PQ across all age groups from public and private health facilities are included. Assuming a population prevalence of G6PD deficiency between 5-10%, programs will need to follow 250-500 PQ treated individuals in order to detect a 25% or greater reduction in hemoglobin (Hb) between enrolment and day 7 for G6PD deficient patients with a Type I error of 0.05. For programs engaged in enhanced monitoring, follow-up visits are performed on or near day 7 after enrolment. Data on patient characteristics, malaria diagnosis and treatment, Hb levels and reported adverse events through history taking and physical examination is gathered. Finger-prick blood samples are taken for Hb, to test for G6PD deficiency, and to collect a dried blood spot. All participants are instructed on identifying symptoms of commonly reported adverse events and to monitor the color of their urine. The tool will be piloted in two low transmission countries in the Asia Pacific region and southern Africa. The design of our safety monitoring tool will be presented and could prove useful for programs planning wide-scale roll-out of single low dose PQ use in routine malaria treatment.

1278

A POSSIBLE THREAT TO THE ELIMINATION: OVERVIEW OF IMPORTED MALARIA IN JIANGSU PROVINCE, P.R. CHINA

Jun Cao, Yaobao Liu, Weiming Wang, Yuanyuan Cao, Huayun Zhou, Qi Gao

Jiangsu Institute of Parasitic Diseases, Wuxi, China

The great successful progress has been achieved in P.R. China, since the malaria elimination program launched on 2010. However, there still remain some possible threats, for example, the overseas imported cases significantly increased over the past few years. In terms of a possible resurgence of the disease, a retrospective study was conducted to describe the epidemiological profile of imported malaria 2001-2011 in Jiangsu Province, where used to be a major malaria endemic area in China. Most of imported malaria cases were acquired from African countries, young male adults with the main travel purpose of exported labors were majority of population of patients. *Plasmodium falciparum* accounted for more than 80% of the infections, and a certain proportion of patients weren't received early diagnosis and proper treatment. In recent years,

the significant growth of investment to Africa and the large number of exported labors caused the increase of overseas imported cases, there is possible increasing risk of re-introduction of malaria to the country from imported cases. The web-based real time disease reporting system is core for surveillance, and the important of having an efficient response mechanism to deal with imported malaria is highlighted.

1279

A TIME-SERIES ANALYSIS OF MALARIA CONTROL AND ITS EFFECTS ON PEDIATRIC BLOOD TRANSFUSIONS IN RURAL ZAMBIA

Alison B. Comfort¹, Philip Thuma², Janneke van Dijk², Sungano Mharakurwa³, Kathryn M. Stillman⁴, Payal Hathi¹, Sonali Korde⁵, Allen S. Craig⁶, Nancy Nachbar⁴, Yann Derriennic⁴, Rose Gabert⁴

¹Abt Associates Inc., Cambridge, MA, United States, ²Macha Research Trust, Choma, Zambia, ³Johns Hopkins Malaria Research Institute, Macha Research Trust, Choma, Zambia, ⁴Abt Associates Inc., Bethesda, MD, United States, ⁵President's Malaria Initiative, Bureau of Global Health, United States Agency for International Development, Washington, DC, United States, ⁶President's Malaria Initiative, Center for Global Health, Centers for Disease Control and Prevention, Lusaka, Zambia

Malaria related mortality remains a serious burden in sub-Saharan Africa, particularly among children. Blood transfusions can reduce mortality among children with severe malarial anemia. There has been little research conducted to date to measure the impact of malaria control on the use of blood transfusions in health facilities. We report findings from a time series analysis of facility and patient record data from a rural referral hospital over an eight-year period (2000-2008). We use multivariate analyses with an auto-regression-moving-average model to assess relationships between the scale-up of malaria control and pediatric blood transfusions. We also investigate the association between malaria control scale-up and the use of blood transfusions in other patient wards. Our results show that in years when malaria control was scaled up there were 21.9 fewer pediatric blood transfusions per month as compared to years when before malaria control scale-up (95% CI 8.1-35.8; p<0.01), a 56% reduction. Pediatric admissions for severe malarial anemia declined over the same period. In the maternity ward, there were 1.1 additional blood transfusions per month during the years of malaria scale-up (95% CI 0.1-2.1; p<0.05) as compared to years before malaria scale-up. This study provides important evidence that malaria control can reduce pediatric admissions for severe malarial anemia and thereby lower the use of pediatric blood transfusions. Our findings also suggest that malaria control may provide indirect benefits to non-malaria patients through greater availability of blood resources.

1280

COMMUNITY BASED MALARIA ELIMINATION EFFORTS IN SOUTHERN ZAMBIA

Anna M. Winters¹, Zunda Chisha¹, Daniel Bridges¹, Benjamin Winters¹, Busiku Hamainza², Mercie Mwanza², Mulakwa Kamuliwo², Sichitamba Wamulume², Duncan Earle³, John Miller³

¹Akros, Lusaka, Zambia, ²Zambian National Malaria Control Program, Lusaka, Zambia, ³MACEPA, Lusaka, Zambia

Progress in malaria control efforts in Zambia resulted in a drop in malaria parasitemia in children under five from 22% in 2006 to 16% in 2010. This success, however, is not uniformly distributed with certain areas of Zambia reporting resurgence in malaria cases while other areas, mainly Lusaka and Southern Provinces have reached sufficiently low levels of malaria transmission to warrant an in-country push towards malaria elimination. Given this level of progress, the Zambian Ministry of Health set a goal of achieving malaria elimination in at least five areas within the country by 2015. This goal warrants the establishment of a robust malaria surveillance system with a high level of sensitivity to detect malaria infections at community level. The existing passive malaria surveillance

system, which detects malaria cases at formal health facilities, has been enhanced by leveraging volunteer community health worker networks to detect hotspots of malaria transmission through follow up and screening of households in proximity of identified index cases. These enhancements have been termed “Step 3” and constitute the final stage of an innovative three-step sequence designed to measure the progress, and move towards malaria elimination. Through Step 3, over 450 community health workers from four districts of Southern Province received a 4-day refresher training in aspects of clinical presentation, testing using rapid diagnostic tests and treatment of uncomplicated malaria according to current Ministry of Health policy. Further trainings were conducted in 2013 and will substantially increase the number of community health workers and the geographical area being considered for possible malaria elimination. Through Step 3, over 20,000 RDTs have been administered. Average positivity rate during community testing has been 11.87. Reporting completeness from community health workers each month has averaged approximately 90%. Initial results show this program increases the sensitivity and timeliness of malaria surveillance such that malaria infections previously undetected by the routine passive surveillance system are now being identified and treated. Data are being monitored by district personnel for hotspot activity to guide interventions. This presentation will highlight the efforts, successes and challenges faced during the implementation of this program.

1281

MALARIA EPIDEMIC SURVEILLANCE SITES IN THE SENEGAL RIVER VALLEY, 2008-2012

Medoune Ndiop¹, Julie Thwing², Mame Birame Diouf³, Moustapha Cisse¹, Sylla Thiam⁴, Mady Ba¹

¹Senegal National Malaria Control Program, Dakar, Senegal, ²Centers for Disease Control and Prevention, Atlanta, GA, United States, ³United States Agency for International Development, Dakar, Senegal, ⁴AMREF, Nairobi, Kenya

As malaria transmission falls in a region, residents may not have sufficient exposure to infective bites to maintain immunity, and it may become epidemic-prone. The Senegal River Valley is epidemic-prone and experienced malaria epidemics in the 1990s. Artemisinin-based combination therapy (ACT) was introduced in 2007, and rapid diagnostic tests (RDTs) in 2008. Mass distribution of insecticide treated nets for children under 5 years took place nationwide in 2009, and universal coverage distribution in 2011. In 2007, the Senegal National Malaria Control Program (NMCP) put in place eight epidemic surveillance sites at health posts in four districts in the Senegal River Valley. Using a standard spreadsheet, sites report the number of total consultations, suspected malaria cases, patients tested, and confirmed cases of malaria. Data quality was assessed with quarterly onsite supervision. After 2008, diagnostic effort (cases tested/cases suspected) consistently surpassed 95% and was 100% annually in half the sites, with near absolute promptness and completeness. Transmission was highly seasonal, with 80% of cases occurring from August to November, with 60% in September and October. The southernmost site was found to be inconsistent with the epidemiologic profile of the others, with a mean annual incidence of symptomatic malaria of 93/1000 over the five years. In the remaining sites, mean annual incidence of symptomatic malaria from 2009-2012 was 1.7/1000; 0.2/1000 in children under 5, 0.6/1000 in pregnant women, and 2.0/1000 in the remainder of the population. Less than 10% of all consultations were suspected malaria, and RDT positivity rate among those tested was 17%. An investigation of the cause of high incidence in the southernmost site was conducted in 2010, but no epidemics occurred during the surveillance period. Given the low incidence and simultaneous scale-up of diagnostics, it was not possible to detect the impact of vector control interventions. Epidemic surveillance sites have performed well in Senegal and increased the districts' capacity in surveillance. The NMCP continues to add sites as transmission decreases, with the goal of detecting and responding to epidemics within two weeks.

1282

WHERE TO START IN ELIMINATING AN INFECTIOUS AGENT?

Thomas Smith, Melissa Penny, Nakul Chitnis

Swiss Tropical and Public Health Institute, Basel, Switzerland

Programs that have been successful in eliminating a disease from a large area have generally concluded that they should have focused their efforts earlier in the places with the highest transmission. These remained a threat after transmission was interrupted elsewhere, leading to the need to maintain potentially expensive surveillance activities in peripheral areas after the disease has been eliminated from them. We use a simple mathematical model of cost effectiveness to consider in which order to eliminate transmission in two connected zones, given that this is technically feasible, but that resource constraints allow an attack phase in only one zone at a time. We make simple sets of assumptions about receptivity, vulnerability, and costs. Irrespective of transmission level, disease burden is minimised by attacking the higher transmission site first. In low transmission areas, costs are minimised by attacking the higher transmission site first, while if both zones have initially very high transmission, costs are minimised by attacking the lower transmission site first. These results are scale-invariant (implying the units might be small patches, villages, districts, or countries), and can be generalized to any number of units. Considerations of equity and efficiency both argue against elimination strategies that concentrate resources in areas with the lowest transmission.

1283

THE ROLES OF VECTOR CONTROL IN ENABLING MALARIA ELIMINATION CAMPAIGNS IN VARYING TRANSMISSION SETTINGS

Philip A. Eckhoff¹, Thomas R. Burkot², Frank H. Collins³, James Gentile³, Neil F. Lobo³, Benoit Raybaud³, Tanya L. Russell², Edward A. Wenger¹

¹Intellectual Ventures, Bellevue, WA, United States, ²James Cook University, Cairns, Australia, ³University of Notre Dame, South Bend, IN, United States

Planning malaria elimination programs requires an understanding of local transmission dynamics and intensities, the local vectors species, their ecologies and behaviors. Computational models of malaria transmission can then be used to simulate the effects of different combinations, timings, and durations of vector control interventions. The EMOD model was used to simulate transmission dynamics for sites in Nigeria, Kenya, Tanzania, Zambia, and the Solomon Islands where a wide range of transmission intensities are exhibited that vary by vector species with different behaviors and population dynamics. Interventions tested in silico included insecticide-treated nets, indoor residual spraying, long-lasting larvicides, spatial repellents, and attractive toxic sugar baits. The impact of timing and duration of spray and larvicide rounds were examined for impact on the human parasite reservoir during the dry season, which affected the ability of dry season drug distribution rounds to eliminate transmission. The impact of vector control interventions depended on both the baseline transmission intensity and the behavior and ecology of each local vector species, with the species composition changing in simulation as interventions were applied. These computational results demonstrate the importance of field entomological data and understanding the transmission context for elimination programs.

1284

IDENTIFYING CHILDHOOD MALARIA HOTSPOTS USING MATERNAL SEROLOGICAL RESPONSES IN ENTEBBE, UGANDA, AN AREA OF HIGH MALARIA ENDEMICITY

Juliet Ndibazza¹, Chris Drakeley², Simon Brooker², Gyaviira Nkurunyingi¹, Hellen Akurut¹, Medi Kakande¹, Pascal Magnussen³, Birgitte Vennervald⁴, Alison Elliott¹

¹Medical Research Council/Uganda Virus Research Institute, Entebbe, Uganda, ²London School of Hygiene & Tropical Medicine, London, United Kingdom, ³Institute for International Health, Immunology and Microbiology, Faculty of Health and Medical Sciences, Copenhagen University, Copenhagen, Denmark, ⁴Section for Parasitology and Aquatic Diseases, Faculty of Health and Medical Sciences, Copenhagen University, Copenhagen, Denmark

Identifying populations with the highest malaria risk can be a valuable preliminary stage in directing targeted malaria control and elimination programmes. Improving malaria surveillance in regions where malaria burden is greatest is undoubtedly essential. We hypothesised that serological markers in pregnancy can be used to identify spatial variation in childhood malaria transmission in highly endemic regions. In a randomised trial on anthelmintic use in pregnancy [ISRCTN32849447] 2,507 women were enrolled between April 2003 and November 2005, and 2,345 live births accumulated. Participants' addresses were geo-referenced using a handheld global position system (GPS). Maternal blood was collected at delivery and an enzyme immunoassay (EIA) was used to detect total IgG antibody concentrations ($\mu\text{g/ml}$) to Apical Membrane Antigen-1 (AMA-1) and Merozoite Surface Protein-1 (MSP-1). Childhood malaria episodes from birth to two years were recorded prospectively, and annual blood samples examined for asymptomatic parasitaemia. Hotspots of malaria transmission were identified by determining spatial patterns in the incidence of childhood malaria (Incidence rate/100pys (95% CI) IR=47.4, (45.3-49.5)), the prevalence of childhood asymptomatic parasitaemia determined by microscopy (10.4%, 95% CI: 8.2-12.6), and maternal levels of AMA-1 (mean \log_{10} =6.26, 95% CI: 6.19-6.34) and MSP-1 (mean \log_{10} =6.65, 95% CI: 6.58-6.71) antibodies, respectively. Two consistent hotspots were identified, and hotspots of maternal antimalarial responses to AMA-1 and MSP-1 overlapped hotspots of childhood clinical and asymptomatic malaria. Serological markers in pregnancy might be useful in identifying spatial variation in childhood malaria transmission at micro-geographic levels in highly endemic regions. Simple descriptive mapping using routine data collected at maternal and child health units, to instantly analyse epidemiological data, could be a cost-effective operational tool to detect hotspots of malaria and support planning and implementation of control activities.

1285

A MODEL FOR DISTRIBUTION OF THE CRYOPRESERVED PFSMZ VACCINE FOR FOCAL ELIMINATION OF MALARIA

Eric R. James¹, Flavia Camponova², Damien Huzard², Naïg Chenais², Frederic Michoud², Martin Page², Klaus Schonenberger², Stephen L. Hoffman¹, Marcel Tanner³

¹Sanaria, Rockville, MD, United States, ²EssentialMed, Lausanne, Switzerland, ³Swiss Tropical and Public Health Institute, Basel, Switzerland

The PfsMZ Vaccine targeting *Plasmodium falciparum* (Pf) comprises attenuated, cryopreserved sporozoites that are stored and distributed through a liquid nitrogen (LN2) vapor phase (LNVP) cold chain using LNVP dry shippers. The vaccine is currently being evaluated in clinical trials in the U.S., Europe, and Africa. LN2 or LNVP cold chains are in common use in veterinary medicine for vaccines and artificial insemination. In human medicine LNVP storage is common, but LNVP cold chains are used on a smaller scale, principally for *in vitro* fertilization, regenerative medicine and anti-cancer vaccines. There are multiple advantages to using a LNVP cold chain, including independence from electricity. We recently reported on modeling the use of the LNVP cold chain for distribution of

the PfsMZ Vaccine for use in the Expanded Program for Immunization (EPI). Using Tanzania as the example, the cost of distributing this vaccine was determined to be no different from that of distributing any newly introduced vaccine through the EPI. However, we are now aiming for use of the PfsMZ Vaccine in mass-administration to all age groups in campaigns targeting elimination of Pf malaria. For countrywide coverage, a new distribution model that incorporates a rolling series of focal campaigns based on zones, each of which utilizes a zonal storage hub, and delivery directly to immunization centers, has been developed. Zonal boundaries are defined by considerations of population density, geography, infrastructure and accessibility, and each is activated in a sequence determined by economics and seasonality of malaria transmission. We have applied this model to the distribution logistics of a 3-dose regimen of PfsMZ Vaccine for Pf elimination in Tanzania: here the model comprises 9 zones, each active for 4 months. Defining components of the distribution model are the number of doses/cryovial, the holding time and capacity of the LNVP dry shippers, the volume of, and rate of production of LN2, and the LN2 production equipment. These components can be modified according to specific zonal requirements. The model for complete population coverage for Tanzania will be presented.

1286

PERFORMANCE OF A FIELD-STABLE LAMP MALARIA KIT IN THE DETECTION OF ASYMPTOMATIC CARRIERS IN ENDEMIC AREAS OF CAMBODIA, ZANZIBAR, SWAZILAND AND COLOMBIA

Iveth J. Gonzalez¹, Nimol Khim², Weiping Xu³, Andrés Vallejo⁴, Bryan Greenhouse⁵, Spencer Polley⁶, Didier Ménard², Berit A. Schmidt³, Sócrates Herrera⁴, Michelle Hsiang⁵, Peter Chiodini⁶, David Bell¹

¹Foundation for Innovative New Diagnostics FIND, Geneva, Switzerland,

²Institut Pasteur du Cambodge, Phnom Penh, Cambodia, ³Karolinska University Hospital, Stockholm, Sweden, ⁴Caucaseco Scientific Research Center, Cali, Colombia, ⁵University of California San Francisco, San Francisco, CA, United States, ⁶Hospital for Tropical Diseases in London, London, United Kingdom

The ability to detect asymptomatic infections at a field level will be fundamental to the success of malaria elimination strategies. This requires highly sensitive screening tests close enough to the community to enable rapid treatment. Very low parasite density infections can be detected by molecular methods such as PCR; however, these techniques require considerable training and are restricted to reference laboratories. A new field-stable CE-marked diagnostic kit for malaria based on loop-mediated isothermal DNA amplification (LAMP) is now commercially available. This LAMP kit targets mitochondrial DNA of all *Plasmodium* (Pan LAMP) or of *Plasmodium falciparum* (Pf LAMP) parasites and is able to detect down to 1 parasite/ μl of blood in less than 40 minutes. This assay is not only faster than PCR, but also requires minimal processing and instrumentation, and allows test reading with the naked eye. Compared to nested PCR and using samples from febrile patients, sensitivity and specificity for Pan LAMP were <97.0% and <99.2% respectively, and for Pf LAMP <93.3% and <85%, respectively. In order to evaluate the feasibility of this LAMP kit as a tool for the detection of asymptomatic malaria, dried blood spots from volunteers in endemic areas of Zanzibar, Cambodia, Swaziland and Colombia were collected. DNA extracted by Chelex-100 or Instagene reagent was used for amplification with Pan LAMP. Nested-PCR or nested-real-time-PCR were used as reference standards. In Cambodia, based on 516 samples, sensitivity and specificity of Pan LAMP were 86.4%(95%CI:76.6-92.7) and 93.3%(95%CI:90.5-95.4) respectively while on 465 samples from Zanzibar, sensitivity and specificity were 90.7%(95%CI:78.9-96.5) and 100%(95%CI:98.8-100) respectively. In Swaziland, 921 samples have been tested by LAMP and a positivity rate of 2.7% was observed. Nested-PCR results from these samples are pending. Sample collection in Colombia is ongoing and results will be available soon. Although LAMP testing was performed in reference laboratories, previous studies have demonstrated that the same performance can be

achieved by technicians without previous training, working in simple laboratory space and with basic equipment. FIND and partners are currently working on the development of a high throughput LAMP assay with a simplified sample processing method suited to large-scale screening campaigns for malaria elimination.

1287

GEOGRAPHIC EFFECTS ON THE DESIGN OF A TRIAL FOR INTERRUPTING THE TRANSMISSION OF MALARIA ON A SMALL ISLAND

Mariabeth Silkey¹, Thomas A. Smith¹, Tobias Homan², Nicolas Maire¹, Alexandra Hiscox², Willem Takken²

¹Swiss Tropical and Public Health Institute, Basel, Switzerland,

²Wageningen University and Research Centre, Wageningen, Netherlands

A cluster-randomized (stepped-wedge) A hierarchical stepped-wedge is implemented in the design of a trial of the use of odour-baited traps to eliminate *P. falciparum* malaria from Rusinga Island, Lake Victoria, Kenya (SolarMal trial). Each of 4062 households to receive the intervention are grouped into clusters of approximately 50 households. Groups of nine clusters are combined into meta-clusters. One randomly selected cluster within a randomly metacluster is selected to receive the intervention each week. Hierarchical randomization sequences ensured that the intervention is rolled out completely within one meta-cluster before moving on to the next randomly selected meta-cluster. A stochastic model of malaria transmission incorporating first-order community effects applied to the household geography and membership was used to measure the efficacy of the intervention at each time step. Bootstrapped confidence intervals derived from several hundred model runs were used to identify those sequences which produced narrow ($\pm 5\%$ width) confidence intervals until at least the last two months of the rollout, i.e., designs with the most power to distinguish differences between the intervened and the not yet intervened groups. Results were heavily influenced by the local variations in population density, a direct effect of the physical geography of the island. Of the random sequences that met these criteria, additional social constraints were applied, e.g., each meta-cluster must have an equal chance of being the first meta-cluster to receive the intervention; households within a given village must all receive the intervention within six months. Ultimately, a set fifty of the most powerful designs were presented to community representatives as alternatives, and the one to be implemented was drawn by lot.

1288

CHARACTERISTICS OF CHILDREN WITH ASYMPTOMATIC MALARIA PARASITEMIA IN A HIGH-TRANSMISSION SETTING OF MALAWI

Laura C. Steinhardt¹, Dyson Mwandama², Adam Wolkon³, Monica Shah¹, John Gimnig¹, Themba Mzilahowa², Ryan Wiegand¹, Don Mathanga², Kim A. Lindblade¹

¹Centers for Disease Control and Prevention, Atlanta, GA, United States,

²Malaria Alert Centre, Blantyre, Malawi, ³Centers for Disease Control and Prevention, Lilongwe, Malawi

Use of molecular diagnostics such as polymerase chain reaction (PCR) has led to the recognition that the majority of prevalent malaria infections are asymptomatic, and modeling suggests they play an important role in malaria transmission. We present data on asymptomatic parasitemia (AP) from a cross-sectional survey of children aged 6-59 months in Malawi enrolled in a cohort study. A census of six villages found 1,667 age-eligible children, of whom 1200 (72%) met inclusion criteria and consented. Caregivers were questioned regarding the child's illness history over the previous two weeks and a finger-prick blood sample was taken for slide microscopy and PCR. In March-April 2012, 440 (37%) out of 1186 providing a blood sample had parasitemia by PCR. Among parasitemic children, 291/430 (68%) had not been ill in the previous two weeks; 88% were not ill at the time of blood collection; and 89% had axillary

temperature <37.5 °C. Among children not ill in the past two weeks, factors related to AP in a multivariate log-binomial model, included: age (16% increased risk per year of age, $p<0.0001$), wealth status (45% decreased risk for those in the wealthiest quintile, $p=0.0002$), and sleeping under a bednet the previous night (31% decreased risk, $p<0.0001$). No measured characteristics of parasitemic children differed between those reporting illness and those not, except antimalarial use in the prior two weeks (28% among symptomatic and 0% among asymptomatic children). Among PCR-positive children with blood smear results ($n=326$), the proportion with submicroscopic parasitemia was 35%. Our results suggest that fever surveys would miss more than two-thirds of malaria infections among children 6-59 months, and mass screen and treat strategies using microscopy or rapid diagnostics with similar sensitivity would miss more than a third of infections. Our results suggest that mass screen and treat with more sensitive diagnostics or mass drug administration may be required to significantly reduce the parasite reservoir in areas of moderate to high malaria transmission.

1289

INITIAL IMPACT OF LONG LASTING INSECTICIDE TREATED MOSQUITO NETS ON MALARIA IN KARIMUI, PAPUA NEW GUINEA

Susan Paul¹, Justin Pulford¹, Ivo Mueller², Peter M. Siba¹, Manuel W. Hetzel³

¹Papua New Guinea Institute of Medical Research, Goroka, EHP, Papua New Guinea, ²Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia, ³Swiss Tropical and Public Health Institute, Basel, Switzerland

Malaria control activities in Karimui, a remote area in the highlands region of Papua New Guinea, have historically had limited success. For example, a national malaria control program involving indoor residual spraying and mass drug administration carried out in the 1960s reduced malaria prevalence in the general population from between 5-10% to 1% across PNG, except for Karimui where the pre-implementation prevalence rate remained unchanged despite exposure to program activities. Karimui is also relatively unique in PNG terms as reliable malaria prevalence data has been collected in the region at several intervals over the past 50 years. After decades of inactivity, the national malaria control program with support from the Global Fund to fight HIV/Aids Tuberculosis and Malaria commenced costless mass distribution of long lasting insecticide treated mosquito nets (LLINs) across PNG in 2006. Drawing on the existing evidence-base, this study aims to assess the initial impact of LLINs on malaria epidemiology in Karimui relative to previous malaria control activities in the region. A household survey (HHS) was conducted alongside an annual census update round in a Karimui-based Sentinel Site in 2011. The HHS included 255 randomly selected households from across the Sentinel site. A structured questionnaire examining household level LLIN ownership and use (among other things) was completed with the head of each participating household. A blood sample was also drawn from all consenting individuals aged 6 months or older residing in each randomly selected household ($n=1135$). The resulting dataset was in the final stages of cleaning at the time of drafting this abstract. Analyses will be completed by July 2013 and will include LLIN coverage and utilisation rates and malaria parasitaemia prevalence in the general population. These findings will be compared and contrasted with earlier malaria epidemiological data obtained from the Karimui region.

1290

ASSESSING THE BURDEN OF MALARIA IN LARGE CITIES OF TROPICAL AFRICA - USE OF MALARIA INDICATOR SURVEYS AND DATA FROM THE MALARIA ATLAS PROJECT**Bob Pond***JSI Research & Training Institute, Inc., Boston, MA, United States*

This presentation will demonstrate a simple method using data from Malaria Indicator Surveys ("MIS files") and/or data from the web site of the Malaria Atlas Project ("MAP files") to measure the prevalence of malaria *parasitemia* among children living in large cities of tropical Africa and compare this to the prevalence among children living nearby. Geo-coordinates for each survey cluster (in the case of MIS files) or research site (in the case of MAP files) were used to determine the distance from the site to the center of the city. Geo-coordinates of any site within 25 km of the city center were entered into Google Earth to obtain a satellite image of the location and determine whether it was within the boundaries of the metropolis. Data from all sites within city boundaries were pooled together and compared to data from all sites outside of city boundaries but within 100 miles of the city center. Data from the Uganda 2009 MIS showed that the prevalence of malaria *parasitemia* among children 6 - 59 months of age living in Kampala was 93% (95% C.I.: 85% - 97%) less than among children living outside the city. Data from the Nigeria 2010 MIS showed that the prevalence of malaria *parasitemia* among children living in Lagos was 95% (95% C.I.: 82% - 99%) less than among children living outside of the city. The prevalence of malaria *parasitemia* among children living in 7 large African cities in malaria endemic areas ranged from less than 1% in Dar es Salaam to 7.9% in Monrovia and was between 72% and 95% lower than in nearby sites outside of these cities. The method provides for a practical way to use existing and easily accessible data to rigorously document the substantially lower burden of malaria in various large cities of tropical Africa.

1291

THE INTERACTION BETWEEN IRON DEFICIENCY ANEMIA AND MALARIA ON ADVERSE BIRTH OUTCOMES**Freya J. Fowkes¹**, Kerry Moore¹, Freya Langham¹, Francesca Baiwo², Julie A. Simpson³, Danielle Stanic², Christopher King⁴, Ivo Mueller⁵, Peter Siba², Stephen Rogerson³, James G. Beeson¹*¹Burnet Institute, Melbourne, Australia, ²Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea, ³University of Melbourne, Melbourne, Australia, ⁴Case Western Reserve University, Cleveland, OH, United States, ⁵Walter and Eliza Hall Institute, Melbourne, Australia*

The World Health Organization recommends iron supplementation and malaria prophylaxis during pregnancy to reduce adverse birth outcomes. However, there are concerns that iron supplementation can increase the risk of malaria and iron deficiency has been shown to protect against malaria. It is currently unknown how iron deficiency anemia and malaria interact to influence birth outcomes such as low birthweight. We determined malariometric and iron deficiency parameters (ferritin, CRP, transferrin receptor) in 470 pregnant women attending antenatal clinics in a malaria-endemic region of Papua New Guinea at enrolment (mean 25 weeks gestation). Women were followed to delivery and birth outcomes including birthweight and gestational age were recorded. The prevalence of iron deficiency anemia was high in this population (70-87%) depending on iron marker and definition. Linear regression showed an inverse relationship between ferritin (a biomarker of body iron stores) and birthweight; for every two-fold increase in ferritin, mean birthweight decreased by 58g (95%CI: -98, -18; $p = 0.023$) i.e. the more iron replete the greater the birthweight. There was some evidence of effect modification by the presence of *Plasmodium spp.* infection whereby the relationship between ferritin and birthweight was stronger in aparasitemic women (-67; 95% CI: -120, -15; $p = 0.004$) compared to parasitemic women (-31; 95% CI: -93, 31; $p = 0.3$). There was no association between iron status and gestational age/pre-term birth. This study provides evidence

that iron deficient women are giving birth to heavier babies than their iron replete counterparts in a malaria-endemic area. Results question the use of universal iron supplementation during pregnancy for the prevention of adverse birth outcomes in malaria-endemic regions. Further research is needed to understand the mechanisms behind the protective effects of iron deficiency on adverse birth outcomes.

1292

SUBMICROSCOPIC GAMETOCYTEMIA AND MALARIA IN MALAWI: MOLECULAR IDENTIFICATION AND IMPLICATIONS FOR TRANSMISSION**Jenna E. Coalson¹**, Jenny A. Walldorf², Matthias J. Marti³, Regina Joyce³, Karl B. Seydel⁴, Miriam D. Ismail¹, Don P. Mathanga⁵, Atupele P. Kapito-Tembo⁵, Terrie E. Taylor⁴, Miriam K. Laufer⁶, Mark L. Wilson¹*¹University of Michigan School of Public Health, Ann Arbor, MI, United States, ²University of Maryland Baltimore, Baltimore, MD, United States, ³Harvard School of Public Health, Boston, MA, United States, ⁴Blantyre Malaria Project, University of Malawi College of Medicine, Blantyre, Malawi, ⁵Malaria Alert Center, University of Malawi College of Medicine, Blantyre, Malawi, ⁶University of Maryland School of Medicine, Baltimore, MD, United States*

Asymptomatic *Plasmodium* parasite infections occur frequently in people where malaria is endemic, and, if gametocytemic, may represent a source of "silent" transmission that is not associated with malaria disease. Microscopy is often considered insufficient to detect gametocyte infections, which occur at low densities relative to asexual parasite stages. A novel, highly sensitive and specific reverse transcription polymerase chain reaction (RT-PCR) assay was recently created that uses 5 markers to distinguish developing and mature *P. falciparum* gametocytes from asexual stages at submicroscopic densities. We evaluated this assay using human blood samples collected during October 2012 in a cross-sectional, all-ages, household-level study of the International Center of Excellence for Malaria Research in Malawi. We aimed to define potential infectious reservoirs by assessing prevalence and predictors of submicroscopic gametocyte infection in three settings representing urban/low (Blantyre), semi-rural/mountainous (Thyolo), and rural/high (Chikhwawa) transmission. Of 2,795 people who were surveyed and sampled for *Plasmodium* microscopy, additional blood from a subset of 629 people was collected into RNAprotect for RT-PCR testing. Of these, 618 had thick smear microscopy readings. Asexual stage parasites were detected by microscopy in 9.3% (16 of 173), 3.2% (7 of 218), and 13.3% (30 of 227) of samples from Blantyre, Thyolo, and Chikhwawa, respectively. Gametocytes were also detected in one person in this subset (from Blantyre). The use of this new RT-PCR assay enabled us to identify a large number of additional submicroscopic gametocyte infections, many of which were asymptomatic in this cross-sectional sample. We present data on the predictors of submicroscopic *gametocytemia* and compare these results with microscopic and molecular results for asexual parasites. A better understanding of which humans may be unrecognized sources of parasite transmission is critical in order to enhance malaria interventions, particularly in areas approaching elimination.

1293

INCIDENCE AND FACTORS ASSOCIATED WITH CLINICAL MALARIA AMONG SCHOOLCHILDREN IN A HIGH MALARIA TRANSMISSION SETTING**Joaniter I. Nankabirwa¹**, Bonnie Wandera¹, Simon Brooker², Moses R. Kamya¹*¹Makare University College of Health Sciences, Kampala, Uganda, ²London School of Hygiene & Tropical Medicine, London, United Kingdom*
Although school aged children bear the highest burden of asymptomatic malaria infections in high transmission settings, little is known about the burden of the clinical disease in this age-group. To investigate

the incidence and factors associated with clinical malaria among schoolchildren in Tororo, Uganda, we studied 248 children aged 6-14 years and enrolled in the placebo arm of a randomized placebo controlled trial investigating the impact of intermittent preventive treatment on malaria morbidity and cognitive function. Clinical malaria was defined as *parasitemia* with either history of fever or axillary temperature of greater than or equal to 37.50C. All children were followed for one year and clinical malaria was assessed by active case detection. Of the 248 children enrolled, 243(98%) completed the one year follow up. At baseline, *parasitemia* was present in 71(32%) of the children and the incidence of clinical malaria was 0.34 episodes/child/year after one year of follow up. Clinical malaria episodes differed significantly by age groups with a 51% (p-value=0.029) reduction in the odds of disease in the older children (11-14 years) compared to younger children. Children infected with helminths were more likely to get clinical malaria than children without infection (OR 1.6 p-value=0.034). Interestingly, no association was observed between being parasitemic at baseline and development of clinical malaria during follow up (OR 0.96 p-value 0.891). Malaria (both asymptomatic *parasitemia* and clinical episodes) is a big health problem among schoolchildren in a high transmission setting and children may benefit from interventions targeted at reducing the malaria burden in this age-group. Combining malaria interventions to the already existing helminth control interventions in schools may provide cost effective means of extending malaria control in school aged children. Finally, in resource limited settings, targeting malaria intervention to younger children may provide considerable benefit in reducing risk of malaria and missed school days.

1294

THE OBSERVED OPTIMAL TEMPERATURE FOR MALARIA TRANSMISSION AT 25°C IS PRECIPITATION DEPENDENT

Torleif Markussen Lunde

University of Bergen, Bergen, Norway

According to the 2007 IPCC report, the distribution and magnitude of malaria will be influenced by climate change. Exactly how is still debated. Previous studies showed that the optimal temperature for malaria transmission is 25°C. Two studies differed with respect to how they were validated. While Lunde et al based the validation on laboratory studies, Mordecai et al used field data which showed that the highest values of EIR was observed around 25°C. Since EIR is not only dependent on temperature, among other the availability of breeding sites, there is a possibility that this observed optimum is a result of more breeding sites in areas with temperatures close to 25°C. To investigate whether the observed R0 maximum at 25°C is due to more breeding sites in areas with temperatures close to 25°C we run a previously described model, OMaWa for 20 years; one simulation with no temperature perturbation, and one simulation where air and water temperatures were perturbed with 2°C. From the simulations we calculate the monthly mean basic reproductive number, R0, and find the breeding site dependent optimal temperature for malaria transmission. We use a non-parametric local maximum smoothing to define the temperature at which malaria is most efficiently transmitted. We find that the breeding site dependent optimum temperature for malaria transmission under current climate is ~24°C. With a two degree increase, the observable optimum temperature for malaria transmission increases by one degree C. The model suggest the optimal temperature for malaria transmission derived from field observations is dependent on the actual air and water temperatures. To understand how climate change, ignoring changes in socio-economic conditions and interventions, influence malaria transmission and other vector borne diseases, there is a need to document the life history of vectors in relation to temperature in the laboratory.

1295

SPATIO-TEMPORAL SURVEILLANCE MODELS FOR THE DETECTION OF ELEVATED MALARIA RISK IN ETHIOPIA AND ZAMBIA

Joshua O. Yukich¹, Adam Bennett¹, Yemane Berhane², Honelgn Nauhasseny², John M. Miller³, Busiku Hamainza⁴, Marie-Reine I. Rutagwera³, Joseph Keating¹, Thomas Eisele¹

¹Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, United States, ²Addis Continental Institute of Public Health, Addis Ababa, Ethiopia, ³PATH Malaria Control and Evaluation Partnership in Africa (MACEPA), Lusaka, Zambia, ⁴National Malaria Control Centre, Lusaka, Zambia

In many African countries malaria transmission is being effectively reduced by broadly applied malaria prevention measures. However, there remains a need to develop methods to rapidly detect and respond to short term increases in malaria transmission. Passive surveillance data transmitted by mobile phones can provide a platform for rapid data transmission from facilities to district, national and international actors. Surveillance systems operating at scale deliver large quantities of data that require improved methods of interpretation and visualization to quickly simplify content for decision-makers. Furthermore, commonly utilized epidemic detection algorithms in most instances fail to make use of the information contained in the spatial structure of the data. Recent computational advances in spatio-temporal risk modeling using Integrated Nested Laplace Approximation (INLA) allow models accounting for spatial and temporal auto-correlation to be rapidly fit and updated, transforming surveillance data into timely and useful mapped risk notifications. Using the INLA package in R, such models were fit with high predictive accuracy for a sentinel surveillance system in Ethiopia (1,528 facility-month reports over a 39 month period in 83 facilities) and on a national HMIS dataset in Zambia (22,227 facility-month reports over a 24 month period in 1,369 facilities). These models made it possible to accurately identify spatio-temporal clusters of increased risk. When exceedence probabilities were set to less than one in 1,000 for Ethiopia and less than one in 10,000 for Zambia, signaling events occurred at relative risk levels of 1.2, 3, and 4 in 121, 32, 13, and 4 facility-months in Ethiopia, and in 4,175, 931, 283, and 133 facility-months in Zambia, respectively. Thresholds can be varied in this framework to balance the desired sensitivity of detection and programs' operational capacity to investigate each event. Such approaches will be of high utility to decision makers by improving both the speed and sensitivity of detection of increased malaria transmission.

1296

MALARIA TRANSMISSION IN HOUSEHOLDS IN BLANTYRE, MALAWI

Jessica W. Cassin¹, Christopher G. Jacob¹, Phillip C. Thesing¹, Oswald M. Nyirenda², Rhoda Masonga², Terrie E. Taylor³, Christopher V. Plowe¹, Miriam K. Laufer¹

¹Malaria Group, Howard Hughes Medical Institute/Center for Vaccine Development, University of Maryland School of Medicine, Baltimore, MD, United States, ²Blantyre Malaria Project, University of Malawi College of Medicine, Blantyre, Malawi, ³College of Osteopathic Medicine, Michigan State University, East Lansing, MI, United States

Epidemiological methods focused on the home, such as indoor residual spraying and the use of insecticide-treated bed nets, have proven effective in reducing the burden of malaria infection. Insight into the transmission of malaria within households might offer new strategies for malaria interventions. In urban areas, where *Anopheles* mosquitoes are rarely detected, we hypothesized that infections within households would be highly related because they were due to a single exposure outside of the urban area. We examined the relatedness of malaria infections in children participating in a clinical trial to their mothers in the city of Blantyre, Malawi. Children were enrolled in the study when they had an episode of uncomplicated malaria. Their mothers were offered the opportunity to be

tested for malaria when they felt ill. Blood spots from all of the mothers' specimens were tested for malaria by real-time PCR. We analyzed 177 new episodes of malaria in mothers among 101 individuals. Infections from the mothers and the infections detected in their children were genotyped using six neutral, unlinked microsatellite markers. Unique parasite genotypes were compared between children and their mothers and the mean proportion of shared microsatellites for the mother-child pair within a household was compared to the mean proportion of microsatellites shared among each child to every mother outside of his or her household by two sample t-test. Intra-household infections were more genetically related than inter-household infections (mean shared alleles 61.7% vs. 28.2% respectively, p value <0.0001). The extent of allele sharing suggests that drug resistant and drug susceptible parasites are passed between adults and children. Infections within a household may originate from a common source or are passed between members. If an exposure during travel outside the home introduces infection into the household, bed nets or chemoprophylaxis with travel may limit spread of malaria infection in urban areas.

1297

USING INTEGRATED LAPLACE APPROXIMATIONS TO ESTIMATE MALARIA PREVALENCE

Samir Bhatt, Daniel J. Weiss, Bonnie Mappin, Peter W. Gething
University of Oxford, Oxford, United Kingdom

Malaria transmission intensity affects almost all aspects of malaria epidemiology, including community prevalence, incidence, and total malaria mortality. The most commonly measured metric of malaria transmission is the parasite rate (PR): the proportion of individuals infected at a given point in time. Previously, models built to predict PR on a global scale (Gething et al 2010) utilised Bayesian hierarchical models fitted by Markov Chain Monte Carlo (MCMC) sampling. While these models have proven to be very useful, MCMC sampling methods become intractable in terms of both convergence and computational time when used on large data sets. This limits their utility for large-scale malaria risk mapping, particularly as the number of available PR survey data continues to grow rapidly. An alternative new framework using simplified integrated nested Laplace approximations (INLA) to compute posterior marginals (Rue et al 2008) provides a powerful and flexible alternative. Here we show that the statistical performance of the two methods for spatial prediction of PR across large areas (using West Africa as an example) is comparable in terms of predictive validation statistics. We then demonstrate the use of the INLA framework to fit larger, more complex models, which could not otherwise be fit using MCMC sampling but which provide substantial improvements in model accuracy.

1298

CREATION OF CONTINENTAL-SCALE, TEMPORALLY DYNAMIC DATASETS FROM REMOTELY SENSED IMAGERY FOR USE IN DISEASE MODELING

Daniel Weiss, Samir Bhatt, Bonnie Mappin, Peter Gething
University of Oxford, Oxford, United Kingdom

The proliferation of remotely sensed data products enables improved characterization of variables known to influence vector disease ecology. However, contamination of imagery by cloud and other data quality issues means dynamic data are often aggregated to synoptic means, limiting their utility for analyzing change. We have built two dynamic data assemblies for quantifying temperature and vegetation conditions (a lagged proxy for moisture) in Africa for use in modeling malaria. A newly designed gap-filling algorithm was central to our approach as an adjustment for persistent cloud cover in equatorial regions. Our resulting datasets consist of monthly estimates for each parameter (2000-2012, 1km spatial resolution, for all of Africa) and represent a noteworthy improvement over synoptic climatic summaries (e.g., single layers such

as mean annual temperature). We discuss the implications of these new datasets for analyzing patterns and causes of changing malaria prevalence through time.

1299

RECOMBINATION AND RESOLUTION: A NOTE ABOUT *PLASMODIUM VIVAX* MEROZOITE SURFACE PROTEIN-3 ALPHA AS A MOLECULAR MARKER

Benjamin L. Rice, Monica M. Acosta, M. Andreina Pacheco, Ananias A. Escalante

Arizona State University, Tempe, AZ, United States

Parasite molecular markers can provide much needed data on *Plasmodium vivax* populations, but there have been few suitable markers identified and analyzed. One marker that has been used extensively is the gene encoding merozoite surface protein-3 alpha (MSP-3 alpha), a blood-stage antigen known to be highly variable. Here, we report the results of a study using an augmented sample of complete MSP-3 alpha gene sequences ($n = 48$) to analyze patterns of parasite diversity at this locus and assess its utility as a genetic marker. In addition to small study populations of Venezuelan ($n = 10$) and Thai ($n = 17$) clinical isolates, we sequenced *P. vivax* strains from a diverse range of geographic locations. Evidence of frequent and variable insertion-deletion mutations and recurrent recombination between MSP-3 α haplotypes in all populations complicated the inference of genetic diversity patterns and reduced the phylogenetic signal at this locus. Comparison to results from the in silico simulation of a polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) protocol commonly used found that PCR-RFLP haplotypes were not informative of a population's genetic diversity and that identical haplotypes could be produced from analogous bands. Therefore, we question the ability of the PCR-RFLP protocol to accurately recapitulate the complex patterns of MSP-3 alpha recombination and polymorphism observed from sequencing. Our data suggest that a high number of genetic differences at the MSP-3 α locus may be segregating between isolates in all *P. vivax* populations. Thus, we must caution against associating MSP-3 alpha allelic diversity with *P. vivax* population diversity, as MSP-3 alpha variability was as high within both local populations studied as in the entire diverse, global sample. High diversity allows the identification and tracking of individual parasite clones through time and space, and we suggest that this may be the most informative implementation of MSP-3 alpha as a molecular marker.

1300

A COMPARISON OF THE GENETIC STRUCTURES AMONG *PLASMODIUM* POPULATIONS FROM AREAS WITH DIFFERENT TRANSMISSION INTENSITIES IN COLOMBIA

M. Andreina Pacheco¹, Andres Vallejo², Socrates Herrera², Myriam Arevalo-Herrera², Ananias A. Escalante¹

¹Arizona State University, Tempe, AZ, United States, ²Caucaseco Scientific Research Center and Centro Internacional de Vacunas, Cali, Colombia

Malaria low-transmission areas are of great interest because of their potential for elimination attempts. Under such conditions, the precise monitoring of infections, including their spatial connectivity (gene flow), is indispensable. In 2011 Colombia reported a total of 61,636 cases, 47% less than in 2010, which may indicate a decreasing trend. About 42% of these cases were reported in four states (departamentos): Chocó, Córdoba, Nariño, and Valle del Cauca (Valle). Some representative areas like Buenaventura, (Valle) reported 979 cases in 2012, whereas Tumaco (Nariño) and Tierralta (Córdoba) reported 1,475 and 7,482 respectively. Furthermore, these areas display differences in the relative importance of *Plasmodium falciparum* (Pf) and *P. vivax* (Pv): Valle Pv 90%, Tumaco Pv 6.9%, and Tierralta Pv 92%. We hypothesized that in Pv infections, given the presence of hypnozoites and the high prevalence of subclinical infections, we should expect higher levels of recombination and multiple infections (MOI) as compared to Pf. We also hypothesized widespread clonal expansions in Pf, due to the effect of strong selection on mutations

conferring resistance in the recent past. We analyzed a total of 120 samples including both Pv and Pf parasite samples collected from these populations using a set of physically linked and unlinked microsatellite loci. We found that levels of heterozygosity varied geographically in both parasites. The frequency of multiple infections (MOI) ranged from 10-20% in Pv and was about 10% in Pf. The relative low level of MOI in Pv indicates that most patients cleared up their previous infections likely due to the easy access to Primaquine. We also found strong linkage disequilibrium (clonal expansions) in both species. Thus, the pattern observed in *P. vivax* is indicative of ongoing reduced levels of recombination due to the parasite demography. Overall, the local ecology appears to explain the turnover of clones/clusters in both parasites at this spatial scale. These processes need to be taken into account when studying gene flow among malaria endemic areas.

1301

MODELING FOR MALARIA CONTROL AND ELIMINATION SCENARIO PLANNING: APPLICATION OF THE EPIDEMIOLOGICAL MODELING (EMOD) MALARIA DISEASE TRANSMISSION KERNEL TO COMMUNITY-BASED INTERVENTION DELIVERY IN SOUTHERN ZAMBIA

Edward A. Wenger¹, Philip A. Eckhoff¹, Megan Littrell², Kafua Silumbe³, Busiku Hamainza⁴, John M. Miller³, Richard W. Steketee²

¹Intellectual Ventures Laboratory, Bellevue, WA, United States, ²Malaria Control and Evaluation Partnership in Africa (MACEPA), PATH, Seattle, WA, United States, ³Malaria Control and Evaluation Partnership in Africa (MACEPA), PATH, Lusaka, Zambia, ⁴National Malaria Control Center, Ministry of Health, Lusaka, Zambia

In the context of ongoing mass-screen-and-treat (MSAT) campaigns in Southern Zambia, we present the results of simulations using the Epidemiological Modeling (EMOD) program for the purpose of identifying optimal intervention strategies at different levels of endemic transmission. The EMOD modeling platform provides geographically-specific, and mechanistic stochastic models of disease transmission simulations through the use of extensive and complex software modeling. Given known or assumed parameters relevant for malaria control and elimination scenario planning for Zambia, we explore the impact of seasonality on optimal campaign timing and frequency; the cost-effectiveness of different modes of distribution, e.g. mass drug administration (MDA); the role of increased distribution and utilization of vector-control measures; and the addition of drugs with enhanced gametocidal and/or prophylactic effects such as primaquine. As malaria control and elimination efforts progress, models that optimize the combination of prevention and treatment strategies for delivery at community level are important to guide a rational approaches to choice of interventions and delivery methods.

1302

FACTORS INFLUENCING URBAN MALARIA: A COMPARATIVE STUDY OF TWO COMMUNITIES IN THE ACCRA METROPOLIS IN GHANA

Ruth C. Brenyah¹, Derick Osakunor¹, Richard Dadzie Ephraim²

¹Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, ²University of Cape Coast, Cape Coast, Ghana

As urban centres in Ghana continue to grow, the scale and impact of urban malaria is increasing. This study was carried out to compare the prevalence of malaria in two communities and how this may be affected by knowledge, attitudes, socioeconomic status and preventive practices of residents in two communities within the Accra metropolis. Giemsa-stained thick blood films were examined for malaria parasites in 400 people (200 each from townships with high and low urban status) from May to November 2009. Questionnaires were administered to determine and evaluate demographics of the participants. All participants lived within the two catchment areas, about 20 km apart. Average malaria prevalence among participants was 8.75%. Prevalence in Kaneshie (12%:

$p=0.032$) was however higher than that of Airport West (5.5%). Illiteracy rate (17.5%), self-medication (81.5%) and the use of coils (21.0%) as a control mechanism was higher among residents of Kaneshie than Airport West. Most of the people (40%) in Kaneshie did not use any form of malaria control method. Insecticide spray was the most preferred malaria control mechanism by the Airport West residents (60.5%). Overall knowledge about malaria, employment status, housing conditions, level of overcrowding and the cost of treatment of malaria was better in Airport West than at Kaneshie. Malaria prevalence and factors influencing its transmission differs within communities in the same urban area. It is therefore essential to develop control and prevention strategies based on the needs of specific communities.

1303

INTERACTION OF MALARIA AND HELMINTH CO-INFECTIONS IN SYMPTOMATIC AND ASYMPTOMATIC CHILDREN IN SOUTHWEST NIGERIA

George O. Ademowo¹, Ayokulehin M. Kosoko², Olawunmi R. Rabi², Olatubosun G. Arinola², Catherine O. Falade²

¹College of Medicine, Ibadan, Nigeria, ²College of Medicine, University of Ibadan, Ibadan, Nigeria

Malaria and intestinal helminth infections are common tropical diseases. Little is understood about their interaction when they coexist. We investigated the effect of co-infection of helminth and *Plasmodium* infections. Asymptomatic school children (304) and febrile children (495) were recruited from selected primary schools and Adeoyo Hospital, Ibadan, Nigeria). Blood samples were used for haematocrit determination while Giemsa stained smears were used for malaria parasite screening by microscopy. Stool samples were used for helminth diagnosis done by Kato-Katz method. Among the school children, 142 (46.7%) were positive for malaria, 181 (59.5%) had helminth only (*Ascaris lumbricoides*, AL - 43.1%, *Trichuris trichiura* TT -2.3% and AL/TT - 14.1%), while 57 (18.8%) had co-infection of helminth and *Plasmodium*. Among the febrile children, 116 (23.4%) were positive for malaria, 45 (9.1%) for worms only (AL - 7.3%, TT - 0.2%, AL/TT - 1.4%, *Taenia* spp - 0.2%) while 16 (3.2%) had co-infection of malaria and helminth. Among asymptomatic children, *Plasmodium* infection was significantly reduced in helminth positive relative to helminth negative. The opposite was the case among febrile children. Anaemia was significantly higher in *Plasmodium* infection alone compared with those with helminth infection. *A. lumbricoides* is the most prevalent helminth. *Plasmodium* infection was negatively and positively associated with helminth infection in asymptomatic and febrile children respectively.

1304

IDENTIFICATION AND MOLECULAR DIAGNOSIS OF A TANDEM DUPLICATION OF THE *PLASMODIUM VIVAX* DUFFY BINDING PROTEIN GENE IN MADAGASCAR

Binta Jalloh

Case Western Reserve University, Cleveland, OH, United States

Previous studies have shown Duffy-negative African individuals are resistant to *Plasmodium vivax* (Pv) infections. However, recent findings in Madagascar confirm that Pv is capable of Duffy-independent red cell invasion. Data analysis has shown that infections from each individual field isolate are comprised of multiple Pv strains. Additionally, our whole genome sequencing of numerous Pv field isolates from Madagascar has led to discovery of a tandem duplication of the parasite's Duffy binding protein (PvDBP). The overall goal of our studies is to identify factors that play a significant role in Duffy-independent *vivax* malaria. For this study samples were collected from regions of western Madagascar where we originally identified Pv infections in Duffy-negative people. All samples were first analyzed by a *Plasmodium* species PCR-based ligation detection reaction fluorescent microsphere assay (LDR-FMA) to diagnose infection by the four species causing human malaria in Madagascar. To evaluate

complexity of Pv infection we developed nested PCR assays targeting Pv apical membrane antigen 1 gene (PvAMA1) and the PvDBP duplication to verify presence of Pv in individual infections. From a total of 138 samples, 42 were LDR-FMA-positive for Pv. Of these 0 were PCR positive for nest 1 PvAMA1, and 0 for nest 1 PvDBP duplication. However, 15 were PCR positive for the nest 2 of PvAMA1, 9 for PvDBP, and 7 were positive for both PvAMA1 and PvDBP. These results suggest that detection of Pv by focus on single-copy sequence requires nested PCR. Additionally, as Pv infections are characterized by the presence of multiple strains, our results indicate that the strains carrying the PvDBP duplication were present in approximately 25% of infections. When a PvDBP duplication strain was present, it made up varying proportions of the overall infection.

1305

SUB-NATIONAL EVALUATION OF THE IMPACT OF MALARIA CONTROL PROGRAMS IN HUAMBO PROVINCE, ANGOLA

James M. Colborn¹, Ricardo Yava², Gabriel Ponce de Leon¹, Adeline Chan¹, Christie Hershey³, Filomeno Fortes⁴

¹Centers for Disease Control and Prevention, Atlanta, GA, United States, ²Ministerio da Saude, Luanda, Angola, ³United States Agency for International Development, Washington, DC, United States, ⁴Programa Nacional de Combate à Malaria, Luanda, Angola

In most sub-Saharan African countries, malaria control activities are carried out at sub-national levels. Nation-wide activities often start with small geographical areas and expand to other areas. Monitoring and measuring the impact of interventions carried out at sub-national scale is vital to scaling these programs up to the national level, and is not always possible using national-level household surveys such as the malaria indicator surveys and demographic health surveys. These surveys are typically powered to generate estimates at either national or alternatively, one level below national scale. In Angola, we used routine health facility data to measure the impact of indoor residual spraying (IRS), insecticide treated net (ITN), and case management campaigns for malaria control that were implemented in three of the 11 municipalities in the Province of Huambo, Angola. Routine health information system data showed that suspected malaria cases in all ages decreased from 160,487 in 2009 to 135,018 in 2011, while deaths in children under 5 years of age suspected to be caused by malaria decreased from 506 to 141 (72%) during the same time period in Huambo Province. Although IRS and case management training programs were solely implemented in the Municipality of Huambo, the largest decrease in suspected malaria cases and suspected malaria mortality occurred in two municipalities that received a mass ITN distribution campaign in April 2011. In these two municipalities, the peak monthly incidence of suspected malaria cases decreased from 6.2 cases per 1000 population per month to 0.35 cases per 1000 population per month from 2011 to 2012. These results show that health facility data may be useful in measuring the impact of malaria control programs, and suggest that while the interventions in case management training and IRS appear to be decreasing the burden of malaria in Huambo Province as a whole, mass ITN distribution may have had the biggest contribution to this decrease. Other factors, such as infrastructure improvements in the Province may also have contributed to reducing malaria burden.

1306

HIGH RESOLUTION MICROSATELLITE "META-LOCI" TO STUDY THE MICROEPIDEMIOLOGY OF PLASMODIUM FALCIPARUM

Alanna Schwartz¹, Jordan Kemere², Molly Elmer-DeWitt¹, Libing Wang³, Philip Rosenthal¹, Grant Dorsey¹, Bryan Greenhouse¹

¹University of California San Francisco, San Francisco, CA, United States, ²Baylor College of Medicine, Houston, TX, United States, ³University of California Berkeley, Berkeley, CA, United States

Genotyping information may be used to provide fine scale data on parasite transmission networks, especially in low transmission areas.

Microsatellites can be easily amplified from field samples and can readily identify alleles from multiple strains present in the blood. However, when performing many pairwise comparisons between samples, the probability of numerous alleles matching between unrelated parasites due to chance is unacceptably high, even when homozygosity at each locus is relatively low (~0.2). To improve genetic resolution, we investigated a "meta-locus" approach, in which the haplotypes of genetically linked microsatellites, instead of individual microsatellites, were used to define each locus. We identified 27 additional microsatellites demonstrating variability located within 15kb (with the exception of one due to an absence of closer microsatellites) of 10 commonly used microsatellites (range 1-4 per locus), and thus unlikely to recombine over a few generations. Multiplex nested PCR methods were developed to increase sensitivity while conserving DNA. These methods were 10-100x more sensitive than individual PCR reactions, amplifying dried blood spot (DBS) samples with parasite densities of 10-100 parasites / ul. Preliminary genotyping data obtained from 50 dried blood spot samples in Uganda demonstrates that discrimination is increased on average 3.8 fold at each locus, with homozygosity decreasing from a median of 14% (interquartile range of 10%-13.5%) to 4% (interquartile range of 3.65%-4.55%). A number of meta-loci had unique signatures for almost all samples tested, indicating that homozygosity may have been overestimated in the samples tested. These methods offer promise for obtaining highly discriminatory multilocus genotypes from field samples. Application of these methods to evaluate fine-scale population structure is in process. In particular, samples from pre-elimination areas are being evaluated to identify the source and spread of malaria infections to better target interventions.

1307

WEALTH STATUS AND DEMAND FOR MALARIA TREATMENT FROM PRIVATE SECTOR RETAILERS IN NIGERIA

Eric Schatzkin¹, Jenny Liu¹, Naomi Beyeler¹, Sepideh Modrek², Anna De La Cruz¹, Dominic Montagu¹

¹University of California San Francisco, San Francisco, CA, United States, ²Stanford, Stanford, CA, United States

Although AMFm subsidies have increased the supply of artemisinin combination therapies to treat malaria, there is little access to reliable malaria diagnostics in Nigeria even though national policy calls for parasitological confirmation prior to treatment. In 2012, we conducted REMEDI, a pilot study of the acceptability of malaria rapid diagnostic tests (RDTs) among adult customers purchasing anti-malarials from retail pharmacy and proprietary and patent medicine vendors (PPMVs) in urban and peri-urban areas of Oyo State in Southwest Nigeria. Using the pilot study data, our analysis aims to (1) assess the representativeness of our sample compared to a national survey and (2) investigate differences in malaria-treatment seeking behavior, acceptability of RDTs, and treatment adherence by individuals of different wealth statuses. To enable external comparison, wealth indexes are constructed using principal components analysis of household assets measures collected in both REMEDI and the 2010 Malaria Indicators Survey (MIS). Indexes are then converted to quintile categories according to cutoff values defined by the MIS and used as the main predictive indicators in subsequent bivariate and multivariate regression analyses. A comparison of wealth quintiles between REMEDI and the MIS shows that the REMEDI sample is substantially wealthier than the national population and concentrated within the top two wealthier quintiles. Regression analyses indicate that individuals in the highest wealth quintile are significantly less likely to be recruited at a PPMV, but more likely to report having gone to a PPMV for the previous episode of suspected malaria. The wealthiest also paid somewhat less for their drugs. No differences in other health-seeking behaviors, types of anti-malarials purchased, or RDT-positivity was detected, but the wealthiest individuals were less likely to take the correct treatment (according to the RDT result) even though they were more likely to consult the treatment advice card given to them by the study nurse. While the wealthiest individuals were also more educated, acceptability and adherence to RDT results may be more problematic and require targeted intervention.

DIFFERENCES IN THE EPIDEMIOLOGY OF MALARIA IN THE GAMBIA, SENEGAL AND MALI

Seydou O. Doumbia¹, Jean-Louis Ndiaye², Abdullahi Ahmad³, Mahamadou B. Toure⁴, Sory I. Diawara⁴, Joseph Okebe³, Ousmane A. Koita⁴, Mahamadou Diakite⁴, Lansana Sangare⁴, Nafomon Sogoba⁴, Joseph Keating¹, Umberto D'Alessandro³, Donald J. Krogstad¹

¹Tulane University Health Sciences Center, New Orleans, LA, United States,

²University Cheikh Anta Diop, Dakar, Senegal, ³Medical Research Council Unit, Fajara, Gambia, ⁴University of Science, Technologies and Techniques, Bamako, Mali

Wide-scale deployment of improved access and coverage with malaria control tools will reduce malaria transmission in highly endemic areas and may ultimately lead to the elimination of malaria as a major public health problem in West Africa. In order to monitor changes in malaria epidemiology related to policy, both cross-sectional and cohort study designs have been used to target representative samples of the local population in 3 West African Countries: The Gambia, Mali and Senegal. Two sites in Mali characterized by high and intense transmission (irrigated sahelian areas of Dioro and Sudan Savana areas of Dangassa) have been selected. In Senegal, the Thies site is urban with moderate seasonal transmission, whereas the Gambian site is rural and has achieved a significant reduction in the intensity of transmission. We report here the results of 2 cross-sectional surveys carried out in the rainy and dry season respectively at the Mali sites and one cross sectional survey performed in the rainy season at the sites of Gambia and Senegal. The prevalence of asymptomatic infection in all age groups included during the rainy season varies from 0.3% (4/1497) in Urban Thies, 3.4% in rural Gambissara (48/1401), 20.4% in irrigated site of Dioro (301/1479), to 42.6% (601/1412) in Sudan Savana of Dangassa. The prevalence of symptomatic malaria within 2 weeks period in the same cohort was 0% in Thies (N=1497), 1.8% in Gambissara (N=1401), 2.1% in Dioro (N=1479) and 9.4% (N=1412) in Dangassa. During the dry season (February-March) the prevalence of asymptomatic infection in the same cohort remained relatively high in Dangassa : 45.8% (N= 1153) and lower in Dioro 8.4%. These results shows the challenges in control in high endemic areas such as Dangassa. In addition to transmission patterns, the differences between these 4 sites may reflect the different levels of use and coverage with malaria intervention tools.

1309

WHO CRITERIA FOR SEVERE MALARIA IN IDENTIFYING SEVERE VIVAX MALARIA: PRELIMINARY DATA FROM A STUDY IN IQUITOS, PERU

Edward S. Smith-Nuñez¹, Salomon Durand¹, G. Christian Baldeviano¹, Antonio M. Quispe¹, Frederique Jacquerioz², Moises Sihuinchá³, Juan C. Celis⁴, Lorena Tapia¹, Karen Campos¹, Kimberly A. Edgel¹, Andres G. Lescano¹

¹U.S. Naval Medical Research Unit - 6, Lima, Peru, ²Tulane University, Lima, Peru, ³Apoyo Iquitos Hospital, Lima, Peru, ⁴Iquitos Regional Hospital, Lima, Peru

Vivax malaria is responsible for 90% of malaria cases in Peru. Severe vivax malaria is defined using the WHO criteria devised for *Plasmodium falciparum*, but may lead to misclassification in vivax malaria. We report preliminary findings from a case-control study for severe vivax malaria. The study is being conducted in Iquitos, in the Peruvian Amazon. Participants were PCR confirmed *P. vivax* mono-infection 5 to 65 years old. Cases were defined using the WHO severe malaria criteria. Controls were uncomplicated vivax malaria, two for each case. Criteria for critically ill malaria case included very severe anemia (hemoglobin <5 mg/dL), lung injury, shock, renal failure, admission to the ICU or cerebral malaria. All cases and controls provided informed consent and were treated by the Ministry of Health following local guidelines.

Thirty cases and 59 controls were enrolled based mainly on clinical criteria. None of the subjects tested positive for dengue or leptospirosis. The main characteristic of cases was prostration (96%). Other characteristics at admission were severe anemia (n=2), seizures (n=1), coma (n=1), jaundice (n=2) and pulmonary alterations (n=3). After 24 hrs, when the laboratory results were available, 11 controls (19%) were re classified as cases due to total bilirubin > 2.5 mg/dL (n=9), glucose < 60 mg/dL, and hematocrit <21% (n=1). No subjects presented with altered renal laboratory parameters. Prostration was the only severity criteria in thirteen cases (32%). Neither of these cases met the criteria for critically ill patients as defined above. Seventeen subjects were critically ill. Prostrated-only cases, compared to controls, had no differences in hemoglobin, platelets or creatinine, but they had higher total bilirubin levels (76% vs 35%, p=0.008) and lower albumin levels (30% vs 93%, p<0.001). All but one subject were discharged from the hospital within three days. There is a need for a specific definition of severe vivax malaria. Prostration may be a sensitive but not specific criteria to identify severe and critically ill vivax cases.

1310

LOOKING FOR GOLD, FINDING MALARIA: 2012 MALARIA SURVEILLANCE IN GOLD MINERS' COMMUNITIES IN SURINAME

Hedley Cairo¹, Deborah Stijnberg², Marjorie Ardjosentono¹

¹Ministry of Health Malaria Program; "Looking for gold, finding malaria", Paramaribo, Suriname, ²Ministry of Health, Paramaribo, Suriname

Despite the marked reduction of malaria incidence in Suriname, malaria continues to affect the migrants' population (n= 15,000) involved in gold mining. Miners have been trained in the use of RDTs and treatment of uncomplicated malaria to provide services in their communities. Blood films are prepared for the quality control of all RDTs performed. They report to the Tourtonne laboratory (TL). The TL in the epicenter of the Brazilian gold miners' community in the city is the other component of malaria surveillance in gold miners' communities. The TL staff executes Active Case Detection Campaigns on a regular basis in gold mining areas. The surveillance data serves as the basis of this paper. In 2012, 321 cases were recorded, representing a decrease of 50.3% from the 646 recorded in 2011. *Plasmodium falciparum*, *P. vivax* and *P. malariae* were identified in 42.4%, 49.5% and 1.9% of cases respectively. 3.1% had a mixed infection. For 3.1% the species could not be determined. 259 (80.7%) cases were imported; the 62 autochthonous cases signify a reduction of 62.4% compared to the 165 reported in 2011. Of the autochthonous cases, 30 (55.6%) were acquired in the Lawa basin, 11 (20.4%) around the Lake, 6 (11.1%) in the Saramacca and 3 (5.6%) in the Marowijne basin. The Upper Marowijne had the lowest number of cases 1 (1.9%). The 62 cases were dispersed over 24 locations with 5 or less cases per location. 52.4% of the locations had only 1 malaria case in 2012. The mean prevalence measured during ACDs was 1.8%. The SPR was 5.9%, ABER 36.2% and API 5.2 per 1000. 98.4% of the infections occurred in Brazilians. 4 cases were reported in pregnant women. Increased access to diagnosis and treatment in the remote gold mining areas, ACD campaigns and the distribution of LLIN to the populations at risk in the gold mining areas appears have contributed to the steep decline in malaria cases. An increasing proportion of the malaria cases appear to be acquired in French Guiana. A regional approach is mandatory to reduce cross-border importation.

1311

THE IMPACT OF MALARIA CONTROL INTERVENTIONS IN ETHIOPIA, 2000-2012

Kesetebirhan Admasu¹, Daddi Jima², Ashenafi Assefa², Hiwot Solomon¹, Asnakew Yeshiwondim³, Zelalem Kebede³, Gunewardena Dissanayake⁴, Hiwot Teka⁴, Sheleme Chibsa⁴, Lia Florey⁵, Cameron Taylor⁵, Jimee Hwang⁶, Joseph Malone⁷, Christine Hershey⁸, Carrie Nielsen⁶, Yemane Berhane³, Amha Kebede²

¹Ethiopian Federal Ministry of Health, Addis Ababa, Ethiopia, ²Ethiopian Health and Nutrition Research Institute, Addis Ababa, Ethiopia, ³Addis Continental Institute of Public Health, Addis Ababa, Ethiopia, ⁴President's Malaria Initiative-United States Agency for International Development, Addis Ababa, Ethiopia, ⁵ICF International, Calverton, MD, United States, ⁶President's Malaria Initiative-Centers for Disease Control and Prevention, Atlanta, GA, United States, ⁷President's Malaria Initiative-Centers for Disease Control and Prevention, Addis Ababa, Ethiopia, ⁸President's Malaria Initiative-United States Agency for International Development, Washington, DC, United States

Malaria transmission in Ethiopia is unstable, usually limited to areas <2000m in altitude, and 57 million people are considered at risk. Periodic, widespread malaria epidemics with high mortality have been historical features. However, since 2004, Ethiopia rapidly scaled up effective malaria interventions including: artemisinin-based combination therapies (ACTs), indoor residual spraying, long lasting insecticidal nets (LLINs), and universal laboratory diagnosis by microscopy or rapid diagnostic tests (RDTs). In addition, the total number of public health facilities increased 5-fold and >34,000 additional health extension workers were trained in malaria case management and supplied with RDTs and ACTs, which significantly increased Ethiopia's outpatient and inpatient malaria care capacity. Multiple data sources including program, survey, and surveillance data were reviewed to assess the scale-up of interventions and its potential impact. Although no ACTs were available in Ethiopia prior to 2004, more than 4 million treatment doses have been distributed yearly since 2006, sufficient to treat the nation's reported *Plasmodium falciparum* cases. Laboratory confirmation of all suspected malaria cases with microscopy or RDTs increased from <25% in 2004 to 83% by 2012. According to the national Malaria Indicator Surveys, 55% of households owned at least one LLIN in 2011 and access to malaria diagnosis and treatment services within 24 hours of fever onset has increased from 15% in 2007 to 51% in 2011. These improvements coincided with a 28% decrease in mortality from 2005 to 2011 among children less than five years of age. In addition, widespread malaria outbreaks have decreased. In 2003, a large-scale malaria outbreak resulted in an estimated 25,000 malaria-related deaths among children less than five years of age affecting 211 districts. Since then, fewer than 12 districts per year have reported malaria outbreaks. The scale up of malaria control interventions, treatment of laboratory-confirmed malaria cases with ACTs, and health systems strengthening are associated with reductions in annual malaria deaths among children less than five years of age and the suppression of malaria epidemics in Ethiopia.

1312

GENETIC DIVERSITY OF *PLASMODIUM VIVAX* INFECTIONS IN A REMOTE FORESTED AREA OF CENTRAL VIETNAM

Nguyen Van Hong¹, Pham Vinh Thanh¹, Peter Van den Eede², Christopher Delgado³, Nguyen Thi Huong Binh¹, Chantal Van Overmeir², Umberto D'alesandro⁴, Duong Thanh Tran¹, Anna Rosanas-Urgell², Annette Erhart²

¹National Institute of Malariology, Parasitology and Entomology, Hanoi, Vietnam, ²Malariology Unit, Institute of Tropical Medicine, Antwerp, Belgium, ³Unit of International Health, Faculty of Medicine, University of Antwerp, Antwerp, Belgium, ⁴Malariology Unit, Institute of Tropical Medicine Antwerp, Belgium; Diseases Control and Elimination Theme, Medical Research Unit, Fajara, Gambia

Plasmodium vivax control is becoming increasingly important in Vietnam where the malaria burden has been drastically reduced and the government has now engaged into a malaria elimination program. Understanding *P. vivax* transmission dynamics is crucial for further improving elimination strategies; however this knowledge remains scarce in most endemic areas. We present the baseline data on the *P. vivax* population genetics in a remote area of Central Vietnam. Two hundred and forty five blood samples collected before treatment (day 0) in *P. vivax* patients were submitted to species-specific PCR for diagnosis confirmation. All *P. vivax* mono-infections were genotyped using 16 previously published microsatellites. The overall genetic diversity and structure of the *P. vivax* parasite population was determined and related changes in space, time and demographic indicators were analyzed. A total of 239 patients were confirmed to be *P. vivax* mono-infections and genotyped. Overall the *P. vivax* population displayed a high genetic diversity with an expected heterozygosity (He) of 0.70 and an average of 1.21 alleles/locus (ranging from 1 to 5 alleles/locus). Most of the infections were polyclonal (75.3%) with an average multiplicity of infection of 2.7 haplotypes/person. The risk of polyclonal infections ranged from 50% to 96% across villages, and was significantly higher in children compared to adults (73.8 % versus 26.2%). Moreover, compared to dry season, the risk of polyclonal infections was 9-fold higher during the rains. In conclusion, in this remote, forested area, the *P. vivax* population was highly diverse and polyclonal, indicating substantial ongoing transmission; interrupting it may require additional and new interventions to those currently deployed.

1313

SEQUENCING OF *PLASMODIUM FALCIPARUM* LIVER STAGE CD8 T CELL ANTIGENS TO IDENTIFY VACCINE CANDIDATES

Xiaoyan Zou, Sri Hadiwidjojo, Jessica Bolton, Joao Aguiar, Thomas Richie, Eileen Villasante, Vince Gerbasi

U.S. Military Malaria Vaccine Program, Naval Medical Research Center, Silver Spring, MD, United States

CD8 T cell mediated immunity is a critical arm of the immune response in radiation attenuated sporozoite (RAS) conferred protection against malaria. When parasite development is halted inside hepatocytes, malaria peptides are presented on the surface of infected hepatocytes through MHC Class I receptors for presentation to CD8 T cells. Characterizing *Plasmodium falciparum* (Pf) peptides presented on the surface of infected hepatocytes holds promise to identify novel liver stage antigens as vaccine candidates. Here we report that by establishing an *in vitro* system of liver stage schizont culture and utilizing state-of-the-art mass spectrometry approaches we have successfully identified Pf peptides expressed on human primary hepatocytes from various donors at 48- or 96-hrs after sporozoite inoculation. From these samples we were able to identify immunogenic Pf liver stage peptides that match several HLA supertypes from primary human hepatocytes. By continuing our screening process we will work to identify the full repertoire of Pf liver stage antigens as a pathway to accelerate pre-erythrocytic antigen discovery.

PLASMODIUM ALVEOLIN 5 IS ESSENTIAL FOR THE NORMAL FORMATION OF INNER MEMBRANE COMPLEX OF OOKINETES

Naoaki Shinzawa¹, Eizo Takashima², Riko Katsube¹, Mamoru Nozaki¹, Mayumi Tachibana¹, Aki Kato², Amporn Thongkukiatkul³, Takafumi Tsuboi², **Motomi Torii¹**, Tomoko Ishino¹

¹Proteo-Science Center, Ehime University, Toon, Ehime, Japan, ²Proteo-Science Center, Ehime University, Matsuyama, Ehime, Japan, ³Department of Biology, Burapha University, Chonburi, Thailand

Malaria parasites undergo multiple developmental stages and adopt a range of cell shapes, including both motile and non-motile forms. While the motility requires the motor complex associated with the plasma membrane of elongated shape, it remains an open question whether the cell shape itself is required for the differentiation to next developmental stage. All invasive stage parasites have submembranous flattened vesicle packed into continuous layer, called inner membrane complex (IMC), supporting the plasma membrane. We found that ALV5, a member of *Plasmodium* alveolin, is essential for the normal formation of IMC of ookinetes using knocking down of ALV5 in mosquito stage. ALV5-deficiency resulted in the developmental arrest at a point of apical end formation from remnant zygote and the extremely low invasion ability to mosquito midgut due to its lost motility. However, intrahemocoel injection of arrested parasites resulted in normal development of sporogonic stage. These findings clearly indicate that the molecular machinery for differentiation is developed independently of cell shape of parasites.

RALP1, A RHOPTRY-NECK, ERYTHROCYTE-BINDING PROTEIN OF PLASMODIUM FALCIPARUM MEROZOITES, IS A NOVEL VACCINE CANDIDATE ANTIGEN

Daisuke Ito¹, Tomoyuki Hasegawa¹, Tsutomu Yamasaki², Thangavelu U. Arumugam¹, Kazutoyo Miura³, Amporn Thongkukiatkul⁴, Satoru Takeo¹, Carole A. Long³, Jetsumon Sattabongkot⁵, Eun-Taek Han⁶, Eizo Takashima¹, **Motomi Torii¹**, Takafumi Tsuboi¹

¹Proteo-Science Center, Ehime University, Matsuyama, Ehime, Japan, ²Department of Life Sciences, Faculty of Science, Okayama University of Science, Okayama, Japan, ³Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, MD, United States, ⁴Department of Biology, Faculty of Science, Burapha University, Chonburi, Thailand, ⁵Mahidol Vivax Research Center, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, ⁶Department of Medical Environmental Biology and Tropical Medicine, School of Medicine, Kangwon National University, Chuncheon, Republic of Korea

Erythrocyte invasion by merozoites is an obligatory stage in *Plasmodium* infection and is essential to malaria disease progression. Proteins in the apical organelles of the merozoites mediate invasion into the erythrocytes, and are potential malaria vaccine candidates. The rhoptry-associated, leucine zipper-like protein 1 (RALP1) in *P. falciparum* was previously found to be specifically expressed in schizont stages and localized to the rhoptry of merozoites based on immunofluorescence assay (IFA). Also, RALP1 has been refractory to gene knockout attempts, suggesting that it is essential for blood stage parasite survival. These characteristics suggest that RALP1 is a potential blood-stage vaccine candidate antigen, and here we aimed to assess its potential in this regard. Antibodies were raised against recombinant RALP1 proteins synthesized using the wheat germ cell-free system. Immunoelectron microscopy demonstrated for the first time that RALP1 is a rhoptry neck protein of the merozoites. Moreover, our IFA data showed that RALP1 translocates from the rhoptry neck to the moving junction during merozoite invasion. Growth and invasion inhibition assays revealed that anti-RALP1 antibodies inhibit invasion of erythrocytes by merozoites. Erythrocyte binding assays revealed that RALP1 possesses

an erythrocyte binding epitope in the C-terminal region, suggesting that RALP1 represents a new *P. falciparum* erythrocyte binding protein. Human sera collected from malaria endemic areas in Thailand and Mali recognized this protein. Overall, our findings indicate that RALP1 is a rhoptry-neck erythrocyte-binding protein, and that it merits additional evaluation as a *P. falciparum* blood-stage vaccine candidate.

NOVEL MOLECULE THAT IS SPECIFICALLY EXPRESSED ON MALE GAMETOCYTE AND MICROGAMETE HAS POTENTIAL ROLE ON EXFLAGELLATION

Mayumi Tachibana, Motomi Torii, Moe Sudo, Yuki Yokouchi, Takafumi Tsuboi, Tomoko Ishino

Proteo-Science Center, Ehime University, Matsuyama, Japan

Plasmodium transmission via mosquitoes required sexual stage parasite development and fertilization in mosquito midguts. After ingestion of gametocytes by mosquitoes, fertilization occurs to form zygotes, which develop into invasive forms, ookinetes. These transmission events occur rapidly within 24 hours after blood meals and many molecules are supposed to be involved. Nevertheless, little is known about molecular mechanisms how parasites transmit to mosquitoes. Previously, we reported a novel male specific protein, designated PyGM75, that is expressed in both gametocyte and gamete stage of *Plasmodium yoelii*. In this study, the subcellular localization of PyGM75 in male gametocytes and gametes were examined by immune-electron microscopy. It is revealed that PyGM75 is localized to the electron dense organelles, named osmiophilic bodies of male gametocytes, then transported to the surface of microgametes. Next, we produced pygm75 gene disrupted parasites to elucidate its function. Pygm75 disrupted parasites can normally differentiate into male and female gametocytes. However, these parasites were drastically impaired the exflagellation ability, therefore they could not form oocysts in the mosquito midguts. Further electron microscopic analysis demonstrated that osmiophilic bodies were disappeared from pygm75 disrupted male gametocytes. These results indicate that PyGM75 plays a crucial role in microgametes formation prior to fertilization.

CONTRASTING ROLES FOR PFACS5 AND PFACS9 IN THE EXPANDED PLASMODIUM FALCIPARUM ACYL CO-A SYNTHETASE GENE FAMILY

Allison Demas, Pamela Magistrado, Sarah Volkman, Ulf Ribacke, Dyann F. Wirth

Harvard School of Public Health, Boston, MA, United States

The remarkable plasticity of the *Plasmodium falciparum* genome allows for adaptation in response to selective pressures and challenges efforts to combat this important human pathogen. Evidence of the adaptive nature of this genome includes the expansion and recent positive selection of the acyl Co-A synthetase (ACS) gene family, which includes four orthologs predicted to activate exogenous fatty acids and play important roles in fatty acid scavenging as well as nine paralogs with unknown function. The evolutionary and functional significance for the expansion of the PfACS9 ortholog to nine paralogs, including PfACS5, is unknown, and we sought to functionally characterize these molecules to understand their biological role in the parasite. We therefore generated parasites with conditional knockdown of PfACS5 and PfACS9, which significantly reduced protein abundance, but led to no difference in intra-erythrocytic parasite growth, under either normal or restricted fatty acid growth conditions. To explore possible neofunctionalization, HA-tagged lines of PfACS5 and PfACS9 were characterized for timing of expression, subcellular localization, and interacting partners. We observed differential localization for these proteins using immunofluorescence assays. Unlike ACS9, ACS5 was clearly exported to the red blood cell cytosol and membrane periphery. Western blots of parasite lysate from subcellular fractions support this differential localization, and show peak expression at 30-36 hours post-

invasion (hpi) for PfACS5 and 38-44 hpi for PfACS9. Exploration of the PfACS interactome through pull down assays further supports distinct functions for these enzymes. We hypothesize that the expansion and recent positive selection of the PfACS gene family are the consequence of metabolic pressures driving parasite evolution, and characterization of this family may identify metabolic chokepoints and potential targets for novel antimalarials.

1318

EFFECTS OF RBC STORAGE CONDITIONS ON *PLASMODIUM FALCIPARUM* INVASION OF RBCS *IN VITRO*

Morgan M. Goheen, Martha A. Clark, Carla Cerami

University of North Carolina Chapel Hill, Chapel Hill, NC, United States

The *in vitro* culture of *Plasmodium falciparum* in red blood cells (RBCs) is essential to studying the molecular and cell biology of the parasite, however, culture methodologies differ between laboratories. One type of variability arises from RBC source and storage conditions. Recent protocols for standard parasite growth suggest collection and storage of RBCs in acid citrate dextrose (ACD), citrate phosphate dextrose (CPD), or citrate-phosphate-dextrose-adenine (CPDA). Most laboratories routinely culture *P. falciparum* in RBCs for up to 4 weeks after RBC collection, although it is known that freshly donated RBC sustain a higher *P. falciparum* growth rate. It is unknown what step of the *P. falciparum* intraerythrocytic life cycle is impacted by RBC storage. Studies on RBC storage for human clinical use in blood transfusions have revealed a relationship between RBC storage and transfusion complications. Current standards for blood banking involve using CPD for RBC collection, removing plasma and leukocytes, then storing RBCs in saline-adenine-glucose-mannitol (SAGM) for up to 42 days at 4°C. Many RBC storage lesions have been documented in these acidic medias, such as decreased deformability, decreased ATP, decreased 2,3-diphosphoglycerate (2,3-DPG), decreased intracellular potassium, increased intracellular NaCl, oxidative damage, lipid peroxidation, changes in membrane phospholipids, and vesiculation of membranes. Using flow cytometry based assays, we have separately examined the effect of RBC storage conditions and time in storage on overall parasite growth, merozoite invasion of RBCs, and merozoite production. We present results on the effects of storing RBCs after two, four, and six weeks in acid citrate dextrose (ACD) and citrate-phosphate-dextrose-adenine (CPDA), as well as in two other solutions known to maintain RBC integrity, RBC buffer (10 mM HEPES, 12 mM NaCl, 115 mM KCl, 5% BSA) and Alsever's solution.

1319

DE NOVO ASSEMBLY OF A FIELD ISOLATE GENOME REVEALS A NOVEL *PLASMODIUM VIVAX* ERYTHROCYTE-BINDING PROTEIN GENE

Jim Hester¹, Ernest Chan¹, Didier Menard², Odile Mercereau-Puijalon³, John Barnwell⁴, Peter Zimmerman⁵, David Serre¹

¹Cleveland Clinic, Cleveland, OH, United States, ²Pasteur Institute in Cambodia, Phnom Penh, Cambodia, ³Pasteur Institute, Paris, France, ⁴Centers for Disease Control and Prevention, Atlanta, GA, United States, ⁵Case Western Reserve University, Cleveland, OH, United States

Recent sequencing of *Plasmodium vivax* field isolates and monkey-adapted strains enabled characterization of SNPs throughout the genome. These analyses relied on mapping short reads onto the *P. vivax* reference genome generated from a monkey-adapted strain. Any locus deleted in this genome would be lacking in the reference sequence and missed in previous analyses. Here, we report de novo assembly of a *P. vivax* field isolate genome. Out of 2,857 assembled contigs, we identify 362 contigs each containing more than 5 kb of contiguous DNA sequences absent from the reference genome sequence. These novel *P. vivax* DNA sequences account for 3.8 million nucleotides and contain 792 predicted genes. Most of these contigs contain members of multigene families and likely originate from telomeric regions. Interestingly, we identify two contigs

containing predicted protein coding genes similar to *Plasmodium* red blood cell invasion proteins. One gene encodes the reticulocyte-binding protein gene orthologous to *P. cynomolgi* RBP2e and *P. knowlesi* NBXPb. The second gene harbors all the hallmarks of a *Plasmodium* erythrocyte-binding protein but clusters separately from all known *Plasmodium* Duffy-binding protein genes. Additional analyses show that this gene is present in most *P. vivax* genomes and transcribed in blood-stage parasites. Our study complements previous genomic analyses and takes full advantage of sequence data to provide a comprehensive characterization of genetic variations in this important malaria parasite. Further analyses of the protein coding genes discovered have the potential to identify genes influencing key aspects of *P. vivax* biology, including novel mechanisms of human erythrocyte invasion.

1320

THE AUTOPHAGY PROTEIN PFATG7 IS THE ACTIVATING ENZYME OF THE *PLASMODIUM FALCIPARUM* PFATG8 LIPIDATION PATHWAY AND IS ESSENTIAL FOR NORMAL PARASITE GROWTH

Dawn M. Walker, Maribeth Spangler, Najmus Mahfooz, Katherine A. Kemme, Viral C. Patel, Mark E. Drew

The Ohio State University, Columbus, OH, United States

The *Plasmodium falciparum* genome encodes a limited number of putative autophagy genes, specifically the four genes involved in Atg8 lipidation, an essential step in formation of autophagosomes. In other eukaryotic systems, Atg8 lipidation requires the E1-type ligase Atg7, an E2-type ligase Atg3, and a cysteine protease Atg4. We have confirmed that these four putative *P. falciparum* ATG (PfATG) genes are transcribed during the parasite's erythrocytic stages. We hypothesize that these putative autophagy genes are the essential players of a functional Atg8 lipidation pathway in *P. falciparum*. Recent effort have focused on dissecting the biochemistry of this pathway. We have genetically engineered parasites to allow for regulatable expression of the activating enzyme PfAtg7. Upon PfAtg7 attenuation, parasites exhibit slow growth in culture, indicating the essentiality of this enzyme for normal parasite growth. We have also modified the PfATG7 locus to introduce a C-terminal hemagglutinin (HA) tag. This has allowed us to immunoprecipitate native PfAtg7 enzyme to confirm its biochemical activity. In an *in vitro* conjugation assay combining native PfAtg7, ATP, and recombinant PfAtg8 followed by non-reducing SDS-PAGE conditions, we detect a PfAtg7-PfAtg8 thioester conjugate at approximately 150kDa using anti-PfAtg8. Upon reduction, the 150kDa conjugate is reduced to PfAtg7 and PfAtg8. This ability to form a thioester linkage with PfAtg8 provides evidence that PfAtg7 is in fact the activating enzyme of this pathway. As to translational implications of this research, specific inhibitors have been developed for E1-type ligases, such as the mammalian NEDD activating enzyme, and are currently in clinical trials as anticancer therapeutics. A similar strategy could be employed in the development of specific and selective PfAtg7 inhibitors. If successful, these inhibitors would represent a new class of antimalarials.

1321

DEVELOPMENT OF A NONRADIOACTIVE HETERODUPLEX TRACKING ASSAY TO MEASURE IN-HOST GENETIC DIVERSITY IN CLINICAL *PLASMODIUM VIVAX* INFECTIONS IN CAMBODIA

Matthew Givens¹, Jessica T. Lin¹, Chanthap Lon², Charlotte Lanteri², Panita Gosi², Oksana Kharabora¹, David Saunders², Jonathan J. Juliano¹

¹University of North Carolina at Chapel Hill, Chapel Hill, NC, United States,

²Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand

Compared to *Plasmodium falciparum*, relatively less is known about the genetic complexity of *P. vivax* infections. Developing assays which can be used in malaria endemic countries to measure in-host diversity can further research into this neglected species. The Heteroduplex Tracking

Assay (HTA) sensitively detects different parasite variants simultaneously existing within an infected person, but relies on the generation of a radioactive probe, limiting its broad application. We developed a novel non-radioactive, fluorescently-labeled capillary electrophoresis-based HTA to measure multiplicity of infection based upon a region between the interspecies conserved blocks 5&6 of merozoite surface protein 1 (PvMSP-1). This new method relies on visualization of peaks that are detected as a heteroduplex formed by a fluorescently-labeled probe and patient-derived PCR amplicon migrate through a nondenaturing polymer, similar to the readout in microsatellite analysis. The new method was applied to *P. vivax* isolates from 25 patients from Anlong Veng, Cambodia. We found that the number of variants within individual persons ranged from 1 to 5 with a mean of 2.4 variants per sample. Virtual heterozygosity was high at 0.892, suggesting good allelic discrimination at the PvMSP-1 locus. In persons with recurrent *vivax* infections, we found reappearance of identical genetic variants in multiple recurrences, suggesting relapse rather than re-infection. We also found novel variants in these recurrent infections, suggesting that there remain minor variants in the initial *parasitemia* that are undetected, or that there are variants that do not emerge in the initial *parasitemia* but emerge in a relapse. These results are consistent with prior HTA studies from this region and reveal significant in-host malaria diversity in Southeast Asia. This new method will allow HTAs to be used in malaria-endemic countries for clinical and research purposes.

1322

CHARACTERIZATION OF A TYPE 2C PROTEIN PHOSPHATASE IN *PLASMODIUM FALCIPARUM*

Bethany J. Jenkins, Thomas M. Daly, Akhil B. Vaidya, Lawrence W. Bergman

Drexel University College of Medicine, Philadelphia, PA, United States

Signaling pathway components, including kinases and phosphatases, have been a growing area of interest in the pursuit of novel antimalarials. Many have been identified as being more closely related to orthologues found in plants or other lower eukaryotes, making them attractive drug targets. In recent years, divergent kinases and phosphatases have been shown to play essential roles in both the human and mosquito stages of the parasite lifecycle. Type 2C protein phosphatases (PP2Cs) are serine/threonine phosphatases characterized by their magnesium dependence. While ten putative PP2Cs have been found in the *Plasmodium falciparum* genome, only one has been characterized, and is involved in the regulation of transcription and translation. We are investigating a PP2C, PfPP2C-1 (Pf11_0362), which diverges from a group of *Apicomplexan* PP2Cs and shares closer homology with those of the plant *Arabidopsis thaliana*. Since *Arabidopsis* PP2Cs are critical for growth and stress responses, we are interested in the role of this late stage PP2C in *Plasmodium* schizogony. We have successfully over-expressed PP2C-1 in *P. falciparum* parasite cultures using the mycobacteriophage recombination system, and found that it localizes to the cytoplasm. While we hypothesized that overexpression of PP2C-1 may lead to deregulation of its signaling pathway, these parasites showed no growth defect or phenotypic differences from wild type parasites. Functional significance of this protein is being assessed through gene knockout and knockdown strategies. We are using co-immunoprecipitation approaches to identify binding partners and potential signaling components of the protein. These studies may reveal hitherto unknown signaling pathways in *Plasmodium* schizogony, and further define the critical role of PP2Cs in these parasites.

1323

GENOMIC STABILITY OF PFHRP2, PFHRP3 AND ITS FLANKING GENES OF *PLASMODIUM FALCIPARUM* WILD ISOLATES FROM THE PERUVIAN AMAZON REGION ADAPTED TO *IN VITRO* CULTURES DURING A YEAR

Paola Larrauri, Maria del Carmen Orozco, Jorge Bendezú, Dionicia Gamboa, Joseph Vinetz

Cayetano Heredia University, Lima, Peru

Plasmodium falciparum parasites lacking *pfhrp2* and/or *pfhrp3* were restricted to laboratory strains which lose those genes during long period *in vitro* cultures. However, wild isolates lacking those genes were also found in the Peruvian Amazon Region as reported in 2010. It is hypothesized that these parasites could be losing both genes spontaneously by mitotic recombination in the asexual stage, similar to laboratory strains during long term cultures. The aim of this study is to assess the presence of *pfhrp2*, *pfhrp3* and its flanking genes as indicative of the subtelomeric regions stability from chromosomes 8 and 13. Six *P. falciparum* wild isolates were adapted and maintained on *in vitro* cultures during a one year period to simulate mitotic replications of the erythrocytic stages under no selective pressure forces. Previously, all samples (blood spots in filter paper) were characterized by PCR in order to confirm the initial *pfhrp2/pfhrp3* gene profiles: 2 (-/-), 1 (+/+), 2 (+/-) and 1 (-/+). Then, these isolates were maintained in cultures for 12 months and one aliquot per month were used to monitor the presence of these genes (*pfhrp2*, *pfhrp3* and their flanking genes) and for the molecular genotyping using 3 genetic markers (*pfmsp1*, *pfmsp2* and *pfglurp*) and 14 microsatellites. All cultures maintained the original *pfhrp2/pfhrp3* and their flanking genes profiles along the period of study (182.5 generations, 1 generation = 48 hrs. of intraerythrocytic cycle). Only 1 isolate presented a switch between the *pfhrp3* profile from its filter paper sample (positive) and all its cultures (negative). The molecular genotyping showed the clonal nature of all the culture samples along the year and allows their monitoring along this period of time as quality control tool. In conclusion it was observed a genomic stability of *pfhrp2/pfhrp3* and their flanking genes in these isolates maintained during one-year *in vitro* culture. The switch in one isolate could be explained by the presence of more than one clone at the beginning of the study that was lost during the culture. Additionally, the classic genetic markers (*msh1*, *msh2* and *glurp*) were cost-effective and enough to determine the genotype of the isolates and as a quality control tool; but microsatellites brought wider information about those genotypes.

1324

PREVALENCE AND DISTRIBUTION OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY AND MUTANT VARIANTS IN MALARIA PATIENTS FROM CAMBODIA

Panita Gosi¹, Charlotte A. Lanteri¹, Soklyda Chann¹, Darapiseth Sea², Sittidech Surasri¹, Saowaluk Wongarunkochakorn¹, Kingkan Pidtana¹, Nillawan Buathong¹, Sabaithip Sriwichai¹, Satharath Prom³, Char Meng Chuor², Youry Se¹, Chanthap Lon¹, David L. Saunders¹

¹*U.S. Army Medical Component-Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand*, ²*National Center for Parasitology, Entomology and Malaria Control, Phnom Penh, Cambodia*, ³*Royal Cambodian Armed Forces, Phnom Penh, Cambodia*

Primaquine is a key component of current malaria control efforts in Southeast Asia. However, the safety of primaquine in patients with glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency remains a substantial safety concern given current diagnostic limitations in most malaria endemic areas. To better understand potential safety concerns and estimate risks for hemolysis that could result from widespread primaquine use, we evaluated the prevalence of G6PD deficiency, and attempted to characterize common G6PD variants in malaria endemic areas with known multidrug resistance along the Thai-Cambodian border.

We measured the prevalence of G6PD deficiency in a total of 1,188 patients in northern, western, central, and southern Cambodia from 2009 to 2012. Results from a qualitative G6PD fluorescence spot test were compared with a high resolution melting (HRM) real-time PCR method to detect G6PD variants. We developed the HRM assay to probe for single nucleotide polymorphisms (SNPs) associated with five of the most common G6PD variants previously reported in Southeast Asia: Viangchan, Mahidol, Canton, Jiangxi, and Chinese-5. Prevalence of qualitative G6PD deficiency among malaria patients was approximately 12%. HRM analysis revealed that the Viangchan variant, typically associated with moderate to severe (WHO Class II) deficiency, was most prevalent. The relatively high proportion of the population at risk with a mutation associated with moderate to severe G6PD deficiency cautions against widespread, unmonitored primaquine administration in Cambodia. In the absence of G6PD screening, and/or careful monitoring for potential hemolysis in unscreened patients, the risk of serious adverse events is high. Correlation with limited quantitative G6PD-deficiency data is currently underway, and will be presented to help estimate risk in this population, and better inform national malaria drug treatment policy in Cambodia.

1325

DELIVERY STRATEGIES FOR MASS CAMPAIGNS TO ACHIEVE UNIVERSAL COVERAGE WITH INSECTICIDE TREATED NETS: WHICH WORKS BEST? A MULTI-COUNTRY COMPARISON

Celine Zegers de Beyl¹, Hannah Koenker², Emmanuel Obi³, Emmanuel Adegbe³, Richmond A. Selby⁴, Albert Kilian⁵

¹Malaria Consortium, London, United Kingdom, ²Center for Communication Programs, Johns Hopkins University, Baltimore, MD, United States, ³Malaria Consortium, Abuja, Nigeria, ⁴Malaria Consortium, Kampala, Uganda, ⁵Malaria Consortium and Tropical Health, Montagu, Spain

The use of insecticide treated nets (ITN) is widely recognized as one of the main interventions to prevent malaria. Mass distribution campaigns are the best approach to rapidly scale up ITN coverage. However, the best strategy to distribute ITN to households is still under debate. Data from 14 post campaign household surveys conducted in Nigeria, Ghana, South Sudan, Senegal and Uganda were merged. These campaigns used a variety of strategies such as stand-alone versus integrated distribution, fixed point versus house to house delivery and targeted or limited versus universal coverage ITN allocation. Survey design and data collection methods were similar across surveys, i.e. representative cross sectional household surveys with a two-stage cluster sampling design and a standard questionnaire. Analysis included 13,901 households and accounted for survey design and sampling probabilities. The main outcome indicators were the proportion of households that received at least one ITN from the campaign and the proportion of households reaching universal coverage on the survey day. None of the ITN campaigns increased the household coverage to the expected target of 80% or more households with sufficient ITN (one ITN for every two people or one ITN per sleeping place). There was no difference in campaign effectiveness comparing various strategies for distribution or delivery, providing that enough ITN are available. There were substantial discrepancies between the quantity of ITN distributed to households and the quantity needed in respect to people or sleeping places, independently of the indicator considered. The effectiveness of ITN campaigns does not depend on the strategy but rather on quality of implementation and ITN availability. Coverage achieved confirms that it is essential to complement mass campaigns with continuous distribution systems to achieve universal coverage targets.

1326

DOES A TORN LONG-LASTING INSECTICIDAL NET FAIL TO PROTECT CHILDREN FROM MALARIA PARASITEMIA? DATA FROM TWO CROSS-SECTIONAL SURVEYS IN WESTERN UGANDA

Albert H. D. Kilian¹, James Ssekitooleko², Anthony Nuwa², Geoffrey Namara²

¹Malaria Consortium and Tropical Health LLP, Montagu, Spain, ²Malaria Consortium, Kampala, Uganda

Durability of long-lasting insecticidal nets (LLIN) is increasingly coming into focus since longer net survival is associated with significant public health savings. However, there is very little data on the extent to which damages to an LLIN limit its protective effect. In the context of malaria control efforts in Western Uganda, physical condition of nets was measured in a random sample of nets from two representative, cross-sectional surveys in July 2011 and October 2012, 18-30 months after mass distribution of LLIN in the area. From a total sample of 1,598 and 3,938 households 592 and 1,313 nets were assessed for physical integrity respectively using a proportionate hole index as recommended by WHO. Of these nets 818 (43%) had been used the previous night by children under five for whom data on malaria *parasitemia* were also obtained. Physical condition of LLIN was considered to be "good" when the total hole surface area on the net did not exceed 100 cm² and as "too torn" when more than 1000 cm². The proportion of the 818 nets in "good" condition decreased from 80% for nets less than 6 months old to 63% for nets 1-2 years old (p=0.02) and then stabilized around 50% suggesting that nets were discarded when too torn. Parasite rates in children 0-59 months of age decreased over time from 23% at the first survey to 15% (p=0.07) but did not vary significantly with physical condition (p=0.4) being 13.2% (95%CI 9.2-18.4) for "good" nets, 16.7% (11.7-32.4) for "damaged" nets and 18.3% (9.5-32.4) for nets "too torn". In a logistic regression model of *parasitemia* child age showed to be a significant determinant with an Odds-Ratio (OR) of 1.3 per each additional year (p=0.01) as well as district (p<0.005), current fever (OR 3.5, p<0.005) and second vs. first survey (OR 0.55, p=0.04). However, no increased risk of *parasitemia* was found for "too torn" nets (OR 1.0, p=0.9). These data suggest that, in the setting of Western Uganda, even seriously torn LLIN still provide sufficient protection for children and nets are discarded before they lose their protective effect.

1327

RISK FACTORS ASSOCIATED WITH MALARIA INCIDENCE AMONG YOUNG CHILDREN AND FEMALE ANOPHELES MOSQUITO COUNTS IN KOROGWE, TANZANIA

Jenny Liu¹, Roly Gosling¹, Brittany Zelman¹, Samwel Gesase², Ramadhan Hashim², Silas Otieno³, Caroline Maxwell⁴, Daniel Chandramohan⁴, Teun Bousema⁴

¹University of California San Francisco, San Francisco, CA, United States, ²National Institute for Medical Research, Tanga, United Republic of Tanzania, ³National Institute for Medical Research, Kilimanjaro, United Republic of Tanzania, ⁴London School of Hygiene & Tropical Medicine, London, United Kingdom

Several studies conducted in Northeast Tanzania have documented a declining trend in malaria transmission beginning well before malaria interventions were scaled up. One explanation for the decline in malaria may be the changes in socioeconomic conditions associated with economic development, and in particular improvements in house construction materials. This analysis has two main objectives: (1) identify risk factors associated with malaria incidence among young children and (2) identify household and environmental factors associated with mosquito density in and around the home. A particular focus is paid to the housing construction materials as determinants in both analyses. For 435 children enrolled in larger trial of intermittent preventive treatment for malaria in infants in Tanga, North-eastern Tanzania, detailed information on their dwelling characteristics were collected. An index scale of housing structure

quality constructed via principal components analysis was converted to decile units for regression analysis. Ordered logistic regressions were used to predict risk factors for child malaria episodes (none, 1-2, or 3+ episodes) and negative binomial regressions were used to predict risk factors for average female anopheles mosquito counts collected in traps in and around the dwelling. Results suggest that, compared to children who reside in houses with better construction materials, residing in the worst type of house significantly increases the risk of malaria two- to three-fold, even when wealth and rural residence is controlled for. Having ceilings is associated with a significant reduction in female anopheles mosquito counts by nearly half, while having cattle around the house increases mosquito counts. In conclusion, these results corroborate findings from other studies of household and environmental risk factors that show associations between malaria risk to poor housing materials. Interventions to reduce the receptivity of an area or exposure via housing type could help to further reduce malaria transmission.

1328

SELECTION AND CHARACTERIZATION OF A NEW, NON-MELANISING, LINE OF ANOPHELES GAMBIAE REFRACTORY TO PLASMODIUM FALCIPARUM

Lenka Richterova, Lisa Ranford-Cartwright

Institute of Infection, Immunity and Inflammation, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, United Kingdom

Anopheles gambiae is a principal vector of *Plasmodium falciparum* malaria in Africa. Some individual mosquitoes within a population are naturally refractory to infection. The only existing refractory line of *An. gambiae* (G3) melanises *P. falciparum* parasites, a refractory behaviour uncommon under natural transmission. Understanding common mechanisms of natural refractoriness could be used for development of transmission blocking vaccines or GMO vector strategies. We have selected a new, non-melanising, refractory line of *An. gambiae* from the outbred Keele line named GU-REF. GU-REF was selected for refractoriness to *P. falciparum* clone 3D7 over 11 generations of selection. At the same time, the GU-CON line was selected at random as a control for inbreeding effects. The refractory line was then tested for genotype specificity, parasite stages affected, timing of blood meal digestion after feeding on infected and uninfected blood, expression of candidate genes previously linked with refractoriness, and fitness parameters (costs of refractoriness). GU-REF mosquitoes exhibit a significantly lower infection prevalence compared to GU-CON and the parent Keele line. The refractory behaviour is not specific to the parasite clone (3D7) used for selection, in that refractoriness is seen to an unrelated parasite, HB3. The refractory mechanism affects the parasite stages before the early oocyst. GU-REF mosquitoes do not appear to exhibit fitness costs associated with refractoriness, as measured by fecundity. Protein digestion of the blood meal is slightly faster in GU-REF after an infectious blood-meal, compared to GU-CON. There is no difference in speed of digestion after a non-infected blood-meal. A new refractory line of *An. gambiae* refractory to infection with *P. falciparum* has been selected. The exact mechanism of refractoriness has not yet been characterised, but could involve the speed of blood-meal digestion or non-melanotic immune responses. The GU-REF line does not appear to have fitness costs associated with refractoriness.

1329

IMPACT OF INSECTICIDE TREATED WALL LINER ON SCHOOL ATTENDANCE IN RURAL WESTERN KENYA

Elizabeth Glaser¹, Adeyemi Okunogbe¹, Jane A. Odhiambo¹, John E. Gimnig², Mary J. Hamel², Grant Ritter¹, Peter Otieno³, George Olang³, Nabie Bayoh³, Donald S. Shepard¹

¹Brandeis University, Waltham, MA, United States, ²Centers for Disease Control and Prevention, Atlanta, GA, United States, ³Kenya Medical Research Institute (KEMRI), Kisumu, Kenya

Results of a cluster randomized trial in rural western Kenya suggest a new form of malaria prevention, insecticide treated wall liner (ITWL) plus insecticide treated nets (ITNs), provide added benefit over that provided by ITN alone, reducing childhood malaria infection by 38% (95% confidence interval [CI], 23%-50%) overall and by 42% (95% CI=26%-55%) in children aged 5-11 years. Prior studies have shown that malaria adversely affects children's academic performance and school attendance. This supplemental study sought to determine whether children from the ITWL plus ITN (intervention) villages had reduced absenteeism when compared to children from the ITN alone (control) villages. We performed a retrospective analysis of attendance registers for children in standards (grades) 1 through 8 via comparison of school attendance in term 1 of the 2010 academic year (prior to ITWL) to term 3 (after ITWL). Data were available from 6 schools serving children from 8 of the 12 villages in the original trial. Using a multilevel mixed effects difference-in-differences regression model, we explored the effect of ITWL on attendance of pupils from intervention vs. control villages between terms 1 and 3. In order to adjust for registers with missing or incomplete recording of absences, mostly in the last weeks of each 13-week term, we choose to limit analysis to attendance from weeks 1-10 in each academic term. We adjusted for clustering by the inclusion of a village-level variable in the multilevel analysis; other covariates used in the analysis were categorical variables for standard, gender, village, and term. The resulting dataset had 1,126 observations, each representing the percentage of school days attended for one child for weeks 1-10 in a term. Overall recorded attendance averaged 90.1 percent (95% CI 88.9%-91.3%) over weeks 1-10 of term 1, so that recorded absenteeism averaged 9.9 percent. The interaction term in the regression showed that attendance improved (and absenteeism decreased) by 4.7 percentage points (95% CI 1.2%-8.1%) for children in intervention compared to control villages (p=0.008), representing a halving of recorded absences. The main limitation was our inability to confirm the overall accuracy of entries from existing school attendance registers. Nevertheless, these favorable preliminary results suggest a beneficial impact on school attendance from adding ITWL to ITN.

1330

PLASMODIUM FALCIPARUM GAMETOCYTES INFECTIVITY FROM POST ASAQ (ARTESUNATE AMODIAQUINE) TREATMENT PATIENTS SUPPLEMENTED WITH AZADIRACHTIN-ENRICHED NEEM EXTRACT

Rakiswendé S. Yerbanga¹, Robert K. Ouédraogo¹, Dari F. Da¹, Franck A. Yao¹, Koudraogo B. Yaméogo¹, Leonardo Lucantoni², Giulio Lupidi², Orazio Tagliatela-scafati³, Anna Cohuet⁴, Annette Habluetzel², Jean Bosco Ouédraogo¹

¹Institut de Recherche en Sciences de la Santé, Direction régionale de l'ouest, Bobo Dioulasso, Burkina Faso, ²Scuola di Scienze del Farmaco e dei Prodotti della Salute, Università di Camerino, Camerino, Italy, ³Dipartimento di Farmacia, Università di Napoli "Federico II", via D. Montesano, Napoli, Italy, ⁴Institut de Recherche pour le Développement, Unité MIVEGEC (IRD 224- CNRS 5290-UM1-UM2), Montpellier, France

Infectivity of malaria species to the mosquito vector has been investigated in the recent years by scientific community. Patients treated with artemisinin-based combination therapy, artesunate amodiaquine (ASAQ), against *Plasmodium falciparum* malaria produce fast clinical responses to

asexual stage of the parasite; but few data are available for sexual forms (gametocytes) responsible for the malaria transmission to human host to mosquito. In this study, *Plasmodium falciparum* gametocytes from naturally infected human after ASAQ 3-day treatment course in presence of azadirachtin-enriched neem (*Azadirachta indica*) extract were assessed for its infectivity to *Anopheles coluzzii*. *Anopheles coluzzii* females were membrane fed on gametocytaemic blood collected from patients after 3 day ASAQ treatment course and supplemented with azadirachtin-enriched neem (Aza) extract. Gametocytes infectivity was evaluated by assessing oocysts prevalence and intensity on mosquito midgut. Oocyst prevalence of 43% (CI₉₅ 23-60) and oocyst intensity of 10.78 (CI₉₅ 0.0-21.9) were still found after ASAQ treatment. However, a single dose of Aza added to gametocytaemic blood, completely block gametocytes infectivity at 60 ppm and reduce the oocyst prevalence to 98% at 50 ppm. This work demonstrated that after 3-day ASAQ treatment, patients are still able to maintain vector infection. But, single dose of Aza at 50 to 60 ppm will help in preventing mosquito infection and in blocking the malaria transmission.

1331

IMPACT OF COMMUNITY CHANGE AGENTS ON LLIN NORMS AND USE IN TANZANIA

Marc Boulay¹, Dana Loll¹, Hannah Koenker¹, Michelle Kaufman¹, Rob Ainslie², Benjamin Kamala², Susan Mlangwa²

¹Johns Hopkins University Center for Communication Programs, Baltimore, MD, United States, ²Johns Hopkins University Center for Communication Programs, Dar es Salaam, United Republic of Tanzania

Since 2009, Tanzania has distributed 27 million LLINs. According to the 2011-12 THMIS, 91% of households now own at least one ITN and 68% of the population used an ITN the night before the survey. To achieve consistent universal net coverage, program planners need more information on the factors that influence net use in net owning households. Social norms are increasingly recognized as an important determinant of a range of health behaviors, although their role in malaria prevention is not understood. This study investigated the role of a Community Change Agent (CCA) program in affecting social norms related to use of long-lasting insecticidal nets. Since 2008, more than 1800 community members have been recruited and trained to become CCAs and to promote malaria awareness and discussion through community meetings, educational events and household visits. This study randomly recruited 1040 men and women living in the Lindi, Rukwa, and Mwanza regions of Tanzania to participate in a behavioral survey. Overall, 81% of respondents in net-owning households reported that everyone in the household slept under a net during the night before the survey. This outcome was significantly related to perceived social norms ($p < 0.001$). Adjusting for background characteristics and number of household nets, universal use in a household increased from 57% in households where the respondent believed few or no households in the community used bed nets to 86% in households where the respondent believed that all households in the community used nets. In addition, controlling for background variables and the actual level of net use in the community, respondents who had interacted with the CCA were significantly more likely to believe that more households in their community used bed nets ($p = 0.01$). The results of this study suggest that exposure to a community change agent indirectly affects net use through CCAs' effects on descriptive social norms.

1332

MALARIA CHEMOPROPHYLAXIS: WHY DON'T THE EXPERTS AGREE? AN INTERNATIONAL OPINION SURVEY

Andy Matheson¹, David Lalloo², Colin Sutherland³, Ron Behrens¹, Christopher Whitty³, Peter Chiodini¹

¹Hospital for Tropical Disease, London, United Kingdom, ²Liverpool School of Tropical Medicine, Liverpool, United Kingdom, ³The London School of Hygiene & Tropical Medicine, London, United Kingdom

The use of malaria chemoprophylaxis is central to pre-journey recommendations made to many of our travellers. We struggle to ensure that travellers understand the importance of strict adherence, and all too often medication is taken irregularly or just left at the bottom of the bag. One possible reason for the poor adherence is the wide variation in advice that is given to the public, with different expert groups recommending different drugs or no drugs for travellers with identical itineraries. We undertook a questionnaire survey of experts from around the world involved in the development of National Malaria Guidelines. There is a notable difference in the chemoprophylaxis recommendations in the National Guidelines produced by different jurisdictions. We aimed to find out what evidence is used by the different experts in the development of their guidelines; to better understand the reasons for the wide variation in chemoprophylaxis recommendations. The respondents were also asked what sort of evidence they would prefer to use if ideal data were available. We were unable to detect a marked difference in the evidence used by the different jurisdictions. This was true even when broken down to specific areas, such as that used for India. There are several possible reasons for the variation in recommendations despite using the same evidence base. It may be that we are interpreting the available data differently; it may be that the available data is too poor quality to be of any use; or it may be that we are just collating the wrong data. It may be that we have good data, but are drawn to alternative conclusions by other factors such as medico-legal risk and drug costs. It is difficult to know which recommendations will be proved correct, and the outcomes from the different policies will be fascinating to observe. However a there will need to be a coordinated effort to pool the traveller data from all countries to make sense of the results. The development of an agreed tool to standardise the weighting given to evidence types would give a clear rationale for any chemoprophylaxis recommendations. This would, ultimately, improve chemoprophylaxis compliance amongst travellers.

1333

IDENTIFYING SUBPOPULATIONS LEAST LIKELY TO USE MOSQUITO NETS AFTER MASS DISTRIBUTION CAMPAIGNS: CASE OF KANO STATE, NIGERIA

Elizabeth Ivanovich¹, Jui Shah², Yazoume Ye²

¹United Nations Foundation, Washington, DC, United States, ²ICF International, Calverton, MD, United States

Insecticide-treated net (ITN) ownership and particularly use remain low in many malaria endemic countries in sub-Saharan Africa (SSA). With the shift from target group to universal coverage approaches there is need to ensure effective use of ITNs among all subgroups of the population. Identifying subgroups least likely to use ITNs could inform targeted messaging to improve overall coverage. This study aimed to identify the subgroups least likely to use ITNs after the mass distribution campaigns which took place in May and July 2009 in Kano State, Nigeria. The study used post-campaign evaluation survey data which was collected from October to November 2009. Individuals (3,056) living in households with at least one ITN and sleeping in the households the night before the survey visit (de facto population) were included in the analysis. Pearson Chi-square and Chi-square Automatic Interaction Detector (CHAID) regression were used to identify predictors of ITN use and the subgroups least likely to use ITNs. Eight covariate variables were included in the initial model. Five of these, including sex, age, wealth quintiles, education of the head of the household, and campaign distribution wave were used in the final

model as predictors of ITN use. Overall ITN use was 53% among all participants, and age and sex were good predictors of use. Males aged 15-25 years were the least likely to use ITNs, with a use rate of only 23%, while rates ranged from 46% to 62% among other subgroups. While further qualitative research may provide additional insight, these findings provide useful information for targeted awareness messaging during the mass distribution campaigns of ITN which are being implemented in several countries in SSA.

1334

EFFECT OF AGE OF ITN OWNED BY HOUSEHOLDS ON MALARIA PARASITE INFECTION AMONG CHILDREN UNDER FIVE YEARS OF AGE IN ANGOLA

Ana C. Franca-Koh, Yazoume Ye

ICF International, Calverton, MD, United States

Insecticide treated nets (ITNs) are effective for malaria control and provide protection to individuals living in households that own them. ITNs are manufactured to have a long lasting protective effect; however, the effect of the age of ITNs in households on malaria *parasitemia* is not well documented. This study examined the association between the age of ITNs in households and malaria *parasitemia* among children under five years of age in Angola. ITNs that were obtained shortly before the survey may not protect children from malaria *parasitemia* because the infection may have happened before the acquisition of the net. Conversely, ITNs that were obtained a longer time ago may be less protective due to wear and tear of the net, or reduction in efficacy of the insecticide. We performed a multivariate logistic regression to assess the association between the age of ITNs in households and malaria *parasitemia* among children under five years of age using the 2011 Angola Malaria Indicator Survey. We adjusted for eight potential confounders: sex of child, age of child, mother's level of education, whether the household had been sprayed or not in the previous 12 months, household size, household wealth, area of residence, and malaria epidemiologic zones. Children from households that had owned ITNs for 2-6 months before the survey were significantly less likely to have malaria *parasitemia* compared to those from households without ITNs (OR = 0.28, 95% CI: 0.10-0.84). ITNs that had been owned for 1 month or less, or for more than 6 months, were not protective. These findings provide useful information, particularly when assessing the impact of ITN interventions on the reduction of malaria burden.

1335

MYANMAR ARTEMISININ RESISTANCE CONTAINMENT (MARC) SURVEY: MALARIA AWARENESS AND PREVENTION

Ohnmar Hlabaw¹, Celine Zegers de Beyl², Thae Maung Maung¹, Sylvia Meek², Krongthong Thimasarn³, Aye Yu Soe⁴, David Sintasath⁵, Thar Tun Kyaw⁶

¹Department of Medical Research (Lower Myanmar), Yangon, Myanmar, ²Malaria Consortium, London, United Kingdom, ³World Health Organization, Yangon, Myanmar, ⁴Three Diseases Fund, Yangon, Myanmar, ⁵Malaria Consortium Asia, Bangkok, Thailand, ⁶Vector Borne Disease Control, Ministry of Health, Nay Pyi Taw, Myanmar

Despite anecdotal evidence of declining malaria transmission in some parts, Myanmar has the malaria burden in the Greater Mekong Sub-region. With the emergence of artemisinin resistance in the region, Myanmar is at the forefront of containing and ultimately eliminating artemisinin resistant parasites. In 2012, a malaria survey of households was conducted in the areas of known and suspected artemisinin resistance (Tier 1 and Tier 2) to serve as a baseline for the Myanmar Artemisinin Resistance Containment (MARC) efforts. The study domain included representative populations living in high to moderate malaria risk areas and utilized a multi-stage sampling approach stratified by Tier. Overall, 1992 household respondents were interviewed using standardized and pre-tested questionnaires in line with similar malaria surveys previously conducted in Cambodia and Thailand. Overall, 66.5% (95%CI 62.2 to

70.6) of household respondents understood "mosquito bites" as a mode for malaria transmission and 17.2% (95%CI 14.2 to 20.6) did not mention any transmission mode. Household coverage with at least one mosquito net was 97.5% (95%CI 95.1 to 98.7) and insecticide treated net (ITN) was 35.1% (95%CI 28.4 to 42.4). Lastly, 76.5% (95%CI 72.9 to 79.8) of all people (n = 9408) used a mosquito net the previous night and 15.9% (95%CI 12.4 to 20.3) slept under an ITN. General awareness of malaria was found to be modest; further efforts should be placed on improving community perceptions and behaviors for malaria prevention. Household coverage of ITN seemed insufficient to have an impact on reducing malaria transmission. Considering the high coverage and use of untreated mosquito nets, the national malaria prevention strategy should explore short to medium-term approaches to convert these untreated nets into ITNs and LLINs. For the longer term, demand-driven strategies should be in place to replace current untreated mosquito nets, building on the existing "net culture" in Myanmar.

1336

INSECTICIDE TREATED NET USE UNDER A COMPREHENSIVE DISTRIBUTION PROGRAM IN KENYA: SUCCESSES AND UNAVOIDABLE SHORTFALLS

Peter S. Larson¹, Noboru Minakawa², Gabriel O. Dida³, Mark L. Wilson¹

¹University of Michigan, Ann Arbor, MI, United States, ²Nagasaki University Institute of Tropical Medicine, Nagasaki, Japan, ³School of Public Health, Maseno University, Kisumu, Kenya

Insecticide treated nets (ITNs) have proven instrumental against holoendemic malaria. As distribution of ITNs throughout sub-Saharan Africa (SSA) is being scaled up, however, maintaining high levels of coverage over time will be instrumental to sustain current gains. We evaluated the impact of an ITN mass distribution campaign in early 2011 to a rural Kenyan community along Lake Victoria. Surveyors collected data on ITN use both before and one year following this distribution. At both times, household representatives were asked to provide a complete accounting of ITNs within the home, including net locations and the ages and genders of people sleeping under them the previous night. Other data on household material possessions, education levels, occupations, and community group memberships were recorded. Patterns of ITN use before and following distribution were compared using spatial and multi-variable statistical methods. At the time of distribution, ~50% of residents reported sleeping under an ITN the previous night, a use rate that rose to 92% one year following mass distribution. However, ITN use varied by age and gender, following a similar pattern both pre- and post-distribution. After infancy, ITN use sharply declined until the late teen years when it began to rise again, plateauing at ~30 years of age. Prior to distribution, socio-economic factors such as parental education and occupation were associated with ITN use. Following distribution, ITN use was similar across social groups. Household factors such as ITN availability and sleeping arrangement negatively impacted use. Our results indicate that mass distribution of ITNs was effective in rapidly scaling up coverage. Free distribution of ITNs using a direct-to-household method can eliminate socio-economic and spatial heterogeneities in ITN possession and use. Age is an important factor in determining consistent ITN use, but problems of sleeping arrangement and ITN disappearance will present a challenge to effective intervention campaigns.

1337

COST EFFECTIVENESS OF INDOOR RESIDUAL SPRAYING IN NYANZA PROVINCE KENYA

Donald S. Shepard¹, Elizabeth Glaser¹, Aggrey Kihombo², Sareh Khoshi¹

¹Brandeis University, Waltham, MA, United States, ²Mzumbe University, Mzumbe, United Republic of Tanzania

From its peak in 2004 to 2010, global malaria mortality fell by 32% from 1.82 to 1.23 million according to a 2012 Lancet paper by Murray et al. The expansion of indoor residual spraying (IRS) and insecticide treated nets (ITN) are considered important contributing interventions to this decrease. However, few empirical studies exist about the cost-effectiveness of IRS as a supplement to ITN, particularly in normal operational programs. We conducted a retrospective cost-effectiveness study of this use of IRS in 2010, combining data from two adjacent districts with perennial malaria transmission (greater Nyando and Rachuonyo) in Nyanza Province, Kenya. We assessed district-level costs by developing spreadsheet templates enumerating the categories of inputs (personnel, recurrent, capital), and the quantities and unit costs of each input within each category. We assessed quantities and unit costs through local and national key informants, consulting catalogs, and checking consistency (e.g. known productivity of spray operators and equipment per operator). We amortized capital inputs based on previous publications of the US President's Malaria Initiative (PMI), and computed cost per person in greater Nyando based on the Kenya census estimates. We estimated clinical malaria cases averted from trial previously published from Rachuonyo, and converted this to discounted life years gained (DLYG) by linking with other previous studies. IRS cost 229 Kenyan shillings (US \$3.16) per person in the population, with shares of 22% for personnel, 69% for recurrent cost, and 10% for amortized capital. The breakdown for recurrent costs was 35% for vehicle rental, 27% for insecticide, 31% for personal protective equipment, and 7% for other. Per 100 person years, the combination of IRS and ITN compared to ITN alone reduced infections from 44 to 18, clinical cases from 27 to 9, and added 2.27 DLYG. These give cost-effectiveness ratios of \$12 per malarial infection averted, \$18 per clinical case averted, and \$139 per discounted life year gained--a ratio substantially below Kenya's per capita GDP of \$795 (a WHO threshold). Our cost per person covered was about half the median reported from 12 PMI countries (\$6.94). While a more systematic addition of national and international overheads would increase costs somewhat, our analysis nevertheless suggests that IRS is a highly cost-effective addition to ITN in this endemic region.

1338

USE OF DEEP SEQUENCING FOR ASSOCIATION MAPPING OF GENES POTENTIALLY INVOLVED IN PYRETHROID RESISTANCE IN Aedes Aegypti

R. Patricia Penilla, Farah Zamira Vera, Corey Rosenberg, Karla Saavedra-Rodriguez, William C. Black, IV

Colorado State University, Fort Collins, CO, United States

Identification of target site based-resistance to insecticides has relied on detection of the single target sites mutations known to affect insecticide resistance in the field. With the advent of next generation sequencing we are now able to sample the whole genome association to detect single-nucleotide polymorphisms (SNPs) associated with insecticide resistance. This study seeks to identify SNPs associated with pyrethroid survival in natural populations of *Aedes aegypti* collected in the Viva Caucel and Vergel populations from Yucatan, Mexico. Four library sequences were built from the DNA of 25 mosquitoes. Two replicate libraries contained DNA from mosquitoes that had survived one hour exposure to a predetermined LC₅₀ (25 µg a.i./bottle) and two contained DNA of mosquitoes that died from the same exposure. Sequences were obtained from an Illumina HiSeq2000/2500 Sequencer. Alignments of paired read data were run in the NextGene software, interrogating each library

sequence with an insecticide resistance library of reference containing 307 genes with 4,039,599 nucleotides. SNPs with coverages <25 or >1000 were excluded as were SNPs that didn't occur in all four libraries. Log Likelihood Ratio Tests were then used to identify SNPs associated with resistance. Novel as well as previously identified genes were found to be associated with resistance. Additional libraries are being sequenced to test for associations with deltamethrin exposure, and permethrin exposure in other *Ae. aegypti* field populations.

1339

INTEGRATED ENTOMOLOGICAL SURVEILLANCE IN ZAMBIA: IMPLEMENTATION OF A PHASED PROGRAM FOR DISTRICT BASED DELIVERY THROUGH ENVIRONMENTAL HEALTH TECHNICIANS

Chadwick Sikaala¹, William Lubemba², Musapa Mulenga¹, Mulakwa Kamuliwo¹, Anna M. Winters², Daniel Bridges², Benjamin Winters², Matthew Burns²

¹Zambian National Malaria Control Program, Lusaka, Zambia, ²Akros, Lusaka, Zambia

Zambia has witnessed a rapid expansion in delivery of insecticidal based interventions such as Indoor Residual Spraying and Long Lasting Insecticidal Nets. Despite intensification of vector control programming, entomological surveillance is conducted sporadically and is geographically limited in coverage. Until now, there has been no routine, decentralized government entrenched longitudinal surveillance system that monitors localized species prevalence and supports routine processing of specimens to measure entomological impact of vector control interventions. A conceptual framework based on phased delivery of individual components of an integrated entomological surveillance system has been designed with supporting tools for districts with ongoing vector control activities. Individual components of the program support training of new and existing recruits, utilization of a standardized field surveillance protocol, data management, intra- and inter-district program performance, species composition mapping, and vector bionomics output associated with local malaria transmission. Nine Environmental Health Technicians who were trained for this program were selected to self-manage surveillance sessions in their respective sentinel sites with Community Health Worker assistance; based on their assessed training performance and their national representation. All sentinel sites were proficient in adopting a standardized collection protocol over multiple months during the wet-season and in yielding specimen data for building localized spatial and temporal species maps and associated bionomics. Findings highlight that the decentralized model of entomological surveillance is an achievable goal for national programs. Further exploration is required to address options that allow for nationally sustainable routes to multiply sentinel sites to ensure comprehensive spatial and temporal mapping of vector species and related parameters and assist the National Malaria Control Centre with evidenced based intervention selection and targeting.

IS INSECTICIDE-TREATED MATERIAL (ITM) USEFUL FOR DENGUE CONTROL? PERSPECTIVES FROM RANDOMIZED CONTROL TRIALS WITH TREATED CURTAINS AND SCHOOL UNIFORMS

Pattamaporn Kittayapong¹, Phanthip Olanratmanee¹, Suporn Thongyuan¹, Teerasak Laksananan², Pongsri Maskhao³, Peter Byass⁴, Valérie R. Louis⁵, Duane J. Gubler⁶, Annelies Wilder-Smith⁴

¹Center of Excellence for Vectors and Vector-Borne Diseases, Faculty of Science, Mahidol University at Salaya, Nakhon Pathom, Thailand, ²Social Medicine Group, Sawanpracharak Hospital, Ministry of Public Health, Nakhon Sawan, Thailand, ³Faculty of Humanities and Social Sciences, Rajabhat Rajanagarindra University, Chachoengsao, Thailand, ⁴Center for Global Health Research, Department of Public Health and Clinical Medicine, Umea University, Umea, Sweden, ⁵Institute of Public Health, Heidelberg University Medical School, Heidelberg, Germany, ⁶Emerging Infectious Diseases Program, Duke-NUS, Singapore, Singapore

Dengue is currently becoming a global public health problem. So far, vector control is the only method used to reduce dengue incidence. Our study aims at finding an alternative solution for dengue control by using insecticide-treated materials (ITM); i.e., treated curtains and school uniforms. Two randomized controlled trials were conducted separately in: 1) an urban city where 2,037 households were used to test ITM curtains, and 2) ten schools with 1,825 enrolled students used to test ITM school uniforms. Evaluation was carried out by entomological parameters and questionnaire interview of participants. The mosquito age was determined by using mosquito population age prediction method which is a tool to determine gene expression of age-related genes. The movement of *Aedes* vectors was evaluated by using sticky mosquito traps. Our results showed a significant reduction in *Aedes* density for both households ($p=0.006$) and schools ($p=0.033$) following an implementation. However, for the school trial, an average number of *Aedes* vectors increased after one month due to reduced efficacy of impregnated uniforms after frequent washing. Interestingly, the trial using impregnated curtains showed a trend of declining mean age of *Aedes aegypti*, i.e., 1.2 vs 8.6 days ($p=0.0002$) in treatment and control areas respectively; and a trend of increased movement of vector populations out of households after a one-year trial, i.e., 11.5% difference in treatment areas while no change was observed in control areas. Surveys with participants showed promising acceptability to the technology. In conclusion, application of ITM in dengue control was useful in either reducing dengue vectors and/or reducing their mean ages, which could have an impact on dengue transmission. We observed a reduction of dengue cases in treatment areas when compared to control areas. Further investigation is needed to decide whether an innovative control method using ITM is practical and effective for a long-term and large-scale implementation.

ASSESSMENT OF THE INSECTICIDE RESISTANCE STATUS OF Aedes Aegypti IN LIMA, PERU

Carmen Flores-Mendoza¹, Jorge Alarcon², Abelardo Tejada², Liz Espada¹, Gabriela Calle¹, Gissella M. Vasquez¹, Roxanne G. Burrus¹

¹U.S. Naval Medical Research Unit - 6, Lima, Peru, ²Instituto de Medicina Tropical Daniel Alcides Carrion Universidad Nacional Mayor de San Marcos, Lima, Peru

In Peru, *Aedes aegypti* was successfully eradicated in 1958 after a 13-year DDT spraying campaign conducted by the Ministry of Health (MoH). However, this mosquito re-infested Lima in 2000, and dengue outbreaks were reported five years later. Current MoH practices for *Ae. aegypti* control consist of temephos applications for larval control and pyrethroid spraying for adult control during dengue outbreaks. Based on the chemical spraying history, evaluating the insecticide susceptibility of *Ae. aegypti* populations from Lima could help prevent potential chemical control failures and guide decisions for an effective mosquito vector control

program. Therefore, the objective of this study was to determine the insecticide resistance status of *Ae. aegypti* from northern Lima. Centers for Disease Control (CDC) bottle bioassays were performed using 3-5 d-old F1 adults. Insecticide susceptibility was evaluated following CDC diagnostic dose and time for alphacypermethrin, deltamethrin, cypermethrin, and lambda-cyhalothrin (10 µg/30 min); permethrin (15 µg/30 min); fenitrothion and malathion (50 µg/30 min); DDT (75 µg/45 min), and benthio carb (12.5 µg/30 min). *Ae. aegypti* New Orleans and Rockefeller strains were also evaluated and used as reference for insecticide susceptibility. *Ae. aegypti* F1 population from Lima was 100% susceptible to all five pyrethroids and to malathion but resistant to DDT (10%). This population was apparently less susceptible to fenitrothion (78%) and benthio carb (3%); however, *Ae. aegypti* susceptible strains were also less susceptible to fenitrothion (<14%) and benthio carb (<2%). Our results suggest that no insecticide resistance exists to the five pyrethroids examined and to malathion, yet this *Ae. aegypti* population is resistant to DDT. The response to fenitrothion and benthio carb should be re-examined at different diagnostic doses and times to determine if *Ae. aegypti* from Lima are actually resistant to these chemical classes.

THE PLASTICITY AND HERITABILITY OF SPATIAL REPELLENCY RESPONSES TO TRANSFLUTHRIN IN Aedes Aegypti

Joseph Wagman, John Grieco, Nicole Achee

Uniformed Services University of the Health Sciences, Bethesda, MD, United States

The potential for spatial repellents to contribute to novel vector control approaches, especially in transmission settings unaffected by traditional tools such as indoor residual spraying and insecticide treated nets, is widely recognized as a research priority. The process of developing new spatial repellent products and strategies has been hampered, however, by the fact that work in this area involves complex behaviors that remain not well defined and/or poorly understood. *In vitro* bio-assays consistently show that disease vectors exhibit a wide range of behavioral responses to repellent chemicals in controlled experimental settings. In order to gain a better understanding of how behavior modification can impact vector populations, the plasticity and heritability of spatial repellency responses in *Aedes aegypti* following exposure to transfluthrin was investigated using a previously described high-throughput bioassay. In general, recently colonized (F₁ generation), non-mated mosquitoes were introduced into an assay system containing a chemical gradient established by dual-ended exposure chambers: a repellent chamber treated with 1.35 mg/m³ transfluthrin and an untreated control chamber. Mosquitoes that were repelled (moving away from the treated chamber) were considered responders and labeled SRA+, while mosquitoes that were not repelled (remained inactive) were considered non-responders and labeled SRA-. After each evaluation, specimens were collected alive and segregated based on observed behavioral phenotype. We present results on 1) the reproducibility of the behaviors in individual mosquitoes retested after a 48 hour resting period and 2) the heritability of spatial repellent behavior through six generations in which male responders were selectively bred with female responders, and non-responders with non-responders.

CARBAMATE AND ORGANOPHOSPHATE RESISTANCE IN ANOPHELES GAMBIAE ACROSS SOUTHERN GHANA: PATTERNS AND PREDICTION

John Essandoh¹, Alexander E. Yawson², David Weetman¹

¹Liverpool School of Tropical Medicine, Liverpool, United Kingdom, ²BNARI, GAEC, Accra, Ghana

Malaria is hyperendemic in Ghana and is a major cause of death and poverty. With strong DDT resistance entrenched throughout much of West Africa, carbamates and organophosphates (OPs) are the preferred alternatives to pyrethroids for IRS. However, resistance to both insecticide

classes has been documented in *Anopheles gambiae* in West Africa: to maintain insecticide efficacy, it is important to predict how and where resistance is likely to occur and spread. *Anopheles* larvae were sampled from 18 sites spanning five distinct ecological zones in southern Ghana from March to Mid-August 2011. Adult mosquitoes were bioassayed with bendiocarb and fenitrothion. Species and molecular characterization were performed using Scott and SINE PCRs respectively. Taqman qPCR assays were used to genotype the ACE-1 G119S resistance-associated locus and ACE-1 alleles were cloned and sequencing to determine possible copy number variation. A higher level of resistance was observed to bendiocarb than fenitrothion, though phenotypes correlated across populations. M-form and S-form were found in sympatry in 15 sample sites but in varying proportions, with three sites harbouring only M-forms. ACE-1 resistant allele (119S) frequency was much higher in S than M forms and a population from Ashiaman, a rice-growing area in Greater Accra, exhibited the highest 119S frequency reported to date (68%). ACE-1 frequency was found to be the strongest independent predictor of phenotypic resistance to both insecticides. However, duplication of ACE-1 was detected, with some individuals displaying multiple distinct alleles. Further work is now required to determine the distribution and resistance-association of ACE-1 duplications in southern Ghana.

1344

MULTIPLE INSECTICIDE RESISTANCE IN *ANOPHELES GAMBIAE* S.L. ACCORDING TO COTTON CULTIVATION SCHEMES IN BURKINA FASO, WEST AFRICA

Moussa Namountougo¹, Frédéric Simard², Abdoulaye Diabaté¹, Thierry Baldet³, Thibaud Martin⁴, Jean Bosco Ouédraogo¹, Géorges Anicet Ouédraogo⁵, Roch Kounborbr Dabiré¹

¹Institut de Recherche en Sciences de la Santé, Bobo-Dioulasso, Burkina Faso, ²IRD/MIVEGEC/BEES, Montpellier, France, ³IRD/CIRAD, Montpellier, France, ⁴CIRAD, Montpellier, France, ⁵UPB, Bobo-Dioulasso, Burkina Faso

In absence of effective vaccine, the most realistic strategy to control malaria is based on vector control relied on the use of synthetic insecticides. Unfortunately, due to the emergence of insecticide resistance in natural vector populations, many malaria vector control programmes are challenging field control failures. Here, we present new data from Burkina Faso, where longitudinal and cross-sectional surveys were conducted to monitor the frequency of the L1014F kdr and G119S ace-1R mutations and the role of metabolic-based detoxifying mechanisms in contributing to insecticide resistance in field *Anopheles gambiae* populations. In Burkina Faso since 2008 two innovative cotton growth systems based on transgenic (Bt) and biological cotton were introduced using no or less insecticide for pest control prospects. In such context, a country-wide survey associating bioassays and molecular investigations carried out from 2008 to 2010 through 26 localities in Burkina Faso. Populations of *An. gambiae* tested showed during these three years survey a generalising resistance status to PYs (permethrin and deltamethrin) and decreased mortality to bendiocarb whereas they remained susceptible to OP (chlorpyrifos methyl and fenitrothion) irrespective to area. The frequency of the L1014F kdr mutation was highest in the sudan region ranging from 0.75 to 0.99 and relatively moderated in the sudano-sahelian area. Results showed also over-expression of detoxifying enzymes such as GST, oxygenases, cytochrome P450 in *An. gambiae* s.s. from the old cotton belt together with kdr and ace-1R mutations indicating the existence of multi-resistance in Burkina Faso. The geographical distribution of resistance in *An. gambiae* s.l. populations was found in sites of cotton cultivation that has expanded dramatically in the last ten years. Until the discovery of new insecticides or formulations of existing insecticides, it is crucial to integrate the regional vector resistance status in the implementation of control interventions that will preserve a long term efficacy of these vector control tools.

1345

THE IMPACTS OF VECTOR CONTROL ON THE EFFECTIVE POPULATION SIZES OF MALARIA MOSQUITOES

Giridhar Athrey¹, Theresa Hodges¹, Kevin Deitz¹, Michael Reddy², Hans J. Overgaard³, Abrahan Matias⁴, Frances Ridl⁵, Immo Kleinschmidt⁶, Agalgisa Caccione², Michel A. Slotman¹

¹Texas A&M University, College Station, TX, United States, ²Yale University, New Haven, CT, United States, ³Norwegian University of Life Science, As, Norway, ⁴Medical Care Development International, Malabo, Equatorial Guinea, ⁵Medical Research Council, Durban, South Africa, ⁶London School of Hygiene & Tropical Medicine, London, United Kingdom

The battle against malaria mosquitoes in sub-Saharan Africa is being fought with two main weapons: indoor residual spraying of insecticides (IRS) and long-lasting insecticidal net (LLIN) campaigns. Although many programs have been successful in reducing malaria infection, demonstrating the impact of these programs on vector populations is typically confounded by numerous variables associated with collection methods. Without accurate ways of measuring the impacts of vector control, it is also difficult to determine the optimal frequency for insecticide spraying to keep transmission rates low. Here, we analyzed more than 2,200 samples of three important malaria vectors - *Anopheles gambiae*, *An. melas*, and *An. moucheti* - from seven sites in Equatorial Guinea that were collected over the course of anti-vector programs in that country (2004-2010). Taking advantage of recently developed coalescent genetic approaches, we addressed two main questions: a) what is the impact of vector control programs on effective population size? and b) how is the effective population size effected by single insecticide spray round? We demonstrate convincingly for the first time that both IRS- and LLIN-based control resulted in dramatically lowered effective population sizes (between 55%-87%) in all populations, with the exception of a single population of *An. melas*. No such reductions were observed in negative control populations. We also found that mosquito populations are dramatically reduced following IRS rounds (65-92%), but rebounded (2,818% increase) between 3-5 months after spraying, indicating that increased spray frequency is likely to greatly improve the impact of IRS on malaria transmission. Our findings are especially important to malaria control because we were able to conclusively link anti-vector interventions to genetic impacts, a linkage that has been difficult to establish in the past.

1346

QUANTITATIVE AND QUALITATIVE ANALYSIS OF GENE DUPLICATION IN INSECTICIDE-RESISTANT *ANOPHELES* MOSQUITOES FROM WEST AFRICA

Luc S. Djogbénou¹, John Essondah Essondah², Edi Constant Constant², Keith Steen Steen², Benoit Assogba Assogba³, Roch Dabiré⁴, Guillaume Ketoh⁵, Martin J. Donnelly², David Weetman²

¹Institut Régional de Santé Publique/Université d'Abomey-Calavi and Liverpool School of Tropical Medicine, Liverpool, United Kingdom, ²Liverpool School of Tropical Medicine, Liverpool, United Kingdom, ³Institut Régional de Santé Publique/Université d'Abomey-Calavi, Ouidah, Benin, ⁴IRSS/Centre Muraz, Bobo-Dioulasso, Burkina Faso, ⁵Université de Lomé, Lomé, Togo

Gene duplication is thought to provide a major source of material for evolutionary innovation. In addition to well-known point mutations that cause Ace-1 target site insensitivity for organophosphate and carbamate insecticides, Ace-1 gene duplication has been found in several West African populations of the primary malaria vector *Anopheles gambiae* s.s. Initially using a PCR-RFLP protocol we recorded excess heterozygosity at the Ace-1 resistance locus (G119S) in several field populations, consistent with the presence of a duplication phenomenon, but specific data on individual specimens could not be inferred. Here, we develop and apply quantitative real-time PCR (qRT-PCR) with SYBR Green detection, alongside both analogue and digital droplet qPCR Taqman assays to investigate

the range of allele-specific Ace-1 copy number variation occurring in natural *An. gambiae* populations in West Africa. Our results reveal that: (a) Ace-1 duplication is widespread across West Africa; (b) is present in unexpectedly high copy number (at least five-fold); and (c) multi-copy resistant homozygotes are not uncommon, despite strong prior evidence for fitness costs in single-copy homozygotes. The pairing of the G119S Taqman assay with our newly-developed copy number qRT-PCR assay provides an informative paired-diagnostic to assess the consequences of Ace-1 mutation and duplication for insecticide resistance phenotypes and fitness in wild *An. gambiae* populations.

1347

RISE OF MUTATION CYS 1534 IN THE VOLTAGE GATED SODIUM CHANNEL GENE IN *Aedes Aegypti* IN MEXICO

Farah Z. Vera-Maloof, Karla Saavedra-Rodriguez, Saul Lozano-Fuentes, William C. Black, IV

Colorado State University, Fort Collins, CO, United States

Aedes aegypti, is the primary vector to humans of dengue and yellow fever flaviviruses (DENV, YFV), and is a known vector of the chikungunya alphavirus (CV). Because vaccines are not yet available for DENV or CV or are inadequately distributed in developing countries (YFV), management of *Ae. aegypti* remains the primary option to prevent and control outbreaks of these arboviral diseases. Permethrin is one of the most widely used active ingredients in insecticides for suppression of adult *Ae. aegypti*. In 2012, we documented a replacement mutation in codon 1,534 of the voltage-gated sodium channel gene (*para*) of *Ae. aegypti* that encodes an cysteine rather than a phenylalanine and confers resistance to permethrin. A total of 86 field collections containing 4,014 *Ae. aegypti* were made throughout México from 1999 to 2012. These mosquitoes were analyzed for the frequency of the Cys1,534 mutation using a melting-curve PCR assay. Dramatic increases in frequencies of Cys1,534 were recorded from the late 1990's to 2012 in several states including Nuevo Leon in the north, Veracruz on the central Atlantic coast, and Yucatan, Quintana Roo and Chiapas in the south. From 1999 to 2012, the overall frequency of Cys1016 was 0.28. In 2000 in Veracruz the frequency was very low and by 2012 the frequency rose to 0.93. In 2008 Martinez de la Torre and Coatzacoalcos had frequencies of 0.94-1. In 2012 the frequency increased to 0.97 and had become fixed in Tuxpan. The earliest detection of Cys1,534 was in Chiapas, Guerrero and Veracruz in 2000. In total, we document a dramatic increase in the frequency of the Cys1,534 mutation in Mexico from 1999 to 2012. This may be related to previous extensive use of DDT and continued heavy use of permethrin. A rotational schedule utilizing different classes of adulticides should be implemented to slow or prevent fixation of Cys1534.

1348

BITING BEHAVIOR AND HIGH RESOLUTION MELTING DETECTION OF INSECTICIDE RESISTANCE IN *ANOPHELES GAMBIAE* IN MALI

Moussa Keita¹, Sidy Doumbia¹, Bilkissou Yagoure¹, Amadou S. Traore², Adam M. Jenkins³, Kimberly Regna⁴, Seydou O. Doumbia¹, Sekou F. Traore¹, Donald J. Krogstad⁵, Mamadou B. Coulibaly¹, Marc A. Muskavitch³

¹University of Science, Technologies and Techniques, Bamako, Mali, ²Tulane University Health Sciences Center, Bamako, Mali, ³Boston College, Chestnut Hill, MA, United States, ⁴Boston College, Boston, MA, United States, ⁵Tulane University Health Sciences Center, New Orleans, LA, United States

Understanding the behavior and detecting insecticide resistance in malaria vectors have important implications for malaria control. In 2012-2013, in four traversal passages (start, middle and end of transmission, and dry season), we have collected mosquitoes in two rural areas, Dangassa and Dioro in Mali, using human landing catches. We have used WHO bioassays to detect phenotypic resistance, and high resolution melting

(HRM) technology to detect target-site mutation frequencies in the *kdr* locus. Preliminary results reveal a nearly even split in the proportion of mosquitoes biting indoors vs. outdoors. The proportions were 47.7% vs. 54.3% (n=1013) in July 2012, 55.7% vs. 44.3% (n=517) in October 2012, 49.7% vs. 50.3% (n=155) in December 2012 and 38.0% vs. 62.0% (n=21) in April 2013 in Dangassa. In Dioro, they were 42.8% vs. 57.2% (n=35) in July 2012, 49.7% vs. 50.3% (n=151) in October 2012, 49.7% vs. 50.3% (n=155) in December 2012 and 57.1% vs. 42.9% (n=7) in April 2013. WHO susceptibility assays detected substantial resistance to DDT at both sites (22% and 14% mortality rates in Dangassa and Dioro, respectively) and susceptibility to bendiocarb and pirimiphos-methyl. The HRM analysis for *kdr* genotypes conducted on a subsample showed frequencies of 0.2 (RR), 0.3 (RS) and 0.5 (SS) at the start of the rainy season, and 0.2 (RR), 0.0 (RS) and 0.8 (SS) during the middle of the rainy season in Dangassa. In Dioro, the *kdr* allele frequencies were 0.4 (RR), 0.3 (RS) and 0.4 (SS) at the start of the rainy season and 0.4 (RR), 0.2(RS) and 0.4 (SS) during the middle of the rainy season.

1349

CHARACTERIZATION OF INSECTICIDES RESISTANCE IN *Aedes Aegypti* POPULATION FROM THE CARIBBEAN REGION OF COLOMBIA

Ronald Maestre Serrano¹, Doris Gómez Camargo¹, Suljey Cochero², Elkin Monterrosa Vergara³, Hugo Soto Lacouture⁴, Zulibeth Florez Rivadeneira⁵, Marcelo Torres⁶, Sergio Goenaga Olaya⁷, Erick Perdomo⁸, Brenda G. Silva⁹, Adriana E. Flores⁹

¹Universidad de Cartagena, Cartagena, Colombia, ²Secretaria de Salud de Sucre, Sincelejo, Colombia, ³Secretaria de Salud de Córdoba, Montería, Colombia, ⁴Secretaria de Salud del Cesar, Valledupar, Colombia, ⁵Secretaria de Salud de la Guajira, Riohacha, Colombia, ⁶Secretaria de Salud Distrital, Barranquilla, Colombia, ⁷Secretaria de Salud del Atlántico, Barranquilla, Colombia, ⁸Secretaria de Salud del Magdalena, Santa Marta, Colombia, ⁹Universidad Autónoma de Nuevo León, San Nicolás de los Garza, Nuevo León, Mexico

We determined the susceptibility to insecticides and biochemical and molecular mechanisms involved in insecticide resistance of nine populations of *Aedes aegypti* in the Caribbean Region of Colombia. Bioassays were performed for temephos in larvae according to WHO and bottle bioassays for adults with the insecticides: lambda-cyhalothrin, cyfluthrin, permethrin, deltamethrin, malathion, fenitrothion and pirimiphos-methyl. The resistance ratios were calculated using the susceptible Rockefeller strain as a control. Additionally, the organochloride DDT was evaluated through the impregnated papers technique. Biochemical resistance mechanisms were identified associated with high level of α , β -esterases, mixed-function oxidases, insensitive acetylcholinesterase and glutathione S-transferases; we identified the mutation Ile1,016 in the gene of the voltage-dependent sodium channel and its frequency. All populations were susceptible to the organophosphates evaluated (RR=1x-4x) with exception of Puerto Colombia and Soledad (Atlántico) strains which demonstrated high and moderate resistance to temephos (RR=15x) and (RR=5x), respectively and Sincelejo (Sucre) with moderate resistance to pirimiphos-methyl (RR=5x). All populations were resistant to DDT (2-28% mortality). Strains evaluated exhibited values of resistance to lambda-cyhalothrin between 4,9-83 fold, for deltamethrin between 0,9-37,8 fold, cyfluthrin with 0,5-33,8 fold and permethrin of 1,8 -17,9 fold. Over-expression of glutathione S-transferases were found in all populations with the exception of Puerto Colombia (Atlántico) and Cartagena (Bolívar); as well as α -esterase in strains: Valledupar (Cesar) and Montería (Córdoba); and insensitive acetylcholinesterase in Puerto Colombia strain (Atlántico). The mutation Ile1,016 was registered in all populations with variability in its frequency.

1350

HYDROLOGICAL DISTURBANCE AFFECTS COMPETITION BETWEEN *Aedes* VECTOR MOSQUITOES VIA CHANGES IN LEAF LITTER

Paul T. Leisnham, Cassandra Smith, T. Zach Freed
University of Maryland, College Park, MD, United States

The invasive mosquito *Aedes albopictus* utilizes water-holding containers for its development where it competes for food as larvae with the native *Aedes triseriatus* in the eastern United States. We tested the hypothesis that prior hydrological disturbance would affect competition between *Ae. albopictus* and *Ae. triseriatus* in containers via changes in leaf litter decomposition, associated microbial resources, and leached tannins. Containers provisioned with senesced litter were treated to mimic three broad hydrological regimes experienced by containers in nature: dry, flooded, and a wet-dry cycle, before varying densities of competing first-instar *Ae. albopictus* and *Ae. triseriatus* larvae were added using a response surface design. We found that hydrological regime affected litter resource quality, water quality, and *Aedes* competition. Previously dry leaf litter decayed more slowly, supported lower microbial abundance, and leached higher tannin concentrations than litter that had been flooded or exposed to a wet-dry cycle. Containers with previously dry litter experienced more intense competitive effects of *Ae. albopictus* on *Ae. triseriatus* population performance than containers that had previously been flooded or exposed to a wet-dry cycle. In contrast, prior hydrological regime did not affect the population performance of *Ae. albopictus*. These results suggest that prolonged wetter conditions prior to *Aedes* utilization of container habitats may relax competitive effects of *A. albopictus* on *A. triseriatus*, and help foster coexistence between the two species. Coexistence of these *Aedes* mosquitoes has implications for understanding mosquito invasions generally and specific disease risks in eastern North America.

1351

DESIGN AND TESTING OF A NOVEL, PROTECTIVE HUMAN-BAITED TENT TRAP FOR THE COLLECTION OF ANTHROPOPHILIC DISEASE VECTORS

Benjamin J. Krajacich¹, Jeremiah R. Slade², Robert T. Mulligan², Brendan LaBrecque², Kevin C. Kobylinski¹, Meg Gray¹, Massamba Sylla¹, Wojtek S. Kuklinski¹, Jonathan A. Seaman¹, Brian D. Foy¹, Timothy A. Burton¹

¹Colorado State University, Fort Collins, CO, United States, ²InfoScitex Corporation, Waltham, MA, United States

Currently, there exists a deficit of safe, active trapping methods for the collection of host-seeking *Anopheles* and other disease-causing arthropod vectors. The gold standard approach for mosquito collection is that of Human Landing Catch (HLC) in which an individual exposes bare skin to possibly infected vectors. Here, we present the development of a new method for mosquito collection, the InfoScitex Tent (IST), which utilizes modern tent materials coupled with a novel trap design. This provides an efficacious, non-labor intensive, and safe method for vector collection. In these initial studies, we found it collected an average of 31.5 *Anopheles gambiae* s.l. per trap per night in rural villages in Southeastern Senegal, and 42.5 *Culex* group V per trap per night in the semi-urban town of Kedougou, Senegal. In direct comparisons to HLC, the tent was not statistically different for collection of *Cx. quinquefasciatus* in crepuscular sampling, but was significantly less efficacious at trapping the highly motile dusk biter *Aedes aegypti*. These studies suggest that the IST tent is a viable and safe alternative to HLC for *Anopheles* and *Culex* sampling in areas of high vector-borne disease infection risk.

1352

HETEROGENEITY IN MALARIA VECTOR DYNAMICS AND BIONOMICS IN NCHELANGE DISTRICT, ZAMBIA

Smita Das

Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States

As part of the Southern Africa International Centers for Excellence in Malaria Research (ICEMR) project, mosquito collections were performed from March-May 2013 in Nchelenge District, Luapula Province, Zambia. Located along the environs of Lake Mweru and Kenani Stream, Nchelenge experiences hyperendemic transmission and has the highest malaria infection rate in children under the age of 5 years despite implementation of indoor residual spraying (IRS) and long-lasting insecticide-treated net (LLIN) distribution. Center for Disease Control light traps (CDC LTs), pyrethroid spray catch (PSC), and larval collections were performed at three villages along Lake Mweru and two villages along Kenani Stream. The collections revealed that *Anopheles gambiae* sensu stricto is the dominant vector in the lakeside villages, whereas *An. funestus* s.s. is the primary vector with secondary contribution from *An. gambiae* s.s. in the streamside villages. Both human malaria infection rates and vector populations were higher near the streamside villages than those of the lakeside villages. Surveys of potential oviposition sites found that temporary water bodies near the stream and the stream itself are the major breeding sites for *An. gambiae* and *An. funestus*. Both vector species are highly anthropophilic and are predicted to have high sporozoite infection rates. The differences in human malaria infection rates and mosquito abundances between the lake and stream sites support the hypothesis that heterogeneity exists in the human blood index, entomological inoculation rates, and multiple blood feeding behavior of the two vectors within Nchelenge District. The insecticide resistance status of both malaria vectors will also be explored. The vector data in Nchelenge present unique opportunities to further our understanding of malaria transmission and the implications for malaria control in high-risk areas.

1353

CEMETERIES ARE EFFECTIVE SITES FOR SURVEILLANCE OF LA CROSSE VIRUS AND VECTOR POPULATIONS IN APPALACHIA

Rebecca T. Trout Fryxell¹, Kimberly Freyman², Armando Ulloa³, Brian Hendricks¹, Dave Paulsen¹, Abelardo Moncayo²

¹University of Tennessee, Knoxville, TN, United States, ²Tennessee Department of Health, Nashville, TN, United States, ³Regional Center for Public Health Investigation, Tapachula, Mexico

In North America, the mosquito-borne disease La Crosse encephalitis is the leading cause of arboviral disease among children, and was previously limited to the upper Midwest. Unfortunately, the Appalachian region, with Tennessee in particular, now has the highest incidence risk in the nation: 228.7 cases per 100,000 children 15 years and younger, and almost 75% of all US cases reported in a year are in Appalachia (Haddow and Odai 2009). In 2012, nine pediatric cases of La Crosse encephalitis occurred in eastern Tennessee, including one death. While *Aedes (Ochlerotatus) triseriatus* has been the historical vector, *Ae. albopictus* and *Ae. (Oc.) japonicus* are two invasive species that may be important accessory vectors. All three vectors oviposit desiccant-tolerant eggs in forest stands and opportunistically oviposit eggs in artificial containers. Use of artificial containers may move La Crosse virus (LACv) from the forest's tree holes and into the urban environment as LACv can be transmitted to mosquito offspring (transovarial transmission). In an attempt to detect LACv in active mosquito populations, our objective was to determine if cemeteries were effective sites for monitoring LACv and the vector population; consequently, we conducted an in-depth vector ecology study centered around the 2012 fatal case. Briefly, 38 cemeteries were selected within 10 radial miles of the fatal case. At each cemetery, four ovitraps baited with water and seed germination paper (egg paper) were placed at the four cardinal directions. Egg papers and water were replaced weekly, from 5

Sept. - 3 Oct. 2012, this yielded a total of 760 egg papers. Recovered egg papers (99.3%) were brought back to the laboratory where eggs hatched and adults emerged. Thus far, we have successfully recovered all 3 vector species representing *Ae. (Oc.) triseriatus* (87.6%), *Ae. albopictus* (12.2%) and *Ae. (Oc.) japonicus* (0.2%), and identified four positive pools of *Ae. (Oc.) triseriatus*. This preliminary data indicates cemeteries are effective sites for surveillance of LACV and vector populations.

1354

ENVIRONMENTAL INVESTIGATION FOLLOWING A LA CROSSE ENCEPHALITIS CASE FATALITY IN TENNESSEE, 2012

Kimberly Freyman¹, Armando Ulloa², Brian Hendricks³, Rebecca Trout-Fryxell³, Dave Paulson³, Abelardo C. Moncayo¹

¹Tennessee Department of Health, Nashville, TN, United States, ²Centro Regional de Investigacion en Salud Publica, Tapachula, Mexico, ³University of Tennessee, Knoxville, TN, United States

La Crosse encephalitis virus (LACV) is an important cause of pediatric encephalitis in the United States. Historically, human cases have been concentrated in the upper-Midwestern states, but in the mid-1990s, the Appalachian region including east Tennessee became a focal point. In 2012, nine pediatric cases of LACV encephalitis occurred in Tennessee, including one death. To detect LACV in the area, oviposition traps, BG sentinel and CDC light traps were placed at forty-nine sites consisting of cemeteries and houses within ten miles of two pediatric infections including the deceased child from September 5 to October 3, 2012. Ninety-one papers have had adults reared and pooled so far. The pools were tested for LACV by real-time RT-PCR. Adult collections from BG and CDC traps at house sites were comprised of 36% *Aedes albopictus*, 29% *Culex erraticus*, 13% *Anopheles punctipennis*, 9% *Cx. pipiens*, 8% *Ochlerotatus triseriatus*, 2% *Ae. vexans*, 2% *An. quadrimaculatus* and 1% other species. Adults emerging from cemetery collected egg papers were *Oc. triseriatus* (87.6%), *Ae. albopictus* (12.2%) and *Oc. japonicus* (0.2%). Papers collected from house sites showed *Oc. triseriatus* (54.8%), *Ae. albopictus* (44.6%) and *Oc. japonicus* (0.6%). During the last two weeks, the percentage of *Oc. triseriatus* emerging from the papers decreased; whereas *Ae. albopictus* increased for house and cemetery sites. Of house sites, 50% showed a composition of two species, 37.5% with three and 12.5% with one. Of cemetery sites, 57.7% had a species composition of two, 27% with one and 11.5% with three species. Some (3.8%) cemetery sites did not hatch. To date, 628 pools of mosquitoes have been tested. All 39 pools from BG and CDC trap collections were negative for LACV. Four pools of *Oc. triseriatus* from egg paper collections were LACV positive. The positive pools came from a cemetery site on October 3, 2012. Along with the successful detection of LACV, these findings suggest a temporal and spatial variation in mosquito activity. *Aedes albopictus* may also be more prevalent near homes and *Oc. triseriatus* near cemeteries.

1355

FIELD EVALUATION OF A PUSH PULL STRATEGY TO CONTROL MALARIA VECTORS IN NORTHERN BELIZE, CENTRAL AMERICA

Joseph Wagman¹, Grieco John¹, Russell King², Ireneo Briceño², Christopher Martinez³, Nicole Achee¹

¹Uniformed Services University of the Health Sciences, Bethesda, MD, United States, ²Ministry of Health, Orange Walk, Belize, ³Uniformed Services University of the Health Sciences, Orange Walk, Belize

Current vector control tools are quickly becoming inadequate for controlling arthropod-borne diseases such as malaria. The reasons for this are complex but combined highlight the need for development of novel approaches to reduce pathogen transmission. Efforts are being carried out to evaluate the use of spatial repellents and mosquito traps in a combined push-pull strategy to reduce the probability of human-vector contact in and around homes. Here, we report on a 16-night, four-arm Latin square experimental hut study in Belize, Central America that evaluated the

ability of this approach to reduce densities of two locally relevant malaria vectors, *Anopheles vestitipennis* and *An. albimanus*, from entering the structures. Utilizing a matched-control (untreated) hut, we measured changes in vector entry patterns at huts receiving either indoor repellent alone (1.4 mg/m³ transfluthrin), outdoor traps (CDC miniature light traps baited with human foot emanations), or both interventions simultaneously. Outdoor light trap yields were also compared between huts with and without repellent. Results show that while light traps alone did not impact mosquito entry into huts, use of repellent alone significantly reduced mosquito entry by more than 60% (\pm 4%) for both species. The combined intervention did not result in any further reduction of mosquito entry over repellent alone. In fact, while not significant in terms of absolute numbers of mosquitoes entering the huts, a post-hoc Wilcoxon Signed Rank analysis indicates that the presence of a baited CDC light trap outside of a hut may reduce the repellency effect of transfluthrin. Interestingly, use of an indoor repellent did increase the average numbers of *An. vestitipennis* (an endophagic species) captured in outdoor light traps by 50% (\pm 27%), but no corresponding effect was seen with *An. albimanus* (an exophagic vector). These results indicate that while a combined push-pull intervention has the potential to reduce human-vector interactions, the baseline ecology and behaviors of the target vector(s) will influence efficacy.

1356

INSECT-SPECIFIC VIRUSES DETECTED IN LABORATORY MOSQUITO COLONIES: IMPLICATIONS FOR EVALUATING VECTOR COMPETENCE EXPERIMENTS

Bethany G. Bolling, Nikos Vasilakis, Hilda Guzman, Vsevolod L. Popov, Saravanan Thangamani, Robert B. Tesh
University of Texas Medical Branch, Galveston, TX, United States

In the past 5 years, there has been a dramatic increase in the detection and description of insect-specific viruses found in field-collected mosquitoes. Evidence suggests that these viruses are widespread in nature and many appear to be maintained by vertical transmission (infected female transmits virus to her progeny). Recent studies also indicate that superinfection exclusion (cells infected with one virus are refractory to infection by a second related virus) may occur between some insect-specific viruses with pathogenic arboviruses, thus altering the vector competence profiles of certain mosquito species. In order to evaluate this phenomenon further, we initiated studies to investigate the presence of insect-specific viruses in our laboratory mosquito colonies. Pools containing 50 male and 50 female mosquitoes collected from each colony were homogenized and virus isolation was attempted in Vero (vertebrate) and C6/36 (invertebrate) cell lines. Cell cultures were examined for cytopathic effect and also screened by electron microscopy for the presence of virus-like particles. Total RNA was extracted from C6/36 cell cultures and submitted for deep sequencing with an Illumina platform. Seven out of 14 colonies were found to contain an insect-specific virus. Phylogenetic analyses and serological tests confirmed the presence of previously described insect-specific flaviviruses as well as several novel viruses. The infection rates detected within the infected mosquito colonies were variable. The potential implications of these findings in regards to vector competence studies will be discussed.

1357

THE EFFECTS OF TRANSIENT IMMUNE ACTIVATION ON TRANSGENIC ANOPHELES STEPHENSI FITNESS

Andrew Pike, George Dimopoulos

Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States

Mosquitoes of the genus *Anopheles* spread the *Plasmodium spp.* parasites responsible for human malaria. Rising resistance and difficulties of distribution have hampered traditional malaria control efforts, which have focused on chemotherapeutic agents to treat cases as they arise and control of mosquito populations through insecticide use, bednets and habitat removal. These issues, coupled with the lack of an effective

vaccine, call for the development of new malaria control methods. Multiple laboratory groups have created transgenic mosquitoes refractory to malaria infection, but no such lines have yet been released as part of a malaria control program. One problem with genetically modified mosquito lines is that they are generally assumed to be less fit than their wild-type conspecifics, which would stop them from replacing the native population and limit their effectiveness. However, previous studies in *Drosophila* and initial data from mosquitoes indicate that temporary immune induction in transgenic insects may have minimal effects on fitness. Therefore, we set out to investigate how short-term induction of the mosquito immune system affects mosquito fitness. We compared various aspects of mosquito fitness, such as; lifespan, fecundity, development time, mating competitiveness, wing length and blood meal consumption in five separate transgenic lines to the same measures in wild-type mosquitoes and have seen few effects. The transgenic lines tested were chosen to test different aspects of transgenesis that may affect fitness, and include the same gene under different promoters, different genes under the same promoter, different isoforms of the same gene and different insertion points of the same construct. These results suggest that the mere presence of a transgene in mosquitoes does not necessarily lead to a large fitness reduction, and indicate that genetically modified mosquitoes may soon be a viable tool for the control of vector-borne diseases.

1358

MODERATE PRECIPITATION CONDITIONS FAVORED INCREASE OF MOSQUITO POPULATION VECTORS OF VENEZUELAN EQUINE ENCEPHALITIS IN LA ALTA GUAJIRA COLOMBIA

Cristina Ferro, Jorge Luis De las Salas Ali, Ligia Lugo, **Betsy Bello**
Instituto Nacional de Salud, Bogota, Colombia

In the past 17 years none outbreak of Venezuelan equine encephalitis (VEE) has been registered in La Guajira and the disease is no longer a public health priority. However, it is important to consider the last two epidemics that took place in 1992 and 1995 when the virus showed that it was still a threat, after its disappearance was speculated. The objective of this work was to monitorize the precipitation conditions that favor the increase in the populations of mosquito vectors (*Diptera: Culicidae*), in order to assess the entomological risk of virus transmission. Different precipitation periods were studied from September 2009 to August 2012 in La Guajira. Mosquitoes were collected using CDC traps and identified to species. Daily average abundance of female mosquito vectors species collected per night was calculated, and compared to the accumulated precipitation register of the previous 16 days of the collecting day. Vector species, *Aedes taeniorhynchus* and *Psorophora confinnis*, achieved their maximum abundance, when rainfall was moderated between 30 to 60 mm., either heavy (above 80 mm), very low or absence rainfall affected negatively their populations. Both species proved to need specific and slightly different climatic conditions. In conclusion the entomological risk of transmission of VEE increases in the rainy season, particularly at the end of it.

1359

TEMPORAL CHANGE IN ANOPHELES DARLINGI DIVERSITY IN SOME MALARIA ENDEMIC PERUVIAN LOCALITIES

William Lainhart¹, Kyle Nadler¹, Sara A. Bickersmith², Marta Moreno³, Marlon Saavedra⁴, Paulo E. Ribolla⁵, Joseph M. Vinetz³, Jan E. Conn²

¹Department of Biomedical Sciences, School of Public Health, State University of New York-Albany, Albany, NY, United States, ²Wadsworth Center, New York State Department of Health, Slingerlands, NY, United States, ³Division of Infectious Diseases, School of Medicine, University of California San Diego, San Diego, CA, United States, ⁴Asociacion Beneficia-PRISMA, Lima, Peru, ⁵Parasitologia, Universidade Estadual Paulista "Julio de Mesquita Filho", Botucatu, Brazil

WHO reported approximately 500,000 malaria cases in the Americas in 2011, of which 22,878 cases were in Peru. In the city of Iquitos in northern Amazonian Peru, *Anopheles darlingi* is the primary malaria vector. The overall aim of this project is to evaluate vector control measures and seasonality by measuring local allelic diversity (A) and effective population size (N_e) in *An. darlingi*. Based on earlier studies that detected mid-range N_e and high gene flow in villages surrounding Iquitos, we hypothesize that neither diversity nor N_e will vary among localities seasonally, although this has not been tested previously. A quantitative measure of vector control effectiveness is a significant reduction in N_e and A . *An. darlingi* microsatellite data from fifteen loci were analyzed for four localities south and west of Iquitos: San Jose de Lupuna (LUP), Villa El Buen Pastor (VBP), Cahuide (CAH) and Santo Tomas (STO). Genetic diversity, differentiation (F_{ST}), N_e , departures from Hardy-Weinberg equilibrium and linkage disequilibrium were measured for 17-50 specimens per collection. Sequential Bonferroni corrections minimized multiple testing biases. Both structure and F_{ST} analyses detected one population of *An. darlingi*, similar to findings of Mirabello et al. (2008). However, in the current study, N_e estimates were lower. Overall genetic diversity was high and similar for the four localities. These results differ from those of Pinedo-Cancino et al. (2006) who used amplified fragment length polymorphism analyses and reported limited diversity in *An. darlingi* in the same region. Differences between February (dry) and April (rainy) in 2011 were only assessed for LUP and VBP. In this analysis, mean A for all loci was stable in both localities, but in VBP, observed heterozygosity (H_o) decreased and expected heterozygosity (H_e) increased. Our results suggest local seasonal environmental changes may influence diversity within this population of *An. darlingi*.

1360

A PHARMACOLOGICAL APPROACH TO VECTOR CONTROL VIA THE ANOPHELES GAMBIAE SEX PEPTIDE RECEPTOR

Kimberly Regna¹, Jamie R. Doyle², Alan S. Kopin², Marc A.T. Muskavitch¹

¹Boston College, Chestnut Hill, MA, United States, ²Tufts Medical Center, Boston, MA, United States

While many vector-targeted control strategies aim to decrease vector survival, there are many mosquito behavioral processes that could serve as targets for strategies that would decrease vectorial capacity. Among such behaviors, mating is a potential target for intervention in many insects, including *Anopheles gambiae*, because there is a dramatic increase in female refractoriness to mating after a single initial mating event. In other insects, including *D. melanogaster*, sex peptide receptor (SPR) has been shown to play a significant role in regulating mating behavior. SPR is a G protein-coupled receptor that is activated by sex peptide (SP), which is present in the male seminal fluid, and by myoinhibiting peptides (MIPs), which are thought to be ancestral ligands for SPR-related receptors. We are investigating the pharmacology of SPR in *An. gambiae* by screening selected MIPs in cell-based assays to identify receptor agonists. Using an agonist-based approach, it may be possible to induce female refractoriness to mating by delivery of these peptides *in vivo*, and thereby decrease

reproductive ability and fitness of agonist-treated mosquitoes, leading to source reduction. We have found that RNAi-based knockdown of the *D. melanogaster* SPR ortholog leads to pre-adult developmental arrest and impaired flight ability, suggesting that SPR antagonists may be of interest for control of *An. gambiae* if the mosquito receptor plays similar roles. The goals of this project are to better understand SPR receptor-ligand activity relationships and to investigate the role of SPR in mosquito behavior and survival, in an effort to validate novel drug targets for development of next-generation insecticides.

1361

FUNCTIONAL CONFIGURATION OF METAGENOME IN THE MOSQUITO GUT ECOSYSTEM

Giannong Xu¹, Phanidhar Kukutla¹, Hongmei Jiang², Lingling An³, Jinjin Jiang¹, Matthew Steritz¹, Wanqin Yu¹, Celeste Alvarez¹, Thomas Gilbreath⁴, Guiyun Yan⁴

¹New Mexico State University, Las Cruces, NM, United States,

²Northwestern University, Evanston, IL, United States, ³University of Arizona, Tucson, AZ, United States, ⁴University of California Irvine, Irvine, CA, United States

Host associated microbes are ubiquitous, yet our understanding of the interactive relationships is very limited. The mosquito gut ecosystem accommodates a complex microbial assemblage. The dynamic gut microbiome profoundly affects various mosquito life traits, such as fecundity and immunity. Besides, bacteria may directly interfere with malaria *Plasmodium* development in the gut before invasion occurs. However, little is known about the genetic structure and functional repertoire of the gut microbiome. In this study we generated 15Gbp metagenomic DNA- and RNA-seq data from the guts of adult mosquito *Anopheles gambiae* under conditions with sugar meals or blood meals. Using an assembly-based pipeline, a 37.1 Mbp metagenomic reference was compiled, which included 49,000 contigs. Similarity based taxonomic classification recognized at least 6 phyla, predominant taxa included Proteobacteria (Enterobacteriaceae, Pseudomonadaceae and Acetobacteraceae) and Bacteroidetes (Flavobacteriaceae). The function annotation was implemented via SEED/Subsystems and COG/KEEG, which recognized 23,550 coding sequences. Among them 42% were assigned into ~700 subsystems. Metabolic reconstruction predicted 1658 reactions and 1266 compounds. In addition to the presence of many ABC transporters, there are large numbers of TonB dependent transporters and polysaccharide utilization *loci*, constituting uptake systems for iron, vitamin B 12 and various biopolymers. The presence of large capacity of resistance to antibiotics and toxic compounds may represent a defense strategy for maintaining community stability. The metagenomic reference was further used for mapping RNA-seq reads to decipher context dependent community functions, which was exemplified by metatranscriptomic analysis of the sugar-fed and blood-fed guts. The metagenomic reference provides insights into the taxonomic and functional configuration in the mosquito gut ecosystems.

1362

DIVERSE SYMPATRIC MALARIA VECTOR SPECIES IN PURSAT PROVINCE, WESTERN CAMBODIA, AN AREA WHERE ARTEMISININ-RESISTANT *PLASMODIUM FALCIPARUM* IS HIGHLY PREVALENT

Becky A. Miller¹, Brandyce St. Laurent¹, Men Sari², Chanaki Amaratunga¹, Seila Suon², Duong Socheat², Robert W. Gwadz¹, Rick M. Fairhurst¹, Jennifer M. Anderson¹

¹National Institutes of Health/National Institute of Allergy and Infectious Diseases/Laboratory of Malaria and Vector Research, Rockville, MD, United States, ²National Center for Parasitology, Entomology and Malaria Control Program, Phnom Penh, Cambodia

Anopheles mosquitoes from a two-year longitudinal entomological collection in Thmar Da commune, Pursat Province, were analyzed to

determine which species transmit malaria to humans along Cambodia's border with Thailand. This region has been a hotspot for the evolution of drug-resistant *Plasmodium falciparum* parasites for decades, so understanding the complex transmission dynamics and the vector species responsible for spreading these parasites is critical for effective malaria prevention, control, and eventual elimination. Using human landing catch and CDC light trap methods, we collected 4,264 anophelines comprising 14 different morphologically-identified species (*An. barbirostris*, *An. dirus*, *An. hyrcanus*, *An. hyrcanus group*, *An. jamesii*, *An. karwari*, *An. kochi*, *An. maculatus*, *An. minimus*, *An. nigerrimus*, *An. philippinensis*, *An. tessellatus*, *An. umbrosus*, and *An. vagus*), all of which have been incriminated as (mostly secondary) malaria vectors elsewhere in southeast Asia. Specimens were analyzed for (i) *Plasmodium* infection using a nested PCR, (ii) bloodmeal source (i.e., human or domestic animal), and (iii) the presence of cryptic molecular species defined by rDNA ITS2 *loci*. Preliminary molecular speciation reveals even more species diversity in this area, with multiple cryptic species present. Several different anopheline species, including *An. maculatus*, *An. dirus* A, and *An. tessellatus*, were found to carry *Plasmodium* parasites. The implications of multiple vector species and their biting behaviors for malaria control and transmission in this region will be discussed. The diversity of vector species in Thmar Da and elsewhere in Cambodia is a challenge for vector control efforts and underlies the need for further characterization of vector ecology, behavior, and population genetics in this country's malaria-endemic areas.

1363

IDENTIFICATION OF *Aedes aegypti* IMMUNE RESPONSES MECHANISMS TO DENGUE VIRUS

Paola A. Caicedo¹, Clara B. Ocampo¹, Carl Lowenberger², George Dimopoulos³, Neal Alexander¹, Idalba M. Serrato¹

¹Centro Internacional de Entrenamiento e Investigaciones Médicas-CIDIEM, Cali, Colombia, ²Simon Fraser University, Burnaby, BC, Canada, ³Johns Hopkins University, Baltimore, MD, United States

In recent years there has been considerable progress in our knowledge of dengue, particularly in vaccine development, the characterization of the immune responses and molecular properties of the virus. However, there are still many aspects that must be investigated in terms of its transmission by the principal vector, *Aedes aegypti*. We have conducted research to elucidate Dengue virus-vector relationships, specifically the innate immune response of *A. aegypti* to dengue virus infection. For this, we identified and selected two strains of *A. aegypti*, from Cali, Colombia with different susceptibility to dengue infection: Susceptible (Cali-S) and refractory with midgut infection barrier (Cali-MIB). We compared the global gene expression of the midguts of Cali-S and Cali-MIB after ingestion of sugar, a bloodmeal, or a bloodmeal containing Dengue-2 virus using microarrays. Preliminary results from the microarrays indicated the expression of a total of 3761 genes. Of these, a total of 165 immune-related genes have been identified. A differential expression between the two strains exposed to DENV-2 virus included genes in different functional groups; immunity, metabolism, proteolysis, redox, replication, transport, and unknown function. Characterization of these genes is underway to elucidate if refractoriness is related to an upregulation or downregulation of specific or multiple genes in the two strains. This study will provide a global overview of gene expression in susceptible and refractory mosquitoes and will be compared with other studies that have looked at specific molecules and pathways. This study will also validate the use of our field derived strains as an important biological model to study Dengue-vector relationships.

1364

OCCURRENCE OF NATURAL *ANOPHELES ARABIENSIS* SWARMS IN AN URBAN AREA OF BOBO-DIOULASSO CITY, BURKINA FASO, WEST AFRICA

Kounbobr R. Dabiré¹, Simon P. Sawadogo¹, François de Sales D. Hien¹, Hamidou Maïga¹, Thierry Baldet², Frédéric Simard³, Abdoulaye Diabaté¹, Louis-Clement Gouagna⁴, Gabriella Gibson⁵, Rosemary S. Lees⁶, Jérémie Gilles⁶

¹Centre Muraz/IRSS, Bobo-Dioulasso, Burkina Faso, ²Centre de Coopération Internationale en Recherche Agronomique pour le Développement (CIRAD), Montpellier, France, ³UMR-MIGEVEC, IRD, Montpellier, France, ⁴UMR-MIGEVEC, IRD, Ile de la Reunion, France, ⁵Natural Resources Institute/University of Greenwich, Central Avenue Chatham Maritime Kent, United Kingdom, ⁶Insect Pest Control Laboratory, FAO/IAEA, Vienna, Austria

The swarming behavior of natural populations of *Anopheles arabiensis* was investigated by conducting transect surveys on 10 consecutive days, around dusk, from March to April and from September to October 2012 in Dioulassoba, a district of Bobo-Dioulasso city in Burkina Faso (West Africa). Swarms were observed outside, around identified larval breeding sites on the banks of the Houet River, as well as in the open-air courtyards found at the centre of many homes in the region. Swarms were found to occur in open sunlit spaces, mostly located above physical or visual cues somehow visually distinct from the surrounding area. Overall 67 and 78 swarms were observed, respectively, during the dry season (March-April) and the rainy season (September-October) of 2012, between 1.5 and 4.5 meters above the ground at their centre. 964 mosquitoes were collected and analyzed from dry season swarms, of which most were male, and all were *An. arabiensis*, as were the few resting mosquitoes collected indoors. Larvae collected from breeding sites found on the banks of the Houet River mostly consisted of *An. arabiensis* and only a minority *An. coluzzii* (formerly identified as *An. gambiae* M form). Of 1694 mosquitoes analyzed from 78 swarms in the wet season collections, a few *An. gambiae* males were identified, and the remainder was *An. arabiensis*. The majority of larvae collected during the wet season from the same breeding sites were identified as *An. arabiensis* and only a minority *An. coluzzii* form and even fewer *An. gambiae* (formerly known as *An. gambiae* S form). The same pattern of species composition was seen in resting mosquitoes, though the proportion of *An. arabiensis* was less overwhelming. These data support the conclusion that *An. arabiensis* is the most prevalent species in this area, though the difference in species composition when using different population sampling techniques is noteworthy. Further studies are required for more detailed investigation of male dispersal, feeding behaviour and mating patterns in an urban setting.

1365

ACCURATE SPECIES IDENTIFICATION IS CRITICAL FOR MALARIA CONTROL: THE UTILITY OF MOLECULAR CHARACTERIZATION OF ANOPHELINE SPECIES ACROSS INDONESIA, A COUNTRY OF DIVERSE VECTORS AND MALARIA TRANSMISSION

Brandyce St. Laurent¹, Puji B. Asih², Siti Zubaidah², Sumardi S.³, David Bretz⁴, Hellen C. Miller⁴, John Mueller⁴, William A. Hawley⁵, Supratman Sukowati³, Dln Syafruddin², Frank Collins⁴, Neil Lobo⁴

¹Eck Institute for Global Health, University of Notre Dame, South Bend, IN, United States, ²Eijkman Institute of Molecular Biology, Jakarta, Indonesia, ³National Institute of Health Research and Development, Jakarta, Indonesia, ⁴University of Notre Dame, South Bend, IN, United States, ⁵Unicef, Jakarta, Indonesia

Identification of malaria vectors is critically important for the evaluation of malaria transmission dynamics. In areas of high biological diversity, morphological species identification may not fully describe the amount of variation that is relevant to malaria transmission. The burden of malaria in Indonesia, a region of high biological and geographical diversity, is

significant and varies across the archipelago, largely due to differences in the types of mosquito species inhabiting each region. In many areas in Indonesia, there are multiple sympatric anopheline species whose specific bionomic traits ultimately determine the dynamics of malaria transmission. Most of these species are isomorphic members of cryptic species complexes. In this study, we used molecular tools to identify anopheline specimens collected from four different sites in Indonesia to molecular species to address site-specific species identification issues as they relate to malaria control. Specimens were collected from four field sites in Indonesia: a low transmission field site in Purworejo, Central Java; a medium transmission field site in Lampung, Sumatra; and high transmission sites in South Halmahera and Papua. 2,840 anopheline samples from different entomological collections, representing 18 different morphological species, were sequenced for ribosomal DNA ITS2 using Sanger sequencing. Molecular species identification revealed 22 different molecular species, a high level of misidentification, and 9 species carrying *Plasmodium falciparum* or *P. vivax* sporozoites. These species include: *Anopheles aconitus*, *An. balabacensis*, *An. farauti* 4, *An. indefinitus*, *An. kochi*, *An. maculatus*, *An. sundaicus* A, *An. vagus*, and *An. vanus*. Accurate species identification is cost-effective for control programs and site-specific evaluation of species compositions at the molecular level is recommended prior to the implementation of any control or monitoring program. These results will contribute to our understanding of the distribution of vector species, their behavioral patterns, as well as provide new diagnostic tools.

1366

PRESENCE OF *AEDES (STEGOMYIA) ALBOPICTUS* (SKUSE, 1894) (DIPTERA: CULICIDAE) IN COLOMBIA

Betsy Bello, Ligia Lugo

Instituto Nacional de Salud, Bogota, Colombia

Aedes (Stegomyia) albopictus (Skuse, 1894), it is the dengue's vector, yellow fever in Southeast Asia and others arbovirus such as chikungunya fever; this vector is an invasive specie that has the ability to reproduce in natural and artificial environments with a widely geographic distribution, being in different countries in Europe, Africa and America. The first record of *Ae. (Stg.) albopictus* in South America was at Brazil in 1986, followed by Bolivia, Colombia, Paraguay, Argentina, Uruguay and Venezuela. Also, inside of the entomological surveillance that is made in Colombia to exotic species of public health importance, we includes the sentinel surveillance sampling is performed in larvitrap and in some cases ovitraps at strategic points such as airports, land and river ports. Being the first record of *Ae. (Stg.) albopictus* in Leticia – Amazonas (Colombia) in 1998, this place is the border zone with Tabatinga-Brazil and Caballo Cocha, Iceland and Santa Rosa - Perú; after that we found this new vector in six of the thirty-two Colombian departments, starting with the Special District, Industrial, Port, and Ecotourism Biodiversity Buenaventura-Valle del Cauca, 2001. Although there are few records of its role as a vector in the Americas, there is one report of natural infection in *Ae. (Stg.) albopictus* with serotypes Den-1 and Den-2 in Colombia in 2006, specimens from the municipality of Buenaventura, Valle del Cauca. Therefore it is likely that this mosquito in the future become a efficient vector of dengue and other arboviruses in our country continue to be important sentinel surveillance through larvitrap and ovitraps and integrate the control of *Aedes (Stegomyia) aegypti* and *Aedes (Stegomyia) albopictus* in the country, as globalization has enabled the generation of new trade routes and through passive transport in less time get more places both the mosquito vector and the virus and the sick.

TUBERCULOSIS IN LAMBARÉNÉ, GABON: FIRST EPIDEMIOLOGICAL AND MICROBIOLOGICAL DATA

Sabine Bélard¹, Jonathan Remppis¹, Davy U. Kombila¹, Saskia Janssen¹, Matthias Frank², Abraham S. Alabi¹, Bertrand Lell¹, Peter G. Kremsner², Martin P. Grobusch³

¹Centre de Recherches Médicales de Lambaréné, Lambaréné, Gabon, ²Institute of Tropical Medicine, Tübingen, Germany, ³Center for Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Division of Internal Medicine, Academic Medical Center, Amsterdam, Netherlands

The central African region is highly affected by the pandemics of HIV and tuberculosis (TB), but systematic data on local epidemiology and drug resistance are scarce, if ever available. The objective of this first prospective observational cohort analysis of 200 TB patients in Lambaréné, Gabon, is to describe demographic, clinical and microbiological characteristics and evaluate treatment outcomes. Patients from three different treatment centers in Lambaréné were included and followed up 2 and 6 months after treatment initiation. Sputum samples were sent to Germany for culture and drug sensitivity testing. To date 120 patients have been included; 74 (62%) were male and 20 (17%) were children. 105/120 (88%) were new TB cases, in 9/120 (8%) and 5/120 (4%) retreatment was started due to default and relapse, respectively. Among the adult patients 75/100 (75%) presented with smear positive pulmonary TB, 18/100 (18%) with smear negative pulmonary TB and 7/100 (7%) with extra-pulmonary TB. HIV co-infection was confirmed in 36/120 (30%), in 12/120 (10%) HIV status was unknown. Of the 54 positive sputum culture results obtained so far 47/54 (87%) were identified as *Mycobacterium tuberculosis* and 7/54 (13%) as *M. africanum*. Full drug sensitivity for the first-line antituberculous drugs (RHZES) was ascertained in 44/54 (81%) patients. Resistance to at least rifampicin and isoniazid (multi-drug resistance, MDR) was found in 3/54 (6%), and mono-resistance to isoniazid and streptomycin in 3/54 (6%) each, and combined resistance of isoniazid plus streptomycin in 1/54 (2%). So far treatment outcome could be evaluated for 36 patients; 17/36 (47%) were classified cured, 3/36 (8%) defaulter, 1/36 (3%) treatment failure, 10/36 (28%) lost to follow-up, and 5/36 (14%) deceased. All deceased patients were HIV co-infected. These first interim results indicate that in Gabon TB is a serious public health threat with a high mortality in HIV co-infected patients and a low cure rate. Besides improvement in basic TB control, implementation of mycobacterial culture and drug sensitivity testing beyond research purposes as well as the establishment of a second-line regimen are urgently needed to halt the further spread of MDR TB.

1368

IMPACT OF RESPIRATORY ILLNESSES DURING PREGNANCY ON NEWBORN'S WEIGHT - A COMMUNITY BASED LONGITUDINAL STUDY AT AN URBAN SLUM IN PAKISTAN

Asad Ali¹, Umer Zaman¹, Samana Zaidi¹, William Petri², Zulfiqar Bhutta¹, Anita Zaidi¹, Molly Hughes²

¹Aga Khan University, Karachi, Pakistan, ²University of Virginia, Charlottesville, VA, United States

Birth weight is a powerful determinant of an infant's long term growth and survival. Although maternal health is widely believed to impact the birth weight of the baby, the exact factors during pregnancy which influence the birth weight are not clearly known. We are conducting a longitudinal observational study at Bilal Colony, a semi urban area of Karachi, Pakistan to assess the effect of maternal morbidities on the weight of the newborn. We are following 400 pregnant women from the first trimester onwards until their delivery. The pregnant women are visited weekly to record any fever or respiratory symptoms during the past seven days, and are referred to the study site clinic for treatment of observed illnesses. Each symptom episode is defined as one or more days of a self-reported symptom (fever, cough, difficulty breathing, runny nose, sore throat, head ache, chills or myalgia) in a pregnant woman who was symptom free for three days before. So far, 288 pregnancies

have concluded as live deliveries, 12 as still births and 31 as spontaneous abortions. We analyzed the data of 243 pregnant women whose newborns were weighed within 14 days of birth. The average age of pregnant women in our study was 24.1 years and average weight of the pregnant woman was 56.1 kg at the time of enrollment. Only 31% of the mothers had primary education or above whereas 38.3% had antenatal visits during their pregnancy. There were 51 (21%) newborns with low birth weight (< 2.5 kg), whereas 192 (79%) had normal birth weight (>= 2.5 kg). In pregnant women who had a low birth weight baby, the average episodes of fever, cough, headache and myalgia were 1.7, 2.3, 4.3, and 4.3 per women respectively. In pregnant women who had a normal birth weight baby, the average episodes of fever, cough, headache and myalgia were 1.7, 2.1, 5.2 and 4.6 per women respectively. The results of this study will help identify the degree to which maternal respiratory illnesses during pregnancy are a risk factor for infant's low birth weight.

1369

MOLECULAR DETECTION OF HUMAN METAPNEUMOVIRUS ON NASOPHARYNGEAL SWABS COLLECTED FROM OUTPATIENTS WITH ACUTE RESPIRATORY TRACT INFECTIONS FROM MBAGATHI DISTRICT HOSPITAL, KENYA IN THE YEAR 2008

Rosemary M. Nzunza¹, Wurapa Eyako¹, Kariuki Njenga², Ongus Juliette³, James Njiri¹, Berhane Assefa¹, Wallace Bulimo¹

¹U.S. Army Medical Research Unit-Kenya, Nairobi, Kenya, ²GDD/IEIP-Kenya, Nairobi, Kenya, ³Institute of Tropical Medicine and Hygiene, Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya

Human metapneumovirus (hMPV) is a leading cause of acute respiratory tract infection in children the elderly and immune compromised persons. In Kenya the extend of hMPV infections in the population remains is unknown. A retrospective study was conducted in the year 2008 in outpatients from ≥2 months of age presenting at the outpatient department of Mbagathi District Hospital for acute respiratory infection. Nasopharyngeal swabs were systematically tested for human metapneumovirus and other respiratory viruses, using real time reverse transcriptase PCR. Epidemiological and clinical characteristics of hMPV-infected children were studied and compared to those of patients with respiratory syncytial virus (RSV) and other viral infections. A total of 498 patients were enrolled in this study. Viral investigations detected a total of 271 viruses. Out of these, 77 (15.5%) were hMPV infections, 78 (15.7%) Seasonal Flu A, 60 (12%) Seasonal Flu B, 13 (2.6%) Panenterovirus, 36 (7.2%) Para Influenza viruses and 6 (1.2%) RSV infections. Human metapneumovirus infections were higher in males 43 (55%) than females 34 (45%), and predominantly in children ≤5 yrs (97%), only 2 (3%) aged between 6-9 yrs. The hMPV infection had peak in January-February, and was uncommon after March. Most of the patients infected with hMPV were under 1 year of age and cough (100%) and difficulty in breathing (75%) were the predominant diagnosis in these patients with clinical symptoms of a lower respiratory tract infection. The severity of the disease was similar to those of RSV patients. These results highlight that hMPV plays an important role in acute respiratory tract infections especially in children. Rapid detection to identify specific viral pathogens causing respiratory tract infections in the wider Kenyan population could aid in patient management.

1370

MOLECULAR CHARACTERIZATION OF HUMAN ENTEROVIRUS 68 ISOLATED IN KENYA DURING 2008 TO 2010

Silvanos M. Opanda

United States Army Medical Research Unit-Kenya (USAMRU-K), Nairobi, Kenya

Human enterovirus 68 (HEV-68) is a rarely detected viral pathogen associated with acute respiratory illness. It is unique among enteroviruses because it shares common biological properties with rhinoviruses. The

virus was first isolated in California, USA in 1962 and has ever since been identified almost exclusively in respiratory samples. HEV-68 infection is associated with several disease manifestations ranging from mild respiratory illnesses to severe acute lower respiratory tract infections including pneumonia, wheezing and bronchitis. During the period 2008 to 2010 an upsurge in the number of clusters of acute respiratory illness associated with HEV-68 was reported in many parts of the world including Asia, Europe and the United States. Human respiratory enteroviruses have not been well characterized in the East African region. We sought to molecularly characterize HEV-68 isolated in Kenya in 2008 to 2010 in order to understand their genetic diversity. A total of six (6) isolates were analyzed. Viral RNA was extracted followed by RT-PCR amplification of VP1 capsid protein coding gene. PCR amplicons were sequenced and the resulting sequences compared to those of Fermon prototype strain and previously characterized strains from other countries. Pair-wise comparison of VP1 sequences of Kenyan HEV-68 isolates revealed 87.2-99.5% nucleotide identity. The Kenyan HEV-68 strains shared 86.0-88.4% and 91-99% nucleotide identities respectively, when compared to Fermon and previously characterized strains reported in Gen Bank. Multiple sequence alignment of VP1 sequences of Kenyan isolates with Fermon revealed 12 amino acid substitutions and one deletion in five of the isolates and 11 amino acid substitutions. Phylogenetic analyses revealed five of the Kenyan isolates clustered closely to HEV-68 strains which circulated in New York, USA and Yamagata, Japan; while only one clustered with those that circulated in the Netherlands, Europe. All the Kenyan isolates clustered away from Fermon indicating divergence from the prototype strain. These findings suggest HEV-68 strains isolated in Kenya during the period 2008 to 2010 were generally similar to those detected in other parts of the world. Majority of the Kenyan isolates were however more closely related to those detected in the United States and Japan. Surveillance and constant monitoring of HEV-68 is important in understanding their evolutionary dynamics.

1371

MICRORNAS AS BIOMARKER FOR ACTIVE TUBERCULOSIS INFECTION IN IMMUNOCOMPETENT AND IMMUNODEFICIENT

Grace W. Mwangoka¹, Paolo Miotto², Ilaria C. Valente², Luca Norbis², Giovanni Sotgiu³, Klaus Reither⁴, Norbert Heinrich⁵, Francesco Aloï⁶, Daniela M. Cirillo²

¹Ifakara Health Institute, Dar es Salaam, United Republic of Tanzania, ²Emerging Bacterial Pathogens Unit, Division of Immunology, Transplantation and Infectious Diseases, S. Raffaele Scientific Institute, Milan, Italy, ³Clinical Epidemiology and Medical Statistics Unit, Department of Biomedical Sciences, University of Sassari, Sassari, Italy, ⁴Swiss Tropical and Public Health Institute, Basel, Switzerland, ⁵Division for Infectious Diseases and Tropical Medicine, Ludwig Maxmillian University, Munich, Germany, ⁶St. Francis, Nsambya Hospital, Kampala, Uganda

One of the most important priorities for tuberculosis control is the accurate diagnosis of individuals with active, infectious TB. This enables prompt treatment that both interrupts TB transmission and cures patients. Circulating nucleic acids (CNAs), including miRNAs present in serum, may serve as potential biomarkers for diagnosis and follow up in active and latent TB infection in immunocompetent and immunodeficient. The study enrolled consented participants, from 2 sites in Italy and 2 site in Africa (Tanzania and Uganda). Participants enrolled included healthy controls (HC), subjects with active TB (PTB), PTB with HIV and latent TB (LTBI). To minimize individual variation; sera from 10 participants from each category were pooled. miRNAs profile were measured using Taqman low density arrays qRT PCR. A Student's t test was used to compare mean concentrations of miRNAs with STATA 11. 672 miRNAs were analysed, 47 wmiRNAs were significantly up or down regulated and observed to be common in the active TB and HCs from both geographic region (P<0.05). 50 miRNAs were significantly expressed in active TB compared to LTBI; 37 and 11 miRNAs were up and down regulated respectively. Analysis performed following validation on single patients confirmed 4 common

miRNAs from both the European and the African participants. Whereby: 7 miRNAs (3 European and 3 African specific and 4 common) were identified as discriminatory biomarkers for active TB disease. In conclusion, results from this study suggest that change in miRNAs expression levels plays a vital role in TB pathogenesis and could be biomarkers for TB diagnosis.

1372

PREVALENCE AND RISK FACTORS FOR LATENT TUBERCULOSIS INFECTION IN MILITARY PERSONNEL IN PERU

Giselle M. Soto¹, Cesar Munayco², Gabriela Soto², Moises Apolaya³, Marianela Ore⁴, Giovana Arenas³, Jorge Fernandez⁴, Juan Silvera³, Antonio Tokumoto³, Patricia Avila⁴, Ruben Valle¹, Mariana Ramos¹, Daniel Ehlman¹, David Moore⁵, Daniel G. Bausch¹

¹U.S. Naval Medical Research Unit - 6, Bellavista, Peru, ²Dirección General de Epidemiología del Ministerio de Salud (DGE), Jesus Maria, Peru, ³Dirección de Sanidad de la Fuerza Aerea del Perú (DISANFAP), Surco, Peru, ⁴Comando de Salud del Ejército Peruano (COSALE), San Borja, Peru, ⁵Laboratorio de Enfermedades Infecciosas, Universidad Peruana Cayetano Heredia, San Martin de Porres, Peru

Tuberculosis continues to be a global threat to public health. About of one-third of the world's population has latent tuberculosis infection (LTBI), with the highest rates generally in developing countries. Understanding the risk factors for LTBI is crucial for tuberculosis control. Populations in closed settings, such as military bases, are often at particularly high risk. Close contact with tuberculosis cases has been used to assess the risk of LTBI as well as active tuberculosis. Use of the tuberculin skin test (PPD) can identify persons with LTBI, but is often considered not useful to assess recent exposures in developing countries because it is assumed that the vast majority of persons are positive. We explored the prevalence and risk factors for LTBI in students and cadets in two military academies of the Peruvian Armed Forces. Participants were interviewed and received PPD placement. A total of 621 participants were enrolled, with a mean age of 19 years and 80% were male. Of 608 participants who returned for PPD evaluation, 118 (20%) were positive, with increasing prevalence with age; the multivariate logistic regression analysis showed that for every year of increased age the odds ratio for LTBI increased by 33%. Gender, area of birth and present residence, and close contact with tuberculosis cases or with relatives/friends with tuberculosis were not associated with LTBI. Despite the assumed high burden of tuberculosis in developing countries and closed settings, a minority of persons in our study were PPD positive and close contact with tuberculosis cases was not a risk factor for LTBI. However, increasing age was a good predictor for LTBI and should form the basis for targeted control efforts. We assume, but cannot be certain, that our study population is representative of the general population of Peru.

1373

INCIDENCE OF RESPIRATORY TRACT INFECTIONS AMONG PASTORALISTS BEFORE AND AFTER THE INTRODUCTION OF PCV-10 VACCINATION IN RURAL NORTHERN KENYA

Stephanie J. Hauck, Stephanie B. Gati, Bryan Grenfell

Princeton University, Princeton, NJ, United States

Worldwide, pneumonia is the top killer of children under five years old, taking the lives of 1.2 million children every year. Developing countries bear the highest burden of childhood mortality, and 30,000 of these yearly childhood pneumonia deaths occur in Kenya. To curb the effects of this killer disease, the Kenyan Ministry of Health introduced the 10-valent pneumococcal conjugate vaccine (PCV) to the routine immunization schedule in late 2010. Despite the introduction of PCV-10 to the schedule, however, inadequate access to vaccination in some parts of Kenya suggests immunization rates are too low to induce herd immunity in these communities. To explore the relationship between immunization for PCV-10 and respiratory infection rates, we conducted a retrospective study of

vaccination and outpatient records from two rural dispensaries who service pastoral populations in Laikipia county, Kenya. We found that PCV-10 coverage is very low, with only 33.3% of children receiving the first dose of PCV-10, 13.6% the second dose, and 6.15% the final dose. T-tests with unequal variance using Satterthwaite's degrees of freedom show no significant decrease in pneumonia incidence after vaccination began in Laikipia in March 2011 at either dispensary (Dispensary A: $t(34.845) = 0.081$, $p = .468$) and (Dispensary B: $t(39.889) = 1.068$, $p = .146$). However, the variance of pneumonia cases in months of high vaccination coverage is significantly lower than the variance of cases during low vaccination months ($F(7,38) = 0.266$, $p = .037$), suggesting that if great numbers of children are vaccinated with PCV-10, significant reductions in pneumococcal disease rates may occur.

1374

EVALUATION OF ACCEPTABILITY AND PERFORMANCE OF STOVE OPTIONS FOR REDUCING HOUSEHOLD AIR POLLUTION IN RURAL WEST KENYA

Nigel G. Bruce¹, Tamara Pilishvili², Bryan Christensen², Debbi Stanistreet¹, Jennifer Loo², Ibrahim Sadumeh³, Justus Muoki⁴, Fuyuen Yip², Lindsey Horton², Michelle Bashin⁵, Mike Sage²

¹University of Liverpool, Liverpool, United Kingdom, ²Centers for Disease Control and Prevention, Atlanta, GA, United States, ³Safe Water and Aids Project, Kisumu, Kenya, ⁴University of Nairobi, Nairobi, Kenya, ⁵Public Health Institute, Oakland, CA, United States

Relationships between household air pollution (HAP) and risk of key diseases suggest low levels are needed to realise most of the health benefit; furthermore, achieving low levels requires that households are willing to use effective stoves for all or most needs. This study aims to identify whether one or more solid fuel stoves are capable of both meeting user needs and delivering low HAP, and hence suitable for intervention studies and scaling up. The study was conducted in west Kenya using mixed methods. Candidate stoves were required to demonstrate $\geq 40\%$ reduction in PM_{2.5} emissions in USEPA tests. A cooking demonstration assessed user views on those most suitable for local needs: the 6 best (2 rocket, 1 chimney rocket, 3 fan-assisted) were then evaluated in a cross-over design in 43 homes. Following baseline measurement of kitchen concentrations (CO, PM_{2.5}), personal women (cook) and youngest child (< 5 yr) CO, and stove use with stove use monitors (SUMS, each home used one stove type for 2 weeks, with repeat assessment in the final 48 hrs. This cycle repeated until all homes used at least 5 stoves. Qualitative interviews at baseline and following use of each stove assessed user views and reasons for multiple stove use. Focus groups (FG) explored user views in comparing all stove types. Initial (Round 1&2) results for kitchen and personal HAP show reductions for all stove types, but not to the low levels sought. SUMS data show multiple stove use occurred, and high kerosene lamp emissions may also help explain post-intervention HAP levels. Qualitative findings indicate preference for the new stoves, women reporting smoke reduction and finding them cleaner, more fuel efficient and easy to use. However, a number of stove improvements are suggested which could reduce multiple stove use. For most women, stove cost is reported as a barrier, but the FGs identified ways these could be made more affordable and marketed. Full results (to be presented) will help guide technology development and adoption to help deliver substantive health benefits at scale.

1375

ANTIBIOTIC USE IN AN INFLUENZA-LIKE ILLNESS COHORT IN PERU, 2009-2011

Lizette O. Durand¹, Yeny Tinoco¹, Matthew R. Kasper¹, Eduardo Azziz-Baumgartner², Candice Romano¹, Hugo Razuri¹, Daniel G. Bausch¹

¹U.S. Naval Medical Research Unit - 6, Lima, Peru, ²Centers for Disease Control and Prevention, Atlanta, GA, United States

Influenza-like illness (ILI) affects 20% of the global population annually. Although over 95% of ILI cases are thought to be viral, several studies have shown that patients and physicians often confuse ILI with respiratory infections caused by bacteria, prompting antibiotic prescription and inducing antibiotic resistance. To date, there has been no study on the use of antibiotics in persons with ILI in Peru. Therefore, we collected data on medication use, both prescribed and over-the-counter, from a multi-site ILI cohort study in four distinct ecological regions of Peru during 2009-2011. We compared antibiotic use associated with region, gender, age, presence of co-morbidities, and use of other medications in the preceding 30 days by chi-square analyses performed in EpiInfo. Data were collected on 6,790 cases of ILI, of whom 53% were female, with a median age of 14.7 years (range newborn-108). Overall, 92% of study participants took some medication for their ILI, of which 13% were prescribed by a physician. Co-morbidities and previous medication use were reported in 15% and 24%, respectively. Virtually all of those who took prescribed medications also took over-the-counter ones. Antibiotics comprised 27% of all medications, of which 51% were prescribed and 62% were penicillin drugs. Interestingly, despite data showing that approximately 20% of ILI cases in the cohort are influenza, no person took an anti-influenza drug, although these are not readily available on the market or in private clinics in Peru. The proportion of antibiotic use was higher than all other drugs taken for ILI. Prescription drugs, including antibiotics, are clearly frequently taken by persons with ILI in Peru. Although the etiologic agent is unknown in the majority of cases, the results almost certainly demonstrate an overuse of antibiotics for ILI, despite universal recommendations against the use of antibiotics for this syndrome. Increased availability of on-site diagnostics and dissemination of guidelines on the management of ILI at healthcare centers could improve this situation.

1376

XPRT MTB/RIF FOR THE DIAGNOSIS OF TUBERCULOSIS IN CHILDREN - A SYSTEMATIC REVIEW AND META-ANALYSIS

Anne K. Detjen¹, **Andrew R. DiNardo**², Jacinta Leyden³, Karen R. Steingart⁴, Dick Menzies⁵, Ian Schiller⁶, Nandini Dendukuri⁷, Anna M. Mandalakas²

¹The International Union against Tuberculosis and Lung Disease, New York, NY, United States, ²Baylor College of Medicine, Houston, TX, United States, ³Rice University, Houston, TX, United States, ⁴Cochrane Infectious Diseases Group, Liverpool School of Tropical Medicine, United Kingdom, ⁵Respiratory and Epidemiology Clinical Research Unit, Montreal Chest Institute, McGill University, Montreal, QC, Canada, ⁶Division of Clinical Epidemiology, McGill University Health Centre - Research Institute, Montreal, QC, Canada, ⁷Division of Clinical Epidemiology, McGill University, Montreal, QC, Canada

In 2011, the WHO recommended Xpert MTB/RIF for the diagnosis of tuberculosis (TB) and MDR TB in all age groups despite a lack of pediatric data at that time. We conducted a systematic review to assess the diagnostic accuracy of Xpert MTB/RIF for pulmonary TB (PTB) in children. We performed database searches for relevant studies in all languages through April 2013. We included randomized-controlled, cross-sectional, and cohort studies involving children (< 15 years) with presumed TB. We extracted data separately for expectorated sputum (ES), induced sputum (IS), nasopharyngeal aspirates (NPA), and gastric aspirates (GA). We performed meta-analysis to determine pooled sensitivity and specificity. We included 10 studies in PTB. Five studies (41.7%) were conducted in

low or lower middle-income countries. Against a reference standard of culture, pooled sensitivities were 69% (95% Credible Interval 55-81) for ES and IS combined (7 studies) and 75% (59-90) for GA (5 studies). In HIV-infected children, sensitivity was 77% (60-89) in ES/IS versus 59% (44-72) in HIV-uninfected children. Sensitivity in ES/IS in children aged 0-4 was 57% (36-74) versus 83% (68-92) in children aged 5-15. Pooled specificity was >95% in all subgroups assessed using culture as a reference standard. In children with smear positive disease, pooled sensitivity was 96% (90-99) for ES and IS and 95% (83-99) for GLA. Pooled sensitivity in smear negative disease was 76% (58-90) for ES/IS and 78% (59-92) for GLA. As Xpert MTB/RIF is being rolled out in TB high burden settings it becomes available for children as an alternative to smear microscopy. Xpert MTB/RIF is highly specific for TB in children. However, sensitivity estimates are estimated with poor precision due to the sparse data available. There is a greater need for pediatric studies of Xpert to support guidelines for use in this population.

1377

COMPARISON OF NASOPHARYNGEAL SWABS COLLECTED FOR PNEUMOCOCCAL COLONIZATION AND NASAL SWABS IN THE IDENTIFICATION OF VIRAL RESPIRATORY INFECTIONS IN PERU

Carlos Grijalva¹, Philip Budge¹, Marie Griffin¹, Ana Gil², Kathryn Edwards¹, Hector Verastegui², Monika Johnson¹, Stella Hartinger², Claudio Lanata², John Williams¹

¹Vanderbilt University School of Medicine, Nashville, TN, United States,

²Instituto de Investigacion Nutricional, Lima, Peru

We sought to determine agreement in detection of respiratory viruses using RT-PCR testing between two different types of samples collected on the same day: nasal swabs preserved in viral transport medium (NS) and nasopharyngeal swabs preserved in skim milk-tryptone-glucose-glycerol [STGG] media (NP). Samples were collected as part of a prospective household-based cohort study of Andean children aged less than 3 years. Nasal swabs were collected during episodes of acute respiratory illness for identification of respiratory viruses including influenza, human metapneumovirus (MPV), respiratory syncytial virus (RSV), human rhinovirus (HRV), parainfluenza virus 3 (PIV) and adenovirus (AdV). NS used a Dacron swab placed into each nostril sequentially, rotated beneath the turbinates, and placed into viral transport medium, which was then aliquoted into lysis buffer and stored at -80C. NP swabs were collected on a monthly basis to study colonization with *Streptococcus pneumoniae*. NP used a Rayon wire-handled swab placed through one nostril into the posterior nasopharynx, rotated for 5 seconds, placed into STGG and stored at -80C. A random sample of paired NP and NS samples collected from the same child on the same day was selected. Nucleic acid was extracted and tested for respiratory viruses by real-time multiplex RT-PCR. We evaluated the agreement between NP and NS samples in viral detection using the kappa coefficient and compared viral loads in NP and NS samples using RT-PCR cycle thresholds (CT). We studied 260 paired NP and NS samples. The kappa coefficient between NP and NS virus testing results was 0.70 (AdV); 0.87 (RSV); 0.88 (influenza); 0.92 (PIV3); 0.96 (HRV); and 0.97 (MPV). Median CT values were not statistically different between NP and NS samples across most respiratory viruses, except for influenza and RSV for which CTs were slightly lower in NP than in NS (all p<0.05). The agreement between NS and NP samples was very high, indicating NP samples could be used as a single, efficient collection strategy for field studies of both respiratory viruses and bacteria.

1378

LOPHOMONAS SP. IN RESPIRATORY TRACT SECRETIONS IN HOSPITALIZED CHILDREN WITH PNEUMONIA AND BORDETELLA PERTUSSIS CO-INFECTION

Rito Zepa¹, Elsa Ore², Carmen Quispe², Lilian Patiño², Margarita Alvarado², Paolo A. Wong¹

¹Instituto de Medicina Tropical Daniel A. Carrión, Universidad Nacional Mayor de San Marcos, Lima, Peru, ²Instituto Nacional de Salud del Niño, Perú, Lima, Peru

Lophomonas sp. is a protozoan that is found in the digestive tract of cockroaches: *Periplaneta americana* and *Blatta germanica*. There are few reports of this emerging protozoan infection in humans, mainly affecting the lower respiratory tract in patients with severe lung disease. *Lophomonas sp.* has recently been reported in patients with asthma, as well as the discovery of protozoa in the respiratory tract of children with pneumonia. The aim of the study was to investigate *Lophomonas* in respiratory samples of children with pneumonia and in patients with a clinical diagnosis of pertussis, treated at the National Institute of Child Health, national reference center for pediatric diseases in Lima, Peru, in the period January to December 2012 and from January to March 2013. 558 samples were worked: 471 from tracheal aspirate, 40 from bronchoalveolar lavage and 47 from nasopharyngeal aspirate. This last group corresponding to children with a clinical diagnosis of pertussis. *Lophomonas* was found in 17/558 (3.04%) samples of children with pneumonia, six of them were diagnosed with pertussis. A sample with *Lophomonas sp.* and *Bordetella pertussis* coinfection was found out. In conclusion, it is necessary to search for *Lophomonas sp.*, emerging protozoan upper and lower respiratory infections, mainly in children with pneumonia and in patients diagnosed with pertussis.

1379

ESTABLISHMENT AND SUCCESSES OF THE UGANDA NATIONAL VIRAL HEMORRHAGIC FEVER SURVEILLANCE PROGRAM AND HIGH-CONTAINMENT LABORATORY, 2010-2013

Trevor Shoemaker¹, Stephen Balinandi¹, Alex Tumusiime¹, Joseph Wamala², Barbara Knust³, Ilana Schafer³, Shelly Campbell³, Debi Cannon³, Bobbie Rae Erickson³, Arideth Gibbons³, Luke Nayakarahuka⁴, Julius Lutwama⁴, Edward Mbidde⁴, Ute Ströher³, Pierre Rollin³, Stuart Nichol³

¹Centers for Disease Control and Prevention-Uganda, Entebbe, Uganda,

²Ministry of Health, Kampala, Uganda, ³Centers for Disease Control and Prevention, Atlanta, GA, United States, ⁴Uganda Virus Research Institute, Entebbe, Uganda

Uganda is endemic for viral hemorrhagic fevers (VHF) and other zoonotic diseases. In July 2010 the Viral Special Pathogens Branch, CDC, the Uganda Virus Research Institute (UVRI), and the Ministry of Health established a first of its kind National VHF surveillance program. In addition, a permanent high-containment laboratory was established at UVRI. This lab serves as the national VHF reference laboratory, and an East Africa regional resource. The laboratory can perform real-time PCR, IgM, IgG and antigen capture ELISA for Ebola, Marburg, Rift Valley fever, and Crimean-Congo hemorrhagic fever viruses. To date, suspect VHF samples from over 20 districts in Uganda, and 5 East and Central African countries, have been sent for rule-out testing. The program has tested over 2000 samples from human surveillance, serosurveys, primates, livestock, and VHF outbreaks. 1364 samples have been tested for surveillance and outbreak activities, resulting in confirmation of 5 independent filovirus outbreaks. Four Ebola outbreaks have occurred: two in Luwero District (2011, CFR=100%; 2012, CFR=57%; both Sudan virus), one in Kibaale District (2012, CFR=71%; Sudan virus), and one in Isiro, DRC (2012, CFR=54%; Bundibugyo virus). One Marburg outbreak occurred in Kabale, Kamwenge, and Ibanda districts in 2012 (CFR=58%). Testing was completed for a national Uganda serosurvey of 587 human blood

samples looking for evidence of past infection with Ebola, Marburg, RVF, and CCHF. The program has also tested 244 primate and livestock samples for VHF, including 204 samples from the Karamoja region where 35% were positive by IgG for CCHF, showing evidence of actively circulating CCHF virus in Uganda. The successes of this program show how having a functional, comprehensive, and timely VHF surveillance system in Uganda, and East Africa, greatly contributes to limiting the extent of outbreaks through early detection and response. This program also advances the knowledge of other high-hazard pathogens of international concern in Uganda, and the region, and should serve as a model for further expansion throughout Africa.

1380

RE-EMERGENCE OF BUNDBUGYO VIRUS AFTER A FIVE YEAR HIATUS -- ISIRO, THE DEMOCRATIC REPUBLIC OF THE CONGO, 2012

Ilana J. Schafer¹, Andrea M. McCollum¹, Barbara Knust¹, Jean-Jacques Muyembe², Robert Shongo³, Benoit Kebela³, Kiyele Musa³, Eric Bergeron¹, Christina Spiropoulou¹, Brian Bird¹, Elisabeth Pukuta², Gary Kobinger⁴, Félix Adima⁵, Claudine Nseye³, Mathias Mossoko³, Félix Mulangu³, Emmanuel Lampaert⁶, Carolina Nanclares⁷, Deborah Cannon¹, Steven Balinandi⁸, Alex Tumusiime⁸, Olimpia de la Rosa⁷, Miriam Alia⁷, Bobbie Rae Erickson¹, Trevor Shoemaker⁸, Ute Ströher¹, Pierre E. Rollin¹, Stuart Nichol¹

¹Centers for Disease Control and Prevention, Atlanta, GA, United States, ²Institut National pour la Recherche Biomédicale, Kinshasa, Democratic Republic of the Congo, ³Ministry of Health, Kinshasa, Democratic Republic of the Congo, ⁴Public Health Agency of Canada, Winnipeg, MB, Canada, ⁵Haut-Uélé District Health Department, Isiro, Democratic Republic of the Congo, ⁶Médecins sans Frontières, Kinshasa, Democratic Republic of the Congo, ⁷Médecins sans Frontières, Barcelona, Spain, ⁸Centers for Disease Control and Prevention, Kampala, Uganda

On August 16, 2012, two patients in Isiro Health Zone, The Democratic Republic of Congo (DRC) tested positive for Bundibugyo virus (BDBV), identifying the second Ebola Hemorrhagic Fever (EHF) outbreak attributed to BDBV – the first occurring in Uganda in 2007. An international response was immediately launched to control the outbreak. Patient epidemiologic and clinical data were collected via a standardized case report form. A field laboratory tested blood samples by RT-PCR, and serology diagnostics were performed in Uganda. Cases were classified as suspect (clinical criteria), probable (suspect plus epidemiologic criteria), or laboratory confirmed. Bivariate data analysis was used to evaluate cases and non-cases for predictors of BDBV infection, and cases for predictors of death. A total of 36 confirmed, 16 probable, and 7 suspect EHF cases were identified, with 133 initially suspected cases ruled out. Among the 52 confirmed and probable cases, the case fatality rate (CFR) was 53.8%, age range was 0 – 70 years (median=40 years), 76.9% were female, and 25.0% were healthcare workers. Among all patients evaluated for EHF, factors significantly associated ($p < 0.05$) with being a case were female gender, fever, vomiting, diarrhea, fatigue, conjunctivitis, difficulty swallowing, difficulty breathing, hiccups, and anorexia. Patients with a cough were significantly less likely to be a case. Among EHF cases, symptoms significantly associated with death were hemorrhagic signs, cough, difficulty swallowing, difficulty breathing, conjunctivitis, and hiccups. Five unlinked chains of virus transmission were identified, indicating that EHF cases remained unidentified. June 1, 2012 was the earliest discovered case onset. Like the 2007 outbreak, this BDBV outbreak had a lower CFR than is seen with *Zaire ebolavirus* and *Sudan ebolavirus* species. The last confirmed case was isolated 57 days after outbreak detection. Prompt local and international efforts in field laboratory establishment, case finding, and case isolation were crucial to the successful containment of the outbreak.

1381

ROTAVIRUS INFECTION IN CHILDREN IN A RURAL COMMUNITY IN PISCO, PERU

Carlos A. Figueroa, Maria E. Silva, Giannina Luna, Claudio Rocha, Drake Tilley, Daniel G. Bausch

U.S. Naval Medical Research Unit - 6, Bellavista, Peru

Rotavirus is the leading cause of severe diarrhea in children under 5 years of age worldwide, causing up to 50% of childhood hospitalizations for diarrhea in industrialized countries, and an even higher proportion in developing countries. However, data on rotavirus transmission rates in the community are much more sparse, especially in developing countries. Community-based data will be vital in assessing the effectiveness of rotavirus vaccination as the vaccine becomes more widely employed. We used data and samples available from a study on water quality to explore the prevalence of rotavirus infection in rural communities outside the town of Pisco, Peru. The study was conducted in 2010, one year after rotavirus vaccination was introduced in Peru's national immunization program, with reported rotavirus vaccine coverage in Ica region at the time of 64%. A convenience sample of 192 houses was selected and stool samples taken from one child age ≤ 5 years old from each household. Stools were tested for rotavirus by real time RT-PCR according to CDC guidelines. Of the 192 children enrolled, 54 (28%) were rotavirus infected. The proportion of rotavirus-infected children did not differ significantly between children who did and did not report an episode of diarrhea in the preceding two weeks: 11/32 (33%) and 43/160 (27%), respectively. The median age of the rotavirus-positive children was 24.5 months (range 5-48 months) and 50% were male. Unfortunately, because the original aim of the study was not oriented toward rotavirus, no specific rotavirus vaccination history on each child was taken. The finding of frequent rotavirus infection in children who did not recently suffer diarrhea suggests that additional factors, such as infectious dose, underlying co-infections or morbidities, or genetic predisposition are involved in producing clinical disease due to rotavirus infection. The results also provide baseline data useful for future assessment of rotavirus vaccine effectiveness in Peru.

1382

NIAKHA VIRUS: A NOVEL MEMBER OF THE FAMILY RHABDOVIRIDAE ISOLATED FROM PHLEBOTOMINE SANDFLIES IN SENEGAL

Nikos Vasilakis¹, Steven Widen¹, Sandra V. Mayer¹, Robert Seymour¹, Thomas G. Wood¹, Vsevolod Popov¹, Hilda Guzman¹, Amelia P. Travassos da Rosa¹, Elodie Ghedin², Edward C. Holmes³, Peter J. Walker⁴, Robert B. Tesh¹

¹University of Texas Medical Branch Health, Galveston, TX, United States, ²University of Pittsburgh, Pittsburgh, PA, United States, ³The University of Sydney, Sydney, Australia, ⁴CSIRO, Geelong, Australia

Members of the family *Rhabdoviridae* have been assigned into eight genera but many remain unassigned. Rhabdoviruses have a diverse host range that includes terrestrial and marine animals, invertebrates and plants. Transmission requires arthropod vectors such as mosquitoes, midges, sandflies, ticks, aphids and leafhoppers, in which they replicate. Here we characterize Niakha virus (NIAV), a previously uncharacterized rhabdovirus isolated from phlebotomine sandflies in Senegal. Analysis of the 11,124 nt genome sequence indicates that it encodes the five common rhabdovirus proteins with alternative ORFs in the M, G and L genes. Phylogenetic analysis of the L protein indicate that NIAV's closest relative is Oak Vale rhabdovirus, although still so phylogenetically distinct that it may be not classified as a member of the eight recognized *Rhabdoviridae* genera. This observation highlights the vast, and yet not fully recognized diversity, of this family, some members of which could potentially jump species boundaries in the future.

1383

EASTERN EQUINE ENCEPHALITIS VIRUS: REEMERGENCE AND EXPANSION IN THE NORTHEASTERN UNITED STATES

Theodore G. Andreadis, Philip M. Armstrong, Goudarz Molaei
Center for Vector Biology and Zoonotic Diseases, The Connecticut Agricultural Experiment Station, New Haven, CT, United States

Eastern equine encephalitis (EEE) virus is the most deadly mosquito-borne pathogen in North America with an estimated human case fatality rate of 35 to 75%. EEE virus activity is most common in and around freshwater hardwood swamps in the Atlantic and Gulf Coast states and in the Great Lakes region, where the primary mosquito vector *Culiseta melanura* resides. Since the discovery of EEE virus in the 1930s, outbreaks in temperate regions have been sporadic, both temporally and spatially, highly focal, and largely unpredictable. However, over the last decade, we have witnessed a sustained resurgence and change in dynamics of EEE virus activity within long-standing foci in the northeastern U.S. and unprecedented northward expansion into new regions where the virus had been historically rare or previously unknown, including northern New England and eastern Canada. This has resulted in severe disease in humans (46 cases with 16 fatalities) and domestic animals (173 cases). The factors responsible for reemergence of EEE virus are largely unknown but are likely complex reflecting ongoing changes in the ecology and epidemiology of this virus. Long-term changes in land-use, including wetlands restoration and suburban development, and increases in human population density near critical habitats may be important components. Weather conditions associated with climate change are also likely to be contributing factors. These include mild winters, hot summers and extremes in both precipitation and drought that increase vector abundance and distribution, elongate the virus transmission season, and increase the intensity of virus transmission by increasing the frequency of blood feeding and rate of virus replication in mosquitoes. These and other underlying factors associated with the introduction, amplification, persistence, and range expansion of EEE virus in the region including: 1) vector mosquito abundance and distribution that drive viral amplification and spillover into human and equine populations, 2) species-specific mosquito-avian interactions that favor amplification, 3) virus titers in primary and secondary mosquito vectors, and 4) genetic variation in regional EEE virus strains that provide evidence for local overwintering, evolution and extinction of EEE virus strains, with periodic reintroduction from southern sources, will be examined.

1384

EMERGING PATHOGENS IN MULTIPLE BAT SPECIES IN MADRE DE DIOS, PERU: LEPTOSPIRA AND PARAMYXOVIRUSES

Karen Segovia¹, Bruno M. Ghersi², Maria E. Silva², Gabriela Salmon-Mulanovich², Enrique Canal², Hugo Razuri², Victor Pacheco³, Matthew R. Kasper², Joel M. Montgomery², Daniel G. Bausch²

¹San Marcos University School of Veterinary Medicine, San Borja, Peru, ²U.S. Naval Medical Research Unit - 6, Lima, Peru, ³Natural History Museum, Universidad Nacional Mayor de San Marcos, Lima, Peru

In recent years, bats have attracted considerable attention as hosts of emerging and other pathogens relevant to public health. We trapped bats and harvested their tissues for analysis near seven communities in the Madre de Dios Region in the southern Amazon basin of Peru as part of a study to explore the impact of anthropogenic habitat perturbation in the region (the building of the Peruvian interoceanic highway) on the distribution of reservoirs and pathogens. Bat kidneys were tested for *Leptospira* by PCR using primers that amplify 16S rRNA. Spleens were tested for paramyxovirus by nested PCR targeting the conserved motifs of the polymerase pol gene. A total of 432 bats from 24 different genera were captured, of which 32 (7%) were positive for *Leptospira*. All positive bats belonged to one of nine genera of the family *Phyllostomidae*, including the genera *Trachops* and *Lophostoma*. Twenty-six (81%) of the

Leptospira positive bats were adults, while age could not be determined in the remaining 6 (19%). Infected animals were identified in 6 of the 7 sites sampled. Sequencing of PCR products is underway to identify the specific species of *Leptospira* implicated. Paramyxovirus testing was performed on 263 bats, of which 3 (1%) were positive. All 3 positive bats were adults of the *Sturnira lilium* species collected in one location in Iberia District. Sequence analysis placed the paramyxoviruses in the Avulavirus or Rubulavirus genera. Avulaviruses are known to date only to infect birds, while rubulaviruses such as Tioman, Mapuera, and Menangle have been described in fruit- and insect-eating bats, making Rubulavirus the more likely genus implicated here. Of note, rubulaviruses have been associated with encephalitis and influenza-like illness in humans. This is the first report of *Leptospira* infection in *Trachops* and *Lophostoma* in Peru, as well as of paramyxovirus infection in any bat in Peru, expanding our understating of the host and geographic range of these potentially emerging pathogens. Testing for other pathogens, including coronaviruses, is underway.

1385

AGE-STRATIFIED SEROLOGICAL SURVEY OF SYLVATIC CHIKUNGUNYA VIRUS IN NONHUMAN PRIMATES IN SENEGAL

Benjamin M. Althouse¹, Mathilde Guerbois², Amadou A. Sall³, Mawlouth Diallo³, Diawo Diallo³, Ousmane Diop³, Brenda Benefit⁴, Evan Simons⁴, Douglas M. Watts⁵, Scott C. Weaver², Kathryn A. Hanley⁴, Derek A. Cummings⁶

¹Santa Fe Institute, Santa Fe, NM, United States, ²University of Texas Medical Branch, Galveston, TX, United States, ³Institut Pasteur, Dakar, Senegal, ⁴New Mexico State University, Las Cruces, NM, United States, ⁵University of Texas at El Paso, El Paso, TX, United States, ⁶Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States

Sylvatic chikungunya virus (CHIKV) has been isolated in Senegal over the past 50 years. Until recently, virus isolation was predominantly from mosquito collections, and the virus was only isolated from nonhuman primates (NHP) after opportunistic capture. Here we present an age-stratified serological survey of CHIKV in three NHP species in Senegal and calculate forces of CHIKV infection for each species. African green monkeys (*Chlorocebus sabaeus*), patas monkeys (*Erythrocebus patas*), and Guinea baboons (*Papio papio*) were collected in the dry season in each of three years (2010-2012) from in Kedougou, Senegal. Primates were trapped, sedated, and bled and sera were tested for IgM by ELISA and IgG by PRNT. Ages of primates were quantified using pattern of tooth eruption and wear determined from photographs and dental casts; weight and other anthropometric measurements were also taken. Force of CHIKV infection was calculated using catalytic models with bootstrap confidence intervals. Random effect logistic models were fit to find associations between age, month of collection, and species with seropositivity. A total of 219 African green monkeys, 78 patas, and 440 baboons were collected between 2010 and 2012. Across all years, 66%, 36%, and 73% were seropositive for CHIKV antibody by PRNT50, respectively. Forces of infection were high, ranging from 0.13 per year (95% Confidence Interval [CI]: 0.07, 0.21) for patas in 2012 to 1.15 per year (95% CI: 0.81, 3.83) for African green monkeys in 2010. Logistic models with random effects for troop indicated age as significantly positively associated with PRNT50 positivity (Odds ratio [OR]: 1.030 (95% CI: 1.023, 1.036)), and significantly less positivity in patas compared to African green monkeys (OR: 0.73, (95% CI: 0.60, 0.89)). To our knowledge this is the first study of CHIKV transmission dynamics in its sylvatic reservoir host. It reveals very high forces of infection of CHIKV for all NHP species tested, with rates of seropositivity approaching 100% as primate age increases. Our demonstration of a CHIKV reservoir carries important consequences for individuals living or working in proximity to primate populations in Senegal, where CHIKV has the potential to cause major morbidity.

HERPES SIMPLEX AS THE MOST COMMON CAUSE OF ENCEPHALITIS IN PERU

Nicanor Mori¹, Silvia Montano¹, Ada Romero¹, Mark P. Simons¹, Drake Hamilton Tilley¹, Joseph Zunt²

¹U.S. Naval Medical Research Unit - 6, Callao, Peru, ²University of Washington, Seattle, WA, United States

Herpes simplex encephalitis (HSE) causes significant morbidity and mortality within developing countries, where the ability to diagnosis and treat HSE is limited. Our aim was to describe the clinical and cerebrospinal fluid (CSF) characteristics of HSE in patients presenting with symptoms of encephalitis to a network of hospitals in Peru. This was a prospective study of patients aged 28 days or older presenting with symptoms of encephalitis at nine Peruvian hospitals in three different geographical regions (coast, mountains and jungle) between February 2009 and March 2012. We enrolled patients presenting with clinical symptoms of encephalitis and diagnosis of HSE was confirmed by detection of HSV DNA in CSF using PCR. In this study 223 patients met clinical criteria for encephalitis and were included in the final analysis. Mean age of the patients was 5.41 years for children and 41.8 years for adults. 66.7% of children and 47.6% of adults were male. The mean time from onset of symptoms to hospital presentation was 9 days (range: 1 - 31). Headache, fever, seizures, neck stiffness, dystaxia, and nausea were the most common clinical symptoms. Seizures were more frequent in children ($p=0.005$), while headaches and neck stiffness were more frequent in adults ($p=0.013$ and 0.048 , respectively). CSF was normal in 5.5% patients with abnormal glucose seen in 55.6%. Leukocyte counts, predominantly lymphocytes, were higher in adults than in children ($p=0.031$). HSV as determined by PCR was the etiology in 36 (16.1%) patients (21 adults, 15 children). The majority of HSE (88.9%) was due to HSV-1. HSV-2 was found in 2 patients from each age group. Co-infections with HIV were found in 5 (13.8%) adults and 3 patients also had *Cryptococcus neoformans* meningitis. HSV-1 was found to be the most common cause of encephalitis in Peru and emphasizes the need for improvements in diagnostic capabilities and acyclovir availability in developing countries.

GENETIC CHARACTERIZATION OF NOROVIRUSES AMONG PERUVIAN ARMY RECRUITS IN THE AMAZON BASIN

Sarah B. Ballard¹, C. Giannina Luna², Sonia Apaza³, Susan Espetia³, Mayuko Saito⁴, Maria E. Silva², Erik J. Reeves², Claudio Rocha², Karla J. Vilela², Drake H. Tilley², David L. Blazes⁵, Robert H. Gilman¹, Daniel G. Bausch⁶

¹Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, ²U.S. Naval Medical Research Unit - 6, Lima, Peru, ³Laboratorio de Investigacion y Desarrollo (LID), Universidad Peruana Cayetano Heredia, Lima, Peru, ⁴University of California San Diego School of Medicine, San Diego, CA, United States, ⁵Uniformed Services University of the Health Sciences, Bethesda, MD, United States, ⁶Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, United States

Norovirus is the number one cause of acute gastroenteritis worldwide, afflicting 21 million Americans and killing 200,000 children under five in the developing world each year. Understanding norovirus genetic variation may be important in the development of an effective vaccine. We assessed the various genotypes of norovirus circulating in a cohort of Peruvian military recruits under active surveillance for acute gastroenteritis between 2005-2011 in Iquitos, Peru. Stool specimens were collected from randomly selected participants, 200 with acute gastroenteritis and 200 healthy controls, and tested for norovirus genogroups GI and GII by real-time RT-PCR. Positive samples were genotyped by sequencing the C region of the capsid gene. Sequence fragments were aligned and compared to norovirus sequences available in the GenBank database. Norovirus was detected in 40/360 (11.1%) samples, 26/184 (14.1%) cases and 14/176 (8.0%) controls (the epidemiologic and clinical significance of these findings are

discussed in a companion abstract). Of the 25 noroviruses that could be genotyped (18 from cases and 7 from controls), 11 were GI and 14 were GII. The predominant GI genotype was GI.4 (7 persons), followed by one each of GI.1, GI.3, GI.5, and GI.7. The predominant GII genotype was GII.4 (6 persons), followed by GII.17 (2 persons) and one each of GII.5, GII.6, GII.14, GII.15, and GII.16. Of the four GII.4 positive cases that could be further differentiated by variant, all were GII.4 Den Haag (2006b). The sample size was too small for meaningful statistical analysis, but the GII.4 genotype was the most prevalent genotype identified in cases, and it was not identified in controls. Multiple norovirus variants circulated in both cases and controls in this study, without other obvious associations with pathogenicity. Further research is needed to explore the possible clinical significance of the numerous variants of norovirus and to guide vaccine development.

RODENT SPECIES AND THEIR CORRELATION WITH HUMAN SEROPOSITIVITY FOR ZONOTIC INFECTIONS IN GHANA

Shirley C. Nimo Paintsil¹, Elisabeth Fichet-Calvet², Emad Mohareb³, Maria Morales³, Joseph H. Bonney¹, Kwesi Obiri-Danso⁴, William K. Ampofo¹, Randal J. Schoepp⁵, Karl C. Kronmann⁶

¹Noguchi Memorial Institute for Medical Research, Accra, Ghana, ²Bernhard-Nocht Institute for Tropical Medicine, Hamburg, Germany, ³U.S. Naval Medical Research Unit - 3, Cairo, Egypt, ⁴Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, ⁵United States Army Medical Research Institute of Infectious Disease, Fort Detrick, MD, United States, ⁶Naval Medical Center, Portsmouth, VA, United States

Rodents serve as reservoirs and/or vectors for several human infections which account for high morbidity and mortality in Africa. The remarkable expansion of human population has brought them into increasing contact with these mammals, thereby disrupting their habitats and increasing opportunities for disease transmission. To investigate possible risk factors for exposure to some of these pathogens, 764 small mammals were collected from ten communities in Ghana together with 657 human sera from healthy adults living in the same communities. Rodents were captured by setting Sherman collapsible traps along marked lines in fields (outdoors) and houses (indoors) totaling 9,269 night traps for three consecutive nights. The small mammals caught constituted ten genera of which whole blood of two rodents (0.3%) *Mus (Nannomys) sp.* tested positive for arenaviruses and one kidney tissue from *Crocidura sp.* tested positive for *Leptospira* by conventional polymerase chain reaction (PCR). All rodent lung tissues were negative for Hantaviruses (Dobrava and Puumala serotypes). Using an in-house enzyme-immunoassay (ELISA), human serum showed evidence of arenavirus antibodies in 34 samples (5%). Antibodies to Puumala and Dobrava serotypes and Leptospirosis were also detected in 11%, 12% and 21% respectively with commercial kits. The occurrence of immunoglobulin G (IgG) antibodies to Dobrava and Puumala serotypes was more common in females (54%) than in males whereas the opposite was observed for Lassa virus (LASV) and Leptospirosis (52%). Human exposure to zoonotic infections was observed to cut across all age groups. Seropositivity was highest for anti-LASV at site 7 (29%), anti-hantavirus (Dobrava serotype) at site 10 (26%), and anti-*Leptospira* at site 8 (19%) located in the Eastern, Brong Ahafo, and Northern Regions respectively. Fifty six individuals had been exposed to more than one of the rodent-borne infections tested whereas 208 had been exposed to only one type of infection. The known reservoirs of the different pathogens that were tested in the human sera were captured in most of the study sites but human exposure could not be linked to their presence. This study suggests that 40% of residents in rural farming communities in Ghana have measurable antibodies to at least one rodent-borne disease (LASV, hantavirus, or Leptospirosis), which is not surprising given the ubiquitous presence of rodents in subsistence farming communities.

1389

PHYLODYNAMIC AND PHYLOGEOGRAPHIC PATTERNS OF EASTERN EQUINE ENCEPHALITIS VIRUS IN THE NEW WORLD

Albert J. Auguste¹, Naomi L. Forrester¹, David Wentworth², Rebecca A. Halpin², Philip M. Armstrong³, Thomas R. Unnasch⁴, Grace Leal¹, Scott C. Weaver¹

¹The University of Texas Medical Branch, Galveston, TX, United States, ²J. Craig Venter Institute, Rockville, MD, United States, ³Center for Vector Biology and Zoonotic Diseases, The Connecticut Agricultural Experiment Station, New Haven, CT, United States, ⁴University of South Florida, Tampa, FL, United States

Eastern equine encephalitis virus (EEEV) is a mosquito-borne alphavirus (Family: Togaviridae) of significant public and veterinary health importance throughout the Americas. EEEV exists as one antigenic complex but can be further classified into four lineages or subtypes based on serologic and phylogenetic analyses. Lineage I primarily consists of North American and Caribbean isolates, and lineages II-IV, which consist of Central and South America isolates, has been proposed to comprise a distinct species. Although EEEV is largely maintained locally (*in situ*), there is evidence of gene flow among and within countries. Lineage I strains utilize different hosts and vectors, and possess distinct neurovirulence characteristics, which are typically not observed among lineage II-IV isolates. This study aims to characterize EEEV genetic diversity, describe its molecular epidemiology, identify genetic determinants of EEEV emergence and virulence, and infer the phylodynamic and phylogeographic histories of EEEV. To this end, we performed a Bayesian analysis of EEEV complete genomes derived using next-generation sequencing. Results suggest differences in selective constraints and substitution rates among EEEV lineages. The data also suggests a Peruvian origin for EEEV, and that the virus spread to north eastern US prior to its expansion into other regions of the US. There is also evidence of significant gene flow within North America, suggesting that state level control measures would be inadequate for local elimination of the virus.

1390

EVASION OF HOST IMMUNE RESPONSE BY SEVERE FEVER WITH THROMBOCYTOPENIA SYNDROME VIRUS (SFTSV)

Félix W. Santiago¹, Lina Covalada¹, Maria Sanchez², Ana Diaz-Virreta¹, Xue-jie Yu¹, Adolfo Garcia-Sastre², Patricia Aguilar¹

¹University of Texas Medical Branch, Galveston, TX, United States, ²Mount Sinai School of Medicine, New York, NY, United States

Severe Fever with Thrombocytopenia Syndrome virus (SFTSV) is a novel member of the family Bunyaviridae, genus Phlebovirus. This virus was recently isolated from patients suffering from fever, thrombocytopenia, and hemorrhagic manifestations. SFTSV displays a mortality rate of 12% to 30% and direct human-to-human transmission has been reported. Due to the recent emergence of this pathogen, limited knowledge is available about the mechanism(s) involved in disease pathogenesis and the molecular mechanism(s) by which SFTSV suppresses innate immune responses. The type I interferon (IFN) responses are crucial for the development of antiviral immunity and therefore many pathogens have developed strategies that subvert these responses by blocking production of IFN or blocking IFN signaling. Indeed, type I IFN suppression has been described in other members of the genus. Likewise, we have observed that SFTSV infection inhibits type I IFN responses. SFTSV infection triggers the formation of cytoplasmic vesicles in which key components of the Type I IFN response, such as the cytosolic viral RNA receptor retinoic acid-inducible gene 1 (RIG-I) and its regulator the E3 ubiquitin ligase TRIM25, co-localize with viral proteins. Interestingly, the expression of the SFTSV nonstructural protein (NSs) is sufficient for the formation of vesicles and the co-localization of RIG-I and TRIM25 within them. SFTSV NSs not only co-localizes but also interacts with RIG-I and TRIM25. Furthermore, NSs inhibits the activation of the IFN- β promoter induced by virus infection or double-stranded RNA (dsRNA). Taken together, these data suggest that

NSs inhibits type I IFN-mediated host protective innate immunity against viral infection by "sequestering" RIG-I and TRIM25 into the NSs-induced vesicles. Our studies provide mechanistic insights into viral pathogenesis and define a novel immune evasion strategy for subversion of host innate immune responses. This information will provide new targets for preventive and therapeutic interventions against SFTSV and other related pathogenic RNA viruses.

1391

NOROVIRUS GASTROENTERITIS AT A SKILLED NURSING FACILITY

Abimbola Ogundimu¹, Mosunmola Lizzy Adeyemi²

¹University of Georgia, Alpharetta, GA, United States, ²Walden University, Minneapolis, MN, United States

In January 2011, symptoms of nausea, abdominal cramps, and diarrhea were reported in a 250-bed skilled nursing facility. Investigations revealed that these symptoms were present in some residents and employees as far back as two days prior, but they were thought to be isolated cases. Upon realization that the cases reported could be an outbreak, immediate actions were put in place to contain the outbreak and to prevent its spread throughout the facility. Immediate actions that were taken included: restrictions of all residents with symptoms in their rooms; staff education that include nursing, environmental, therapists and other caregivers; increasing hand hygiene; restricting visitors to the facility. Sick visitors were asked to stay away; signs were posted on all floors; increasing frequency of cleaning of "high touch" surfaces; using bleach to clean high touch surfaces; notification of the County Department of Health; continued surveillance for immediate identification of new cases and monitoring of old ones; hydration protocol for affected residents to prevent debilitating effects of the virus; sending of samples to the County Department of Health for definitive identification; restrictions of affected employees from care areas; education provided by County Public Health Nurse on the first week of this outbreak. Overall, the outbreak involved over 70 facility residents and the following departmental staff: Nursing, Nutritional Services, Office and Maintenance. On the average, the symptoms lasted about 48 hours for each individual. The norovirus gastroenteritis transmission subsided once the control recommendations (above) were implemented within three weeks after the index case occurred.

1392

INFLUENZA A VIRUS IN SWINE FARMS FROM GUATEMALA: EVIDENCE OF ZONOTIC TRANSMISSION FROM HUMANS

Ana S. Gonzalez Reiche¹, Ana L. Ramirez², María L. Müller³, Silvia M. Sosa³, David Orellana⁴, Daniel R. Perez¹

¹University of Maryland, College Park, MD, United States, ²Prince Leopold Institute of Tropical Medicine, Antwerpen, Belgium, ³Centro de Estudios en Salud, Universidad del Valle de Guatemala, Guatemala, Guatemala, ⁴Ministerio de Agricultura Ganadería y Alimentación, Guatemala, Guatemala

In 2009 the emergence of the pandemic H1N1 (pH1N1) strain of influenza A virus (IAV) of potential swine origin, highlighted the need of surveillance of influenza virus in pigs. In Central America, Guatemala is the country with the largest pork production; however the circulation of IAV in the swine population has not been investigated in detail. The main objectives of this study were to determine the presence of IAV in the swine population in Guatemala and identify the circulating subtypes including pH1N1. Two nation-wide multistage random surveys for IAV were conducted. Nasal swabs and blood samples were collected from swine farms and backyard operations during October 2010 and from June to August 2011. Samples were collected from 171 herds in 2010 (n=500) and 136 herds in 2011 (n=499). Herd prevalence for IAV detected by rRT-PCR was 33% for both years. From rRT-PCR positives 4 viruses were isolated, based on their full genome sequences, 3 were fully pH1N1 and one a fully H3N2 seasonal human-like strain. Additionally, antibodies

against IAV were detected by ELISA with herd prevalences of 17.5 and 5.1% for 2010 and 2011 respectively. The H1N1 and H3N2 subtypes from different genetic clusters (swine and human-like) were detected by hemmagglutination inhibition assay. These results suggest that different IAV circulate in the swine population of Guatemala and that human-animal contact may play a role for the introduction of novel strains into the swine population. Global and local methods were used to establish if spatial correlation exists in the IAV positive swine farms from each year. This study is the first in Guatemala analyzing AIV prevalence and its distribution in swine farms from the country.

1393

DEVELOPMENT OF SYSTEM FOR THE APPLICATION OF ANTIRABIC VACCINES IN UKRAINE

Serhiy Nychyk, Ivan Polupan, Alina Nikitova, Vitalii Nedosekov
IVM, Kiev, Ukraine

In order to develop and implement an effective program for rabies eradication in Ukraine, a collection of samples of pathological rabies-positive materials selected from 17 animal species and humans was founded in 2008 on the basis of regional veterinary laboratories of Ukraine. The collection is regularly updated and now includes 1,340 samples from all regions of Ukraine. We performed a Molecular-genetic study of the collection material using 156 pathological samples/probes from animals having rabies. We performed PCR tests and virus isolation with further sequencing. The study resulted in the determination of two genetic clusters and their clear geographical division in relation to river Dnieper. The genetic clusters' prevalence mapping for the last 5 years showed that cluster II isolates circulate in the regions with maximum rabies spread. Antirabic vaccine efficiency against the two cluster strains circulating in environment was evaluated on the stage of the work. Commercial vaccines obtained with the employment of the rabies virus vaccine strains SAD (Street-Alabama-Dufferin) and Wistar PM/WI were used for the evaluation. The study showed that all the vaccines were 30 % less effective for the cluster II rabies viruses than for the cluster I viruses. The performed research demonstrated genetic and antigen difference between environmental rabies viruses and the strains used for the vaccines production. The obtained results enable one to assume the low efficiency of antirabic vaccines against genetic cluster II rabies viruses as a potential reason for the high rabies prevalence in certain territories. The study results will be employed for the efficiency elevation of antirabic vaccine use in Ukraine on the basis of differential approach depending on vaccine immunogenic activity as well as geographical distribution of rabies virus strains. The performed work also points at the necessity of the development of new regional rabies virus vaccine strains in future.

1394

SEARCH OF ANTHROPURGIC REASONS FOR RABIES IN UKRAINE

Serhiy Nychyk, Ivan Polupan, Alina Nikitova, Mykola Ivanov, Vitalii Nedosekov
IVM, Kiev, Ukraine

Rabies is an acute viral encephalomyelitis that affects wild and domestic mammals. Worldwide, human death due to rabies makes approximately 55,000 cases annually. Red foxes (*Vulpes vulpes*) are natural reservoirs of rabies virus in Ukraine. We used the monitoring and mathematical methods for this research. Despite considerable financial expenses on oral immunization of foxes and parenteral immunization of dogs and cats, considerable results have not been achieved in the fight against rabies in Ukraine. It is observed a tendency to increasing of rabies cases in dogs and cats which are the main source of rabies in people. In epidemic section in Ukraine, cats pose the highest hazard, as they are the basic source of infection for humans - 41.3 %, while the rates for dogs and foxes are 24.1 % and 20.7 %, respectively. The rest cases appear from other undefined contacts. When analyzing data, the most important epidemic

route for rabies in Ukraine was defined. This could be depicted as follows - fox→cat→human. Over the last decade, nearly 10.5 thousand cases of rabies in cats were detected (average cats morbidity index in Europe is 13.2 %); herewith, 42 % of these cases were registered in Ukraine. The situation analysis based on the reports from veterinarians and veterinary service representatives in urban areas on quantity of fox bites in animals, showed that one of the reasons was the close location of fox inhabitation to urban areas, and their contacts with cats due to the common nutritive base - murine rodents. One more reason was a weak control over the execution of domestic animals' keeping rules, irresponsibility of their owners especially at suburban areas, and small percentage of cats vaccinated against rabies. For instance, 85 % of cats infected with rabies were kept by owners without timely provided vaccination against rabies. With intent to improve the situation with rabies in Ukraine, it is necessary to strengthen control over the rules for keeping domestic animals, increase responsibility of animals' owners for breaking the rules and ensure complete preventive vaccination of cats in endemic zones.

1395

APPLICATION OF GUANCID TO ENSURE BIOLOGICAL SAFETY DURING WORK WITH AUJESZKY'S DISEASE VIRUS

V. L. Kovalenko, A. V. Pozymniuk
IVM, Kiev, Ukraine

The purpose of a research was to detect the optimal exposure time for the elimination of Aujeszky's disease agent and define Guancid disinfectant safe concentration for animals and humans. The Guancid active component is polyhexamethyleneguanidine hydrochloride. Pig embryo kidney (PEK) and young pig testicle (YPT) cell culture were cultured on well bottoms of 96-well microplate in the form of a monolayer. Different media (RPMI 1640, DMEM, GLA), series 07 bovine blood serum, and phosphate-buffered saline (PBS) were employed for the cell culturing. The "Clone-B" vaccine strain of Aujeszky's disease agent (ADA) was used as the control virus. In order to define the disinfectant antiviral effect, different concentration Guancid solutions in PBS were employed: 0.01; 0.03; 0.05; 0.1; 0.5; 1.0; 2.0; and 3.0 %. After the solution application to the wells, ADA viral suspension with the activity of 107TCD50/cm³ (a dose of virus that causes cytopathic effect in PEK and YPT cells in 24-28 hours without treatment with disinfectant). The virus-disinfectant interaction was performed within 1-60 minutes. Subsequently, the well content was applied onto the surface of cell monolayer to absorb the virus, which was not inactivated by the disinfectant. After 20-minute contact, the microplate was triply washed with PBS and filled with a supporting medium with 2 % of bovine blood serum and incubated. 16 wells with cell cultures were left without disinfectant as the control. Microscopy of wells was conducted twice a day. Results were assessed prior the moment of degenerative changes in the control wells of the microplate. Virus cytopathic effect on the cell cultures was determined at Guancid solution concentrations of up to 0.05 % and at 60 minute exposure. The disinfectant displayed this effect at 2 and 3 % concentrations and at 20 minute exposure. No virus or disinfectant cytopathic effect was detected after 30-minute exposure using Guancid solution concentrations from 0.1 to 1.0 %. It could be concluded that Guancid concentrations from 0.1 to 1.0 % and 30-minutes exposure should be used to ensure biological safety during work with ADA. The disinfectant could be employed for preventive disinfection in veterinary in the presence of animals and humans.

1396

GEOGRAPHIC DISTRIBUTION OF ZONOTIC AND VECTOR-BORNE SELECT AGENTS IN KENYA: A SEROLOGIC SURVEY USING A SUBSET OF SERA SAMPLES COLLECTED THROUGH THE KENYA AIDS INDICATOR SURVEY (KAIS)

Leonard Nderitu¹, Lilian Waiboci², Rob Breiman³, Joel Montgomery², John Neatherlin², Stella Gikunju¹, Cyrus Wachira¹, Kabura Wamburu¹, Lilian Wakhule¹, Mamo Umuro⁴, Margret Mbuchi⁵, Alfred Muia⁶, Charles Magiri⁵, Raymond Nyoka², Brian Owino¹, Barry Fields²

¹Kenya Medical Research Institute/Centers for Disease Control and Prevention, Nairobi, Kenya, ²Centers for Disease Control and Prevention, Nairobi, Kenya, ³Emory Global Health Institute, Atlanta, GA, United States, ⁴National HIV Reference Laboratory, Nairobi, Kenya, ⁵Kenya Medical Research Institute/U.S. Army Medical Research Unit, Nairobi, Kenya, ⁶Kenya Medical Research Institute, Nairobi, Kenya

Zoonoses are diseases and infections which are transmitted naturally between vertebrate animals and man. Vector-borne diseases are infections that are transmitted by the bite of an infected arthropod. Of all human infectious diseases, 61% are zoonotic while 75% of human Emerging Infectious Diseases (EID) are zoonotic. Out of these zoonoses, 33% have a human to human transmission. The dynamics of population growth and lifestyle increases the human-animal-vector encounters and as such exposing humans to zoonotic infections. The incidence and prevalence information of select zoonotic and vector-borne diseases in Kenya is either limited or unknown even though they have been documented to cause outbreaks. An assessment of exposure levels to select zoonotic and vector-borne agents, will determine the most at risk populations to infections as well as outbreaks and therefore target public health interventions. An assessment of co-infection between the select agents will determine what role do co-infections play in prognosis. A total of 15,853 blood samples were collected and analyzed during the 2007 Kenya AIDS Indicator Survey (KAIS). During data collection, serum from participants that consented to storage of their specimens for future testing were separated into several cryovials for processing, including a "storage vial" which was stored in -70°C for future testing. A nationally representative subset of the samples (1091 specimens) was selected and tested for Anthrax, Brucella, Chikungunya, Dengue, Rift Valley Fever, *Rickettsia* and *Leishmania* by IgG Enzyme Linked Immunosorbent Assay (ELISA). Preliminary findings give an indication of geographical hotspots in some regions in Kenya. Of the 1091 serum samples tested, analysis was done by province, residence (rural/urban) and by wealth quintiles. A Dengue, RVF and Rickettsial analysis by province shows coast province to have the highest prevalence of antibodies against the 3 select agents followed by North Eastern. The least affected province is Rift Valley. In relation to residence, the rural dwellers were more affected than their urban counterparts. When analyzed by wealth quintiles, the lowest quintile was seen to have the highest prevalence, while the middle quintile had the lowest prevalence of antibodies against the select agents.

1397

CHARACTERIZATION OF NEUTRALIZING ANTIBODY RESPONSES FOLLOWING NATURAL PRIMARY INAPPARENT AND APPARENT DENGUE VIRUS INFECTIONS

Kizzmekia S. Corbett¹, Hasitha Tissera², Dharshan de Silva³, Aravinda M. de Silva¹

¹University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, ²Sri Lanka Ministry of Health, Colombo, Sri Lanka, ³Genetech Research Institute, Colombo, Sri Lanka

Dengue virus is the most significant arthropod-borne virus of humans. Primary dengue infection induces both neutralizing antibodies towards the infecting dengue serotype and cross-reactive non-neutralizing antibodies to other dengue serotypes. The theory of antibody dependent enhancement predicts that cross-reactive antibodies enhance secondary

dengue infections, thus resulting in severe disease. During a pediatric fever surveillance cohort study in Colombo, Sri Lanka, sera samples were collected at regular yearly intervals and during and soon after dengue fever episodes. Here, we report on studies that were conducted, using prospectively-collected samples from that cohort, to compare the quality and quantity of dengue-specific antibodies in children with inapparent and apparent infection. Both dengue-specific IgG levels and neutralizing antibody responses induced by primary inapparent and apparent infections were similar. We followed primary dengue cases for up to two years to hone in on the specifics of neutralizing antibody decay over time. Primary infections induced broad-neutralizing antibodies that gradually became monospecific to the infecting serotype over time. The presence of dengue-specific IgM was correlated with broad neutralization. In children exposed to secondary infections, we observed that children with pre-existing monospecific neutralizing antibody responses were more likely to develop fever upon a secondary dengue infection than children with broadly neutralizing antibody pre-existing responses. In all, our findings provide unique insight about development and timing of the neutralizing antibody response following natural primary dengue infection and how such a neutralizing antibody response may influence fever outcome upon secondary infection.

1398

MUTATIONS THAT MODULATE DENGUE VIRUS "BREATHING" HAVE A SIGNIFICANT IMPACT ON SENSITIVITY TO ANTIBODY-MEDIATED NEUTRALIZATION

Kim A. Dowd¹, Swati Mukherjee¹, Richard Kuhn², Michael S. Diamond³, Daved Fremont³, Ted Pierson¹

¹National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, United States, ²Purdue University, West Lafayette, IN, United States, ³Washington University School of Medicine, St. Louis, MO, United States

Flaviviruses explore multiple conformations via the structural dynamics of viral envelope proteins in the virion. This adds complexity to the antigenic surface of the virion, as virus "breathing" varies the epitopes available for antibody (Ab) binding. A recent study explored the structural basis for genotypic differences in the neutralization potency of a DENV-1 specific mAb (Austin et al., PLOS Pathogens, 2012). mAb E111 binds a poorly exposed domain III epitope on the envelope (E) protein and neutralizes strain 16007 >4000x better than the related strain WP. This result could not be explained by differences in the affinity of E111 for each of these strains. Instead, the ensemble of structures sampled by these two viruses was hypothesized to differ. To further investigate differences in the "breathing" of these two DENV strains, reciprocal WP and 16007 mutants were generated that individually expressed all 13 amino acid differences in the E protein. Using DENV reporter virus particles, these variants were tested for their stability in solution (intrinsic decay) and neutralization sensitivity to a panel of mAbs. Strikingly, differences in the behavior of WP and 16007 mapped to E protein residue 204, located well outside the E111 epitope in domain III. The intrinsic decay rate of WP was ~2x greater than 16007; this difference could be reversed in a reciprocal fashion in the presence of this 204 substitution. The large difference in neutralization sensitivity of these two strains to mAb E111, and a related domain III mAb E98, was significantly modulated by the same residue. Our results demonstrate that neutralization susceptibility can be altered in an epitope-independent manner by subtle mutations (K→R) that alter the overall structural ensemble. That different conformational ensembles of flaviviruses can affect the landscape available for Ab binding, as well as virus stability, has important implications for vaccine development and antibody mapping studies.

THE ANTIGENIC DETERMINANTS OF SEROTYPE SPECIFICITY FOLLOWING NATURAL DENV-3 AND DENV-4 INFECTION

William B. Messer¹, Ruklanthi de Alwis², Scott Royal³, Boyd Yount³, Jeremy P. Huynh¹, Ralph S. Baric³, Aravinda M. de Silva²

¹Oregon Health and Sciences University, Portland, OR, United States,

²University of North Carolina Chapel Hill School of Medicine, Chapel Hill, NC, United States, ³University of North Carolina Chapel Hill School of Public Health, Chapel Hill, NC, United States

Dengue virus (DENV) occurs as four serotypes, DENV-1 through DENV-4, and is the most important arthropod-borne viral disease of humans worldwide. Infection with one serotype confers protective immunity to that serotype but not the remaining serotypes—rather, subsequent infection with a heterotypic serotype is associated with an increased risk of severe disease. Despite its worldwide importance, the antigenic determinants on each DENV serotype targeted by protective human antibodies have not been well defined. This knowledge gap has significantly hampering vaccine development. We have recently described the hinge region between domain I and II of the dengue E protein as a target of some human monoclonal antibodies that neutralize DENVs. In the current study we have transplanted the EDI-II hinge between serotypes to determine if this region is the main target of serotype specific neutralizing Abs that develop following primary DENV infections. Transplantation of EDI-II hinge from DENV-4 into DENV-3 leads to a near complete loss of DENV-3/4ic neutralization by monotypic DENV-3 human immune sera and the near complete gain of sensitivity to neutralization by monotypic DENV-4 sera. These results have important implications for vaccine design strategies as well as basic studies of dengue virus biology, immunity, and immunopathogenesis.

STUDY OF EPITOPES, AVIDITY AND NEUTRALIZING POTENCY OF FLAVIVIRUS GROUP-REACTIVE HUMAN MONOCLONAL ANTIBODIES DERIVED FROM SECONDARY DENGUE VIRUS INFECTION

Wei-Kung Wang¹, Wen-Yang Tsai¹, Chih-Yun Lai¹, Yi-Chieh Wu¹, Hong-En Lin², Carolyn Edwards³, Amonrat Jumnainsong³, Srisakul Kliks⁴, Scott Halstead⁴, Juthathip Mongkolsapaya³, Gavin R Screaton³

¹Tropical Medicine, JABSOM, University of Hawaii at Manoa, Honolulu, HI, United States, ²Microbiology, National Taiwan University, Taipei, Taiwan, ³Imperial College of London, London, United Kingdom, ⁴Pediatric Dengue Vaccine Initiative, International Vaccine Institute, Seoul, Republic of Korea

The envelope (E) protein of dengue virus (DENV) is the major target of neutralizing antibodies (Abs) and vaccine development. Previous studies of polyclonal human sera after DENV infection revealed that a significant proportion of anti-E Abs were cross-reactive to all four DENV serotypes and to one or more other flaviviruses, known as group-reactive (GR). Studies of mouse anti-E monoclonal antibodies (mAbs) reported that GR mAbs were weakly or non-neutralizing compared with type-specific mAbs; GR response was thus regarded as useless for vaccine strategy. The epitopes of human GR mAbs remain largely unknown. In this study, we investigated the epitopes, binding avidity and neutralization potency of 32 human GR anti-E mAbs. The epitopes involved either fusion loop (FL) residues in E protein domain II only or both FL and bc loop residues in domain II; these residues were highly conserved by different flaviviruses and absolutely conserved by the four DENV serotypes. The neutralization potency and binding avidity of GR mAbs derived from secondary DENV infection were stronger than those derived from primary infection. Analysis of repertoire of anti-E mAbs derived from patients with primary DENV infection revealed that the majority were GR, low avidity and weakly neutralizing, whereas those from secondary DENV infection were primarily GR, high avidity and potent neutralizing. Our observations suggest the weakly neutralizing GR anti-E Abs generated from primary DENV infection

become potent neutralizing against four serotypes after secondary infection. The finding that dengue immune status of host affects the quality of cross-reactive Abs generated may have implications for different strategies of DENV vaccine.

QUANTIFICATION OF TYPE I INTERFERON SIGNALING IN CELLS INFECTED WITH FIELD STRAINS OF DENGUE VIRUS

Freddy A. Medina¹, Giselle Torres², Gilberto A. Santiago¹, Juan F. Medina¹, Luis M. Santiago¹, Amanda J. Chase³, Jorge L. Muñoz-Jordán¹

¹Centers for Disease Control and Prevention, San Juan, PR, United States,

²University of Puerto Rico Medical Science Campus, San Juan, PR, United States, ³Mercer University School of Medicine, Macon, GA, United States

Dengue virus (DENV), as well as other flaviviruses, circumvent the anti-viral response induced by type I interferon (IFN- α/β) by blocking key players of the JAK/STAT pathway. The relevance of the IFN- α/β system with regards to pathogenic outcomes has been highlighted in gene expression studies of DENV-infected patients showing suppression of interferon stimulated genes in patients with severe dengue. Some studies have suggested that not all DENV or flaviviruses are capable of blocking IFN- α/β signaling. Furthermore, studies of JEV and WNV have suggested a correlation between disease severity and the ability to inhibit IFN- α/β signaling. We have compared the relative inhibition of IFN- α/β signaling by DENVs using a new method that combines flow cytometry and a four-parameter logistic regression model. Clinical isolates from all DENV serotypes and isolates encompassing the five DENV-2 genotypes (Asian, American, Asian/American, Cosmopolitan, and Sylvatic) were selected and analyzed for their IFN- α/β blocking ability. We used the prototypical DENV-2 strain 16681 as a reference strain to normalize the quantitation of IFN- α/β inhibition by DENVs. The inhibitory effect of other DENVs on STAT1 phosphorylation was compared to 16681 using calculations obtained from a four-parameter logistic (4PL) model. All of the DENV serotypes and DENV-2 genotypes analyzed were able to inhibit STAT1 phosphorylation. Modest differences were observed in DENV-3 and DENV-2 sylvatic viruses. We were unable to correlate the relative strength of DENVs to inhibit IFN- α/β signaling with their plaque size or replication capacity. The quantitative method we developed allows us to determine the relative IFN- α/β blocking ability among DENV strains. Contrary to previously published studies of DENV and other flaviviruses, the majority of DENV strains analyzed in this study show a highly conserved ability to inhibit IFN- α/β signaling with a similar magnitude to that observed with DENV strain 16681. Therefore, the probability of correlating pathogenic outcomes in dengue to IFN- α/β signaling inhibition appears to be slim.

EXPLORING THE MECHANISM AND SIGNIFICANCE OF CELL TYPE-DEPENDENT NEUTRALIZATION OF FLAVIVIRUSES

Swati Mukherjee¹, Kimberly A. Dowd¹, Carolyn J. Manhart¹, Anna P. Durbin², Stephen S. Whitehead¹, Ted C. Pierson¹

¹National Institutes of Health, Bethesda, MD, United States, ²Johns Hopkins School of Public Health, Baltimore, MD, United States

Flaviviruses assemble at and bud into the endoplasmic reticulum as immature virions containing two glycoproteins, envelope (E) and premembrane protein (prM), arranged in heterotrimeric spikes. Virion maturation involves the cleavage of prM by the cellular serine protease furin. While this cleavage is required for infectivity, it may be inefficient, leading to release of partially mature virions with uncleaved prM. The maturation state of the virion has been shown previously to impact neutralization via changes in epitope accessibility. In this study, we explored the possibility that virion maturation may contribute to cell type-dependent neutralization patterns observed with many monoclonal antibodies (mAbs). We characterized the neutralization activity of a panel of mAbs using multiple target cell types. Several mAbs were significantly

less potent when assayed on Vero or BHK cells, as compared to Raji cells expressing DC-SIGNR; antibody dose-response curves revealed a resistant fraction reminiscent of our studies with antibodies sensitive to the maturation state of the virion. Our data revealed that the apparent inability of antibodies to neutralize WNV when assayed on Vero or BHK was due to the differential impact of uncleaved prM on the specific infectivity of the virus on a given cell type rather than the capacity of the antibody to block infection per se. prM+ viruses are under-represented in neutralization studies using the Vero/BHK cellular substrates typically used in neutralization assays. Analysis of sera from recipients of two live-attenuated dengue virus vaccines revealed a strong correlation between the impact of virion maturation and cell-type dependent patterns of neutralization. The neutralizing potential of cross-reactive responses may be significantly under-represented by the "gold-standard" plaque reduction neutralization test that employs Vero cells.

1403

COHERENT IMMUNE REPERTOIRE SIGNATURES IN HUMAN DENGUE

Poornima Parameswaran¹, Yi Liu², Krishna Roskin³, Katherine Jackson³, Vaishali P. Dixit³, Ji-Yeun Lee³, Karen Artiles³, Simona Zompi¹, Maria José Vargas⁴, Birgitte B. Simen⁵, Bozena Hanczaruk⁵, Kim R. McGowan⁵, Muhammad A. Tariq⁶, Nader Pourmand⁶, Daphne Koller², Angel Balmaseda⁴, Scott Boyd³, Andrew Z. Fire⁷, Eva Harris¹

¹Division of Infectious Diseases and Vaccinology, School of Public Health, University of California Berkeley, Berkeley, CA, United States, ²Department of Computer Science, Stanford University, Stanford, CA, United States, ³Department of Pathology, Stanford University, Stanford, CA, United States, ⁴Laboratorio Nacional de Virología, Centro Nacional de Diagnóstico y Referencia, Ministerio de Salud, Managua, Nicaragua, ⁵454 Life Sciences, A Roche Company, Branford, CT, United States, ⁶Baskin School of Engineering, University of California Santa Cruz, Santa Cruz, CA, United States, ⁷Departments of Pathology and Genetics, Stanford University, Stanford, CA, United States

Dengue, caused by dengue virus (DENV), is the most prevalent mosquito-transmitted viral disease of humans. The lack of early prognostics, licensed vaccines and therapeutics contributes to tremendous disease burden in endemic areas. In this study, we employed high-throughput sequencing methodologies to capture B cell-associated rearranged immunoglobulin variable heavy chain (V_H) signatures in peripheral blood mononuclear cells (PBMCs) from individuals enrolled in two ongoing dengue studies in Nicaragua. PBMCs were sampled from 44 dengue patients during acute symptomatic dengue (2-5 days post-symptom onset, "dpo"), convalescence (7-47 dpo) and post-convalescence (~180 dpo); 8 individuals with non-dengue febrile illness during the acute phase of disease; and 8 healthy individuals with no prior history of dengue. In addition, an independent set of 16 individuals with symptomatic dengue was sampled during the acute phase of illness. Analysis of V_H sequences from total PBMCs revealed clonal B cell expansion in acute dengue that was greater in secondary than primary DENV infections and not observed in convalescent and post-convalescent samples. We also identified convergent DENV-specific antibody sequences within the hypervariable complementarity determining region 3 (CDR3) that define prevalent and specific indicators of DENV infection; these CDR3 signatures were present in acute symptomatic dengue, significantly reduced after clearance of DENV infection, and not observed in non-dengue samples. The convergent CDR3 regions originated from distinct V_H sequences that were encoded by multiple V genes and were derived from B cell populations that had undergone affinity maturation and accumulated somatic mutations in response to DENV infection. These CDR3 regions and their associated CDR2 and CDR1 sequences have similar amino acid physiochemical profiles that uniquely position them as immune repertoire indicators in human dengue. This is the first report of convergent antibody sequences elicited in response to dengue, and, notably, in response to any natural infection in humans. Similar approaches using samples from individuals

infected with different DENV serotypes (and genotypes) could facilitate identification of serotype-specific (and possibly genotype-specific) immune repertoire signatures. Future efforts will also be directed at assessing the antigen specificities of these convergent antibodies.

1404

INCIDENCE OF ACUTE GASTROENTERITIS-ASSOCIATED MORTALITY AMONG CHILDREN UNDER FIVE YEARS OF AGE IN BANGLADESH, 2010-12

Makhdum Ahmed¹, Abdullah Al-Mamun¹, Jaynal Abedin¹, Stephen P. Luby², Syed M. Satter¹, Repon C. Paul¹, Marc-Alain Widdowson², Katharine Sturm-Ramirez², James D. Heffelfinger², Mahmudur Rahman³, Emily S. Gurley¹

¹International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh, ²Centers for Disease Control and Prevention, Atlanta, GA, United States, ³Institute of Epidemiology, Disease Control and Research, Dhaka, Bangladesh

In Bangladesh, diarrhea-related deaths are common among children <5 years. The objective of this study was to estimate acute gastroenteritis-related mortality among children <5 years. We randomly selected 20 unions, the smallest administrative unit in Bangladesh, from the catchment areas of 11 tertiary hospitals from July to December 2012. We used social-networking to identify children aged <5 years who died in the previous two years in the targeted communities. Family members who had taken care of children during the illness preceding death were interviewed about disease symptoms and the types of healthcare sought during the illness. We classified a death as being associated with acute diarrhea if caregivers reported sudden onset of loose, watery stool ≥ 3 times a day within 14 days of death; we classified a death as related to acute abdomen if caregivers reported sudden onset of abdominal pain without diarrhea within a week of death. We calculated the incidence of acute gastroenteritis-related mortality by dividing the number of deaths associated with acute diarrhea or acute abdomen by the age-specific census population of the study unions. We identified 312 deaths among children <5 years; 41 (13%) following acute diarrhea and 12 (4%) following acute abdomen. Of the 53 children who died with acute gastroenteritis, 43 (81%) were aged <2 years and 26 (49%) were male. The annual incidence of acute gastroenteritis-related deaths per 10,000 children <5 years was 3.7 (95% CI 2.7-4.8), and 3.0 (95% CI 2.2-4.0) for acute diarrhea-related death. Twenty eight of 53 (53%) children died in November to February during 2010-12. Thirty five of 53 (66%) received treatment from certified physicians or hospitals within four days of illness onset and 28 of 53 (53%) died at home. The burden of acute gastroenteritis-associated mortality was highest among children <2 years. The months in which deaths peaked correspond with seasonal peaks of rotavirus circulation in Bangladesh, suggesting that this pathogen may contribute importantly to child deaths. The planned introduction of rotavirus vaccine could substantially reduce childhood mortality in Bangladesh. Many children did not seek care from trained providers, and more than half died even after seeking qualified care, suggesting that quality care may not have been accessible to these children. Improving access to prompt management of childhood gastroenteritis could save lives.

HOME-BASED DIARRHEA CASE MANAGEMENT AND THE RISK OF ALL-CAUSE MORTALITY IN THE KENYA GLOBAL ENTERICS MULTICENTER STUDY (GEMS) SITE

Arthi Vasantharopan¹, Ciara O'Reilly², Richard Omoro³, Karen Kotloff⁴, Tamer Farag⁴, Myron M. Levine⁴, Kayla Laserson⁵, Robert F. Breiman⁵, Eric D. Mintz², Pavani K. Ram¹

¹University at Buffalo, Buffalo, NY, United States, ²Division of Foodborne, Waterborne and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, United States, ³Kenya Medical Research Institute/Centers for Disease Control and Prevention, Kisumu, Kenya, ⁴University of Maryland, Baltimore, MD, United States, ⁵Kenya Medical Research Institute/Centers for Disease Control and Prevention, Kisumu, Kenya and Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA, United States

Modeling studies suggest that oral rehydration solution (ORS) may prevent most diarrheal deaths if universal coverage is achieved. Globally, only one-third of children with diarrhea receive ORS, the form of rehydration for diarrhea recommended in the Integrated Management of Childhood Illness guidelines. Achieving 100% ORS use will require substantial financial input and behavior change efforts. To strengthen the case for promoting appropriate diarrhea case management at home, we evaluated whether home-based diarrhea treatment methods reduced the risk of death in children with moderate to severe diarrhea (MSD). At the GEMS Kenya field site, we enrolled children <59 months old with MSD. Health workers asked caretakers about diarrhea case management at home during the time preceding enrollment. Survival status was determined at follow-up 50-90 days after enrollment. We calculated risk ratios (RR) and 95% confidence intervals (CI) to describe associations between the following and death: oral rehydration therapy (ORT) consisting of ORS, recommended home-fluids, or increasing fluids; ORS with or without other fluids; and continued feeding (CF). During 2008-11, 1,476 MSD cases were enrolled; 1,419 (96%) were followed up. At home, 65% of children received one or more forms of ORT, 14% received ORS with or without other fluids, and 19% were offered continued feeding. Between enrollment and follow-up, 52 deaths occurred (case fatality rate 3.7%), 35% of which reportedly occurred < 7 days after enrollment. Children with MSD who later died were more likely to present with slow return skin pinch and restless/irritable mental status at enrollment, and to require intravenous hydration and hospitalization during treatment than those who survived ($P < .0001$ for all). Home diarrhea case management strategies were not significantly associated with mortality (ORT: RR=0.92 [CI 0.53-1.61], ORS: RR=1.65 [CI 0.87-3.16], and CF: RR=0.45 [CI 0.18-1.12]). In Kenya, children with MSD experienced a high case fatality rate, but few were offered ORS and continued feeding at home. Clinical signs suggesting dehydration were associated with mortality. A small number of deaths and low rates of ORS use and CF reduced our ability to identify protective effects of ORT, ORS, and CF among children with moderate-to-severe diarrhea.

ASSOCIATION BETWEEN ENTEROPATHOGENS, DIARRHEA AND GROWTH IN THE MAL-ED COHORT

James Platts-Mills¹, Benjamin J. McCormick², Monica McGrath², Mark Miller², Jean Gratz¹, Margaret Kosek³, Alexandre Havt⁴, Samie Amidou⁵, Anita Zaidi⁶, Gagandeep Kang⁷, Rashidul Haque⁸, Ladaporn Bodhidatta⁹, Eric Houpt¹, On behalf of the MAL-ED Network

¹University of Virginia, Charlottesville, VA, United States, ²Fogarty International Center, National Institutes of Health, Bethesda, MD, United States, ³Asociación Benéfica PRISMA, Iquitos, Peru, ⁴Federal University of Ceara, Fortaleza, Brazil, ⁵University of Venda, Thohoyandou, South Africa, ⁶Aga Khan University, Karachi, Pakistan, ⁷Christian Medical College, Vellore, Tamil Nadu, India, ⁸International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh, ⁹Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand

The pathogenicity of enteric infections is typically defined by their association with diarrhea. However, enteric infection has also been linked to stunted growth and decreased cognitive development. It is not clear whether the pathogens most clearly associated with diarrhea are equally important for these long-term outcomes. We performed an interim analysis of the association between enteropathogens and both diarrhea and poor linear growth in the multisite MAL-ED cohort study. To estimate pathogen-specific burdens of diarrhea, we calculated the population attributable fraction (AF) of diarrhea for each pathogen that had a statistically significant association with diarrhea. We constructed models using nine-month linear growth intervals to estimate the association between enteropathogen infections and linear growth. We then developed pathogen-specific models to determine the relative effect of symptomatic and asymptomatic infections on growth. In the first year of life, the top three causes of community diarrhea were rotavirus (aggregated AF 4%), astrovirus (3%), and enterotoxigenic *E. coli* (ETEC; 3%). *Campylobacter sp.* had the highest burden of diarrhea at three sites (Brazil, Peru, and South Africa) but was not significantly associated with diarrhea at the other sites. In the second year of life, rotavirus (aggregated AF 7%), *Shigella* (4%), astrovirus (4%), ETEC (4%), and *Cryptosporidium* (4%) had the highest burdens of diarrhea. The pathogens associated with poor linear growth were *Campylobacter* (aggregated average height loss of 0.06cm per nine-month interval), *Giardia* (0.03cm) and *Cryptosporidium* (0.01cm). In the pathogen-specific models, most of this growth burden was mediated by asymptomatic infection. Our preliminary findings suggest that the pathogens associated with growth shortfalls are different than those associated with diarrhea. These findings have substantial implications for prioritizing interventions designed to address both the mortality and morbidity associated with these infections in children in low-income countries.

ENTEROAGGREGATIVE *ESCHERICHIA COLI* ASSOCIATED WITH MALNOURISHED CHILDREN IN THE MAL-ED CASE-CONTROL STUDY IN FORTALEZA, CEARÁ, BRAZIL

Aldo A. Lima¹, Ila F. Lima¹, Nadia Boisen², Álvaro M. Leite¹, Alessandra F. Moura¹, Noélia L. Lima¹, Alberto M. Soares¹, José Q. Filho¹, Alexandre Havt¹, Francisco S. Junior¹, Reinaldo B. Oriá¹, James P. Nataro³, Richard L. Guerrant³

¹Federal University of Ceara, Fortaleza, Brazil, ²University of Maryland, Bethesda, MD, United States, ³University of Virginia, Charlottesville, VA, United States

Enterotoxigenic *Escherichia coli* (EAEC) is an important enteric pathogen worldwide, but the disease pathophysiology remains obscure. This case-control study aimed to describe the prevalence of EAEC and potential associations of its VRGs with risk or protection to malnourished (moderate to severely underweight children, determined by weight for age Z score (WAZ) <-2) and nourished (age, sex, and neighborhood matched controls

presenting WAZ >-1) Brazilian children. Stool samples were collected from 259 children, 132 cases and 127 controls, aged 6 to 24 months that visited the specialized clinic in infant malnutrition (IPREDE) in Fortaleza, Ceará, Brazil, from Aug/2010 to Jul/2012. The specimens were cultured for *E. coli*, which was screened using microbiological standard methods. *E. coli* strains were tested for EAEC by polymerase chain reaction (PCR). For each sample, a pool of up to 5 single colonies from original MacConkey plates were examined for the EAEC diagnostic genes (*aaiC* and *aatA*). Some positive strains were individually analyzed by multiplex PCR to identify 18 VRGs. EAEC (*aaiC*+ and *aatA*+) was significantly found in 34% (45/132) of cases and 21% (27/127) of controls ($P=0.021$). Among these positive strains, 62 EAEC isolates obtained from 19 children, 15 cases and 4 controls, were further investigated by multiplex PCR. All EAEC strains carried at least three of the 18 assayed VRGs. The transcriptional activator *aggR* was the most common (98.54%), followed by genes encoding the mucinase *pic* (95.2%) and the hypothetical cryptic protein *orf3* (93.5%). Heat-stable toxin EAST-1 and hypothetical hemolysin *orf61* genes were strongly associated with cases among the EAEC strains tested ($P=0.0003$, $OR=31.47$, 95%CI=1.77-557.8; and $P=0.006$, $OR=8.25$, 95%CI=1.89-35.98, respectively). In addition, genes encoding the toxin *sat* and protease *sepA* were significantly more detected in controls compared to malnourished children ($P=0.0001$, $OR=0.03$, 95%CI=0.002-0.48; and $P=0.023$, $OR=0.21$, 95%CI=0.06-0.73, respectively). These data confirm a high prevalence of EAEC strains in the studied population and the higher association with malnourished children. Our plans include completing the EAEC VRGs characterization in all isolates to determine the importance of a combination of these VRGs potential associated with its pathogenesis.

1408

SOCIO-ECONOMIC, MOTHER CHARACTERISTICS AND CHILD CARE RISK FACTORS ASSOCIATED WITH MALNOURISHED CHILDREN IN THE MAL-ED CASE-CONTROL STUDY IN FORTALEZA, CEARÁ, BRAZIL

Aldo A. Lima¹, Álvaro M. Leite¹, Alessandra F. Moura¹, Noélia L. Lima¹, Reinaldo B. Oriá¹, Alberto M. Soares¹, José Q. Filho¹, Alexandre Havt¹, Ila F. Lima¹, Josiane S. Quetz¹, Francisco S. Junior¹, Cláudia B. Abreu¹, Francisco S. Mota¹, Richard L. Guerrant²

¹Federal University of Ceara, Fortaleza, Brazil, ²University of Virginia, Charlottesville, VA, United States

In Fortaleza, located in the poorest region of Brazil, there is a large socioeconomic and cultural disparity that maybe influences the prevalence of malnutrition and its serious consequences for growth and cognitive development in children. The aim of this study was to evaluate the risk factors related to the child and the mother, as well as environmental and socioeconomic factors associated with the development of malnutrition in children in this population. A total of 345 children aged 6 to 24 months that visited the specialized clinic in infant malnutrition (IPREDE) in Fortaleza, Ceará, Brazil, from Aug/2010 to Mar/2013 were enrolled in this study. Cases (N=165) were defined as children with weight-for-age (WAZ) z-score less than -2 and control (N = 180) healthy children with WAZ more than -1. The children were monitored for anthropometric parameters and morbidity at baseline and at quarterly visits for a year. Specific questionnaires were developed and used for data acquisition on risk factors. The children in both groups did not differ by gender and age. The controls had a better birth weight, length and head circumference compared to cases ($p<0.01$). In relation to breastfeeding the controls showed a significant increase in the percentage in the first 24 hours ($p<0.01$) as well use more colostrum ($OR=0.24$; $CI_{95\%}:0.11-0.55$; $p<0.01$) than the cases and maintained breastfeeding longer than cases ($OR=0.60$; $CI_{95\%}:0.38-0.94$; $p=0.01$). The pattern of introducing liquids in the first three months of life was significantly more favorable for the controls ($p<0.01$). Regarding to mother's educational level there was a significant increase in school years in controls compared with cases ($OR=0.38$; $CI_{95\%}:0.17-0.87$; $p=0.01$). The controls had a higher percentage in the use of piped water in the house compared to the cases ($OR=2.16$;

$CI_{95\%}:0.93-5.12$; $p=0.05$). A multivariate hierarchical analysis is needed to determine the influence of variables on the combined outcomes and it is in progress now. In conclusion, the data showed that the weight, length and head circumference at birth, delayed initiation of breastfeeding after birth, deficit in the colostrum intake, low maternal education and poor quality of sanitation are risk factors associated with infant malnutrition in this population.

1409

CATCH-UP GROWTH OCCURS WHEN DIARRHEA BURDEN IS LOW IN EARLY CHILDHOOD

Stephanie A. Richard¹, Robert E. Black¹, Robert H. Gilman¹, Richard L. Guerrant², Gagandeep Kang³, Claudio F. Lanata⁴, Kåre Mølbaek⁵, Zeba A. Rasmussen⁶, R. Bradley Sack¹, Palle Valentiner-Branth⁵, William Checkley⁷

¹Johns Hopkins University, Bloomberg School of Public Health, Baltimore, MD, United States, ²University of Virginia School of Medicine, Charlottesville, VA, United States, ³Christian Medical College, Vellore, India, ⁴Instituto de Investigacion Nutricional, Lima, Peru, ⁵Statens Serum Institut, Copenhagen, Denmark, ⁶Fogarty International Center, National Institutes of Health, Bethesda, MD, United States, ⁷Johns Hopkins University, School of Medicine, Baltimore, MD, United States

Diarrhea and linear growth faltering continue to burden low-income countries and are among the most important causes of illness and death during early childhood. Diarrhea is thought to adversely affect linear growth, but catch-up growth can occur if no further insults are experienced. We sought to characterize catch-up growth in relation to frequency of diarrhea in a multi-site setting. Using longitudinal anthropometry and diarrheal surveillance from seven cohort studies in four countries, we examined the relationship between diarrhea prevalence and length velocity in 3- to 6-month periods using linear mixed effect models. The velocity during each period was calculated from the models as a function of age using linear splines. We incorporated the longitudinal prevalence of diarrhea in both current and previous periods into the model. Diarrhea during the current period was associated with slower growth in all age groups except for 0-3 months. Faster (catch-up) growth in length was observed in children with no diarrhea in the current period following a period in which diarrhea was experienced (6.01-12 month age group: 0.03 mm per month for each percent diarrhea prevalence in the previous period (95% CI: 0.009, 0.05); 12.01-18: 0.03 (0.02, 0.05); 18.01-24: 0.03 (0.002, 0.06)). Similar results were observed when weight was the outcome variable. When diarrhea episodes are followed by diarrhea-free periods in the first two years of life, catch-up growth is observed. Catch-up growth can allow children to regain their original trajectories given no or reduced diarrhea burden in subsequent periods. Diarrhea burdens are high throughout the first two years of life in developing countries, therefore reducing the likelihood of catch-up growth. Extending diarrhea-free periods may result in improved catch-up growth and a lower level of stunting. Diarrhea-free periods can be attained through expanded implementation of well-documented interventions (e.g., rotavirus vaccine, breastfeeding, zinc supplementation, and improved water and sanitation).

1410

PREVALENCE OF NON-*JEJUNI/COLI* *CAMPYLOBACTER* SPECIES DETECTED BY ENZYME IMMUNOASSAY AND CULTURE IN THE MAL-ED COHORT STUDY

James A. Platts-Mills¹, Jie Liu¹, Jean Gratz¹, Esto Mduma², Caroline Amour³, Ndealilia Swai³, Mami Taniuchi¹, Sharmin Begum⁴, Julian Flores⁵, Ben Parker⁶, James Fox⁷, Margaret Kosek⁸, Rashidul Haque⁴, Eric Houpt¹

¹University of Virginia, Charlottesville, VA, United States, ²Haydom Lutheran Hospital, Haydom, United Republic of Tanzania, ³Kilimanjaro Clinical Research Institute, Moshi, United Republic of Tanzania, ⁴International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh, ⁵Asociación Benéfica PRISMA, Iquitos, Peru, ⁶Johns Hopkins University, Baltimore, MD, United States, ⁷Massachusetts Institute of Technology, Boston, MA, United States, ⁸Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States

Methods for detection of *Campylobacter* species include culture, enzyme immunoassay (EIA) and PCR. A large discrepancy in detection by culture and EIA was noted in diarrheal and asymptomatic surveillance samples tested by both methods in the MAL-ED cohort study: 4.0% vs. 32.4% respectively in Bangladesh and 4.4% vs. 20.0% in Peru. To better understand this discrepancy, we randomly selected a total of 436 samples comprised of diarrheal cases and matched controls from children 0-12 months of age from Tanzania, Bangladesh, and Peru. According to the study protocol, all samples had previously been tested by the ProSpect *Campylobacter* ELISA as well as by selective culture in Bangladesh and Peru. Additionally, we tested all samples with a duplex PCR assay for *C. jejuni/coli* (cadF) and *C. species* (16S rRNA). 71.6% of EIA positive samples were positive for cadF and 100% were positive for *Campylobacter* 16S rRNA, suggesting that EIA positivity was associated with non-*jejunii/coli* *Campylobacter* species. Next, we used 16S rRNA-based primers to sequence 60 EIA-positive samples for which the 16S rRNA quantification cycle (Cq) was at least 10 cycles lower than the cadF Cq. A sequence was successfully obtained for 50 of the samples, which most closely matched known 16S rRNA from *C. hyointestinalis* subsp. *lawsonni* (48%), *C. troglodytis* (30%), *C. jejuni/coli* (16%), and *C. upsaliensis* (6%). Of these, 7 were positive by selective culture, of which 4 were *C. hyointestinalis* subs *lawsonni*, 2 were *C. troglodytis*, and one *C. jejuni/coli*. *C. hyointestinalis* was the most frequently matched species in Tanzania and Peru, and *C. troglodytis* was the most frequently matched species in Bangladesh. Eight 16S positive/cadF positive samples with a less than 10x discrepancy in 16S and cadF burden were also sequenced, which most closely matched *C. jejuni/coli* (87.5%) and *C. troglodytis* (12.5%). PCR reveals a high burden of non-*jejunii/coli* *Campylobacter* in infants in these settings, some of which is detected by enzyme immunoassay and culture. *C. hyointestinalis* subsp. *lawsonni* is of porcine origin while the reservoir for *C. troglodytis* is not clearly established. We would estimate that approximately 10-20% of EIA positive samples from this age group from these sites represent non-*jejunii/coli* *Campylobacter* species, the clinical importance of which is not known.

1411

COMPARISON BETWEEN POST-TREATMENT REACTIONS AFTER DEC OR IVERMECTIN IN SUBJECTS WITH LOIASIS

Jesica A. Herrick¹, Fanny Legrand¹, Raceline Gounoue², Jean Bopda³, Steve Bickmen Tchana³, Bienvenu Etogo Ondigui², Céline Montavon⁴, Thomas Nutman¹, Joseph Kamgno³, Amy D. Klion¹

¹Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, United States, ²Université de Yaounde, Yaounde, Cameroon, ³Center for Research on Filariasis and Other Tropical Diseases, Yaounde, Cameroon, ⁴Institut de recherche pour le développement; Faculté des Sciences, Montpellier, France
Diethylcarbamazine (DEC) treatment of loiasis is complicated by severe adverse reactions that are related to the number of circulating

microfilariae (MF). The cause of these reactions is unknown, but they are accompanied by a dramatic increase in IL-5 and absolute eosinophil count (AEC). Clinically similar reactions have been seen following mass drug administration of ivermectin (IVM) for control of onchocerciasis in *Loa*-endemic areas and impact the success of filariasis control programs. To directly compare post-treatment responses following DEC and IVM, we randomized 12 subjects with loiasis and <2000 MF/mL blood to receive single-dose DEC (8 mg/kg) or IVM (200 mcg/kg). Adverse events (AE), AEC and MF counts were assessed at baseline, 4, 8 and 24 hours, and 2, 3, 5, 7, 9, and 14 days. Serum was stored at all time points for additional analyses. Baseline characteristics were comparable between the two treatment groups. All study subjects experienced mild to moderately severe AEs in the first 3 days post-treatment that were similar in character and frequency in the two groups. In the DEC group, AEC decreased from baseline levels within 24 hours in all subjects (from GM 3269/ μ L to 1139/ μ L, $p=.03$). This was followed by a slow rise in AEC, peaking between days 2 and 9. In contrast, all subjects in the IVM group experienced a transient increase in AEC during the first 24 hours (GM 1761/ μ L to 4081/ μ L, $p=.03$) with return to baseline levels by day 2. MF counts decreased dramatically in all subjects by 24 hours post-therapy (GM 1074 to 0 MF/ml in the DEC group, $p=.03$, and 355 to 32 MF/ml in the IVM group, $p=.03$), although the proportion of subjects with measurable MF counts was greater in the IVM group at all time points ($p<0.05$ at days 1, 3 and 5). These data suggest that DEC and IVM have differing effects on microfilarial clearance and post-treatment eosinophilia. This may have important implications with respect to interventions to prevent post-treatment reactions.

1412

COMPARISON OF THE IMMUNE RESPONSE PROFILE IN SUBJECTS WITH *LOA LOA* INFECTION AFTER A SINGLE-DOSE OF DIETHYLCARBAMAZINE OR IVERMECTIN

Fanny Legrand¹, Jesica Herrick¹, Celine Montavon², Michelle Makiya¹, Raceline Gounoue³, Jean Bopda⁴, Steve Bickmen Tchana⁴, Simon Metenou¹, Godwin Nchinda⁵, Joseph Kamgno⁴, Amy D. Klion¹

¹Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, United States, ²Institut de recherche pour le développement, Montpellier, France, ³Faculté des Sciences, Université de Yaounde, Yaounde, Cameroon, ⁴Center for Research on Filariasis and Other Tropical Diseases, Yaounde, Cameroon, ⁵Laboratory of Immunology, The Chantal Biya International Reference Centre for Research on HIV/AIDS Prevention and Management (CIRCB), Yaounde, Cameroon

Post-treatment reactions can occur in patients with loiasis following administration of either diethylcarbamazine (DEC) or ivermectin (IVM) and are believed to be due to host immune responses to dying microfilariae (MF). Although a dramatic increase in IL-5 driven eosinophilia has been described post-DEC treatment of loiasis, little is known about immune responses post-IVM. To compare the immune responses following administration of these two drugs, 12 subjects with loiasis and ≤ 2000 MF/mL blood were randomized to receive a single oral dose of IVM (200 mcg/kg) or DEC (8 mg/kg). Complete blood counts were performed and serum collected for mediator analysis at baseline, 4, 8 and 24 hours, 2, 3, 7 and 9 days post-treatment. Whole blood flow cytometry was performed at baseline, 1 and 3 days post-treatment to assess T cell and eosinophil activation. In the DEC group, the absolute eosinophil count (AEC) decreased from baseline levels at 8 hours in all subjects; whereas, all subjects in the IVM group experienced a transient increase in AEC during the same time frame. The absolute neutrophil count increased at 8 hours post-treatment in all subjects, regardless of treatment group. Eosinophil surface expression of CD69 increased in 11/12 subjects on day 1 post-treatment. In contrast, eosinophil surface expression of CD25 increased by a median of 96% in the subjects who received DEC, but decreased by a median of 60% in the subjects who received IVM. Similar discordance was seen with respect to CD25 expression on CD4+ T cells, with a 19% increase in the DEC group and a 46% decrease in the IVM group. Serum

IL-5 levels rose significantly post-treatment in all subjects, but peaked earlier in subjects who received DEC compared to those who received IVM (8 hours vs. 2 days). Serum IL-10 and MCP-1 levels increased post-treatment only in the DEC group. The observed differences in immunologic profiles of subjects with loiasis who received DEC as compared to those who received IVM suggest that these two drugs may exert their microfilaricidal effects through different mechanisms.

1413

IS ONCHOCERCA VOLVULUS SUBOPTIMAL RESPONSE TO IVERMECTIN A RESULT OF SELECTION UNDER IVERMECTIN PRESSURE? INSIGHTS FROM A STUDY COMPARING IVERMECTIN AND MOXIDECTIN IN AREAS WITHOUT PRIOR IVERMECTIN MASS TREATMENT

Didier Bakajika¹, Eric Kanza², Hayford Howard³, Nicholas Opoku⁴, Jean-Pierre L. Tchatchu¹, Kambale Kataliko², Mawolo Kwapor³, Simon K. Attah⁴, Michel Vaillant⁵, Piero L. Olliaro⁶, Christine M. Halleux⁶, Annette C. Kuesel⁶

¹Centre de Recherche en Maladies Tropicales de l'Ituri, C.R.M.T-ITURI, Hôpital Général de Référence de Rethy, Rethy, Democratic Republic of the Congo, ²Centre de Recherche Clinique de Butembo (CRCB), Université Catholique du Graben (UCG), Butembo, Democratic Republic of the Congo, ³The Liberian Institute for Biomedical Research, Clinical Research Center Bolahun, Bolahun, Liberia, ⁴Onchocerciasis Chemotherapy Research Centre, Hohoe, Ghana, ⁵CCMS CRP-SANTE, Luxembourg, Luxembourg, ⁶UNICEF/UNDP/World Bank/World Health Organization Special Programme for Research and Training in Tropical Diseases, Geneva, Switzerland

Control and progress towards elimination of onchocerciasis in Africa currently rely on annual ivermectin (IVM) mass treatment (CDTI). Concern has been raised about longterm CDTI selecting for parasites with 'suboptimal response', i.e. higher skin microfilaria (mf) levels than considered 'adequate response', threatening control objectives. We analysed data from a study in Ghana, Liberia and DRC in areas without CDTI for indication of 'suboptimal' response. IVM and moxidectin (moxi) had been given to 494 and 978, respectively, males and females ≥ 12 years with ≥ 10 mf/mg skin. For the 97.2% of IVM treated and the 96.6% of moxi treated with 12 months follow up, baseline levels were 41.1 ± 31 and 39.1 ± 30.9 , respectively (mean \pm SD mf/mg). Ivermectin treated: 1, 6, and 12 months post dose, mf levels were $>17\%$ of baseline in 10.2%, 14.1% and 46%, and $>40\%$ of baseline in 4.6%, 3.5% and 18.3% of subjects. Maximum levels were 150%, 159% and 375% of baseline, respectively. The % of IVM treated with undetectable levels was 42.7%, 11.3% and 5.2% at 1, 6 and 12 months. Moxidectin treated: 1, 6, and 12 months post-dose, mf levels were $>17\%$ of baseline in 0%, 0% and 4.8% and $>40\%$ of baseline in 0%, 0%, and 1.1% of subjects. Maximum levels were 8.1%, 8.5% and 58.5 % of baseline, respectively. The % of moxi treated with undetectable levels was 83.2%, 91.6% and 46.5% at 1, 6 and 12 months. The data did not indicate site or pre-dose level dependency. While the higher efficacy of moxi relative to IVM ($p < 0.0001$ for all endpoints tested) shows that IVM efficacy is not optimal, comparison of the data of IVM treated with criteria and analyses in the literature shows that significant percentages of 'suboptimal responders' to ivermectin are present in populations which have not been under IVM selection pressure. This suggests that the natural variability of response to IVM is larger than commonly assumed, which needs to be taken into account during the design and analysis of studies on the origin, frequency and potential impact of 'suboptimal' IVM responders.

1414

THE DEVELOPMENT OF THE LYMPHATIC FILARIASIS QUALITY OF LIFE TOOL BANGLADESH (LF-QOL BANGLADESH)

Lynne Zeldenryk¹, Marion Gray², Susan Gordon¹, Richard Speare¹, Wayne Melrose¹

¹James Cook University, Douglas, QLD, Australia, ²Southern Cross University, Sunshine Coast, QLD, Australia

Lymphatic Filariasis (LF) is the world's leading cause of physical disability. Despite this, little is known about LF-disability across the stages of disease progression/manifestation, gender, age and socio-economic groups. A lack of quality data on LF-disability impact makes it difficult to develop evidence based interventions targeted to key areas of need and disease stages. A review of tools currently used in the field found that they demonstrably fail to measure the majority of known impacts of LF-disability and are culturally and linguistically inappropriate for LF-endemic populations. A Lymphatic Filariasis Quality of Life Tool was developed through a multi-staged mixed methods research process including a review of known impacts of LF-disability, in-country focus groups, cross-cultural testing and refinement and reliability studies. The final tool, the LF-QOL Bangladesh, is a 72 item, four point response format tool which measures LF-disability experience across four domains: daily activity and participation, body functions, environmental factors (community supports and barriers) and psychological impacts. In-depth in-country cognitive interviewing refined and confirmed the cultural and linguistic validity of the tool. Reliability studies found the overall internal consistency (0.917) and Corrected Item-Total correlation scores (0.91-0.926) to be excellent. The results have implications for disability measurement broadly across neglected tropical diseases (NTDs) and for the development of disability measures for intervention planning and outcome measurement.

1415

CAPACITY STRENGTHENING FOR LYMPHATIC FILARIASIS MORBIDLY MANAGEMENT: EXPERIENCE FROM PANGANI HYDROCECTOMY CAMP

Mwelecele N. Malecela¹, Upendo J. Mwingira¹, Mabula Mchembe², Serigne M. Gueye³, Sunny Mante⁴, Wilfred Lazarus¹, Bernard Kilembe¹, Mbutolwe E. Mwakitalu¹, William J. Kisoka¹, Prince Mutalemwa¹, Yusuf Makange⁵, Rehema Majjid⁶, Charles Mackenzie⁷, Sidney Yongolo²

¹National Institute for Medical Research, Dar-es-salaam, United Republic of Tanzania, ²Muhimbili University of Health and Allied Sciences, Dar-es-salaam, United Republic of Tanzania, ³Cheik Anta Diop University, Dakar, Senegal, ⁴Military Hospital, Accra, Ghana, ⁵Pangani District Hospital, Pangani, United Republic of Tanzania, ⁶Tanga Regional Hospital, Tanga, United Republic of Tanzania, ⁷Michigan State University, East Lansing, MI, United States

The Pangani hydrocelectomy Camp was the first ever organised by the National Lymphatic Filariasis Programme in Tanzania in consultation with Department of surgery Muhimbili University of Health and Allied Sciences (MUHAS) and West African hydrocectomy programme. The Funding for this Camp was through The President Kikwete LF Fund. Village Health Workers (VHW) registered over 400 Patients during MDA, which was followed up by screening by the surgeons at Pangani District hospital and final confirmation from specialist surgeons from MUHAS and PAUSA. As well as the standard clinical examination patients were also examined for presence of microfilaria and Circulating Filarial Antigen (CFA). The camp was organised such that specialist surgeons from tertiary hospitals trained District surgeons who then worked together to carry out the surgeries. A manual from the West African hydrocelectomy Programme was reviewed and adapted for use during this camp. The focus was in the use of the Excision technique, which required the excision of the tunica vaginalis to ensure no recurrence. A total of 202 patients with an age range was between 9 and 86 years, were operated on in the 10 days. Out of the 200 patients 101(50.0%) had bilateral 20(10.0%)had hydroceles with hernia

and 5(2.5%) had hydrocele with testicular complications like atrophy, tumour and necrosis. Hydrocele fluid was collected for biochemical analysis and tissue sections of the Tunica *vaginalis* were preserved in formalin for histopathology. The Surgeons trained village health workers who looked after the patients post surgery in the village. A special algorithm on wound care management and danger signs was provided to all VHW and findings recorded in daily diaries, which were reviewed after 7 days. The experience indicated that large-scale camps are useful especially when they involve local personnel at district level. It also showed that Village Health workers could support postoperative care and hence the involvement of Village Health Workers in morbidity management is crucial. The camp was also a great advocacy activity inspiring more men to register for hydrocelectomies.

1416

COMPLIANCE TO LYMPHEDEMA MANAGEMENT TECHNIQUES AND ITS IMPACT ON THE RATE OF ADENOLYMPHANGITIS (ADLA) EPISODES IN KHURDA DISTRICT, ORISSA STATE, INDIA

Katherine E. Mues¹, Michael Deming², Aishya Prakash³, Jonathan Rout³, LeAnne Fox²

¹Emory University/Centers for Disease Control and Prevention, Atlanta, GA, United States, ²Centers for Disease Control and Prevention, Atlanta, GA, United States, ³Church's Auxiliary for Social Action, Bhubaneswar, India

Lymphedema management programs have been shown to decrease episodes of ADLA, but the impact of compliance with specific lymphedema management techniques has not been explored in detail. Our objectives were to determine the rate of ADLA episodes over time for patients enrolled in a community-based lymphedema management program and determine predictors of compliance to the program. A community-based lymphedema management program was implemented in Orissa State, India from 2007-2010 by the Indian non-governmental organization, Church's Auxiliary for Social Action, in consultation with the Centers for Disease Control and Prevention. Patients (n=374) were followed over 24 months. The 30-day rate of ADLA episodes decreased from 0.34 episodes per person at baseline to 0.23 episodes per person at 24 months (P=0.0043). From baseline until 24 months after the program began, the average of compliance with each separate lymphedema management technique (limb washing with soap, anti-fungal cream use, elevation of the limb, limb exercise, and use of footwear outdoors) increased from 19.3% (2.9%-41.8%) to 65.4% (34.2%-92.2%) (p<0.0001). Ordinal logistic regression models found increasing age (OR=1.02 [1.01, 1.03]), paid work (OR=1.71 [1.21, 2.41]), and use of a mosquito net (OR=1.45 [1.08, 1.95]) to be significantly associated with compliance to limb washing with soap. Increasing lymphedema stage (OR=1.16 [1.02, 1.30]), increasing age (OR=1.05 [1.04, 1.07]) and increasing number of ADLA episodes in the last 6 months (OR=1.15 [1.06, 1.25]) were associated with compliance to wearing footwear outside the home. This study demonstrates improvement in ADLA episodes within a community-based lymphedema program. In addition, it illustrates characteristics of persons who complied with lymphedema management techniques and can assist programs in targeting those who may be less compliant in lymphedema management programs.

1417

REPURPOSED LABORATORY EQUIPMENT PROVIDE A FIELD-FRIENDLY, POINT-OF-CARE METHOD FOR QUANTIFYING LOA LOA MICROFILARAEMIA IN ADVANCE OF "TEST AND (NOT) TREAT" STRATEGY PREVENTION OF POST-TREATMENT SERIOUS ADVERSE EVENTS

Sasisekhar Bennuru¹, Sebastien D. Pion², Joseph Kamgno³, Samuel Wanji⁴, Thomas B. Nutman¹

¹National Institutes of Health, Bethesda, MD, United States, ²Filariasis and Other Tropical Diseases Research Center, Yaounde, Cameroon and UMI 233, Institut de Recherche pour le Développement (IRD), Montpellier, France, ³Filariasis and Other Tropical Diseases Research Center, Yaoundé, Cameroon and Faculty of Medicine and Biomedical Sciences, University of Yaoundé, Yaoundé, Cameroon, ⁴Research Foundation in Tropical Diseases and the Environment and Department of Microbiology and Parasitology, University of Buea, Buea, Cameroon

Administration of ivermectin as part of mass drug administration (MDA) campaigns for onchocerciasis and/or lymphatic filariasis in areas co-endemic for *Loa loa* has resulted in severe post-treatment adverse events (SAEs) including encephalopathy and death. This has led to the suspension of MDA in some of these co-endemic areas of Central Africa. One simple, potential solution aimed at preventing *Loa*-associated post-treatment SAEs is to identify and exclude individuals at risk (high levels of microfilaraemia) from the MDA in a program termed "Test and (Not) Treat" (TNT). We describe the adaptation and optimization of an existing technology for a rapid, point-of-care method for quantifying microfilariae in the blood of infected individuals. By repurposing a handheld microfluidics-based cell counter (Scepter™), we demonstrate that microfilariae can be identified and quantified using minimal volume of whole blood (20µl) after lysis with 10% saponin. A highly significant correlation (r=0.9182, p<0.0001) was observed between counts obtained by microscopy and those obtained using the Scepter™ study using 20µl of blood with microfilariae of *Brugia malayi*, *Dirofilaria immitis* or *L. loa*. Preliminary proof of concept studies in Cameroon with 20µl of *L. loa* infected human blood (n=30) and experimentally infected baboons (n=4) with a wide range of microfilaria levels demonstrated that the counts obtained by calibrated thick blood smears and those by Scepter™ were highly correlated (r=0.8504, p<0.0001), though at very low levels of microfilaria, there was a loss of sensitivity with the Scepter™. Moreover, the time from blood draw to microfilarial count for the Scepter™ was between 1-2 minutes whereas for the calibrated thick smear the time ranged between 4 hours and 2 weeks. The data suggest that we have a sensitive, rapid, point-of-care and quantitative test to identify individuals with levels of *L. loa* microfilariae that put them at risk for SAEs. In addition, it requires minimal blood volumes, is highly portable, independent of ambient temperature and humidity and provides ease of data storage and accessibility.

1418

GLOBAL RISK MAPS OF THE LEISHMANIASES

David M. Pigott¹, Yves Balard², Patrick Bastien², Samir Bhatt¹, John S. Brownstein³, Kirsten Duda¹, Dylan B. George⁴, Monica F. Myers¹, Francine Pratloug², Simon I. Hay¹

¹University of Oxford, Oxford, United Kingdom, ²Centre National de Référence des Leishmania, Montpellier, France, ³Harvard Medical School, Boston, MA, United States, ⁴Fogarty International Center, Bethesda, MD, United States

The *Leishmaniases* are a collection of complex infections caused by *Leishmania spp.*, ranging from localised cutaneous lesions to forms with visceral complications. Annual incidence is estimated to be around 1.5 million new cases of cutaneous leishmaniasis, and 0.5 million cases of visceral leishmaniasis. The interplay between humans, the Phlebotomine sandfly vectors and reservoir hosts complicates epidemiological understanding as well as control efforts; research has therefore tended to concentrate on solving clinical and epidemiological aspects of the

disease at small spatial scales. This, combined with the comparatively little funding and research attention the leishmaniasis garner, has resulted in no attempt to provide a global evidence-based risk map of these diseases. For each sub-national province, an assessment of cutaneous and visceral leishmaniasis was performed incorporating data from the WHO Expert Committee and the Global Infectious Diseases and Epidemiology Network as well as peer-reviewed disease occurrences and reported annual caseloads. These data were used to quantitatively assess certainty of the diseases' presence or absence on a continuous scale. A global database of close to 20,000 geo-positioned data points was collected from peer-reviewed literature using Web of Knowledge and PubMed searches and lab confirmed case data. Using a predictive Boosted Regression Trees modelling approach, separate continuous global risk maps for Cutaneous and Visceral Leishmaniasis were produced. We predict Leishmaniasis risk throughout Central and Southern America, as well as from the Mediterranean Basin to Western China, with other foci in Central and Southern Africa. Climatic and environmental variables were identified as important in defining this distribution. It is hoped that such a map will help inform not only future epidemiological studies but also public health policy directed towards these diseases, allowing improved targeting of specific control efforts with humans, vectors and reservoirs, as well as identify suitable areas for surveillance both active and passive.

1419

GLOBALLY FIRST TIME SYSTEMATICALLY CASE-BASED INTRODUCTION OF LLIN (LONG LASTING INSECTICIDE TREATED NET) AND ITS IMPACT IN KALA-AZAR (VISCERAL LEISHMANIASIS) ELIMINATION IN HYPER ENDEMIC SUB-DISTRICTS OF BANGLADESH

Tanveer A. Choudhury

Medical Officer, Directorate General of Health Services, Ministry of Health and Family Welfare, Bangladesh, Dhaka, Bangladesh

Bangladesh along with Nepal and India is committed to Eliminate Kala-azar (Visceral Leishmaniasis) by 2015. Effective Integrated Vector Management (IVM) is one of the main strategies for Kala azar elimination and LLIN (Long Lasting Insecticide treated Net) is one of the tools for this IVM for preventing human- vector contact. The objective of systemically case based LLINs distribution is to implement the Integrated Vector Management strategy for Elimination of Visceral Leishmaniasis in Hyper Endemic sub-districts of Bangladesh and thus pave the way for elimination status by 2015 and to examine the effectiveness of LLIN tool in reducing the human- vector (Sand fly) contact, and improving awareness building in community for helping in identification of new KA /PKDL (Post Kala-azar Dermal Leishmaniasis) cases through Campaign distribution approach. Total 9494 patient both kala-azar and PKDL, registered since 2008 in 8 hyper endemic sub district of Bangladesh had received the nets. Village-unit approaches were followed. Baseline data was collected and selection of sub-district was done on endemicity criteria and cases were identified from 2008 -- August 2012. A LLIN distribution strategy and Micro plan were developed and also for BCC material (pre and post distribution). Active case search and selection of patient through field visit was done and advocacy meetings were arranged at Sub-district level to create mass awareness on LLINs. Village wise campaigns were arranged for distribution of LLINs among new and old cases. --one LLIN for each patient and extra one for his/her family members. Proper monitoring, evaluation, follow-up program was done by the field managers. Globally practiced for first time, as a tool for Integrated Vector Management (IVM) for Visceral Leishmaniasis Elimination Program, case based LLIN distribution was successfully implemented and can be practiced in other countries. To reduce the transmission of Kala azar from reservoir to Vector, LLIN distribution can play a vital role for PKDL patients. Also lessons were learned that LLIN distribution among KA/KDL cases, with prior campaign for community participation can act as Catch-up strategy for new case identification.

1420

MULTI-SCALE MIGRATION PATTERNS OF *TRITATOMA INFESTANS* IN AN URBAN ENVIRONMENT AND IMPLICATIONS FOR LONG TERM PREVENTION OF CHAGAS DISEASE

Corentin M. Barbu¹, Karthik Sethuraman¹, Jennifer M. Manne², Javier E. Quintanilla Calderón³, Malwina Niemierko¹, Víctor Quispe-Machaca⁴, Michael Z. Levy¹

¹University of Pennsylvania, Philadelphia, PA, United States, ²Harvard School of Public Health, Boston, MA, United States, ³Asociacion Benefica PRISMA, Lima, Peru, ⁴Universidad Peruana Cayetano Heredia, Lima, Peru

Arequipa, with close to one million inhabitants, is Peru's second largest city. It is currently undertaking a campaign to control *Triatoma infestans*, the main vector of Chagas disease. *T. infestans* mobility has long been linked to human movement, suggesting that separate vector populations in large, interconnected urban centers such as Arequipa may behave as a large connected population. Treated households could potentially be recolonized by vectors from households that did not participate in the control campaign or by neighborhoods still awaiting treatment. Here, we develop a new spatial model-based methodology to estimate *T. infestans* migration patterns at the city-block, neighborhood, and city level. We apply this method to spatio-temporal infestation data collected during vector control activities. We estimate that an existing infested household will generate a secondary infestation in a completely susceptible population on average every 1.12 years [0.9-1.3]. We find that the rate of dispersal to neighboring city blocks is on the same order of magnitude as longer-distance dispersal and that both of these are much less common than dispersal within a city block. These estimates are compatible with previously observed auto-correlation patterns of infestation showing a strong barrier effect of streets and with genetic diversity patterns observed using microsatellite markers. The relative importance of migration to distant households suggests that propagation of infestation outside a city-block is largely due to passive transport and probably linked to human movements and is much less determined by distance than by active insect dispersal. In the context of low participation rates in the control campaign (60-85%) along with a high infestation prevalence prior to control (10-30%), we discuss the impact of migration on vector surveillance requirements over time and more generally how long-term vector control planning can be based on epidemiological data routinely collected during control efforts.

1421

SCREENING OF ANTI-INFECTIVES AGAINST *PLASMODIUM* AND KINETOPLASTIDS: A SERVICE FOR THE RESEARCH COMMUNITY

Jessey L. Erath, Grasiella Andriani, Ana Rodriguez

New York University School of Medicine, New York, NY, United States

The Anti-Infectives Screening Core, a non-profit entity created to facilitate early drug development for neglected diseases, takes advantage of the specialized facilities and expertise at NYU Parasitology for testing candidate molecules for parasitic diseases *in vitro* and *in vivo*. Currently, the core tests anti-infectives for four parasitic neglected diseases: Malaria, Chagas Disease, Human African Trypanosomiasis, and Leishmaniasis. Compounds are provided by users and shipped to the core for testing without revealing structures or any IP involvement. We have set up *in vitro* assays that determine the potency of compounds (EC50) for specific parasites: *Trypanosoma cruzi* (intra-host cell amastigotes), *Trypanosoma brucei brucei* (bloodstream forms), *Leishmania amazonensis* (promastigotes, axenic amastigotes or intra-macrophage amastigotes), *L. donovani* (promastigotes), *L. major* (promastigotes), and *Plasmodium falciparum* asexual stages, in addition to quantification of the cytotoxicity (TC50). Each assay contains negative and positive controls and each determination is performed in duplicate. *In vivo* assays take advantage of transgenic parasites that express luciferase, which allows rapid automated

quantification of infection. Groups of five mice are infected with any of the parasites of study: *T. cruzi*, *T. brucei brucei*, *L. amazonensis* and *P. berghei* (liver, blood stage, gametocyte or mosquito transmission). When infection has progressed, mice are imaged to quantify the luminescence signal, which is proportional to the parasite load (baseline infection level). Treatment with the test compounds begins, normally administered via i.p. injection or oral gavage. One day after the last treatment dose, mice are imaged again to determine the level of infection. Results are expressed as the ratio of infection at the end of treatment versus the base infection for each animal. Testing includes a negative control and positive control groups with a well-known drug for each disease. <http://ocs.med.nyu.edu/anti-infectives-screening>

1422

ESTABLISHING BIOMARKERS OF *LEISHMANIA DONOVANI* INFECTION: POTENTIAL ENDPOINTS FOR VACCINE TRIALS

Aarthy C. Vallur¹, Caroline Reinhart¹, Yeung Tutterrow¹, Dinesh Mondal², Khondaker R. Bhasker², Malcolm S. Duthie¹, Rhea N. Coler¹, Steven G. Reed¹

¹Infectious Diseases Research Institute, Seattle, WA, United States,

²International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh

Visceral leishmaniasis in the Indian sub-continent has been targeted for elimination by 2015. The realization of this goal is dependent upon identifying early infection in asymptomatic individuals, who present no overt symptoms and are potential reservoirs for spreading infection and developing disease. We studied asymptomatic individuals in the *Leishmania donovani*-hyper endemic Mymensingh district in Bangladesh over a period of 24 months to define the natural dynamics of *Leishmania*-specific antibodies and DNA and reveal their utility as biomarkers of infection. Samples were analyzed by DAT; *L. donovani* whole cell lysate and rk39 ELISA; and quantitative PCR. Serological tests indicated the sustained presence of antibodies at study intake and at a 12-month follow up interval. By DAT, 57% tested positive at both time points while by ELISA, 82% and 89% were positive at baseline and 75% and 92% tested positive at 12 month follow-up to *L. donovani* whole cell lysate and rk39, respectively. In contrast, though 84% tested positive by PCR at baseline, only 28% remained positive at follow-up. During the course of the study, 3 of the 56 study subjects developed symptomatic VL, with each consistently testing positive for antibodies or nucleic acids. Our results reflect the transient nature of asymptomatic *L. donovani* infection in this endemic area. Used together, the presence of *Leishmania*-specific antibodies and nucleic acids can predict individuals who are at the highest risk of progression to disease and thus will gain most from intervention. Based on our results, we suggest means by which tests for *Leishmania*-specific antibodies and circulating *Leishmania* DNA can be used in active surveillance of endemic areas. We conclude that these bio markers will be valuable in identifying populations for vaccine trials as well as serve as end points to evaluate the effectiveness of the trials.

1423

NOVEL NANOTECHNOLOGY TO CONCENTRATE AND PRESERVE *TRYPANOSOMA CRUZI* ANTIGENS IN URINE FOR EARLY DIAGNOSIS OF REACTIVATION OF CHAGAS DISEASE IN PATIENTS CO-INFECTED WITH HIV VIRUS

Yagahira E. Castro¹, Robert H. Gilman², Melissa Reimer³, Carolina Carolina Mejia¹, Eduardo Valencia Eduardo¹, Lance Lance Liotta⁴

¹Universidad Peruana Cayetano Heredia, Lima, Peru, ²Johns Hopkins University, Baltimore, MD, United States, ³University of South Alabama, Alabama, AL, United States, ⁴George Mason University, Manassas, VA, United States

We developed harvesting nano-porous particles to capture, concentrate and preserve *Trypanosoma cruzi* antigens in urine of HIV/*T. cruzi* patients.

Diagnosis of reactivation of chronic Chagas disease in HIV/*T. cruzi* patients is based on detection of *parasitemia* by micromethod but lacks sensitivity. Antigenuria has been shown to be correlated with *parasitemia*, but has also low sensitivity. Poly N-isopropylacrylamide (NIPAm) based particles are functionalized with chemical baits (trypan blue, TB) that capture antigens with high affinity (KD<10-12 M) within minutes, antigens captured can be eluted in a small volume yielding a concentration factor that is the ratio between the initial volume of urine and the final elution volume. In this study, model urine samples were incubated with poly(NIPAm)/TB particles. Antigens eluted from the particles were detected by Western Blot using a polyclonal antibody against *T. cruzi* H49 antigen. Nano-porous particles increased the sensitivity of antigenuria by *T. cruzi* more than 100 fold (detection limit was 0.8 ng/ml with particle treatment compared to 100 ng/ml without particle treatment). This assay was applied to a cohort of HIV/*T. cruzi* co-infected patients (N=39, 20 *T. cruzi* positive and 19 *T. cruzi* negative). Sensitivity of antigenuria in the particle-concentrated urines was 100% (2/2), 90% (9/10) and 80% (16/20) compared to micromethod, PCR and ELISA, respectively. The specificity was 100%. Positive results of antigenuria were correlated to high levels of *parasitemia* ($p<0.05$). Particle-sequestered *T. cruzi* H49 antigen was protected from enzymatic degradation by trypsin digestion and in urine over seven days at room temperature, showing that particles protected urinary antigens from degradation. Nano-porous particles effectively concentrated *T. cruzi* antigens in urine. Nanotechnology-enhanced antigenuria test could be an early predictor of reactivation and can be adapted for monitoring HIV/*T. cruzi* co-infected patients. Particle integration in urine collection is envisioned for sample handling and shipment at room temperature.

1424

AN7973: A NOVEL OXOBOROLE FOR THE TREATMENT OF AFRICAN ANIMAL TRYPANOSOMIASIS

Yvonne R. Freund¹, Tsutomu Akama¹, Kirsten Gillingwater², Virginia Sanders¹, Wei Bu¹, Grant B. Napier³, Tim Rowan³, Michael Witty³, Bakela Nare⁴, Jacob J. Plattner¹, Eric Easom¹

¹Anacor Pharmaceuticals, Inc., Palo Alto, CA, United States, ²Swiss Tropical and Public Health Institute, Basel, Switzerland, ³Global Alliance for Livestock and Veterinary Medicine, Edinburgh, United Kingdom, ⁴SCYNEXIS, Inc., Research Triangle Park, NC, United States

African animal trypanosomiasis (AAT) is a parasitic disease caused by tsetse fly-transmitted trypanosomes, which include *Trypanosoma congolense* (*T.c.*), *T. brucei brucei* (*T.b.b.*), and *T. vivax*. AAT results in serious economic losses in livestock due to reduced productivity from anemia, emaciation and fever. AN7973 is a novel boron-containing molecule that demonstrates excellent potency against *T. congolense* *in vitro* as well as *in vivo* efficacy against *T.c.* infection in mice, goats, and cattle. AN7973 has an IC₅₀ of 0.057 μ M and 0.098 μ M against *T. c.*, and *T. b. b.*, respectively. Compound wash-out experiments demonstrate that a 10 h exposure to AN7973 results in irreversible killing at concentrations as low as 1.25 μ g/mL (3.3 μ M). By 24 h, 99% of the parasites were killed at concentrations of 0.15 μ g/mL (0.40 μ M), demonstrating the trypanocidal of AN7973. PK studies were performed in mouse, rat, dog, and cattle. Intramuscular (IM) injection of 5 mg/kg in cattle resulted in a C_{max} of 2.05 μ g/mL, AUC_(0-24h) of 89.1 h* μ g/mL and a terminal half life of 22.6 h. AN7973 was tested for *in vivo* efficacy in a murine model of *T.c.* infection. A single dose of 10 mg/kg showed 100% cure, 60 days after treatment. In a goat model of *T.c.* infection, 10 mg/kg by IM injection demonstrated 100% cure at Day 100. In a cattle efficacy study, using a diminazene- and isometamidium-resistant strain of *T.c.*, a single IM dose of 10 mg/kg or 2 doses of 5 mg/kg, 24 h apart, also demonstrated 100% survival at 100 days post-treatment, reflecting complete cure. The plasma concentration in the cattle efficacy study at 1 x 10 mg/kg was 1.93 μ g/mL at t = 24 h, well above the concentrations necessary for cidal activity. The plasma exposure (AUC_(0-24h)) was determined to be 46.1 h* μ g/mL. AN7973 was well tolerated in a cattle safety study during which AN7973 was dosed at 30mg/kg three times with

2 weeks separation between doses. In summary, AN7973 demonstrates excellent efficacy against *T.c.* in the target animal, and shows promise as a novel chemical entity for treatment of AAT.

1425

VILLAGE-LEVEL CHARACTERISTICS ASSOCIATED WITH SPATIAL DISTRIBUTIONS OF MALARIA-INFECTED INDIVIDUALS IN AN AREA OF SOUTHERN ZAMBIA RECEIVING MASS SCREENING AND TREATMENT

David A. Larsen¹, John M. Miller², Joseph Keating³, Joshua Yukich³, Jeffrey Shaffer⁴, Busiku Hamainza², Kafula Silumbe⁵, Thomas Eisele³

¹Department of Public Health, Food Studies and Nutrition, Syracuse University, Syracuse, NY, United States, ²Malaria Control and Evaluation Partnership in Africa (MACEPA), a program at PATH, Lusaka, Zambia, ³Center for Applied Malaria Research and Evaluation, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, United States, ⁴Department of Biostatistics, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, United States, ⁵Malaria Control and Evaluation Partnership in Africa (MACEPA), a program at PATH, New Orleans, LA, United States

Malaria clusters across space and time; malaria interventions may be targeted to maximize the efficiency of scarce resources. However, how to target malaria interventions toward small foci of transmission is not well understood. An ongoing mass screening and treatment (MSAT) intervention in southern Zambia has provided census data at 4 different time from Dec 2011 – Nov 2012. The difference in K function, which assesses spatial regularity or clustering compared to randomness at any distance, was used to assess the spatial distribution of malaria-infected individuals observed during each census. Individuals with a malaria infection clustered within households at all prevalence levels and month of the census. Beyond the household, individuals with malaria infections were distributed differently in space depending both on village parasite prevalence and month of the census. Because the spatial distribution of malaria-infected individuals varied by prevalence level, malaria parasite prevalence aggregated to the village level was then modeled to determine factors that may explain the differing spatial distributions. A linear mixed effects model including altitude, enhanced vegetation index, nighttime temperature, round of MSAT (categorized as round 1-4) and the topographical position index (whether a village was located in a valley, ridge, plain, or slope) accounted for 82.5% of the variation in village malaria parasite prevalence. This technique also revealed that an increase in altitude of 100m was associated with an absolute 2.5% decrease in village parasite prevalence ($p < 0.001$). An increase from 0 (dry, brown foliage) to 1 (green dense foliage) in the enhanced vegetation index was associated with an absolute 44% increase in village parasite prevalence ($p < 0.001$). A 1-degree increase in nighttime temperature was associated with an absolute 0.4% increase in village parasite prevalence ($p < 0.01$). Multiple rounds of the MSAT intervention were also associated with decreased village malaria parasite prevalence; 3 rounds were associated with an absolute 9.6% decrease (relative 38.6%) from the baseline round ($p < 0.001$). Varying spatial distributions of malaria-infected individuals appear to be driven by vector abundance and gametocyte prevalence in the population. The ability to clearly delineate village malaria prevalence may assist in developing mechanisms for focused interventions to optimize their effectiveness.

1426

RAPID SCALE-UP OF LONG-LASTING INSECTICIDAL NETS ASSOCIATED WITH A DECREASE IN SEVERE MALARIA INCIDENCE AND AN UPWARD SHIFT IN THE MEAN AGE OF SEVERE CASES AMONG CHILDREN IN LUANGWA DISTRICT ZAMBIA

Thomas P. Eisele¹, Adam Bennett¹, David A. Larsen², Benjamin Kalayjian³, Josh Yukich¹, Joseph Keating¹, John M. Miller⁴, Busiku Hamianza⁵, Richard W. Steketee⁶

¹Center for Applied Malaria Research and Evaluation, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, United States, ²Syracuse University, Syracuse, NY, United States, ³Tulane University School of Medicine, New Orleans, LA, United States, ⁴PATH-MACEPA, Lusaka, Zambia, ⁵National Malaria Control Centre, Lusaka, Zambia, ⁶PATH-MACEPA, Seattle, WA, United States

Long-lasting insecticidal nets (LLINs) have been shown to reduce malaria transmission by as much as 90% with concomitant reduction in malaria incidence and all-cause child mortality in the African Africa. Ecological data have also shown the mean age of severe malaria to shift from younger to older children as transmission decreases in these settings. In late 2005 and 2006 16,100 LLINs were distributed free of charge to all households (approximately 4,000) in the Luangwa District of Zambia, resulting in rapidly achieving high household coverage of LLINs (73%), from very low coverage prior to 2005. We assessed trends in the mean age of children under 10 years old admitted to the two hospitals serving Luangwa District from January 2003 through August 2009. A difference-in-difference analytic approach was used in a linear regression model to assess change in the mean age of reported child hospital admissions (primary outcome), categorized as malaria or non-malaria diagnosis, before and after LLIN scale-up (before and after January 2007), while controlling for hospital, malaria transmission season, and lagged monthly vegetation index and mean temperature. This approach allowed us to assess the relative change in the mean age of reported in-patient severe malaria cases compared to all hospitalized admissions due to causes other than malaria over this time period. Total reported in-patient admissions among children under 10 years old decreased from 63.8 per 1,000 in 2003 to 41.2 per 1,000 in 2009. Reported in-patient severe malaria admissions decreased from 41.7 to 21.5 per 1,000 population over this same period; severe malaria as the cause of admission decreased from 64.6% in 2003 to 51.6% in 2009. The mean age of non-malaria admissions stayed relatively constant over the observation period at 23.9 months, while the mean age of severe-malaria admissions increased from 17.1 months prior to LLIN scale-up (before 2007) to 23.5 months post LLIN scale-up (coefficient for malaria diagnosis X pre-post LLIN period interaction term = 0.47 (in years); p -value < 0.001). Results suggest a decline in reported severe malaria admissions following LLIN scale-up, with a coinciding upward shift in the mean age of severe malaria admissions. These results suggest that the rapid LLIN scale-up in Luangwa district was associated with a marked decrease in malaria transmission, severe illness, and modifications in the age distribution of those afflicted.

1427

SUSTAINED DECLINING BURDEN OF MALARIA AT COMMUNITY LEVEL IN NORTHEASTERN TANZANIA

Acleus S. Rutta, Filbert Francis, Bruno P. Mmbando, Deus S. Ishengoma, Samuel Sembuche, Ezekiel K. Malecela, Johari Y. Sadi, Mathias L. Kamugisha, **Martha M. Lemnge**

National Institute for Medical Research, Tanga, United Republic of Tanzania

The reported decline of malaria in most parts of Tanzania has some implication on accuracy of malaria diagnosis and management, especially following the introduction of expensive artemisinin combination therapy (ACT) with artemether/lumefantrine (ALu). Traditionally, fever has been the back-bone of malaria case management; but with declining malaria and

introduction of expensive ACTs, this approach poses a major challenge. In our previous and ongoing malaria passive case detection in 4 villages of Korogwe, northeastern Tanzania, we demonstrated that provision of early diagnosis and treatment of malaria by community owned resource persons (CORPs) using rapid diagnostic tests (RDTs) and ALU is an effective strategy for malaria control. We now provide updates on sustained impact of these interventions on malaria in communities where the transmission has significantly declined. In 2006, individuals with history of fever within 24 hours or fever ($\geq 37.5^{\circ}\text{C}$) at presentation were presumptively treated with sulphadoxine/pyrimethamine. Between 2007 and 2012, individuals aged 5 years and above with positive RDTs were treated with ALU while under-fives were treated irrespective of RDT results. A total of 18,981 cases were attended and 17.2% were positive for malaria parasites by microscopy. Malaria prevalence and incidence decreased across the years, from 34.6% to <1% and 235/1000 to <8/1000 person years at risk for 2007 and 2012, respectively. The highest incidence of malaria shifted from children aged 5-9 years to individuals aged 10-19 years from 2009. Despite these changes, fever prevalence remained high at >40.0% in under-fives and >20.0% among individuals aged 5 years and above. The significant reduction in malaria prevalence and incidence observed might be attributed to different interventions including early diagnosis and prompt treatment through CORPs strategy. Studies to investigate causes of fevers other than malaria are recommended for better case management. The current remarkable and sustained decline in malaria suggests that these areas might be moving from control to pre-elimination levels.

1428

RESERVOIRS OF ASYMPTOMATIC MALARIA IN MALAWI: RESULTS OF TWO CROSS-SECTIONAL STUDIES

Jenny A. Walldorf¹, Lauren M. Cohee¹, Jacqueline Fiore², Andy Bauleni³, Jenna E. Coalson⁴, Themba Phiri³, Don Mathanga³, Clarissa Valim⁵, Atupele P. Kapito-Tembo³, Terrie E. Taylor², Miriam K. Laufer¹

¹University of Maryland, Baltimore, MD, United States, ²Blantyre Malaria Project, University of Malawi College of Medicine, Blantyre, Malawi, ³Malaria Alert Center, University of Malawi College of Medicine, Blantyre, Malawi, ⁴University of Michigan School of Public Health, Ann Arbor, MI, United States, ⁵Harvard University School of Public Health, Boston, MA, United States

Malaria surveillance in endemic countries typically focuses on young children who are at highest risk of malaria morbidity and mortality. As we develop strategies to eliminate malaria, it is critical to expand our understanding of sources of malaria transmission. The Malawi International Center for Excellence in Malaria Research conducted cross-sectional surveys in the 2012 rainy and dry seasons in three transmission settings in southern Malawi with the goal of estimating prevalence of asymptomatic malaria infection and assessing risk factors for asymptomatic *parasitemia* in each setting. Districts were selected to represent urban/low (Blantyre City), rural/high (Chikhwawa), and semi-rural/mountainous (Thyolo) malaria transmission. We randomly selected 30 households in 10 enumeration areas in each district. Demographic, malaria intervention, and current health status data were collected through household interviews; blood samples were obtained from all individuals over six months of age. Among 5099 individuals with smear results in Blantyre, Chikhwawa, and Thyolo, total parasite prevalence was 11.7%, 13.1%, 11.0% in rainy and 3.9%, 17.4%, 9.4% in dry seasons respectively. Asymptomatic *parasitemia* represented 46.2%, 41.7%, 49.3% and 76.7%, 69.5%, 79.0% of total parasite prevalence in the two seasons, respectively. In multinomial regression using aparasitemic individuals and age 6-59 months as reference groups and controlling for district, individual net use and indoor residual spraying, ages 5-15 years was strongly associated with asymptomatic *parasitemia* in the rainy season (Odds ratio (OR) = 6.7, [95% Confidence interval (CI): 3.3, 13.7]) and also in the dry season (OR = 1.5 [95% CI: 1.1, 2.2]). Age >15 years was not significantly associated with asymptomatic *parasitemia* in the rainy season but was protective (OR = 0.64, [95% CI: 0.45, 0.92]) in the dry season. In Malawi and potentially in

other endemic settings, school age children represent important reservoirs of asymptomatic infection and should be targeted for interventions to interrupt transmission.

1429

MICROEPIDEMIOLOGY OF SUB-MICROSCOPIC PLASMODIUM FALCIPARUM INFECTION: IMPLICATIONS FOR DETECTION OF HOTSPOTS WITH IMPERFECT DIAGNOSTICS

Jacklin Mosha¹, Hugh Sturrock², Bryan Greenhouse², Brian Greenwood¹, Daniel Chandramohan¹, Colin Sutherland¹, Drakeley Chris¹, Sharan Atwal¹, Nahla Gadalla¹, Gibson Kibiki³, Teun Bousema¹, Roly Gosling²

¹London School of Hygiene & Tropical Medicine, London, United Kingdom,

²University of California San Francisco, San Francisco, CA, United States,

³Kilimanjaro Christian Medical Centre, Moshi, United Republic of Tanzania

At the local level, malaria transmission clusters in hotspots, which may be a single household or group of households that experience higher than average exposure to infectious mosquitoes. Active case detection (ACD), often relying on rapid diagnostic tests (RDTs) for mass screen and treat campaigns, has been proposed as a method to detect and treat individuals in hotspots. Here we used data from a cross sectional survey conducted in north-western Tanzania to examine the spatial distribution of *Plasmodium falciparum* to establish whether RDTs are likely to have sufficient sensitivity to target ACD interventions aimed at reducing transmission. Dried blood spots were collected from all consenting individuals from four villages in a single ward during a survey conducted between August and November 2010. These were analyzed by PCR for the presence of *P. falciparum*, with the parasite density of positive samples being estimated by quantitative PCR. Household exposure was estimated using distance-weighted PCR prevalence of infection. Results showed that mean distance-weighted PCR prevalence per household was 34.5% (range 0 - 94.7%). Infection density was highest in children 5-10 years old and lowest in those >40 years old. Infection density was negatively associated with transmission intensity with the odds of an infection being sub-microscopic increasing with household exposure (OR 1.09 per 1% increase in exposure, $p < 0.001$). This relationship, which is potentially explained by exposure-related immunity, suggests that RDTs and microscopy have the lowest sensitivity in transmission hotspots. Simulations of different targeted mass drug administration (tMDA) strategies showed that treating all individuals in households where RDT prevalence was above 20% increased the number of infections that would have been treated from 43% to 55%, however, 45% of infections remained untreated. Even using a single RDT positive as a trigger for household MDA resulted in around 35% of infections remaining untreated. Taken together, these results suggest that community wide MDA, instead of screen and treat strategies, may be needed to successfully treat the asymptomatic, submicroscopic parasite reservoir and reduce transmission in similar settings.

1430

OPERATIONAL APPROACHES FOR DETECTING FOCI OF MALARIA INFECTION: HOW DO SCHOOL AND HEALTH FACILITY SURVEYS COMPARE AGAINST A COMMUNITY-BASED APPROACH

Gillian H. Stresman¹, Jennifer Stevenson¹, Chrispin Owaga², Elizabeth Marube², Wycliffe Odongo², Shehu Shaggari², Teun Bousema¹, Chris Drakeley¹, Jonathan Cox¹

¹London School of Hygiene & Tropical Medicine, London, United Kingdom,

²Kenya Medical Research Institute, Kisumu, Kenya

There is increasing evidence of heterogeneity manifested through presence of foci of malaria infection. Tailoring interventions to reflect this heterogeneity is likely to bring benefits in terms of their impact and cost effectiveness. For such a targeted approach to be effective in the long term, strategies are needed to enable local malaria control teams to reliably identify and target the true foci of infection in the community.

In July 2010, 4987 children were tested for malaria across 46 schools in Rachuonyo South district in western Kenya and the compounds of 4888 children (98%) were geolocated. Two surveys were conducted in 5 health facilities in the same area (Oct 2011, July 2012) with a combined total of 3034 people tested for malaria. Of the participants sampled, spatial coordinates of the compound were obtained for 30% of the participants. All participants sampled at school and health facilities were tested for malaria by rapid diagnostic test and samples from all surveys were assessed for antibody response to *Plasmodium falciparum* AMA1 and MSP1. The results were compared to foci of infection identified during a community cross-sectional survey of 17506 individuals. Preliminary results indicate that if positive for malaria by RDT or serology, participants had twice the odds of residing in foci of infection ($p < 0.0001$). Seropositivity in schools surveys had a sensitivity of 64.1% in identifying children that reside in known foci whereas RDT results obtained during the health facility surveys were 86.8% specific in identifying children that do not reside in known foci of infection. Results indicate that school and health facility surveys may provide an alternative approach to detect foci of infection in the community. However, the definition of foci of malaria infection from both an operational and academic perspective is in need of further discussion.

1431

USING SEROLOGICAL MARKERS FOR ESTIMATING MALARIA TRANSMISSION INTENSITY AND ASSESSING INTERVENTION EFFICACY IN WESTERN KENYA

Jacklyn Wong¹, Mary J. Hamel¹, Chris J. Drakeley², Simon K. Kariuki³, Ya Ping Shi¹, John M. Vulule³, John E. Gimnig¹

¹Centers for Disease Control and Prevention, Atlanta, GA, United States,

²London School of Hygiene & Tropical Medicine, London, United Kingdom,

³Kenya Medical Research Institute, Kisumu, Kenya

Accurate measurement of local malaria transmission is critical for evaluating control interventions. Serological conversion rates (SCRs) have been used to estimate the force of malaria infection in populations. In low to moderate transmission settings, systematic reductions in incidence (e.g., due to effective interventions) can be measured through a single retrospective serological survey. Our objective was to validate, in a malaria hyperendemic region, the accuracy of serological markers for 1) estimating transmission intensity and 2) retrospectively detecting a decline in incidence. Asembo, western Kenya, is an area that experiences high, perennial malaria transmission. From 1997-1999, Asembo was the site of a community-wide insecticide-treated bed net (ITN) trial that reduced malaria transmission by 90%. Serological samples collected pre-ITN (1994) and post-ITN (2009) were tested by indirect ELISA for antibodies against *Plasmodium falciparum* circumsporozoite protein (CSP), merozoite surface protein-1 (MSP-1), and apical membrane antigen-1 (AMA-1). Age-specific seroprevalence data were fitted to catalytic conversion models to estimate SCRs for 1994 and 2009. Post-ITN (2009) age-seroprevalence curves were also examined for tiered trends to denote when transmission declined. Between 1994 and 2009, SCRs for CSP, MSP-1, and AMA-1 fell by 50%, 25%, and 49%, respectively. SCRs corresponded closely with entomological inoculation rates, which dropped from >100 to 10 infectious bites/person-year during this 15 year period. Post-ITN (2009) SCRs were uniform across all ages rather than tiered; older age groups born before the trial did not exhibit higher SCRs than young age groups born after. We conclude that serological markers provide reliable estimates of malaria transmission intensity near the time of sample collection. Because we were unable to pinpoint when the drop in transmission occurred, however, this model did not appear to be accurate in malaria hyperendemic areas for retrospective reconstruction of historical trends associated with control interventions.

1432

INNATE LYMPHOID CELL POPULATIONS DRIVE THE TH2 IMMUNE RESPONSE TO *LITOMOSOIDES SIGMADONTIS* IN BALB/C MICE

Alexis Boyd¹, Kristin E. Killoran², Edward Mitre², Thomas B. Nutman¹

¹National Institutes of Health, National Institute of Allergy and Infectious Diseases, Bethesda, MD, United States, ²Department of Microbiology and Immunology, Uniformed Services University of the Health Sciences, Bethesda, MD, United States

A group of innate cells, termed nuocytes, multipotent progenitor (MPP) cells or innate helper cells (IHC) [collectively referred to as innate lymphoid cells (ILCs)] have been identified at barrier surfaces and are involved in propagating a Th2-type response following infection with intestinal helminths in mice. *Litomosoides sigmodontis* (Ls) is a filarial parasite of rodents that lives in the pleural cavity and develops a Th2-response at patency (when microfilariae are produced) at day 42 post infection (p.i.). To assess whether the pleural cavity also utilizes ILCs to drive a Th2 response, Balb/c mice were infected with 40 infective stage larvae (L3) of Ls and the frequencies of ILC subpopulations were determined by multiparameter flow cytometry of cells isolated from the spleen and pooled samples from the pleural cavity on days 5, 14, 36, 42, and 60 p.i. ILCs were defined as lineage-*c*Kit⁺ and were further divided by Sca1+ (MPPs), Sca1-/CD90.2+/CD44+ (IHCs) and Sca1+/CD90.2+/CD44+/ST2+ cells (nuocytes). Each of these ILC subpopulations was identified in the spleen and pleural cavity of infected and uninfected mice. Two of the 3 ILC subpopulations were significantly expanded in the spleen at day 42 p.i., compared to uninfected matched controls (nuocytes: $p = 0.021$, IHC: $p = 0.044$). In the pleural cavity, there was an increased frequency of MPPs and nuocytes at day 36 and day 42 p.i. compared to controls and an increase of IHCs at day 42 p.i. The cellular infiltrate in the pleural cavity during infection showed that neutrophils (22-fold day 36, 68-fold day 42), eosinophils (23-fold day 36, 9-fold day 42) and macrophages (26-fold day 36, 6-fold day 42) increased markedly at day 36 to day 42 p.i. This increase was accompanied by an increase from baseline in the levels of IL-4 (16-fold day 36, 34-fold day 42), IL-5 (144-fold day 36, 218-fold day 42), IL-13 (167-fold day 36, 3-fold day 42) and IL-10 (1.5-fold day 36, 27-fold day 42) in the pleural lavage fluid and by increases in plasma IL-5 levels ($p = 0.0097$ day 36, $p = 0.0570$ day 42) and levels of IgE (p -value = 0.0079 day 42) and IgG1 (p -value = 0.0079 day 42) antibodies. These data confirm the induction of a Th2-dominant response both locally and systemically by Ls and suggest that ILCs may be a major contributing factor. Since these ILCs are typically induced by barrier cell-expressed IL-25 and IL-33, the cellular sources of these cytokines and their influence on ILC/Th2 cell induction are currently under study.

1433

M2A MACROPHAGES ARE NECESSARY AND SUFFICIENT TO MEDIATE EOSINOPHIL-DEPENDENT IMMUNITY TO FILARIAL HELMINTH INFECTION

Joseph D. Turner¹, Ana de Castro Guimaraes¹, Alice Halliday¹, Kathryn J. Else², Nico van Rooijen³, Andrew Steven¹, Darren Cook¹, Mark J. Taylor¹

¹Liverpool School of Tropical Medicine, Liverpool, United Kingdom,

²University of Manchester, Manchester, United Kingdom, ³Vrije Universiteit, VUMC, Amsterdam, Netherlands

Eosinophils are effector cells in the immune control of tissue dwelling helminths. Whilst eosinophil responses are induced by Th2 adaptive immunity, it is not known how eosinophils are instructed to home from the blood to target migratory stages of parasites. Here we provide evidence from an experimental model of filarial infection (*Brugia malayi* mouse model) that eosinophils are a crucial component of the anti-filarial response that limits establishment of infectious larvae. *B. malayi* infectious larvae also induce M2a macrophage activation (alternative activation)

of tissue resident macrophages, which is further pronounced following vaccination with heat-killed larvae. Absence of a functional interleukin 4 receptor α chain (IL-4R α) leads to failure of M2a activation, impaired eosinophil recruitment and susceptibility to *B. malayi* establishment to the adult phase. To test the functional relevance of M2a development in the eosinophil larvicidal response, we undertook targeted depletion of macrophages by clodronate liposome (CL) treatment. CL-treatment rendered mice highly susceptible to infection with associated impaired eosinophil recruitment. Add-back of purified M2a into CL-treated WT mice restored both M2a expansion and eosinophil influx. Th2 responses were intact in CL-treated WT mice, suggesting that M2a development directly regulated eosinophil recruitment at the infection site. Consistent with this, an increase in CCL11 transcripts from immune cells derived from the infection site of WT but not IL-4R α ^{-/-} mice was apparent. We therefore tested the direct role of M2a in eosinophil regulation and parasite killing by adoptively transferring purified WT M2a into susceptible severe combined immune-deficient mice (SCID). WT M2a SCID recipients induced a rapid eosinophil response and killing of infectious larvae. In a complementary approach, supplying an exogenous source of IL-4 to condition resident macrophages toward an M2a phenotype at the point of infection rendered SCID mice more resistant to larval establishment. Thus we conclude that M2a conditioning via IL-4R α is both necessary and sufficient in the absence of additional adaptive immune activation to induce resistance to filarial infection via larvicidal eosinophil recruitment.

1434

ALTERNATIVELY ACTIVATED MACROPHAGES (AAM) IN SCHISTOSOMA MANSONI LIVER GRANULOMAS ARE DERIVED FROM MONOCYTES AND ARE PHENOTYPICALLY AND FUNCTIONALLY DISTINCT FROM AAM DERIVED FROM TISSUE MACROPHAGES INDUCED BY LITOMOSOIDES SIGMODONTIS INFECTION

P'ng Loke, Natasha M. Girgis, Uma M. Gundra, Lauren N. Ward, Kirsten E. Wiens, Mynthia Cabrera, Ute Frevort

New York University School of Medicine, New York, NY, United States

Alternatively activated macrophages (AAM) are induced by helminth infections. We investigated the origins of AAM found in the liver granulomas of mice infected with *Schistosoma mansoni*. CX3CR1GFP/+ mice were used to track monocytes and AAM through a combination of intravital microscopy and flow cytometry. GFP+ monocytes in the liver sinusoids arrest upon encountering parasite eggs in the vessels. GFP+ cells with macrophage-like morphology accumulate around the eggs, are incorporated into hepatic granulomas and express markers of AAM. To determine if Ly6Clow or Ly6Chigh monocytes serve as AAM precursors, we transferred pure populations of these cells from CX3CR1GFP/+ mice into infected congenic mice. Ly6Chigh monocytes extravasated into the tissue more efficiently and upregulate PD-L2 suggesting that they are the source of AAM during *S. mansoni* infection. However, when transferred Ly6Chigh monocytes extravasated into the tissue they became Ly6Clow, suggesting that Ly6Chigh monocytes may transition through a Ly6Clow state when differentiating into AAM. In addition to monocytes, AAM can also be derived from tissue resident macrophages that proliferate during *Litomosoides sigmodontis* infection. AAM derived from these different sources may be phenotypically or functionally distinct. We find that while both monocyte and tissue derived AAM express high levels of ARG1, YM1/CHI3L3 and FIZZ1/RELMA, tissue derived AAM expressed high levels of F480, but low levels of MR1 and PDL2. In contrast, monocyte-derived AAM were F480int and expressed high levels of MR1 and PDL2. Monocyte-derived AAM upregulate the enzyme RALDH2, have high levels of Aldefluor activity indicating the production of retinoic acid (RA), whereas tissue derived AAM do not. Consistent with RA production, only monocyte derived AAM can promote the differentiation of FoxP3+ CD4+ cells when used to stimulate naïve CD4+ cells. Therefore, monocyte derived and tissue derived AAM are phenotypically and functionally distinct.

1435

MOLECULAR CLONING AND CHARACTERIZATION OF NOVEL GLUTAMATE-GATED CHLORIDE CHANNEL SUBUNITS FROM SCHISTOSOMA MANSONI

Vanessa Dufour¹, Claudia Wever², Conor R. Caffrey³, Robin N. Beech¹, Paula Ribeiro¹, Joseph A. Dent², Timothy G. Geary¹

¹McGill University, Sainte-Anne-de-Bellevue, QC, Canada, ²McGill University, Montreal, QC, Canada, ³University of California San Francisco, San Francisco, CA, United States

Neuronal receptors of schistosomes are attractive targets for drug development because these parasites depend entirely on neuronal modulation to control functions vital to their survival and reproduction. Cys-loop ligand-gated ion channels (LGIC) are proven drug targets in nematodes and arthropods, but are poorly characterized in flatworms. We have previously cloned 3 glutamate-gated chloride channel (GluCl) subunits from *Schistosoma mansoni* (Sm), and characterized them by two-electrode voltage clamp (TEVC) in *Xenopus* oocytes. Concentration-response relationships revealed that the SmGluCl receptors affinity for glutamate is among the highest reported for GluCl to date, with EC50 values of 6.87- 26.28 μ M. In addition, TEVC showed that SmGluCl receptors are insensitive to ivermectin (IVM), indicating that they do not belong to the highly IVM-sensitive GluCl α subtype group. These SmGluCl subunits appear to be the only non-acetylcholine Cys-loop LGICs found in *S. mansoni*. Phylogenetic analyses suggested that they belong to a novel clade of flatworm GluCl, which also includes putative genes from other trematodes and cestodes. This flatworm GluCl clade is evolutionarily distinct from the nematode-arthropod and mollusc GluCl clades, and from all GABA receptors. Using confocal microscopy, we showed that SmGluCl are distributed throughout the central and peripheral nervous systems of *S. mansoni*. Further work is in progress to provide a detailed description of SmGluCl distribution in males, females, cercaria and somules. Finally, we have initiated RNAi-based functional studies to assess the roles played by SmGluCl in schistosomes. Altogether, these results provide the first molecular evidence showing the contribution of GluCl receptors to L-glutamate signaling in *S. mansoni*, an unprecedented finding in flatworms. This project has uncovered a completely new aspect of neuronal modulation in flatworms, and brings attention to very appealing new anthelmintic targets which could be used to address the urgent need for new chemotherapeutic options for schistosomiasis.

1436

IGE ANTI-SJ6-8 ANTIBODIES PREDICT RESISTANCE TO REINFECTION WITH SCHISTOSOMA JAPONICUM

Hai-Wei Wu¹, Sunthron Pond-Tor¹, Mario Jiz², Luz Acosta², Dipak K. Raj¹, Grant Jolly¹, Jennifer F. Friedman¹, Jonathan D. Kurtis¹

¹Rhode Island Hospital, Providence, RI, United States, ²Research Institute of Tropical Medicine, Manila, Philippines

Our goal is to discover novel vaccine candidates for schistosomiasis japonica by identifying the parasite targets of naturally acquired protective human antibodies. We applied our differential, whole proteome screening method using plasma and epidemiologic data from a longitudinal treatment-reinfection study conducted in Leyte, The Philippines to identify new *Schistosoma japonicum* antigens associated with resistance. Individuals in our cohort (age 8-30 yrs, n=616) were *S. japonicum* infected at baseline, treated with praziquantel and followed with quarterly stool examination for 12 months. We pooled plasma from 10 resistant (RP) and 10 susceptible (SP) individuals, with careful matching for potential confounders, and performed differential screening experiments using an *S. japonicum* adult worm cDNA expression library. We screened 500,000 clones and identified Sj6-8, a 25 kDa hypothetical protein with an IG domain that is uniquely recognized by antibodies in RP but not SP. We have expressed and purified the immuno-relevant region (aa 20-176) in *E. coli* and designated the protein rSj6-8A. Rabbit anti-Sj6-8A recognized a 75 kDa band in adult worm excretory-secretory products and localized

Sj6-8 to the exofacial surface of the tegument and gastrodermis of adult worms by confocal immunofluorescence analysis and immunogold electron microscopy. We developed a bead-based assay to measure anti-rSj6-8A antibody levels in the entire cohort of volunteers. In repeated measures models, individuals with anti-rSj6-8A IgE levels in the upper quartile (n=140) had 58% lower intensity of reinfection measured 12 months after treatment than individuals with anti-rSj6-8A IgE levels in the lowest quartile (n=140, $P < 0.001$) after adjusting for potential confounders including directly observed water contact, village, age, sex, and baseline intensity of infection. Together, these results validate our field-to-lab-to-field based strategy for the rational identification of vaccine candidates and support Sj6-8 as a novel vaccine candidate for schistosomiasis japonica.

1437

IFN- γ ELISPOT RESPONSES AGAINST WHOLE SPOOROZOITES AND PF ANTIGENS IN VOLUNTEERS IMMUNIZED WITH PROTECTIVE PFSPZ MALARIA VACCINE

Martha Sedegah¹, Robert Seder², Jun Huang¹, Harini Ganeshan¹, Maria Belmonte¹, Steve Abot¹, Arnel Belmonte¹, LeeJah Chang³, Mary Enama², Eric James⁴, Peter Billingsley⁴, Sumana Chakravarty⁴, Judith Epstein¹, Eileen Villasante¹, Thomas Richie¹, Barney Graham², Stephen Hoffman⁴

¹Naval Medical Research Center, Silver Spring, MD, United States, ²National Institutes of Health/VRC, Bethesda, MD, United States, ³National Institutes of Health/National Institute of Allergy and Infectious Diseases, Bethesda, MD, United States, ⁴Sanaria, Rockville, MD, United States

In animals, protective immunity induced by irradiated sporozoites (SPZ) is dependent on CD8+ T cells (mice, monkeys) and IFN- γ (mice). We therefore studied IFN- γ responses in 32 subjects immunized multiple times with escalating doses (7.5×10^3 , 3.0×10^4 or 1.35×10^5 PfSPZ) of radiation-attenuated, purified, cryopreserved *Plasmodium falciparum* SPZ (PfSPZ Vaccine, Sanaria) by IV injection. There was a dose response in regard to protection. None of the volunteers were protected at the lowest total dosage and all were protected at the highest total dosage (R. Seder et al. submitted). This provided the opportunity to begin studying the association between immune responses and protection. Because the antigens involved in protective immunity induced by immunization with the PfSPZ Vaccine are unknown, we used IFN- γ ELISpot assays on freshly isolated PBMC to assess recall responses to pools of overlapping 15-mer peptides representing 5 pre-erythrocytic stage proteins, CSP, AMA1, SSP2/TRAP, LSA1 and CelTOS, comparing these responses to those recalled by PfSPZ or the blood stage antigen PfMSP1 as positive and negative controls, respectively. Responses to each of the 5 Pf antigens were of lower magnitude ($25-75$ sfc/ 10^6 PBMC) than were responses to PfSPZ. Analysis is ongoing, but in general there was a dose response for PfSPZ and several antigens, most strikingly, AMA1 and SSP2/TRAP. The combination of small numbers and the dose responses make it difficult to assess whether ELISpot responses to any particular antigen were associated with protection, but there was an indication that responses to AMA1 and PfSSP2/TRAP may be so associated. Based on the premise that protective responses targeting multiple antigens could be additive, we summed the responses to the 5 tested antigens, and correlated this with responses to PfSPZ. The two magnitudes were similar, and positively correlated. These preliminary data provide a foundation for prospective studies designed to determine the targets and mechanisms of the high level protective immunity induced by PfSPZ.

1438

IMMUNIZING AGAINST MALARIA BY INDUCING ANTIBODY AND CD8 T CELL MEDIATED PROTECTION

Sumana Chakravarty¹, Minglin Li², Richard E. Stafford², Meredith L. Leong³, Yun Wu², Edward E. Lemmens³, Bill Hanson³, Peter Lauer³, Dirk G. Brockstedt³, Thomas W. Dubensky, Jr.³, Stephen L. Hoffman⁴, B. Kim Lee Sim⁴

¹Sanaria, Rockville, MD, United States, ²Protein Potential, Rockville, MD, United States, ³Aduro BioTech, Berkeley, CA, United States, ⁴Protein Potential and Sanaria, Rockville, MD, United States

The malaria vaccine, RTS,S/AS01 is safe and delays the onset of clinical malaria by 30%-50% depending on age group. Protection is thought to be primarily mediated by antibodies against the repeat region and possibly CD4+ T cell responses against the C' terminus of the PfCSP. The vaccine does not induce meaningful CD8+ T cell responses. RTS,S/AS01 is not being considered for preventing malaria in non-immune travelers and elimination campaigns, because its protective efficacy is too low. A vaccine for these indications needs to provide >80% protective immunity for at least 6 months. We hypothesize that by adding highly functional, protective CD8+ T cell responses to antibody responses against the PfCSP, such protective immunity can be achieved. This response should be multifunctional as opposed to the high response obtained with adenoviral based vaccines that have not translated protective efficacy in humans. We are using live-attenuated *Listeria monocytogenes* (Lm) as a vaccine platform due to its demonstrated properties of effectively stimulating robust, multi-functional, cell-mediated immunity, as a result of its intracellular lifecycle and ability to directly infect, deliver antigen to, and stimulate DCs *in vivo*. We have developed an attenuated Lm-based vaccine platform (Lm Δ actA Δ inlB) that has been evaluated in multiple clinical trials in patients with malignant and infectious diseases. This live-attenuated Lm Δ actA Δ inlB strain is genetically defined with 2 virulence determinants deleted, resulting in a greater than 1,000-fold attenuation as compared to wild-type Lm, but retaining the immuno-stimulatory potency of the fully virulent wild-type pathogen. We used a prime-boost regimen combining selected molecular adjuvants formulated with recombinant PfCSP protein (rPfCSP) and Lm expressing PfCSP (Lm-PfCSP), to induce PfCSP-specific inhibitory antibodies and CD8+ and CD4+ T cell responses. We will discuss the high levels of inhibitory antibodies as assessed by inhibition of liver stage development and assess long term memory seen with our strategy.

1439

IMMUNE RESPONSES OF RHESUS MONKEYS TO A SELF-ASSEMBLING PROTEIN NANOPARTICLE (SAPN) VACCINE DISPLAYING PLASMODIUM FALCIPARUM CSP B- AND T-CELL EPITOPES

David E. Lanar¹, Margaret E. McCoy¹, Hannah E. Golden¹, Xiaoyan Zou², Zeyana S. Rivera¹, Qin Guo¹, Debleena Dasgupta¹, Stephen A. Kaba¹, David Fryauff², Walter R. Weiss², Randall F. Howard³, Carter Darrick³, Steven G. Reed³, Vincent R. Gerbasi², Peter Burkhard⁴

¹Walter Reed Army Institute of Research, Silver Spring, MD, United States, ²Naval Medical Research Center, Silver Spring, MD, United States, ³Infectious Disease Research Institute, Seattle, WA, United States, ⁴University of Connecticut, Storrs, CT, United States

We have previously studied in mice the immune responses induced against *Plasmodium falciparum* circumsporozoite protein (PfCSP) epitopes using a self-assembling protein nanoparticle (SAPN) platform. As a path to testing this vaccine in humans, we conducted safety and immunogenicity studies in rhesus macaques. We hypothesized that an SAPN displaying B- and T-cell PfCSP epitopes would be safe and induce significant responses in macaques with and without the use of an adjuvant. Therefore, we constructed a PfCSP-KMY-SAPN displaying 60 copies of the PfCSP internal repeat sequence (NANP)₄ and 60 copies each of three previously identified human MHC-restricted CD8 T-cell epitopes (KPKDELDTY, MPNDPNRNV and

YLNKQNSL). Monkeys received four immunizations with the PfcSP-KMY-SAPN with or without the adjuvant GLA-SE. No adverse events developed in any of the animals as a result of immunizations. Antisera and PBMC's were obtained and evaluated by multiple criteria to determine their PfcSP immune specificity. Titer to NANP repeats by ELISA was about 5×10^2 following immunizations of PfcSP-KMY-SAPN in saline, but increased 20-fold to $\sim 1 \times 10^4$ in combination with GLA-SE. Passive transfer of purified IgG from rhesus immunized with PfcSP-KMY-SAPN/GLA-SE prevented infection of 100% of C57Bl/6 mice by a lethal challenge of a transgenic *P. berghei* sporozoite displaying full length *P. falciparum* CSP. Furthermore, serum from these same PfcSP-KMY-SAPN/GLA-SE-immunized monkeys inhibited *P. falciparum* sporozoite infection of primary human hepatocyte cultures by 90%. PBMC were purified and are undergoing evaluation for epitope-specific IFN- γ , IL-2 and TNF α responses. In conclusion, a PfcSP-KMY-SAPN vaccine for malaria was safe and immunogenic in rhesus monkeys. Immune responses to the vaccine were greatly enhanced if the nanoparticle was formulated with the adjuvant GLA-SE.

1440

PROFILING OF ANTIBODIES IN LYMPHOCYTE SUPERNATANTS (ALS) FROM *PLASMODIUM FALCIPARUM* INFECTED PATIENTS IN PERU

Li Liang¹, Emmanuel Y. Dotsey¹, Chris Hung¹, Katherine Torres², David Huw Davies¹, Peter D. Crompton³, Joseph M. Vinetz⁴, Philip L. Felgner¹

¹University of California Irvine, Irvine, CA, United States, ²Malaria Laboratory, Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru, ³Laboratory of Immunogenetics, Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, MD, United States, ⁴University of California San Diego, San Diego, CA, United States

Currently available serologic assays cannot distinguish between circulating antibodies secreted by long-lived plasma cells generated in response to remote infections from antibodies secreted by plasmablasts generated in response to acute or recent infections. To address this technological gap in the context of malaria we developed a high throughput assay to profile Antibodies in Lymphocyte Supernatants (ALS) which are representative of antibodies secreted by circulating plasmablasts. Serum samples and peripheral blood lymphocytes were collected from Peruvian adults with either symptomatic or asymptomatic *Plasmodium falciparum* infection as well as from uninfected controls. Serum samples and supernatants from lymphocyte culture supernatants were probed against protein microarrays containing 500 *P. falciparum* and 500 *P. vivax* proteins. Strong antibody responses were detected in ALS from asymptomatic patients, whereas reactivity in symptomatic patients was much lower, and reactivity in control individuals was negligible. *P. falciparum* antigens differentially recognized by asymptomatic and symptomatic parasitemic individuals were identified. The antibody profiles of the corresponding serum samples were also determined and compared to ALS, and cross-reactivity with the *P. vivax* orthologous was also examined. These data demonstrate the feasibility of separately profiling the antigen specificity of antibodies from plasmablasts resulting from recent exposure, from antibodies circulating in serum that are derived from mature long lived plasma cells. Applied to various study designs involving natural and/or experimental infections with *P. falciparum* and other pathogens, this relatively simple technology will likely provide important insights into the nature of the antibody response to *P. falciparum* and other infections.

1441

DECIPHERING THE EXPRESSED ANTIBODY V GENE REPERTOIRE IN MALARIA

Severin Zinöcker¹, Jean-Nicolas Schickel², Eric R. Meffre², Susan K. Pierce¹

¹National Institutes of Health, Rockville, MD, United States, ²Yale University, New Haven, CT, United States

Individuals living in malaria endemic areas gradually acquire conventional parasite-specific memory B cells (MBC) as well as a large population of atypical MBCs that are associated with chronic infectious diseases, including AIDS. At present, we know little about the molecular mechanisms underlying the generation of conventional and atypical MBCs in response to malaria. To gain insight into these processes we are sequencing the variable (V) gene segments of the immunoglobulin heavy (H) and light (L) chain genes from hundreds of conventional and atypical MBC clones from the peripheral blood of children and adults living in a malaria endemic area of Mali. The analyses of paired V_H and V_L sequences on the clonal level will allow us to determine the germline V_H and V_L gene usage in the conventional and atypical MBC population and the relationship between the two. In addition, the number and the nature of somatic hypermutations in V_H and V_L genes will provide insights to the role of antigen-driven selection in the development of those cell types. By this analysis we aim to gain a better understanding of the generation of both conventional and atypical MBC during the acquisition of antibody-dependent immunity in malaria.

1442

THE PFRH AND EBA INVASION LIGANDS OF *PLASMODIUM FALCIPARUM* ARE IMPORTANT TARGETS OF HUMAN INHIBITORY ANTIBODIES AND FUNCTION TO EVADE NATURALLY ACQUIRED IMMUNITY

Linda Reiling¹, Kristina E. Persson², Freya J. Fowkes¹, Fiona J. McCallum³, Nimmo Gicheru⁴, Jack S. Richards¹, Christine Langer¹, Alan F. Cowman⁵, Peter M. Siba⁶, Chetan Chitnis⁷, Takafumi Tsuboi⁸, Ivo Mueller⁵, Kevin Marsh⁴, James G. Beeson¹

¹The Burnet Institute, Melbourne, Australia, ²Karolinska Institutet, Stockholm, Sweden, ³Army Malaria Institute, Enoggera, Australia, ⁴Kenya Medical Research Institute, Kilifi, Kenya, ⁵The Walter and Eliza Hall Institute, Melbourne, Australia, ⁶Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea, ⁷International Centre for Genetic Engineering and Biotechnology, New Delhi, India, ⁸Ehime University Graduate School of Medicine, Toon, Japan

Acquired antibodies are important in human immunity to malaria and can inhibit *Plasmodium falciparum* invasion of erythrocytes, but key target antigens of protective and functional antibodies are largely unknown. Phenotypic variation by *P. falciparum* merozoites can mediate the evasion of inhibitory antibodies, contributing to the capacity of *P. falciparum* to cause repeated and chronic infections. However, antigens involved in mediating immune evasion have not been defined, and studies of the function of human antibodies are limited. We have studied immune responses to *P. falciparum* reticulocyte binding homologues (Pfrh1, Pfrh2, Pfrh4, and Pfrh5) and erythrocyte-binding antigens (EBA175, EBA140, and EBA181), which are two families of invasion ligands that play important roles in invasion of erythrocytes and are potential vaccine candidates. We used novel and complementary approaches to determine the importance of Pfrh proteins and EBAs as targets of protective human and invasion-inhibitory antibodies, and we defined their role in contributing to immune evasion through variation in function. We evaluated the invasion-inhibitory activity of acquired antibodies from malaria-exposed children and adults using *P. falciparum* lines with targeted disruption of genes encoding different Pfrh and EBA ligands in functional assays, and the invasion-inhibitory activity of human affinity-purified antibodies to Pfrh and EBA ligands. Furthermore, we examined the association between antibodies to different Pfrh and EBA ligands

and protection from malaria in a longitudinal cohort study of children. Considering all data together, our findings provide important evidence that PfRh and EBA ligands are major targets of invasion-inhibitory and protective human antibodies, and that variation in the expression and function of the PfRh and EBAs mediates evasion of acquired antibodies. This knowledge will help to advance malaria vaccine development and understand how the immune response targets multiple invasion ligands to overcome the capacity of *P. falciparum* for immune evasion.

1443

DEMONSTRATION OF ENHANCED STRAIN-SPECIFIC *PLASMODIUM FALCIPARUM* MULTIFUNCTIONAL T CELL CYTOKINE EXPRESSION AMONG MALIAN CHILDREN IMMUNIZED WITH THE FMP2.1/AS02A VACCINE

Shawna F. Graves¹, Bourema Kouriba², Issa Diarra², Amadou Niangaly², Modibo Daou², Drissa Coulibaly², Yamoussa Keita², Matthew B. Laurens³, Johan Vekemans⁴, W. Ripley Ballou⁴, David Lanar⁵, Sheetij Dutta⁵, D. Grey Heppner⁵, Lorraine Soisson⁶, Carter L. Diggs⁶, Mahamadou A. Thera², Ogobara K. Doumbo², Christopher V. Plowe³, Marcelo B. Szein¹, Kirsten E. Lyke¹

¹University of Maryland, Center for Vaccine Development, Baltimore, MD, United States, ²University of Bamako, Malaria Research and Training Center, Bamako, Mali, ³University of Maryland, Center for Vaccine Development and Howard Hughes Medical Institute, University of Maryland, Baltimore, MD, United States, ⁴GlaxoSmithKline Vaccines, Rixensart, Belgium, ⁵Walter Reed Army Institute of Research, Silver Spring, MD, United States, ⁶The Malaria Vaccine Development Program, U.S. Agency for International Development, Washington, DC, United States

Based on *Plasmodium falciparum* (Pf) apical membrane antigen 1 (AMA1) from strain 3D7, the malaria vaccine candidate FMP2.1/AS02A was tested in a Phase 2 clinical trial in 400 Malian children (aged 1-6 years) randomly assigned to receive 3 doses of the AMA1 vaccine or a control rabies vaccine on days 0, 30 and 60. A subset of 10 Pf(-) (i.e., no clinical Pf episodes) and 12 Pf(+) (clinical malaria episodes with parasites with 3D7 or Fab9-type AMA1 cluster 1 loop [c1L]) AMA1 recipients, and 10 controls were randomly chosen for analysis. Peripheral blood mononuclear cells (PBMCs) isolated on days 0, 90 and 150 were stimulated with full-length 3D7 AMA1 and with c1L from strains 3D7 and Fab9 (identical to 3D7 c1L except for amino acid 197) to assess allele-specific cell-mediated responses. T cell expression of INF- γ , TNF- α , IL-2, and/or IL-17A was analyzed by 11-color flow cytometry. Among AMA1 recipients, 19/21 evaluable samples stimulated with AMA1 demonstrated significantly increased levels of INF- γ , TNF- α and IL-2 derived from CD4+ T cells by D150 compared to 0/10 in the control group ($P < 0.0001$). CD4+ cells expressing both TNF- α and IL-2 were increased in Pf(-) children (median=28.4% of cytokine-expressing cells) compared to Pf(+) children in the AMA1 vaccine group (median=8.6% of cytokine-expressing cells). Low prevalence of double- (INF- γ +TNF- α +) and triple-positive (INF- γ +TNF- α +IL-2+) CD4+ cytokine-expressing cells were noted. When PBMCs were stimulated with c1L from 3D7 and Fab9 separately, 5/19 AMA1 recipients with an AMA1-specific CD4+ response had a significant response to one or both c1L. This suggests that AMA1 vaccination induced an AMA1-specific CD4+ response; however, recognition of the vaccine antigen is not dependent upon c1L alone. In summary, AMA1-specific T cell cytokine expression was notably increased in children vaccinated with an AMA1-based vaccine compared to rabies. The possible role of CD4+ TNF- α +IL-2+-expressing T cells in vaccine-induced strain-specific protection against clinical malaria requires further exploration.

1444

DETECTION AND SEMIQUANTITATION OF VENOM AND ANTIVENOM IN THE BLOOD OF TWENTY PATIENTS WITH EVIDENT NEUROTOXIC ENVENOMATION IN GUINEA

Blanca Ramos-Cerrillo¹, Mamadou C. Baldé², Achille Massougbodji³, Jean-Philippe Chippaux⁴, Roberto P. Stock¹

¹Instituto de Biotecnología (Universidad Nacional Autónoma de México), Cuernavaca, Mexico, ²Institut Pasteur de Guinée, Kindia, Guinea, ³Faculté des Sciences de la Santé (UAC), Cotonou, Benin, ⁴Institut de Recherche pour le Développement, Paris, France

In Guinea, elapids are responsible for about 20% of envenomations. Recent studies have shown that case fatality rate falls between 15 and 30% regardless of treatment. We obtained blood samples from 20 patients who presented typical neurotoxic syndromes. All patients were treated with 40 ml of antivenom neutralizing the main species of Elapidae in the region: *Dendroaspis polylepis* (Dp), *D. viridis* (Dv), *Naja melanoleuca* (Nm) and *N. nigricollis* (Nn). Blood samples were spotted onto Guthrie paper before antivenom treatment (hour 0, H0) and two hours after antivenom administration (H2). The samples were analyzed by a custom sandwich ELISA for venom of each of the four species using rabbit antibodies purified against the venom of each species by affinity chromatography and adsorbed against the other three species. The presence of antivenom was also established for all samples. Five patients died. Samples on H0 were missing for 2 patients and samples on H2 were missing for another 2. Of the 18 H0 samples tested, a clear and high venom signal was detected in 4: 2 patients who died were strongly positive for Dp, including a patient who died before treatment, 1 patient was strongly positive for Dv (who also died) and one patient who survived was strongly positive for Nn. Antivenom was detected in the H2 samples of 14 patients. For the 2 patients for whom a clear venom signal was detected at H0 and for whom H2 samples were available, residual venom was detected using an ELISA assay based on immunopurified horse antibodies. A competition ELISA test in which venom was titrated with increasing amounts of antivenom showed that the venom detected by means of this ELISA assay is likely to be free residual venom. The ELISA assays performed on samples spotted and dried on Guthrie paper are robust, very specific but not very sensitive. They have nonetheless permitted, for the first time, an immunodiagnosis of the species of African elapid causing envenomation in 4 of 18 patients, including those 3 (of 5) who died during the study. They have also shown that residual "free" venom was present in two patients after antivenom administration, suggesting that the dose of antivenom administered may have been insufficient to completely neutralize the venom present in some of these victims of snakebite.

1445

USE OF JAPANESE ENCEPHALITIS VACCINE IN U.S. TRAVEL MEDICINE PRACTICES IN GLOBAL TRAVEPINET

Bhushan Deshpande¹, Sowmya R. Rao², Gary Brunette³, Mark J. Sotir³, Mark D. Gershman³, Emily S. Jentes³, Susan L. Hills⁴, Marc A. Fischer⁴, Edward T. Ryan⁵, Regina C. LaRocque⁵

¹Tufts University, Medford, MA, United States, ²University of Massachusetts Medical School, Worcester, MA, United States, ³Centers for Disease Control and Prevention, Atlanta, GA, United States, ⁴Centers for Disease Control and Prevention, Fort Collins, CO, United States, ⁵Massachusetts General Hospital, Boston, MA, United States

Japanese encephalitis (JE) vaccine is recommended for high-risk travelers to Asia and the western Pacific. Few data regarding the use of this vaccine in clinical practice are available. We evaluated international travelers to JE-endemic regions who were seen at U.S. Global TravEpiNet (GTEN) sites between September 2009 and August 2012, when IXIARO was in use. We categorized travelers as higher or lower risk for JE based on the destination country, travel plans, and duration of travel. We compared the demographic and clinical features of higher and lower JE risk travelers and

performed multivariable analyses to identify factors that were associated with travelers not being offered or declining the JE vaccine. We identified 711 higher JE risk travelers and 7,578 lower JE risk travelers in our analysis. Higher JE risk travelers were younger than lower JE risk travelers (median age 29 years vs. 40 years, $p < 0.001$) and traveled for longer durations of time (median 50 days vs. 14 days, $p < 0.001$). 43% of higher JE risk travelers were offered the JE vaccine, and 62% of these travelers accepted it. Short time to departure, rural travel, travel to visit friends and relatives, leisure travel, and travel for humanitarian service work were each independent predictors of declining the JE vaccine. Additionally, 40% of higher JE risk travelers were judged by their clinician to not require the JE vaccine. Travel to visit friends and relatives, leisure travel, travel to India, and travel to China were independent predictors of a higher JE risk traveler not being offered the JE vaccine. Clinicians did not recommend the JE vaccine to many travelers who met the indications offered by the Advisory Committee on Immunization Practices, and there are disparities with regard to subpopulations that receive the vaccine.

1446

EOSINOPHILIA AS A POTENTIAL SURROGATE FOR THE DIAGNOSIS OF STRONGYLOIDIASIS IN AN IMMIGRANT POPULATION AND THE UTILITY OF ABSENT SS-NIE ANTIBODIES AS A BIOMARKER FOR CURE

Rojelio Mejia¹, Kathryn E. Spates², Nicole Holland², Amara G. Pabon², JeanAnne Ware², Thomas B. Nutman²

¹National School of Tropical Medicine, Baylor College of Medicine, Houston, TX, United States, ²National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, United States

Determining the cause of persistent eosinophilia in immigrants to the United States can be hampered by costs needed to evaluate suspected parasitic infections. Thus, diagnosing eosinophilia-causing helminth infections by stool examination or serology is often beyond the means of community health clinics that commonly serve immigrant populations. To define the causes of persistent eosinophilia among an immigrant population seen at a single community free health clinic, 54 patients (originally from Central and South America, Africa, Asia and the Middle East) who arrived in the United States 1-27 years (median 7 years) previously--were found to have an absolute eosinophil count (AEC) > 500 uL and were referred to the National Institutes of Health for further testing. Of the 54 referred patients, 43 (80%) had positive *Strongyloides stercoralis* (Ss)-specific serology. 1/43 (2%) also had schistosomiasis, 3/43 (7%) hookworm, and 2/43 (5%) trichuriasis. There were no differences in baseline eosinophil counts and serum IgE levels between those with Ss and the 11/54 without (probably reflecting the referral criteria). All patients with a definitive parasitologic diagnosis received ivermectin and (when appropriate) praziquantel and/or albendazole treatment and followed over the course of a year. Not unexpectedly, there was a dramatic and significant ($p < 0.0002$) decrease in AEC following treatment with all returning to normal levels by 1 year. IgE levels also fell dramatically following treatment. Most importantly, antibodies to the *Strongyloides*-specific recombinant antigen (Ss-NIE) using a luciferase immunoprecipitation assay (LIPS) also became negative in all those with Ss treated successfully with ivermectin. Thus, in community clinics that provide health care to immigrants well after arrival in the United States, an AEC can be used as a surrogate for stool examination, and serology may be a trigger for empiric treatment when testing is limited by cost. If available, newer serologic tests may replace insensitive stool examinations as tests of cure.

1447

RISK FACTORS AND SEROPREVALENCE OF TRYPANOSOMA CRUZI INFECTION IN TEXAS

Melissa S. Nolan, Peter Hotez, Laila Woc-Colburn, Kristy Murray
Baylor College of Medicine, Houston, TX, United States

Chagas' disease has emerged as an important neglected tropical disease in the United States; particularly in Texas. Chagas' disease is caused when the parasite *Trypanosoma cruzi* (*T. cruzi*) is transmitted to humans by a *Triatominae* insect. One-third will develop chronic infection that can result in cardiac myopathy and death. This study aimed to determine risk factors and estimate disease burden of Chagas disease in Texas. Data was collected from five major blood centers in Texas on those tested for *T. cruzi* from 2008-2012. We only included original donations tested from each donor, and duplicate donations were excluded for seroprevalence analysis by stratification. Risk factors were analyzed by zip-codes with and without a reported case to the Chagas' Biovigilance Network and/or a major Texas blood center. We found 1 per 3,500 population were positive for *T. cruzi* in Texas. Seroprevalence was similar between genders. Infection rate increased with age with ages 41-50 (40 per 100,000) and 51+ (41 per 100,000) having the highest infection rate. As expected, Hispanics had the highest infection rate (43 per 100,000). Caucasians (14 per 100,000) and African Americans (24 per 100,000) had the lowest infection rates. We calculated a total cost to society of \$215 million for these cases. *T. cruzi* positive cases were significantly more likely to live in zip-codes that have a higher percentage of foreign born residents ($p < 0.001$) and urban land use ($p < 0.001$). In conclusion, blood Centers are an important component in understanding *T. cruzi* transmission in Texas. Approximately 1 per 3,500 blood donors test positive for *T. cruzi*. Chronic cases accrue \$215 million in lifetime societal cost to Texans. Minorities, urban areas, and areas with high foreign born population are at highest risk for *T. cruzi* infection.

1448

SPATIAL DISTRIBUTION OF PODOCONIOSIS IN RELATION TO ENVIRONMENTAL FACTORS IN ETHIOPIA: A HISTORICAL REVIEW

Kebede Deribe¹, Simon J. Brooker², Rachel L. Pullan³, Asrat Hailu⁴, Fikre Enquesselasse⁵, Richard Reithinger⁶, Melanie Newport⁷, Gail Davey⁷

¹School of Public Health, Addis Ababa University, Addis Ababa, Ethiopia and Brighton and Sussex Medical School, Falmer, Brighton, United Kingdom, Addis Ababa, Ethiopia, ²Kenya Medical Research Institute-Wellcome Trust Research Programme, Nairobi, Kenya and Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom, ³Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom, ⁴School of Medicine, Addis Ababa University, Addis Ababa, Ethiopia, ⁵School of Public Health, Addis Ababa University, Addis Ababa, Ethiopia, ⁶Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom, School of Public Health and Health Sciences, George Washington University, Washington, DC, RTI International, Washington, DC, United States, ⁷Brighton and Sussex Medical School, Falmer, Brighton, United Kingdom

An up-to-date and reliable map of podoconiosis is needed to design geographically targeted and cost-effective intervention in Ethiopia. Identifying the ecological correlates of the distribution of podoconiosis is the first step for risk and distribution maps. The objective of this study was to investigate the spatial distribution and ecological correlates of podoconiosis using historical and contemporary survey data. Data on the observed prevalence of podoconiosis were abstracted from published and unpublished literature into a standardized database, according to strict inclusion and exclusion criteria. In total, 10 studies conducted between 1969 and 2012 were included through structured searches, and data were available for 401,674 individuals older than 15 years of age from 229 locations. A range of high resolution environmental factors were

investigated to determine their association with podoconiosis prevalence, using logistic regression. The prevalence of podoconiosis in Ethiopia was estimated at 3.4% (95% CI: 3.3%-3.4%) with significant regional variation. We identified significant associations between altitude, mean annual Land Surface Temperature (LST), mean annual precipitation, topography of the land and fine soil texture and high prevalence of podoconiosis ($p < 0.001$). The derived maps indicate both widespread occurrence of podoconiosis and a marked variability in prevalence of podoconiosis, with prevalence typically highest at altitudes > 1500 m above sea level (masl), with > 1500 mm annual rainfall and mean annual LST of 19-21°C. No (or very little) podoconiosis occurred at altitudes < 1225 masl, with annual rainfall < 900 mm, and mean annual LST of > 24 °C. Podoconiosis remains a public health problem in Ethiopia over considerable areas of the country, but exhibits marked geographical variation associated in part with key environmental factors. This is work in progress and the results presented here will be refined in future work.

1449

DISCOVERING THE PATHOGENS OF CENTRAL NERVOUS SYSTEM INFECTION IN NEPAL

Abhisek Giri¹, Amit Arjyal¹, Samir Koirala¹, Abhilasha Karkey¹, Sabina Dangol¹, Sudeep Dhoj Thapa¹, Olita Shilpakar¹, Rishav Shrestha¹, **Radheshyam Krishna KC²**, Le Van Tan³, Jeremy Farrar⁴, Buddha Basnyat¹

¹Oxford University Clinical Research Unit-Patan Hospital, Kathmandu, Nepal, ²Patan Academy of Health Sciences, Kathmandu, Nepal, ³Oxford University Clinical Research Unit-Vietnam, Ho Chi Minh City, Vietnam, ⁴Center for Tropical Medicine, Oxford University, Oxford, London, United Kingdom

Central nervous system (CNS) infection is one of the common causes of hospital admission in Nepal. Due to the absence of specific tests to diagnose the definitive cause of meningitis, the treatment is often empirical. The condition is more challenging when there is prior use of antibiotics. Such-conditions alter the possible outcomes, which ultimately affects treatment and management. Therefore, the aim of this study is to find the possible etiological agents responsible for meningitis in adults in Nepal. We conducted a prospective hospital based study to identify the possible pathogens of CNS infections in adults admitted in Patan Hospital from February 2009-April 2011. The pathogens of CNS infections were confirmed in cerebrospinal fluid (CSF) using molecular diagnostics, culture (bacteria) and serology. 87 patients were recruited for the study and the etiological diagnosis was established in 38% (n=33). The bacterial pathogens identified were *Neisseria meningitidis* (n=6); *Streptococcus pneumoniae* (n=5) and *Staphylococcus aureus* (n=2) in 13/87(14%). Enteroviruses were found in 12/87 (13%); Herpes Simplex virus (HSV) in 2/87(2%). IgM against Japanese encephalitis virus (JEV) was detected in CSF of 11/73 (15%) tested samples. In conclusion, our study is the first (RT) PCR and serology based CSF analysis from Kathmandu, Nepal that attempts to identify the causative organisms of infectious syndromes of the central nervous system in adults. JEV and enteroviruses were the most commonly detected pathogens.

1450

SEVERE MALARIAL ANEMIA IS ASSOCIATED WITH LONG-TERM NEUROCOGNITIVE IMPAIRMENT

Paul Bangirana¹, Robert O. Opoka¹, Richard Idro¹, James S. Hodges², Michael J. Boivin³, Chandy C. John²

¹Makerere University, Kampala, Uganda, ²University of Minnesota, Minneapolis, MN, United States, ³Michigan State University, East Lansing, MI, United States

Cerebral malaria (CM) is associated with long-term cognitive impairment in children 5 years of age and older. No prospective studies have assessed cognitive impairment in children with CM < 5 years of age, or in children with severe malarial anemia (SMA), a more common manifestation of

severe malaria that is estimated to affect > 5 million children annually. Children < 5 years of age who presented to Mulago Hospital, Kampala, Uganda, with CM (n=80) or SMA (n=86) were assessed for overall cognitive function, attention, and declarative memory one week after discharge and 6 and 12 months later. Age-adjusted z-scores for each domain were generated from the scores of 61 healthy community children (CC), who were also tested at enrollment and 6 and 12 months later. Groups were compared using mixed linear models. For the full one-year period of follow-up, children with CM had significantly worse scores than CC in overall cognitive function (-1.00 vs -0.12; $P < 0.0001$), attention (-0.51 vs -0.06; $P = 0.004$), and declarative memory (-0.41 vs 0.04; $P = 0.0003$). Children with SMA also had significantly worse scores than CC in overall cognitive function (-0.52 vs -0.12; $P < 0.0001$) and attention (-0.25 vs -0.06; $P = 0.03$), but not declarative memory (-0.03 vs 0.04; $P = 0.99$). Scores for overall cognitive function and attention did not differ significantly between children with CM vs. SMA. In children < 5 years of age, CM is associated with long-term impairment in overall cognitive function, attention, and declarative memory, and SMA is associated with long-term impairment in overall cognitive function and attention. SMA may be a major cause of long-term neurocognitive impairment in children in sub-Saharan Africa.

1451

EPIDEMIOLOGICAL, CLINICAL AND LABORATORY DESCRIPTION OF ONCHOCERCIASIS IN AN AREA OF HIGH PREVALENCE - JIMMA, ETHIOPIA, 2013

Francisca Abanyie¹, Paul Cantey¹, Sindew Mekasha², Markos Sleshi², Nicholas Ayebazibwe³, Shoshana Oberstein¹, Elizabeth Thiele¹, Anne Moore¹, Mark Eberhard¹, Vitaliano Cama¹

¹Centers for Disease Control and Prevention, Atlanta, GA, United States, ²Ethiopian Health and Nutrition Research Institute, Addis Ababa, Ethiopia, ³African Field Epidemiology Network, Kampala, Uganda

Onchocerciasis, transmitted by blackflies, still infects at least 37 million people worldwide, but elimination of onchocerciasis through mass drug administration (MDA) with ivermectin is feasible in parts of Africa. However, evidence-based tools to evaluate program endpoints are lacking. Clinical specimens characterized with epidemiologic, clinical, and laboratory data were collected and analyzed to evaluate the existing diagnostic tests for onchocerciasis and to identify the best tests to measure programmatic endpoints. Five-hundred specimens were collected in three onchocerciasis-endemic areas in Jimma, Ethiopia, where one round of ivermectin MDA had been given five months before the study. Laboratory analysis in country included blood smears to detect *Loa loa* and *Mansonella perstans*, immunochromatographic card tests (ICT) for filariasis, and skin snip examination for *Onchocerca volvulus*. Plasma, serum, blood smears, dried blood spots, and preserved skin snips were sent to CDC for further analysis. The median age of participants was 45 (range 6-90 years); 276 (55%) were male. Though only 57 (11%) participants reported living near a river, 244 (49%) spent the majority of the day near rivers where blackflies typically bite. Eight (2%) participants had *O. volvulus* microfilaria present in the anterior chamber (N=2) or cornea (N=6). At least one skin nodule was noted in 319 (64%) participants (range 1-11); 312 (62%) had other onchocercal skin manifestations; 74 (15%) had evidence of lymphedema. The skin snip was positive for *O. volvulus* in 19 (4%) participants, with a mean load (average of both snips) among those with at least one positive snip of 19.5 microfilaria/slide (range 0.5-180); 15 (3%) had positive ICTs. The paucity of positive skin snips despite the high prevalence of nodules is unexplained and needs further investigation. *Wuchereria bancrofti* may be co-endemic in the areas studied. Additional laboratory evaluation is pending. The performance of these tests in the African context will help determine their use in the evaluation of elimination program endpoints.

COMPLEMENTARY USE OF COMPREHENSIVE SURVEILLANCE AND TRANSMISSION ASSESSMENT SURVEYS FOR ASSESSING PERSISTENCE OF LYMPHATIC FILARIASIS IN SRI LANKA FOLLOWING MASS DRUG ADMINISTRATION

Udaya S. Ranasinghe¹, Ramakrishna U. Rao², Kumara C. Nagodavithana¹, Sandhya D. Samarasekera¹, Sunil Settinayake¹, Gary J. Weil²

¹Antifilaria Campaign, Ministry of Health and Nutrition, Colombo, Sri Lanka, ²Washington University School of Medicine, St. Louis, MO, United States

The Sri Lankan Anti-Filariasis Campaign (AFC) provided mass drug administration (annual diethylcarbamazine plus albendazole) according to WHO guidelines to some 10 million people in 8 endemic districts between 2002 and 2006. All districts met WHO criteria for lymphatic filariasis (LF) elimination in 2008, but spot surveys showed low-level persistence of microfilaria (Mf) in some sentinel sites. Comprehensive surveillance of suspected hotspots (in 2 public health inspector areas per district) was initiated in early 2010, and WHO recommended TAS surveys were conducted in 2012-13. Comprehensive surveillance included community surveys for Mf and filarial antigenemia (ICT), school surveys for ICT and anti-filarial antibodies (Bm14 ELISA) in children 6-8 years of age, and mosquito surveys to detect filarial DNA in *Culex* mosquitoes collected by gravid traps (molecular xenomonitoring, MX). TAS surveys involved ICT testing of ~1,500 children in 30 to 35 randomly selected schools in each evaluation unit. Provisional targets for LF elimination in hotspot surveys were <0.5% for Mf (community surveys), <2% for ICT (community), <2% for antibody in first grade primary school children, and <0.25% for filarial DNA in mosquitoes. We now report results from 13 hot spot surveys that were conducted in 6 formerly endemic districts. Community Mf and ICT prevalence rates were between 0-0.9% and 0-3.4%, respectively. ICT rates in school children were < 1% in all 13 sites, but antibody rates in school children exceeded 2% in 9 sites. Filarial DNA rates in mosquitoes exceeded the target rate in 7 of 13 study sites, and all of these LF indicators exceeded our targets in one site. Thus, many hot spots had evidence of low level persistence of LF some 6 years after MDA. TAS survey results showed that ICT rates in primary school children satisfied WHO targets in all 8 districts. These results suggest that antibody testing of children and MX are more sensitive tools for detecting low-level persistence of filariasis in communities than TAS. We recommend using enhanced surveillance tools to complement TAS surveys for post-MDA surveillance. We also recommend close follow-up for areas that failed to meet elimination targets to determine whether further intervention is required in these areas.

ACTIVE TRANSMISSION OF FILARIASIS IN ZANZIBAR AFTER MDA HAD BEEN STOPPED FOR FIVE YEARS

Maria Rebollo Polo¹, Khlafan Mohammed², Said Mohammed³, Ali Iddi Simba Khamis², Brent Thomas¹, Jorge Cano⁴, Lorenzo Savioli⁵, Moses J. Bockarie¹

¹Liverpool School of Tropical Medicine, Liverpool, United Kingdom, ²MoH, Zanzibar, United Republic of Tanzania, ³Public Health Laboratory, Chake Chake, Pemba, Zanzibar, United Republic of Tanzania, ⁴London School of Hygiene Tropical Medicine, London, United Kingdom, ⁵World Health Organization, Geneva, Switzerland

The Global Programme to Eliminate Lymphatic Filariasis (GPELF) recommends annual mass drug administration for 4-6 years to interrupt transmission of the disease. Zanzibar, in the United Republic of Tanzania, was the first country to complete five rounds of treatment using a combination of albendazole and ivermectin at 100% geographic coverage and achieving effective coverage rate of over 65% during all five years. MDA implemented through filarial prevention assistants (FPAs) selected that were resident in the communities and aware of public health

activities to various degrees. Total treatment coverage averaged from 70 to 80% in all five rounds mainly due to a very effective social mobilization programme. Impact assessment at two sentinel sites showed that the prevalence and intensity of microfilaria decreased significantly after the first round of MDA and the decline continued after subsequent MDA rounds. MDA was stopped in 2006 after sentinel site surveys revealed prevalence below 1%. In early 2012, transmission assessment surveys (TAS) were conducted to determine if transmission of LF had been interrupted on the two islands. The TAS surveys involved a total of 72 schools; 36 from each of the two Evaluation Units (EUs) in Pemba and Unguja islands. A total of 1298 children were surveyed on Pemba where 70 (5.4%) were found to be positive. In Unguja, 19 (0.95%) of the 1980 pupils tested were positive. The EU on Pemba exceeded the critical cut-off of 18, thereby failing the TAS criteria and implying that transmission had resumed. On the other hand the number of positives from Unguja just fell short of 20, suggesting that the level of exposure, though high, may not be sufficient to sustain transmission. Based on the TAS results it was recommended that MDA be restarted on both islands in 2013 because of the efficiency of the *Culex* vector. Another TAS will be conducted after two rounds. This study confirms the recommendation that effective surveillance and possible continued actions after the achievement of the elimination target may be required to prevent re-establishment of transmission

TRANSMISSION OF ONCHOCERCIASIS IN CENTRAL NIGERIA: ONGOING TRANSMISSION OR DISEASE ELIMINATION?

Darin Evans¹, Kal Alphonsus², John Umaru², Abel Eigege², Elias Pede³, Christopher Ubugadu⁴, Carlos Gonzales⁵, Frank Richards¹

¹The Carter Center, Atlanta, GA, United States, ²The Carter Center, Jos, Nigeria, ³Plateau State Ministry of Health, Jos, Nigeria, ⁴Nasarawa State Ministry of Health, Lafia, Nigeria, ⁵CCI, Chula Vista, CA, United States

Mass drug administration (MDA) with ivermectin is the WHO recommended strategy for control of onchocerciasis. Recent evidence has shown that after 15-17 years of treatment, elimination of the disease in Africa may be possible. In Plateau and Nasarawa states in North-Central Nigeria, MDA has been ongoing since 1991. Since 2000, albendazole has been co-administered with ivermectin for treatment of lymphatic filariasis (LF), which is co-endemic. In 2009, 5 districts were determined to have stopped LF transmission. We set out to evaluate the status of onchocerciasis transmission in these 5 districts to determine onchocerciasis transmission had also been interrupted. Using the 2001, WHO criteria for elimination of onchocerciasis, we sought to achieve a microfilariae (MF) and seroprevalence of <1/1,000 infected individuals and a rate of infective blackflies of <0.05/1,000. We evaluated adults and children in six sentinel sites and children only in eight spot-check villages. Skin snips, blood spots, and nodules were collected and fly catches were conducted at six river sites. We sampled a total of 5,182 persons: 4,441 children ages 3 to 12 and 746 adults ≥20 years in 14 communities. In adults, Mf prevalence had decreased 99.3% from a mean baseline of 43.0% to 0.27% (p<0.001). In children, no Mf were detected but a seroprevalence of 0.16% (n=7, 0.32% upper 95%CI) was found. A total of 1,568 blackflies were assessed in six capture sites. While no infective larvae were found, the number of flies caught was insufficient for determining whether transmission has been interrupted. In conclusion, current criteria from APOC use parasitologic and entomologic indicators for determining elimination status. In areas where the blackfly vector is less abundant, however, the number of flies needed to definitively decide may not be possible to obtain in a timely manner. In Plateau and Nasarawa states, we have found that, while we meet the parasitologic criteria, we cannot achieve the necessary number of flies needed to definitively determine if transmission has been interrupted despite the fact that no infective flies have been found. In this case, we have opted to include the 2001 WHO criteria to examine serologic evidence in children and have found that transmission may be ongoing.

1455

MALARIA AND FILARIASIS COINFECTIONS IN PAPUA NEW GUINEA

Daniel J. Tisch¹, Rajeev K. Mehlotra¹, Zachary Kloos¹, Peter M. Siba², James W. Kazura¹, Peter A. Zimmerman¹

¹Case Western Reserve University, Cleveland, OH, United States, ²Papua New Guinea Institute for Medical Research, Goroka, Papua New Guinea

Malaria and lymphatic filariasis (LF) elimination programs are predicated on efficient and effective surveillance and monitoring tools. Simultaneous detection of all four primary malaria species and *Wuchereria bancrofti* (Wb) using a post-PCR oligonucleotide ligation detection reaction-fluorescent microsphere assay (LDR-FMA) has been recently demonstrated in samples from the Dreikikir region of Papua New Guinea where malaria and filariasis are co-endemic and transmitted by Anopheline mosquitoes. In this setting mass drug administration has been deployed against LF beginning in the mid 1990s and long-lasting insecticide-treated nets were distributed in 2009. The present study evaluates a population of 2700 individuals in this region to quantify co-infection dynamics and characterize the complex epidemiology of these important parasitic diseases. Overall, our results showed that 84.1% of the individuals tested were assay-positive for at least one malaria species and 13.4% were positive for Wb. Among individuals infected with *Plasmodium* species parasites, 38.0%, 29.4%, 13.4%, and 3.3% of individuals were infected with 1, 2, 3, or 4 species of malaria, respectively. Diagnosis of Wb infection prevalence did not differ significantly according to the quantity of malaria species co-infections ($p=0.350$), even after stratifying for intensity of Wb infection (using ICT card grade or microfilaremia) or malaria LDR-FMA optical densities. Furthermore, Wb prevalence was not significantly different among malaria positive or negative individuals (13.6% vs 12.0%, $p = 0.380$). Interestingly, we observed that Wb infections were slightly more common in malaria infected (37.6) vs. uninfected individuals (28.0%) ($p=0.044$) among the subset of individuals residing in a geographic area traditionally characterized as having higher LF transmission prevalence. 35.6% of individuals in the higher LF transmission site and 7.6% of individuals in the lower LF transmission site were Wb positive by LDR-FMA whereas malaria prevalence was similar across sites (79.5% and 85.6%, respectively). Simultaneous multiple parasite detection such as LDR-FMA may be useful to integrated disease monitoring and elimination strategies.

1456

EVALUATION OF TEN YEARS IMPACT OF IVERMECTIN TREATMENT FOR ONCHOCERCIASIS ON LYMPHATIC FILARIAIS: A CASE STUDY FOR THREE OVERLAPPING DISTRICTS IN TANGA REGION, TANZANIA

Upendo J. Mwingira¹, Maria J. Chikawe¹, Mwelecele Malecela², Oscar Kaitaba³, Rehema Maggid⁴, Aferwork Hailemariam⁵, Andreas Nshala³

¹NIMR/NTD Control Programme, Dar es Salaam, United Republic of Tanzania, ²NIMR, Dar es Salaam, United Republic of Tanzania, ³NTD Control Programme, Dar es Salaam, United Republic of Tanzania, ⁴NTD Control Programme, Tanga, United Republic of Tanzania, ⁵APOC, Ougadougou, Burkina Faso

Tanzania is endemic with 5 of the PCT targeted NTDs namely Lymphatic Filariasis - LF, Onchocerciasis, Trachoma, Schistosomiasis and Soil Transmitted Helminthiasis - STH. MDA activities implemented in phases in various implementation units. Tanga region has been implementing consecutive Ivermectin MDA for Onchocerciasis control since 2000 and Ivermectin + Albendazole MDA for LF since 2004 and has completed over 5 effective Mass Drug Distribution rounds and the average coverage being above 65%. The study aim was to evaluate the impact of 10 rounds of Ivermectin treatment for Onchocerciasis on Lymphatic Filariasis. The Survey districts were Lushoto, Muheza and Korogwe. Six sites for lymphatic filariasis were selected from the participating districts. One village with high prevalence of Onchocerciasis and another one with high prevalence

of Lymphatic Filariasis were selected from each district. All hamlets in selected villages were surveyed. A cluster survey was applied involving communities. For LF survey, eligible population were individuals aged 5 years and above. A systematic random sampling of households was done to get 600 participants from each village. Enrolled individuals from the community were tested for Circulating Filarial Antigen (CFA) using ICTs. 100microlitres of blood sample from participants was collected from a finger prick, ICT was done and results provided after 10 minutes. For all ICT positive results night blood was collected between 10pm and midnight and microfilaria(mf) count was done using counting chamber technique. A total of 1887 people participated in the LF survey, 1020 (54.1%) were females and 867(45.9%) were males. All of the participants were tested for CFA with ICT, 40(2.1%) were ICT positive. Mf count was done to 34 of the ICT positives and 6 were positive. Results indicate that LF is still prevalent in the evaluated districts with different CFA prevalence levels and thus MDA should continue for few more round before conducting Transmission assessments survey (TAS).

1457

FORECASTING DEMAND FOR ONCHOCERCIASIS TREATMENT TO ACHIEVE ELIMINATION AND ERADICATION

Young Eun Kim¹, Jan H.F. Remme², Peter Steinmann¹, Fabrizio Tediosi¹

¹Swiss Tropical and Public Health Institute, Basel, Switzerland,

²Independent Consultant, Ornex, France

Recent evidence indicates that mass onchocerciasis treatment with ivermectin can interrupt transmission and eliminate the parasite in endemic foci if high treatment coverage greater than 65% is maintained for a decade or more. Realistic estimates of the coverage levels needed to achieve elimination and eradication can inform donors' investment decisions. We estimated the number of treatments needed to go from the current control level to elimination and eradication of onchocerciasis as the geographic and therapeutic coverage is scaled up. Scenarios were developed assuming treatment continues until the population of female adult worms is reduced to a threshold where it is expected to irreversibly move to its demise. The number of treatments required, from 2012 to 2040, was predicted using historical data. The years of introduction and the coverage rates were collected from APOC treatment database, while for untreated areas they were predicted based on the expected launching year of APOC's budget plan, political and operational challenges, nodule prevalence, at-risk population, and average treatment coverage rates in the country. The treatment duration was predicted based on the existing results of a micro simulation model (ONCHOSIM). The estimated number of treatments needed in sub-Saharan countries is around 75 million in 2012. If the current strategy continues, the annual demand will increase to around 120 million by 2030. In the elimination scenario, the annual demand would decrease to around 30 million by 2030 because many endemic areas will not require treatment any longer. The treatment demand is expected to further decrease to less than 12 million by 2030 in the eradication scenario, whereby challenging areas with post-conflict situation or co-endemicity with loiasis will be treated with locally tailored approaches, so that treatment won't be required in the end. The results show that scaling up ivermectin coverage to achieve elimination and eradication would eventually lead to potential cost savings.

1458

WHAT HAVE WE LEARNED FROM GWAS STUDIES OF INSECTICIDE RESISTANCE IN ANOPHELES GAMBIAE?

David Weetman, Craig S. Wilding, Martin J. Donnelly
Liverpool School of Tropical Medicine, Liverpool, United Kingdom

Driven by advances in marker availability and screening technologies, the last six years has seen an explosion of genome-wide association studies (GWAS) in humans, most aimed at detecting genetic variants linked to common diseases. With a well-assembled genome, unquestioned medical

importance, and dwindling insecticide susceptibility a major threat to control, *Anopheles gambiae* insecticide resistance represented a natural target for the earliest GWAS in insects. Employing sequentially increasing numbers of markers, our studies have confirmed known causal variants and provided new field-applicable markers for pyrethroid resistance, but, in common with GWAS in humans, have yet to discover the novel variants of major effect that were initially anticipated. We highlight a number of design-related issues, recognition of which will aid future work. These include: (1) poor performance of designs inherited from human studies for mosquitoes and especially for insecticide resistance; (2) closer attention to phenotype definition, and (3) greater attention to environmental variation as a source of 'missing' trait heritability. With appropriate design alterations, GWAS can benefit considerably from imminent advances such as quality genome assemblies for multiple *Anopheles* disease vectors and a validated SNP-call database for *An. gambiae*.

1459

A SINGLE MUTATION IN THE GLUTATHIONE-S TRANSFERASE GENE (GSTE2) IS RESPONSIBLE FOR INSECTICIDE RESISTANCE IN THE MAJOR MALARIA ANOPHELES FUNESTUS

Jacob M. Riveron¹, Cristina Yunta¹, Sulaiman S. Ibrahim¹, Helen Irving¹, Rousseau Djouaka², Hanafy M. Ismail¹, **Charles Wondji**¹
¹Liverpool School of Tropical Medicine, Liverpool, United Kingdom, ²IITA, Cotonou, Benin

Metabolic resistance to insecticides is the biggest threat to the continued effectiveness of existing malaria vector control interventions. But its underlying molecular and genetic basis, crucial for successful resistance management, remains poorly characterised. In this study, using a genome-wide transcriptional analysis, we showed that the up-regulation of the glutathione-S transferase gene GSTe2 is strongly associated with DDT resistance. Using a GAL4/UAS transgenic expression of this gene in *Drosophila*, we demonstrated that over-transcription of this gene alone was necessary and sufficient to confer DDT resistance but more importantly also cross-resistance to pyrethroids. We showed that besides quantitative differences, qualitative changes in GSTe2 were also significantly contributing to the high DDT resistance as *In vitro* metabolic assays demonstrated that the resistant allele was more active in metabolizing DDT than the susceptible alleles. For the first time in mosquitoes, we identified an amino acid change (L119F) that strongly associates with DDT resistance and designed a molecular diagnostic assay that accurately detects the resistance in field populations. Structural analysis of the GSTe2 indicated that L119F located in the DDT-binding pocket confers the high DDT resistance by significantly increasing the size of the DDT binding cavity allowing more binding of the DDT molecule leading to its increased metabolism. The distribution of this L119F mutation across Africa shows a strong correlation with known patterns of DDT resistance. Furthermore, we showed that GSTe2 is under strong directional selection in resistant populations, and a restriction of gene flow is observed between African regions, enabling the prediction of the future spread of this resistance. This study represents a comprehensive and detailed dissection of the genetic, molecular and structural basis of metabolic resistance to insecticides and provides the first resistance marker for metabolic resistance in mosquitoes.

1460

INSECTICIDE RESISTANCE IN SYMPATRIC ANOPHELES GAMBIAE AND AN. ARABIENSIS FROM UGANDA: EVIDENCE FOR EVOLUTIONARY CONVERGENCE IN THE RESISTANCE ASSOCIATED GLUTATHIONE-S TRANSFERASE GSTE4

Craig S. Wilding¹, David Weetman¹, Henry D. Mawejje², Emily J. Rippon¹, Martin J. Donnelly¹

¹Liverpool School of Tropical Medicine, Liverpool, United Kingdom,

²Infectious Diseases Research Collaboration, Kampala, Uganda

In Tororo, eastern Uganda, a high malaria transmission setting, and Jinja (approximately 110km from Tororo) where transmission intensity is lower, we have demonstrated extensive resistance to pyrethroid insecticides. This in the absence of universal distribution of ITNs or any IRS programme. In whole-genome microarray analysis of pyrethroid resistant *Anopheles gambiae* (Tororo) and *An. arabiensis* (Jinja) the glutathione-S transferase GSTe4 is significantly up-regulated in both species, suggestive of a role in the resistance phenotype. Where *An. gambiae* and *An. arabiensis* are sympatric we find a low level (0.22% $N=7,202$) of hybrid samples, and using a multiplex SNP array we demonstrate that in addition to F1s there are individuals which are the progeny of advanced backcrossing. This raised the possibility that introgression of selected genes, such as an insecticide resistance associated GSTe4 variant, may have occurred. Sequencing of GSTe4 haplotypes was not supportive of our hypothesis of introgression of GSTe4 variants but comparison of non-synonymous and synonymous changes were suggestive of marked functional constraints/sequence convergence of GSTe4. Biochemical assays, showed that whilst GSTe4 does not actively metabolise pyrethroids, it is strongly inhibited by them, indicative that GSTe4 may play a role in sequestering insecticides in both species. This region of Uganda is experiencing marked flux in resistance status and species composition. We are using next generation whole genome sequencing of *An. gambiae* and *An. arabiensis* in order to better understand the consequences of hybridisation for the transfer of traits relevant to insecticide resistance between these important vectors.

1461

A UNIQUE MUTATION ON THE ACE-1 GENE OF THE MALARIA VECTOR ANOPHELES ALBIMANUS PROVIDES EVIDENCE FOR BALANCING SELECTION IN AN AREA OF HIGH INSECTICIDE RESISTANCE IN PERU

Kelly A. Liebman¹, Jesus A. Pinto², Jorge Valle², Lucrecia R. Vizcaino¹, William Brogdon¹, Audrey Lenhart¹

¹Centers for Disease Control and Prevention, Atlanta, GA, United States,

²Instituto Nacional de Salud, Lima, Peru

Acetylcholinesterase (AChE) insensitivity has previously been associated with resistance to organophosphate (OP) insecticides in arthropods. A single point mutation on the *ace-1* gene (G119S) has been identified in three anopheline species, including the New World malaria vector *Anopheles albimanus*. High levels of resistance to multiple classes of insecticides have recently been detected in the local *An. albimanus* vector population along the NW coast of Peru. To identify the mechanisms of resistance, the abdomens of 77 engorged females were excised and DNA was extracted, while the heads and thoraces of these individuals were used for biochemical analyses. Elevated levels of AChE insensitivity were detected in the biochemical assays, suggesting that this was a likely mechanism of resistance. A species-specific primer set was designed to amplify the region of the *ace-1* gene that includes the G119S mutation site. Sequencing the region showed that the individuals were highly polymorphic, with all individuals being heterozygous (G/T) at the first base. An additional, novel polymorphism was identified at the adjacent locus, where the individuals were all either heterozygous (G/C; $n=63$) or homozygous (C/C; $n=14$). The potential amino acids for individuals heterozygous at both *loci* are glycine (susceptible), serine (resistant), cysteine and alanine. For homozygous individuals at the second base, the only potential amino acids are serine and alanine, suggesting this

novel substitution may be associated with greater AChE insensitivity. This hypothesis is supported by analysis of biochemical and genetic data from the same individuals, which indeed suggests that individuals homozygous at base two presented higher levels of AChE insensitivity than heterozygotes. The G119S mutation appears to have arisen independently in this population, as the polymorphisms that result in serine are unique to what has been previously described. The occurrence of heterozygotes at 2 *loci* suggests that balancing selection could be the driving force behind the maintenance of OP resistance in this population.

1462

INSECTICIDE RESISTANCE SELECTION DRIVES GENETIC DIFFERENTIATION AMONG *Aedes aegypti* FROM YUCATAN

Karla L. Saavedra-Rodriguez¹, Meaghan Beaty¹, Steven Denham¹, Saul Lozano-Fuentes¹, Julian Garcia-Rejon², Guadalupe Reyes-Solis², Carlos Machain-Williams², Maria A. Lorono-Pino², Barry Beaty¹, Lars Eisen¹, William C. Black, IV¹

¹Colorado State University, Fort Collins, CO, United States, ²Universidad Autonoma de Yucatan, Merida, Mexico

The mosquito *Aedes aegypti* is the main vector of dengue viruses. Population reduction involves removal of larval breeding sites and uses insecticides for larval and adult control. In Mexico, permethrin has been used for mosquito control over the last 12 years and widespread resistance has been reported. Knockdown and mortality rates obtained by cone assay were highly variable among Yucatan collections and are highly correlated with point mutations in the voltage gated sodium channel gene (VGSC). We sought to determine if permethrin pressure reduces gene flow by comparing SNP variation at neutral gene markers and with variation at markers putatively associated with insecticide resistance. We tested for patterns of gene flow among 27 collections from Yucatan made in 2011. Three groups of nested collections were made around Merida and five collections were in towns outside Merida. A total of 1,301 mosquitoes were genotyped using 13 single nucleotide polymorphism markers (SNPs). Eight SNPs were in putatively insecticide neutral genes: amylase, apyrase, gluco-phosphate isomerase, early trypsin, vitellogenic carboxypeptidase precursor, chymotrypsin and maltase. Two SNPs were in the VGSC gene (C1534 and I1016), two were in cytochrome P₄₅₀ genes (CYP9J32 and CYP9J29) and one was in a carboxyl/choline esterase gene (CCEae1C). F_{ST} for neutral SNPs was low (0.012 - 0.063) and F_{ST} for potential insecticide metabolic genes were similar (0.031 - 0.049). However, F_{ST} for SNPs at the VGSC were much higher (0.222 and 0.135 for C1534 and I1016, respectively). AMOVA among all *loci* indicated little variation (3%) among collections from different cities. However, locus by locus analysis showed that C1534 and I1016 cause 22 and 13% of the variation among cities, respectively. In the face of high effective migration rates, local insecticide selection pressure created large variation in VGSC mutations.

1463

THE RAPID SELECTION OF PYRETHROID RESISTANCE IN *Anopheles gambiae* IN A SINGLE YEAR: AN INVESTIGATION INTO THE UNDERLYING CAUSES AND POTENTIAL IMPACT

Hyacinthe K. Toe¹, Christopher M. Jones², N'Fale Sagnon¹, Moussa W. Guelbeogo¹, Moussa W. Guelbeogo¹, Antoine Sanou¹, Roch K. Dabire³, Hilary Ranson²

¹Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso, ²Liverpool School of Tropical Medicine, Liverpool, United Kingdom, ³IRSS/Centre MURAZ, Bobo-Dioulasso, Burkina Faso

Resistance to pyrethroids was first reported in *Anopheles gambiae* from the rice growing region of Vallee de Kou in Burkina Faso over 14 years ago. The proportion of resistant mosquitoes has steadily increased since then and it is now rare to find any mosquitoes from this region surviving standard WHO susceptibility diagnostic dose assays. However, without

data on the magnitude of resistance it is difficult to predict the impact that this may have on malaria vector control. To address this, we determined the LT50 of the predominant vector from Vallee de Kou, An *gambiae* M form, in 2011 and again in 2012. Remarkably, in just one year, the LT50 had increased > 10 fold. This dramatic increase in the strength of resistance was not accompanied by an increase in *kdr* frequency, as the frequency of the 1014F allele was >0.8 in both years and the 1575Y allele decreased slightly between the years to 0.27 in 2012. However, using a stringent microarray experiment, with comparisons with multiple susceptible strains, we identified a number of detoxification genes strongly correlated with resistance to deltamethrin. Expression of a subset of these genes, including cytochrome P450 and cuticular genes increased significantly between 2011 and 2012 and may explain the dramatic increase in resistance observed recently. Data on the impact of this very strong resistance phenotype on the efficacy of long lasting insecticide treated bed nets in use in the region, obtained using both cone bioassays and experimental huts will also be presented.

1464

DISSEMINATION OF A POTENT PUPACIDE BY ADULT *Aedes aegypti* UNDER FIELD CONDITIONS: MECHANISMS OF A POTENTIAL CONTROL TOOL

Gregor John Devine¹, Elvira Zamora Perea², Nicole Achee³

¹Tropical Public Health Services, Cairns, Australia, ²Instituto Leonidas e Maria Deane, Manaus, Brazil, ³Uniformed Services University of the Health Sciences, Bethesda, MD, United States

Recent studies show that the behaviour of adult mosquitoes can be exploited for the dissemination of insecticides to aquatic habitats. This requires further characterization and optimization if it is to be widely adopted. A "lure and disseminate" device was designed that 1) contaminated wild mosquito populations with a potent pupacide and 2) released those mosquitoes to auto-disseminate pupacide to larval habitats. These dissemination tools were deployed in the field in Iquitos, Peru. Using coloured markers, the patterns and mechanics of dissemination between lures and sentinel oviposition habitats were examined. The potential contamination of the adult population was high and mark-recapture data revealed an even distribution of contaminated mosquitoes among sentinel aquatic habitats and a high frequency of contamination events at those habitats (ca 1 event every 4 days). Male mosquitoes, and other mosquito genera (particularly *Culex* spp) contributed to the dissemination process. The coloured markers were replaced with finely-milled pyriproxyfen (PPF) granules, and the impact of its subsequent dissemination by dispersing mosquitoes was assessed. Variation in juvenile mortality between aquatic habitats and trials was large (0-100%) but when all trials were averaged, 85% of sentinel larvae failed to develop. More than 75% of deaths occurred at the pupal stage. Affected aquatic habitats retained their pupacidal impact for 4 days after the contaminating devices had been removed from the trial site. The exposure of adult females to PPF using these dissemination tools also affected their reproductive potential. Only 46% of eggs laid at sentinel oviposition sites hatched. In contrast, 97% of eggs laid during control periods eclosed. These field results provide an essential understanding of the factors driving the remarkable efficacy of the auto-dissemination technique. These include 1) potency of the pupacide, 2) precise targeting of the insecticide by the mosquito, 3) amplification in coverage between the contaminating tools and the aquatic habitat, 4) persistence of the pupacide and 5) pupacides are unaffected by density dependent processes in the aquatic environment. The auto-dissemination technique, demonstrated here using a standardized contamination tool, a WHO-recommended pupacide, and a naturally-occurring mosquito population has enormous potential.

1465

CHARACTERIZATION OF STRAIN-SPECIFIC EFFECTS ON TRANSMISSION AND MAINTENANCE OF WEST NILE VIRUS

Alexander T. Ciota, Greta A. Van Slyke, Dylan J. Ehrbar, Kiet A. Ngo, Laura D. Kramer

Wadsworth Center, New York State Department of Health, Slingerlands, NY, United States

West Nile virus (WNV; *Flaviviridae*, *Flavivirus*) cases in New York State (NYS), as well as nationwide, were historically high in 2012. In addition, maximum likelihood estimates based on testing of NYS mosquito pools demonstrated the highest prevalence in *Culex* mosquitoes since the introduction of WNV to NYS, with approximately 7.5 WNV-positive *Culex* per 1000 tested. Although environmental factors are likely important in driving epidemiological shifts, the role of both WNV consensus and intrahost genetic variation in governing temporal shifts in vectorial capacity has not been adequately assessed. In addition, variation in the capacity for vertical transmission and, therefore, overwintering success, has not been evaluated. Previous studies demonstrate that WNV effects on *Culex* life-history traits are strain-specific, establishing the need to evaluate factors beyond vector competence, including strain virulence in mosquitoes and alteration to both bloodfeeding and reproductive patterns, in order to accurately measure strain-specific differences in transmissibility and maintenance. To begin to evaluate these relationships, we used deep-sequencing to genetically characterize WNV strains isolated from *Culex* pools in Suffolk County, NY in both 2005 and 2012, representing low and high activity years, respectively, and performed subsequent phenotypic analyses including quantifying vector competence, life-history traits following exposure, and vertical transmission. Genetic analyses suggest consensus substitution rates of approximately 6×10^{-4} base/year, which is comparable to what has been measured in previous studies, yet identification of single nucleotide polymorphisms (SNPs) demonstrate substantial differences in mutant swarm breadth between isolates, with 19 minority SNPs identified in a 3kb region of the WNV 2005 genome, relative to 9 for the WNV 2012 isolate. Preliminary studies also demonstrate differences in infectivity in *Cx. pipiens*; and initial assessment of life-history traits following exposure suggests potentially important strain-specific effects. Taken together, these data begin to inform our understanding of the relationship between WNV genetic variation and temporal fluctuation in WNV activity.

1466

NS3-249 AMINO ACID SUBSTITUTIONS ALTER AVIAN PATHOGENESIS OF BOTH LINEAGE 1 AND 2 WEST NILE VIRUSES

Aaron C. Brault¹, Angela Bosco-Lauth¹, Michael Anishchenko¹, Stanley A. Langevin², Christy C. Andrade², Joanie L. Kenney¹, Hannah Romo³, Anna Papa⁴, Richard A. Bowen³

¹*Centers for Disease Control and Prevention, Fort Collins, CO, United States*, ²*University of California, Davis, CA, United States*, ³*Colorado State University, Fort Collins, CO, United States*, ⁴*Aristotle University of Thessaloniki, Thessaloniki, Greece*

Previous studies using selection modeling and experimental avian inoculations identified a single West Nile viral genetic *loci* (NS3-249) of lineage 1 WNVs to be under the effect of positive selection and to be a virulence determinant (NS3-249P) associated with increased replicative capacity and virulence in American crows (AMCRs), a sentinel species utilized in North America to track the spread of the virus. Although a lineage 2 virus was isolated from a moribund goshawk in Hungary in 2004, viruses from this lineage have not been associated with significant avian mortality. All genetically characterized lineage 2 viruses have been identified to have a His at the AMCR virulence locus, NS3-249; however, WNV isolates made from a large lineage 2 WNV outbreak in Greece in 2010 were identified to have a Pro at this site. A WNV infectious cDNA of a South African strain isolated in 1989 was subsequently generated

and an NS3-H249P mutation incorporated to assess the potential modulatory effect of this locus in an alternative WNV lineage. Inoculation of AMCRs with the parental South African or cDNA clone-derived virus demonstrated mean peak viremias of 7-7.5 log₁₀ PFU/mL sera and exhibited approximately 30% mortality. In contrast, the NS3-H249P lineage 2 mutant virus demonstrated 100% mortality in AMCRs with an approximate 100-fold higher mean peak viremia (9.6 log₁₀ PFU/mL sera), indicating the potential importance of this specific genetic alteration within the lineage 2 genome for eliciting high replicative capacity in avian hosts. These results confirm the vital role of this locus for avian virulence potential and indicate the selective advantage of different NS3-249 residues for increased avian replication within both lineage 1 and lineage 2 WNV genetic backbones.

1467

SEQUENCE AND PHENOTYPIC ANALYSES OF 2012 WEST NILE VIRUS ISOLATES FROM TEXAS FAIL TO ASSOCIATE VIRAL GENETIC FACTORS WITH OUTBREAK MAGNITUDE

Nisha Duggal, Roger Nasci, Aaron C. Brault

Centers for Disease Control and Prevention, Fort Collins, CO, United States

In 2012, the U.S. experienced the largest outbreak of WNV human encephalitis since 2003. In order to determine whether the increase in WNV transmission in 2012 could have been due to recent sequence changes in the WNV genome, we sequenced 17 full-length isolates made from mosquito pools in Texas in 2012 and compared them to isolates from previous years. We found a similar amount of divergence in the 2012 Texas isolates compared to isolates from previous years, with most of the genome evolving under purifying selection and genetic drift. Further, we compared isolates from Dallas County, that exhibited a 2012 incidence rate of 16 WNV cases per 100,000 population, to isolates from Montgomery County, with a 2012 incidence of 3 WNV cases per 100,000 population. While genetic differences did exist between Dallas and Montgomery County viral populations, weak evidence supports genetic population subdivision or adaptive changes in the Texas isolates. Finally, *in vitro* growth rates of Dallas and Montgomery County WNV isolates with the aforementioned genetic differences were assessed in mammalian and mosquito cells. Results demonstrated that isolates with variable amino acids exhibited indistinguishable replication profiles compared to one another or to the NY99 strain, indicating that these 2012 WNV genetic differences did not afford an *in vitro* replication advantage. Together, these data do not support genetic viral adaptation as an explanation for increased WNV incidence in 2012.

1468

SMALL RNA RESPONSE OF CULEX QUINQUEFASCIATUS TO WEST NILE VIRUS INFECTION: RELATIONSHIP TO VECTOR COMPETENCE

Abhishek N. Prasad¹, Darci R. Smith¹, Doug E. Brackney¹, Benjamin Dodd¹, Thomas D. Harrison¹, Corey L. Campbell¹, Jennifer E. Beane², Gregory D. Ebel¹

¹*Colorado State University, Fort Collins, CO, United States*, ²*Boston University, Boston, MA, United States*

Culex mosquitoes are among the most important vectors of animal viruses worldwide. These include West Nile virus, Japanese Encephalitis virus, Rift valley fever virus and others. However, our understanding of the molecular events that influence their ability to transmit pathogens (vector competence) is incomplete. Variation in vector competence occurs between individual mosquitoes, between populations of the same species, and between taxonomically distinct species. When exposed to the same virus-containing bloodmeal, some mosquitoes fail to become infected, others become infected but limit virus replication and dissemination, while others develop disseminated infection and ultimately transmit virus. Vector competence has been shown through several studies to be a quantitative trait under the control of several genes and other factors. RNAi is widely

regarded as the most important antiviral pathway in mosquitoes, but its role in shaping mosquito vector competence is poorly understood. Moreover it is not clear how RNAi influences vector competence in non-transgenic "wild-type" vector mosquitoes. Therefore, we sought to characterize the mosquito RNAi response to WNV infection and determine its influence on vector competence using colonized *Cx. quinquefasciatus* mosquitoes. Mosquitoes were exposed to WNV in an artificial bloodmeal and held for various extrinsic incubation periods. Small RNA (sRNA) profiles were obtained using next-generation sequencing. To characterize the early sRNA responses to WNV, midguts were removed from mosquitoes 12 and 24 hours after feeding and sRNAs mapped to the WNV genome. To assess the relationship between sRNA responses and virus dissemination from the midgut (a prerequisite for virus transmission), midguts and legs were removed from mosquitoes at 7 and 14 days post feeding. sRNA responses from mosquitoes that permitted WNV dissemination from the midgut into peripheral tissues were compared to those with WNV limited to the midgut. Overall, these studies will characterize the sRNA responses of mosquitoes to WNV infection and determine the extent to which RNAi influences vector competence in this system.

1469

EVALUATION OF CHIMERIC JAPANESE ENCEPHALITIS VIRUS/ DENGUE VIRUS TYPE 4 VACCINE CANDIDATES IN MICE

Gregory D. Gromowski, Cai-Yen Firestone, Christopher T. Hanson, Stephen S. Whitehead

National Institutes of Health, Bethesda, MD, United States

Japanese encephalitis virus (JEV) is a leading cause of viral encephalitis worldwide and vaccination is one of the most effective ways to prevent disease. A suitable live attenuated JEV vaccine could be formulated with a live attenuated tetravalent dengue vaccine for the control of these viruses in endemic areas. Toward this goal, we previously generated chimeric vaccine candidates by replacing the precursor membrane (pM) and envelope (E) structural genes of dengue virus type 4 (DEN4) or attenuated DEN4Δ30 with those of JEV India/78. These first generation JEV/DEN4 chimeric viruses were attenuated for neurovirulence and neuroinvasiveness in weanling mice compared to the wild-type JEV parent, which warranted their further development as vaccine candidates. Adventitious mutations in E, NS3 and NS4B proteins that arose during adaptation of first generation chimeric viruses for replication in Vero cells were engineered into a second generation of JEV/DEN4 chimeric viruses. Novel 3'UTR deletions, similar to those found in DEN4Δ30, were also introduced. Sequencing revealed that chimeric viruses lacking engineered Vero cell adaptive E protein mutations acquired adventitious mutations. This suggests that at least one adaptive E protein mutation is required for genetic stability of JEV/DEN4 chimeric viruses propagated in Vero cells. The second-generation chimeric viruses were attenuated for neurovirulence and neuroinvasiveness in weanling mice. They were also significantly more attenuated for neurovirulence in suckling mice than the wild-type JEV parent and the JEV SA14-14-2 live-attenuated vaccine strain, based on LD50 values and survival times. Deletions in the 3'UTR also increased attenuation for suckling mice. By contrast, a single E protein mutation that is shared by JEV SA14-14-2 significantly increased neurovirulence in suckling mice and replication in Vero cells for one chimeric virus. We are currently evaluating these chimeric vaccine candidates in mice for immunogenicity and protection from challenge with wild-type JEV.

1470

ESTIMATING THE BURDEN OF YELLOW FEVER IN AFRICA

Tini Garske¹, Maria D. Van Kerkhove¹, Sergio D. Yactayo², Olivier Ronveaux³, Rosamund F. Lewis⁴, William Perea², **Neil M. Ferguson**¹, na Yellow Fever Expert Committee²

¹Imperial College, London, United Kingdom, ²World Health Organization, Geneva, Switzerland, ³World Health Organization, Ouagadougou, Burkina Faso, ⁴Ottawa Public Health, Ottawa, ON, Canada

Yellow fever is a vector-borne disease affecting humans and non-human primates in tropical areas of Africa and South America. While eradication is not possible due to the wildlife reservoir, large scale vaccination activities in Africa in the 1940s to 1960s reduced yellow fever incidence for several decades. However, after a period of low vaccination coverage, yellow fever has resurged in the continent. Since 2006 there has been substantial funding for preventive mass vaccination campaigns for yellow fever in the most affected countries in Africa to curb the rising burden and control future outbreaks. Generalised linear regression models were fitted to a dataset of the locations of yellow fever outbreaks in the last 25 years to estimate the probability of outbreak reports across the endemic zone. Environmental variables and indicators of surveillance quality in the affected countries were used as covariates. By comparing probabilities of outbreak reports estimated in the regression with the force of infection estimated for a limited set of locations for which serological surveys were available, the detection probability per case and the force of infection were estimated across the endemic zone. The yellow fever burden in Africa was estimated for the year 2013 as 130,000 (95% CI 84,000 - 170,000) severe cases including 44,000 (95% CI 29,000 - 60,000) deaths, taking into account the current level of vaccination coverage. The recent mass vaccination campaigns are estimated to have reduced this burden by 27% (95% CI 23 - 30%) across the region, achieving up to 82% reduction in countries targeted by these campaigns. With the estimation method presented here, spatial estimates of transmission intensity can be combined with vaccination coverage levels to evaluate the impact of past or proposed vaccination campaigns, thereby helping to allocate resources efficiently for yellow fever control. *Expert Committee: Donald Burke, Fernando De La Hoz, Bryan Grenfell, Peter Hansen, Raymond Hutubessy, Rosamund Lewis, William Perea, Olivier Ronveaux, Erin Staples, Sergio Yactayo.

1471

ISOLATION AND CHARACTERIZATION OF PARAISO ESCONDIDO VIRUS: A NEW FLAVIVIRUS IN LUTZOMYIA (PSATHYROMYIA) ABONNENCI SANDFLIES FROM ECUADOR

Cigdem Alkan¹, Sonia Zapata², Laurence Bichaud¹, Gregory Moureau¹, Gregory Moureau¹, Xavier de Lamballerie¹, Jerome Depaquit², **Remi N. Charrel**¹

¹Aix Marseille University - IRD French Institute of Research for Development - EHESP French School of Public Health, Marseille, France,

²Université de Reims Champagne-Ardenne - ANSES, Reims, France

Flaviviruses consist of mosquito-borne, tick-borne, insect-only and non-vectored viruses. Sandflies are not recognized as principal vectors of flaviviruses. We report here the discovery (detection, isolation and full-length sequence) of a novel flavivirus in *Lutzomyia (Psathyromyia) abonnenci* that was provisionally named Paraiso Escondido virus. Twenty six pools of *Lutzomyia* flies were screened for the presence of flaviviruses. One pool of female (neither gravid nor engorged) *Lutzomyia (Psathyromyia) abonnenci* was found to contain flavivirus RNA through real time RT-PCR assay targeting all flaviviruses, as previously reported. Assuming that one sandfly only was infected in the pool, quantitative real-time PCR estimated that > 1012 genome copies were in the infected insect individual. Virus isolation was obtained in C6/36 cells. The complete genome was sequenced using next generation sequencing technology based on Ion-torrent PGM. The genome consisted of 10,760 nucleotides encoding 3441 AA with 5'- and 3'-UTR of 119 and 316 nts,

respectively. A series of cysteine residues and potential glycosylation sites were identified. The enzymatic domains (serine-protease, helicase/ NTPase, methyltransferase and RNA-dependent RNA polymerase) of Paraiso Escondido virus were found to be highly conserved in comparison with other flaviviruses. The putative cleavage sites of the polyprotein were identified and found substantially different from those of other flaviviruses. The AA distances observed ranged 53-85%, 40-72%, 35-56% with envelope, NS3 and NS5 proteins. Phylogenetic analyses based on amino acid alignments showed that Paraiso Escondido virus clustered together with *Aedes*-borne flaviviruses although it is clearly distinct from other known flaviviruses. In the New world, *Lutzomyia* sandflies are the vectors of viruses (vesicular stomatitis virus, Orbivirus, Punta Toro virus), parasites (leishmaniasis) and bacteria (bartonellosis). Therefore they should be considered as possible vectors of viruses of potential medical and veterinary importance. Further investigations are on-going to determine whether Paraiso Escondido virus is capable to infect vertebrates and humans.

1472

INTEGRATED, COMMUNITY-BASED SURVEYS OF INTESTINAL PARASITIC INFECTIONS WITH TRACHOMA IMPACT ASSESSMENTS IN AMHARA NATIONAL REGIONAL STATE, ETHIOPIA

Tekola Endeshaw¹, Woyneshet Gelaye², Elisabeth Escher³, Aisha P. Stewart⁴, Genetu Alemtay², Sileabatt Melaku², Zerihun Tadesse¹, Peter Odermatt³, Jürg Utzinger³, Paul M. Emerson⁴, **Jonathan D. King**⁴

¹The Carter Center, Addis Ababa, Ethiopia, ²Amhara Regional Research Laboratory, Bahir Dar, Ethiopia, ³Swiss Tropical and Public Health Institute, Basel, Switzerland, ⁴The Carter Center, Atlanta, GA, United States

In the Amhara National Regional state of Ethiopia we integrated assessment of intestinal parasitic infections into large-scale trachoma impact surveys to establish baseline prevalence upon which to monitor the impact of integrated control measures of improved hygiene, water, sanitation, and preventive chemotherapy. Both trachoma and intestinal parasites (*Schistosoma mansoni*, soil-transmitted helminths, and intestinal protozoa) were assessed in systematically selected clusters from a geographic listing of communities by district. One child aged 6-15 years per household in selected clusters was randomly selected to provide a stool sample of which about 1 g was preserved in sodium acetate-acetic acid-formalin, processed using formol-ether concentration and examined under a microscope by experienced laboratory technicians. A total of 6,732 stool specimens were collected from 368 communities. The prevalence of *S. mansoni* was 6.6% (range by district 0-40.9%), but prevalence in 55 communities was $\geq 10\%$. The overall prevalence of any soil-transmitted helminth infection was 22.5% (range by district 3.0-77.7%). Approximately 3 in 4 children were infected with at least one intestinal protozoa. The prevalence of *Giardia intestinalis* was 18.9% (range by district 5.4-41.0%) and *Entamoeba histolytica*/E. dispar was 12.5% (range by district 2.9-22.5%). Associations between soil-transmitted helminth infections and community-level indicators of hygiene, water, and sanitation were explored. According to World Health Organization guidelines, preventive chemotherapy targeted to school-aged children is warranted for the control of schistosomiasis in 10 and for the control of soil-transmitted helminths in 39 out of 59 districts. Integration of deworming with mass distribution of antibiotics for trachoma might further expand health benefits to co-endemic communities. Integrating assessment of intestinal parasitic infections with community-based trachoma prevalence surveys may be a feasible method for evaluating impact of neglected tropical disease control programs.

1473

INTEGRATED SCHOOL-BASED SURVEILLANCE FOR SOIL-TRANSMITTED HELMINTH INFECTIONS AND FOR LYMPHATIC FILARIASIS IN GAMPAHA DISTRICT, SRI LANKA

Nipul K. Gunawardena¹, Sharmini Gunawardena², Ganga Kahathuduwa³, Nadira D. Karunaweera², Nilanthi de Silva¹, Udaya S. Ranasinghe³, **Ramakrishna U. Rao**⁴, Maria Rebollo⁵, Gary J. Weil⁴

¹University of Kelaniya, Ragama, Sri Lanka, ²University of Colombo, Colombo, Sri Lanka, ³Antifilaria Campaign, Ministry of Health and Nutrition, Colombo, Sri Lanka, ⁴Washington University School of Medicine, St. Louis, MO, United States, ⁵Centre for Neglected Tropical Diseases, The Liverpool School of Tropical Medicine, Liverpool, United Kingdom

The Sri Lankan Anti-Filariasis Campaign (AFC) conducted 5 rounds of annual mass drug administration (MDA) with albendazole and DEC in 2002-2006 in 8 districts that were endemic for lymphatic filariasis (LF) (target population approximately 10 million). AFC conducted transmission assessment surveys (TAS) in 2012, about 6 years after the last round of MDA. This study explored the practicality of integrating surveillance for soil transmitted helminth (STH) infections with TAS for LF in Gampaha district (population 2.3 million). The district was divided into two Evaluation Units (EUs), coastal and inland. Each TAS tested 1st and 2nd grade school children drawn from 30 randomly selected schools (N=1,462 inland, 1,642 coastal). Tests included the ICT card test for filarial antigenemia (performed by AFC personnel) and the Kato-Katz test for detection of STH ova (performed by university personnel). ICT rates were 0% and 0.1% (0.01-0.3% CI) in the inland and coastal EUs, respectively. These results suggest that LF transmission rates are very low in Gampaha District. The STH survey was conducted at the same time as the TAS in the inland EU (955 stools from 1,211 children) and several weeks after the TAS in the coastal EU (927 stools from 1,586 children). STH infection rates and stool sample participation rates were 0.8% and 79% in the inland EU and 2.8% and 58% in the coastal EU. Most of the STH infections detected were low-intensity *Trichuris* (present in 73% of positive stools). The low STH rates are probably due to the country's national school deworming program (mebendazole in grades 1, 4, and 7) and relatively good sanitation in Gampaha district. The cost for STH testing was approximately \$5,000 per EU. These results suggest that it is feasible for national NTD programs to integrate school based surveillance for STH and LF. Further work is needed to streamline procedures and to determine optimal sampling strategies for STH surveys, because these may not require as many samples or sampling sites as TAS.

1474

QUANTIFYING THE QUALITY OF SURVEY DATA FOR THEIR USE IN THE DESIGN OF SOIL TRANSMITTED HELMINTH AND SCHISTOSOMIASIS CONTROL PROGRAMS

Birgit Nikolay¹, Charles S. Mwandawiro², Sammy M. Njenga², Rachel L. Pullan¹, Simon J. Brooker¹

¹London School of Hygiene & Tropical Medicine, London, United Kingdom, ²Kenya Medical Research Institute, Nairobi, Kenya

Generous medication donations and increasing political commitment has led to the launch of numerous national neglected tropical diseases (NTD) control programmes. The first step in developing these programmes is often country-wide mapping of disease, which might be unnecessary if data from previously conducted studies exist. Thus, large scale surveys would waste resources and cause unnecessary delays for medication distribution. As the quality of previously collected data can vary in terms of study design and data collection, we developed guidelines for the use of available soil transmitted helminth (STH) and schistosomiasis survey results to support programme implementers during the process of programme design. These guidelines allow identifying areas where sufficient information already exists and others that should be prioritised for surveys. The approach is based on three steps: i) the identification of ecological

zones within the country, ii) the identification and classification of available surveys and iii) the classification of each ecological zone based on characteristics of individual surveys. The country is divided into ecological zones based on environmental data and a systematic literature research is performed to capture all relevant studies. The quality of the identified surveys is assessed based on the following characteristics: We considered the time since surveys, as well as expected substantial changes in transmission. Additionally, the representativeness of the study population is taken into account, as well as the sampling design and sample size. The accuracy of diagnostic methods is graded based on published comparative studies of diagnostic tools. Furthermore, the level of available information is assessed in terms of geographic information (precise locations of surveys vs. district or province summary estimates) and infection information (species specific prevalence vs. STH summary estimates). According to the coverage and quality of identified surveys, each ecological zone is classified independently into five groups i) mapped as recommended, ii) mapped, iii) mapped with low quality data, iv) mapped with questionable data, and v) not mapped. Based on the grading of ecological zones, we further provide recommendations for the design of national surveys. Finally, we demonstrate the application of the proposed guidelines on the example of Kenya and discuss their potential constraints.

1475

TREATMENT COVERAGE OF INTEGRATED MASS DRUG ADMINISTRATION FOR NEGLECTED TROPICAL DISEASES IN TOGO

Monique A. Dorkenoo¹, Rachel N. Bronzan², Kwame C. Amlaga³, Michel G. Datagni³, Kangni Adadé⁴, Touka M. Djato⁴, Boakye A. Boatin⁵, Koffi S. Sognikin⁶, Kodzo A. Anthony³

¹Lymphatic Filariasis Programme, Ministry of Health, Lomé, Togo, ²Health and Development, International, Rockville, MD, United States, ³Health and Development, International, Lomé, Togo, ⁴Onchocerciasis Control Programme, Ministry of Health, Lomé, Togo, ⁵Lymphatic Filariasis Support Centre, Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, Ghana, ⁶Neglected Tropical Diseases Program, Lomé, Togo

Since 2009, the country of Togo has implemented a program for the integrated control of neglected tropical diseases. Under this program, onchocerciasis, schistosomiasis, and soil transmitted helminths are targeted using community-based distribution of ivermectin (IVM), praziquantel (PZQ), and albendazole (ALB). Drugs are given to selected populations based on local prevalence of each disease. A nationwide integrated mass drug administration (MDA) was conducted in July 2012; while reported treatment coverage was high, integrated MDA campaigns are logistically complex and reported coverage may not reflect the actual coverage achieved. In November 2012, Togo conducted a survey to validate coverage for all three diseases. Four cluster surveys were conducted, one in each of three geographically disparate districts, and a fourth in areas with high prevalence of onchocerciasis. In each district 30 to 45 villages were selected with probability proportional to size. Ten houses were selected in each village and all household members were asked about receipt of drugs in July 2012. Each household head answered questions about knowledge of the diseases. In the four clusters a total of 9511 persons in 1187 households were interviewed. Coverage varied by district: 74-84% of the population received IVM, 80-94% of school-age children (SAC) received PZQ, and 84-94% of SAC received ALB. Measured coverage for PZQ and ALB exceeded WHO targets; coverage for IVM was below WHO target in two districts. In one district measured coverage was lower than reported for all drugs ($P < 0.05$), and in two others measured coverage was lower than reported for ALB. Coverage validation surveys are an important part of program evaluation. The sampling for this survey was challenging and novel since the targeted diseases and populations vary by village and no clear guidelines exist for sampling in such a complex distribution scheme. Results from this study will be used to refine MDA training and supervision, and will also contribute to decisions regarding control and/or elimination strategies for these diseases.

1476

"COORDINATED" MAPPING FOR NEGLECTED TROPICAL DISEASES IN COTE D'IVOIRE

Anna E. Phillips

Imperial College, London, United Kingdom

Where geographic overlap among NTD distribution exists, coordinated mapping could result in significant resource savings. There are few data on the geographic distribution of NTDs in post-conflict Cote D'Ivoire. To guide intervention, by the recently established national Lymphatic Filariasis, Schistosomiasis and Soil Transmitted Helminth Control Programme, a coordinated prevalence survey for schistosomiasis, soil-transmitted helminth (STH) infection and lymphatic filariasis (LF) was conducted. The aim was to design a resource efficient protocol to establish which communities required mass drug administration (MDA), according to World Health Organization thresholds. The sampling frame was the health district with a total of eight health districts sampled. Within each health district 20 communities were surveyed for schistosomiasis and STH, sampling 50 school-age children per village. Among the 20 communities selected, two were also surveyed for LF with 100 adults sampled in each. In total 8,000 school-aged children were tested for both urinary and intestinal schistosomiasis and STH. A further 1600 adults were tested for circulating *Wuchereria bancrofti* antigen using immunochromatographic card tests (ICT). Preliminary analysis has shown prevalence of *Schistosoma haematobium* and *S. mansoni* ranged from 2-69% and from 0-76%, respectively. The main STH species was hookworm, ranging from 2-41% by village. LF and cost-analysis results are under-going preliminary analysis. This was the first attempt at using a coordinated survey design for this group of infections in Cote D'Ivoire. The approach proved practical and the results show that only a few areas need to be targeted with MDA, thus confirming the importance of detailed mapping for cost-effective control.

1477

BARRIERS TO COMPLIANCE WITH MASS DRUG ADMINISTRATION FOR NTD CONTROL PROGRAMS

Achille Kabore, Philip Downs

RTI International, Washington, DC, United States

Compliance with mass drug distribution is a determinant of success for national neglected tropical diseases (NTD) control programs. Persistent non-compliance can maintain diseases transmission as a reservoir for potential re-infection. Out-of school children, women of reproductive age and hard-to-reach remote populations might repeatedly miss opportunities for mass drug distribution (MDA); creating systematic non-compliant groups for preventive chemotherapy. An analysis of semi-annual reports and post MDA coverage surveys from the USAID funded NTD control programs and other NTD projects was conducted to identify barriers to adhering to MDA treatment schedules and keys factors amenable to corrective measures. The review identified several groups of individuals including institutionalized people, non-enrolled school age children, and people from high socio-economic status as persistently non-compliant during MDAs. Also identified were 47% of women excluded from MDA due to pregnancy or nursing of babies under 1 month of age, and who later qualify for treatment but did not attend consecutive rounds of annual MDAs. Large sections of urban populations in endemic settings remain consistently untreated because they present specific challenges in terms of acceptability of drugs distributed by non health professionals. Other reasons for recurrent non participation in mass campaigns include: 1) fear of adverse event, 2) non perceived benefit, and 3) lack of disease awareness. The authors also explore campaign fatigue resulting from the long standing drug distribution programs. Strategies to overcome barriers and to increase compliance involve refinement of pre-MDA plans, comprehensive registration of all eligible populations, intensive IEC campaigns, implementation of flexible distribution mechanisms, and routine facility-based post campaign drug administration. The authors

recommend adapting MDA to the local environment and making use of platforms and local opportunities to increase NTD programs visibility and drug coverage.

1478

MONITORING AND EVALUATING INTEGRATED NTD CONTROL: FIVE-YEAR IMPACT OF TREATMENT ON INFECTION IN NIGER AND BURKINA FASO

Anna E. Phillips

Schistosomiasis Control Initiative, Imperial College, London, United Kingdom

Monitoring and evaluation (M&E) is an essential element of national NTD control that guides a programme on how to strengthen its approach. Standard epidemiological monitoring methods, used to measure the impact of treatment through annual parasitological examinations at school sentinel sites, are being employed across all SCI countries. The findings from two countries are presented here. A longitudinal cohort of 718 and 2405 children aged 7-12 years in Niger and Burkina Faso, respectively, were recruited at baseline (2004) and parasitological examinations carried out at yearly intervals before and after large-scale treatment for schistosomiasis and STH. Preventative chemotherapy (PCT) was integrated against five NTDs (lymphatic filariasis, schistosomiasis, STH, onchocerciasis and trachoma) in 2007. In order to monitor the impact of combined mass drug administration, integrated (schistosomiasis, STH, and trachoma) sentinel schools were added in 2008. Data from the longitudinal cohort demonstrated that a significant decrease in the odds of detectable trachoma, as well as *Schistosoma haematobium* infection, was found at follow-up two years post-baseline. Children who benefited most from anthelmintic treatment, in terms of increased haemoglobin concentrations, were those who had presence of anaemia and highly positive microhaematuria scores at baseline. This study demonstrates that chemotherapy can have a substantial impact on both *S.haematobium* and trachoma infection, and its associated morbidity in children, even after integrating PCT for several NTDs. These are the first known integrated sentinel sites to examine all three NTDs, the results of which will demonstrate whether the presence of co-infection affects the impact of treatment as well as the cost-efficiency of combining M&E for multiple infections.

1479

THE UTILITY OF DIAGNOSTIC TESTS FOR TYPHOID FEVER AT CHITTAGONG MEDICAL COLLEGE HOSPITAL (CMCH), CHITTAGONG, BANGLADESH

Rapeephan R. Maude¹, Katja de Jong², Lalith Wijedoru¹, Masako Fukushima³, Aniruddha Ghose⁴, Rasheda Samad⁴, Abdullah A. Sayeed⁴, Mahtab U. Hasan⁴, Md. Amir Hossain⁴, Md. R. Karim⁴, Stannie van den Ende², Thomas van der Vaart², Tran V. Nga⁵, Pham T. Duy⁵, Richard J. Maude¹, James I. Campbell⁵, Stephen Baker⁵, Joost W. Wiersinga², Tom van der Poll², Nicholas P. Day¹, Arjen M. Dondorp¹, Md. Abul Faiz¹, Christopher M. Parry¹

¹Mahidol-Oxford Tropical Medicine Research Unit (MORU), Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, ²Center for Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, Netherlands, ³Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom, ⁴Chittagong Medical College Hospital, Chittagong, Bangladesh, ⁵Wellcome Trust Major Overseas Programme, Oxford University Clinical Research Unit (OUCRU), Ho Chi Minh City, Vietnam

Typhoid fever (TF) is commonly diagnosed in febrile patients in Bangladesh but confirmatory tests are unsatisfactory. We evaluated BactAlert® blood cultures; an in-house real time PCR; and rapid antibody diagnostic tests (RDT) for TF in febrile adults and children admitted to CMCH. The RDTs were Life Assay Test-it™ Typhoid IgM lateral flow assay detecting IgM antibodies against *S. enterica* Typhi (ST) O antigen; CTKBiotech Onsite

Typhoid IgG/IgM Combo Rapid-test cassette lateral flow assay detecting IgG and IgM antibodies against ST O and H antigens; and SD Bioline line assay for IgG and IgM antibodies against ST proteins. Background antibody levels were studied 40 local adult healthy controls: Life Assay RDT was positive at 1+ in 30 controls but at > 1+ in only one control; the CTK and SD Bioline kits were negative in all controls. We studied 303 febrile patients admitted to CMCH with a median (IQR) age of 13 (5-31) years and median (IQR) duration of illness before admission of 5 (2-8) days. TF was diagnosed in 57 (18.8%): 19 positive by blood culture with ST (3 also blood PCR positive); 20 blood culture negative but PCR positive in blood (15), urine (4) and faeces (2); and 18 blood culture and PCR negative but with a compatible clinical syndrome. Of the 246 patients without TF, 13 had a significant positive blood culture with other bacteria. We calculated the sensitivity, specificity, positive and negative predictive values of the three RDTs comparing those patients who had blood culture and/or PCR confirmed typhoid (n=39) with those without TF (n=246). For the Life Assay IgM LFA at a cut-off of ≥ 2+ the sensitivity, specificity, PPV and NPV were 36%, 89%, 35% and 90%; for CTK IgG/IgM assay the values were 54%, 74%, 25% and 91%; and the SD Bioline IgG/IgM assay values were 21%, 97%, 50% and 89%. The performance characteristics of the RDTs were insufficient to be clinically useful. Although the addition of PCR to BC increased the number of laboratory confirmed cases, the evaluation of RDTs is still hampered by the lack of a gold standard for TF diagnosis.

1480

THE FORGOTTEN SCOURGE: MODELING DYNAMICS AND CONTROL OF ENDEMIC TYPHOID IN KATHMANDU, NEPAL

Cayley Bowles¹, Virginia Pitzer², Bryan Grenfell³

¹Harvard School of Public Health, Boston, MA, United States, ²Yale School of Public Health, New Haven, CT, United States, ³Princeton University, Princeton, NJ, United States

Typhoid is a paradoxically widespread yet neglected disease. Recent estimates place the global typhoid burden from 13.5 – 26.9 million cases and 190,000 – 216,000 deaths annually, which provides a motivation to better understand typhoid dynamics. We developed an age-structured, compartmental model that was representative of the pathogen's natural history and human immune response to the infection. We fit the model to incidence data from 1997-2011 collected from Patan Hospital in Kathmandu, Nepal in order to estimate unknown model parameters. The model assumed indirect transmission was a function of rainfall and reproduced the timing of annual peaks very well, but failed to account for an upward trend in cases that began in 2000. An adjusted form of the model that incorporated antibiotic resistance reproduced both the timing and magnitude of the epidemic peaks over the entire dataset. This lends support to the hypothesis that increased use of fluoroquinolones drove the clonal expansion of the H58 haplotype, which confers nalidixic acid resistance through a mutation in DNA gyrase *gyrA*. The inclusion of migrant male workers entering Kathmandu with no previous typhoid exposure helped explain an observed shift in the age and gender distribution of cases, suggesting migration patterns partially underlie typhoid dynamics. The calibrated model estimated the basic reproductive number (R_0) to be ~4.5 in this setting. School-based vaccination was predicted to produce indirect protection and decreased typhoid incidence in the short-run, but the incidence rate is expected to rebound in about 5 years, shortly after vaccine-induced immunity wanes. As the Nepali government begins to implement school-based vaccination, government and public health authorities must recognize the limitations and potential adverse effects of a one-time vaccination campaign. Water and sanitation improvements will be critical to typhoid elimination.

1481

BURDEN OF LABORATORY-CONFIRMED SHIGELLOSIS INFECTIONS IN GUATEMALA 2007-2012: RESULTS FROM A POPULATION-BASED SURVEILLANCE SYSTEM

Sonia T. Hegde¹, Stephen Benoit¹, Beatriz Lopez², John P. McCracken², Chris Bernart², Wences Arvelo¹, Aleida Roldan², Cesar Rancancoj², Blanca Chinchilla³, Leonard Peruski¹, Joe Bryan¹

¹Centers for Disease Control and Prevention, Atlanta, GA, United States,

²Universidad de Valle de Guatemala, Guatemala City, Guatemala,

³Ministerio de Salud y Asistencia Social, Guatemala City, Guatemala

In Guatemala, diarrhea is the second most common cause of morbidity and mortality in children <5 years of age. The proportion of diarrheal disease caused by *Shigella* sp. remains unknown. Using data collected from the two hospitals and 10 clinics in active population-based surveillance sites in Quetzaltenango (Average High Temperature: 22°C) and Santa Rosa (Average High Temperature: 31°C) Departments, we describe the epidemiology and antimicrobial susceptibility patterns of culture-confirmed *Shigella* infections. Clinical, epidemiological, and laboratory data were collected on patients presenting with acute diarrhea (≥ 3 loose stools in 24 hours), from June 2007 - August 2012. Of 5,399 stool specimens collected from patients who met the case definition, 261 (4.8%) yielded *Shigella* sp.. Most were *S. flexneri* (59.2%) followed by *S. sonnei* (35.6%). Most (51%) infections occurred from May to August, during the rainfall season. During the 5 years, the incidence of laboratory-confirmed infections varied from 5.0 to 24.1 per 100,000 in Santa Rosa and 0.31 to 6.2 in Quetzaltenango. Most (57.9%) cases occurred in children <5 years of age; incidence in this age group were 91.9 per 100,000 in Santa Rosa and 31.1 in Quetzaltenango. Thirty (12%) patients were hospitalized, including 6 who were admitted to the intensive care unit. Three patients experienced convulsions, 5 bloody diarrhea, and 17 vomiting; there was 1 death. Over half (56%) of cases were treated with oral rehydration solution within three days of enrollment and 76% of hospitalized cases received intravenous fluids. Antimicrobial susceptibilities were tested for 260 isolates; 238 (96%) were resistant to tetracycline, 210 (83%) to trimethoprim-sulfa, and 141 (61%) to ampicillin. No isolates were resistant to the quinolone antibiotics tested. *Shigella* is an important cause of bacterial diarrhea in children <5 years of age in Santa Rosa and Quetzaltenango. Though limitations exist in the surveillance reporting, the reported incidence is likely an underestimate and highlight the importance of optimizing treatment regimens. Identification of specific risk factors for infection may allow for targeted prevention interventions.

1482

EPIDEMIOLOGY OF STREPTOCOCCUS SUIIS INFECTION IN THE SOUTH OF VIETNAM

Nghia Ho Dang Trung¹, Constance Schultz², Hoa Ngo Thi², Hien Tran Tinh², Jeremy Farrar²

¹Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Vietnam,

²Centre for Tropical Medicine, Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

Human *Streptococcus suis* infection is an emerging zoonotic disease in Southeast Asian countries. It is the most common pathogen caused bacterial meningitis at two referral hospitals for infectious diseases in Ha Noi and Ho Chi Minh City, Vietnam. To date, there has not been any information related to this pathogen in other hospitals as well as the incidence rate of this disease in Vietnam. A prospective hospital-based descriptive surveillance study was conducted from 08/2007 to 04/2010 at thirteen hospitals in central and southern Vietnam, including one district hospital, ten provincial hospitals and two central referral hospitals. Patients were recruited if they met all of the following inclusion criteria: at least one month of age; fever ≥ 38.0 C (axillary); at least one of the following symptoms or signs: headache, neck stiffness, altered consciousness and focal neurological signs; and a cerebrospinal fluid (CSF) sample taken. *S. suis* was confirmed in CSF and blood samples by using

classical microbiology and molecular diagnostics. A total of 1740 patients suspected central nervous system infection were recruited, in which *S. suis* was confirmed in 149 cases. *S. suis* was not found in children but it was reported as the most common pathogen of adult bacterial meningitis (149/302, 49%) in most of provincial hospitals. Overall incidence rate was 0.57/100,000 adult person-years. Incidence rate increased significantly with incremental age group. The ratio between males and females was 4:1. Pig exposures, such as breeding pigs at home, slaughtering pigs and eating raw or undercooked blood/organs, were described in 59/149 (40%) patients. Bacterial meningitis, the most common manifestation of *S. suis* infection, was responsible for 146/149 (98%) cases, and septic shock, the most serious manifestation, was reported in 3/149 cases (2%) and the overall case fatality rate (CFR) was 8% (12/149). While seasonality of *S. suis* meningitis was reported at Hue Central hospital (a tertiary hospital of the North Central of Vietnam), of which the peak month was estimated as July ($p < 0.001$), it was not observed in other southern provinces ($p = 0.31$). In conclusion, this study indicated that *S. suis* serotype 2 meningitis is endemic in Vietnam. Health education program on prevention should be applied to high risk groups to reduce the loss of health and economics of community.

1483

EPIDEMIOLOGY AND RISK FACTORS OF SEROGROUP W135 MENINGOCOCCAL DISEASE OUTBREAK IN THE GAMBIA, FEBRUARY-JUNE 2012

M. Jahangir Hossain¹, Anna Roca¹, Grant A. Mackenzie¹, Momodou Jasseh¹, Ilias Hossain¹, Shah Muhammad¹, Manjang Ahmed¹, Osuorah Donatus Chidiebere¹, Ndiaye Malick¹, Bilquees Shah Muhammad¹, Usman N. Ikumapayi¹, Baba Jeng², Baba Njie², Mamady Cham², Beate Kampmann¹, Tumani Corrah¹, Stephen Howie¹, Umberto D'Alessandro¹

¹Medical Research Council Unit, The Gambia, Banjul, Gambia, ²Ministry of Health, Republic of The Gambia, Banjul, Gambia

In the African meningitis belt, meningococcal disease is endemic with regular outbreaks, mostly (80%) due to *Neisseria meningitidis* (Nm) serogroup A. In 2002-2003, a large epidemic of NmW135 occurred in this region, but not in The Gambia, where the last cases were reported in 1995. In 2012, another NmW135 epidemic occurred in the meningitis belt, including The Gambia. Between February and June 2012, the Gambian Ministry of Health and the Medical Research Council (MRC) Unit, The Gambia, investigated this outbreak in the Central (CRR) and Upper (URR) River Regions. Suspected cases were identified in Bansang Hospital, CRR, and Basse Health Centre, URR, and by visiting NmW135 cases' households. A suspected case was defined as any patient with history of acute fever and any of the following: altered consciousness, unable to feed, neck stiffness, convulsion, petechial rash or bulging anterior fontanel. Cerebrospinal fluid and blood samples were collected from hospitalized cases to identify the pathogens by culture and latex test. A confirmed case was a suspected case in which NmW135 was identified by culture and/or an antigen-specific test. A matched case-control (1:1) study was carried out. Healthy controls were matched with confirmed cases by age and village. We identified 469 suspected cases of which 114 were confirmed for NmW135. Most (65%) of them were in children <5 years old. The overall attack rate was 111/100,000 population but in children <5 years it was 5 times higher (485/100,000) than in older children and adults. The epidemic threshold (10 cases/100,000 population/week) exceeded in February and continued until April in all ages and until June in children <5 years. In the multivariate analysis, male gender (OR 1.9; 95% CI 1.0-3.7), contact with cases (OR 4.8; 95% CI 1.3-17.8), difficult breathing (OR 6.8; 95% CI 1.4-33.4) and itchy eyes (OR 4.4; 95% CI 1.3-14.4) were significantly associated with NmW135 cases. Enhanced surveillance of meningitis and multi-serogroup conjugate vaccine are recommended for the control and prevention of meningococcal epidemics.

RODENT CONTROL PROGRAM AND LEPTOSPIROSIS PREVENTION IN SALVADOR, BRAZIL

Federico Costa¹, Jose E. Hagan¹, Guilherme S. Ribeiro², Renato B. Reis¹, Nivison J. Rocha¹, Maria G. Rodrigues³, Helena M. Farias³, Mitermayer G. Reis¹, Peter J. Diggle⁴, Albert I. Ko⁵

¹Oswaldo Cruz Foundation, Brazilian Ministry of Health, Salvador, Brazil, ²Institute of Collective Health, Salvador, Brazil, ³Zoonosis Control Center, Salvador, Brazil, ⁴Lancaster University, Lancaster, United Kingdom, ⁵Department of Epidemiology and Public Health, Yale School of Medicine, New Haven, CT, United States

Effective interventions for leptospirosis have not been identified which can be feasibly implemented in urban slum communities. Rodent Control Programs (RCP) constitute the principal strategy to prevent leptospirosis in Brazilian cities. However, RCPs are expensive and their efficacy has not been evaluated. We evaluated the efficacy of a municipal RCP to decrease rat infestation and leptospirosis incidence in Salvador (2.6 million pop.). Residences of patients with laboratory confirmed leptospirosis (years 2005-10) were geolocated and used to define 11 areas (15% of the city), containing 2,078 blocks, of equal risk for leptospirosis. During a pre-epidemic season (January-April), households from selected blocks were surveyed for rat infestation and received rodenticide application. Efficacy of the RCP was evaluated after the intervention by assessing two outcomes: 1) rat infestation by surveying 10% of treated blocks, and 2) change on incidence of leptospirosis. Kilograms of applied rodenticide and proportion of treated houses per block were used as measures of treatment intensity. These intensity proxies were used to build two mathematical models and evaluate the risk ratio of incidence of leptospirosis between pre- (2005-08) and post-intervention (2009-10) periods. A total of 671 blocks were treated in 2009 and 1,129 blocks in 2010. Surveys identified rat infestation of 25% and 26% in 2009 and 2010, respectively. 92% of the infested households in 2009 had evidence of *Rattus norvegicus*. After intervention, rat infestation decreased from 25% to 7% ($p < 0.001$) in 2009 and from 26% to 15% ($p < 0.001$) in 2010. The incidence of leptospirosis in the study blocks was 32.2 and 11.3 per 100,000 pop. during the pre and post-intervention periods, respectively. Using the models, the predicted reduction in incidence after maximum rodent intervention, as measured by either completeness of block coverage or kg of rodenticide, had large confidence intervals limiting our ability to evaluate the efficacy of RCP. Our study indicates that a high proportion (>25%) of households are infested with *R. norvegicus*. The RCP was able to decrease rat infestation, but because severe leptospirosis cases are rare events, it was not possible to evaluate their efficacy to decrease incidence. Further evaluations, considering more frequent events, such as mild *Leptospira* infection, may be necessary to evaluate the effectiveness of these costly interventions.

DEVELOPMENT OF DIAGNOSTIC AIDS TO DISCRIMINATE PARTIALLY TREATED BACTERIAL MENINGITIS (PTBM) FROM VIRAL MENINGITIS/ENCEPHALITIS (VM/EN)

Hong Chau T. Tran¹, Marcel Wolber², Tan Le², Hoang Mai Nguyen², Thanh Hang Hoang³, Nghia Ho Dang Trung³, Rogier Van Doorn¹, Jeremy Farrar⁴

¹Hospital for Tropical Diseases, Ho Chi Minh, Vietnam, ²Centre for Tropical Medicine, Oxford University Clinical Research Unit, Ho Chi Minh, Vietnam, ³Pham Ngoc Thach University of Medicine, Ho Chi Minh, Vietnam, ⁴Centre for Tropical Medicine, Oxford University Clinical Research Unit, Ho Chi Minh, Vietnam

The diagnosis of ptBM is difficult. Discrimination of cases from those of VM/EN by clinical features alone is often impossible. We aimed to create a simple diagnostic aid for ptBM in adults on the basic laboratory features. We compared the laboratory features on admission of 374 adults at HTD, Vietnam who satisfied diagnostic criteria for ptBM (n=291) or VM/

EN (n=83). Laboratory features independently predictive of ptBM were modelled by logistic regression according to Bayesian information criterion (BIC) and by classification- tree (C-T) method. Prognostic accuracy was summarized by sensitivity/ specificity / positive predictive value (PPV)/ negative predictive value (NPV). To assess potential over fitting of our models, all performance measures were bootstrap corrected for optimism. BIC defined three characteristics independently predictive of a diagnosis of ptBM from VM/EN: cerebrospinal fluid (CSF) neutrophil proportion (N%), CSF: blood glucose, and log₂ (CSF lactate). Using these three predictors we developed a diagnostic nomogram. Our C-T constructed on two predictors (CSF lactate and CSF white cell count) which is more simple than nomogram but less sensitivity, specificity, PPV and NPV than those in BIC (0.979, 0.923, 0.978 and 0.929, and 0.984, 0.962, 0.988 and 0.950, respectively). This study suggests that simple laboratory data can help in the diagnosis of adults with ptBM, particularly in setting with limited microbiological resources.

VACCINATION WITH A GENETICALLY MODIFIED FILARIAL CYSTEINE PROTEASE INHIBITOR-2 PROTECTS GERBILS AGAINST *BRUGIA MALAYI* AND MICE AGAINST *ONCHOCERCA VOLVULUS* INFECTION

Sridhar Arumugam¹, Bin Zhan², David Abraham³, Jessica Hess³, Simon A. Babayan⁴, Judith E. Allen⁵, David W. Taylor⁵, Danielle Ward¹, Thomas R. Klei¹, Sara Lustigman⁶

¹Louisiana State University, Baton Rouge, LA, United States, ²Baylor College of Medicine, Houston, TX, United States, ³Thomas Jefferson University, Philadelphia, PA, United States, ⁴Institute of Biodiversity, Animal Health and Comparative Medicine, University of Glasgow and Moredun Research Institute, Glasgow, United Kingdom, ⁵University of Edinburgh, Edinburgh, United Kingdom, ⁶Lindsley F. Kimball Research Institute, New York Blood Center, New York, NY, United States

Cysteine protease inhibitors or cystatins are reversible, tightly binding inhibitors of cysteine proteases. Filarial cysteine protease inhibitors have been ascribed to participate in worm's development as well as to contain immunomodulatory properties. They are hypothesized to play an important role in the establishment of infection by suppressing host immune responses, and therefore are good candidates for vaccine development. Expressed recombinant wild-type *B. malayi* cysteine protease inhibitor-2 (Bm-CPI-2) and *Onchocerca volvulus* cysteine protease inhibitor-2 (Ov-CPI-2) in *E. coli* showed strong inhibitory activity against Cathepsin L. Since the wild-type cystatin is a strong immune suppressor and therefore could inhibit host immune response upon immunization, the amino acid Asn at position 66 related to its asparaginyl endopeptidase inhibition activity was mutated to Lys66 in order to inactivate its immune suppressive activity and therefore enhance its protective immunity. DNAs encoding the Bm-CPI-2 or Ov-CPI-2 minus the signal peptides, with Asn66 mutated to Lys66 (Bm-CPI-2M, Ov-CPI-2M) were synthesized by GenScript and subsequently subcloned and expressed in the *E. coli* expression vector pET41a. Mongolian gerbils were immunized with 25 µg of the recombinant Bm-CPI-2M intraperitoneally with alum as the adjuvant three times, two weeks apart. The gerbils were challenged with infective L3 larvae subcutaneously and the parasites were recovered on day 42 post-infection. Vaccination with Bm-CPI-2M resulted in 48% reduction in worm burden in comparison to the Alum control group. Measurement of Bm-CPI-2M specific IgG by ELISA showed elevated levels of specific antibody response in the Bm-CPI-2M vaccinated gerbils. Vaccination of mice with the *O. volvulus* modified cystatin, Ov-CPI-2M, in alum also induced protection against larvae implanted subcutaneously within diffusion chambers, resulting in a 27% reduction in parasite survival. The immunized mice developed antigen-specific IgG responses. Our results confirm the CPI-2M vaccine-mediated protection obtained in the murine model of filariasis *Litomosoides sigmodontis* (Babayan et al. 2012), and extend it to filarial parasites of humans. In conclusion, the genetically modified filarial cysteine protease inhibitor-2 is a promising candidate for use in prophylactic vaccines against filariasis.

1488

EARLY DNA METHYLATION EVENTS IN UROGENITAL SCHISTOSOMIASIS AND THEIR IMPLICATIONS FOR INFLAMMATION-INDUCED BLADDER CANCER

Simon Conti, Jared Honeycutt, **Michael Hsieh***Stanford University School of Medicine, Stanford, CA, United States*

Urogenital schistosomiasis is linked to inflammation-associated bladder cancer. Inflammation-induced DNA methylation of tumor suppressor genes has been implicated in various forms of carcinogenesis. We hypothesized that some of these DNA methylation changes could be detected early after induction of experimental urogenital schistosomiasis. We combined our established mouse model of urogenital schistosomiasis with reduced representation bisulfite sequencing (genome-wide methylation analysis). Mice underwent sub-epithelial bladder injections of *Schistosoma haematobium* eggs or vehicle. Other mice received drinking water containing nitrosamine, an established urothelial carcinogen. After two weeks of exposure mice were sacrificed and their urothelia dissected from the detrusor and granuloma. DNA was extracted from each specimen and the restriction enzyme Msp1 used to cleave CpG islands. After bisulfite treatment samples were purified to a length of 175-225 bp and amplified by PCR. Next generation sequencing was performed with the Illumina Hi-Seq platform. The output was aligned with the UCSC M. Musculus genome v10 using Bismark software. Methylation analysis was performed with MethylKit and IGV. Egg-injected mice featured major alterations in their methylome (vs control mice) after two weeks of treatment. Bases with a depth of sequencing of less than 10 were excluded from analysis, and differential methylation was defined as a different of greater than 25% with a p-value of less than 0.05. 13,333 cytosines were hypermethylated and 6,244 were hypomethylated. Of these differentially methylated bases 1019 were found to be within 1000 base pairs of a transcription start site for a known gene. Six of these genes are part of the Wnt canonical pathway, which is related to cell proliferation. A CpG upstream of the Wnt Inhibitory Factor-1 gene, a gene silenced by hypermethylation in bladder tumors and other cancers, was methylated 54% of the time in egg-injected mice, 34% in nitrosamine-fed mice and 7% in control mice. This methylation event, along with our profiling of the DNA methylome of mice with experimental urogenital schistosomiasis, is the first of its kind, and may lead to an understanding of the sentinel events of urogenital schistosomiasis-associated bladder carcinogenesis.

1489

INFECTION WITH CARCINOGENIC LIVER FLUKE *OPISTHORCHIS VIVERRINI* MODIFIES INTESTINAL AND BILIARY MICROBIOME

Jordan L. Plieskatt¹, Raksawan Deenonpoe², Jason P. Mulvenna³, Lutz Krause³, Banchob Sripa², Jeffrey M. Bethony¹, **Paul J. Brindley**¹

¹The George Washington University, School of Medicine and Health Sciences, Department of Microbiology, Immunology and Tropical Medicine, Washington, DC, United States, ²Tropical Disease Research Laboratory, Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, ³Queensland Institute of Medical Research, Brisbane, Australia

Opisthorchis viverrini is a fish-borne trematode endemic in East Asia. Following ingestion, the flukes locate to the biliary tract, where chronic infection frequently leads to cholangiocarcinoma (CCA). The precise mechanism(s) by which *O. viverrini* infection culminates in CCA is not known. One unexplored aspect is its influence on the host microbiome. In the Syrian hamster, infection with this pathogen reliably leads to CCA. Genomic DNAs of microbiota from colorectal contents and bile of hamsters and *O. viverrini* were examined in this model of fluke-induced CCA. Sequences of regions 7, 8 and 9 of prokaryotic 16S rRNA genes were amplified, pyrosequenced, operational taxonomy units classified, and analysis of community diversity undertaken. Of

~1,000,000 sequences, 536,009 could be assigned to 20 phyla and 273 genera of bacteria or Archaea. Diversity analyses revealed that fluke infection perturbed the gastrointestinal tract microbiome, increasing Lachnospiraceae, Ruminococcaceae and Lactobacillaceae while decreasing Porphyromonadaceae, Erysipelotrichaceae and Eubacteriaceae ($p \leq 0.05$). In addition, >60 prokaryote species were detected in the biliary system, which confirmed bacteriobilia and a remarkable community associated with the parasites. These fluke-associated microorganisms included potential pathogens from the *Enterobacteriaceae* and *Listeriaceae* and others from external environments including cyanobacteria and Deinococci. Given that opisthorchiasis is distinguished from other helminth infections by a robust inflammatory phenotype, with conspicuously elevated interleukin 6, and that inflammation of the biliary system leads to periductal fibrosis that is a precursor to CCA, the flukes as well as their microbiota might together drive this distinctive immune response.

1490

IMMUNOMICS-BASED IDENTIFICATION OF SCHISTOSOMIASIS VACCINE ANTIGENS: AN INTEGRATED DISCOVERY AND VALIDATION APPROACH

Mark S. Pearson¹, Soraya Gaze¹, Patrick Driguez², Tiago Mendez³, Denise Doolan², Angela Trieu², Don McManus², Fernanda Cardoso², Rie Sasaki⁴, Philip Felgner⁴, Jeffrey Bethony⁵, Alex Loukas¹

¹James Cook University, Cairns, Queensland, Australia, ²Queensland Institute of Medical Research, Brisbane, Queensland, Australia, ³Federal University of Minas Gerais, Belo Horizonte, Brazil, ⁴University of California, Irvine, CA, United States, ⁵George Washington University, Washington, DC, United States

Schistosomiasis is a neglected tropical disease affecting >230 million people and causes over 200,000 deaths annually. To identify new vaccine antigens and assess their potential protective efficacy and safety, we used an immunomics approach with sera from putatively resistant (PR) and chronically infected (CI; stratified by infection intensity) people in a high transmission area for schistosomiasis in Brazil. We selected mostly tegumental *Schistosoma mansoni* and *S. japonicum* proteins, produced them using an *in vitro* rapid translation system (RTS) and printed them to generate the first protein microarray for a multi-cellular pathogen. Arrays were screened to detect IgG subclass and IgE responses; antigens which showed preferential/unique recognition by IgG1/3 from PR individuals were up-selected, and those that were the target of potentially deleterious IgE responses (in terms of vaccine-induced hypersensitivity) were down-selected. We detected strong correlations between the number of antigens recognized and infection intensity for all antibody subclasses, most notably IgE. Surprisingly, PR individuals produced little IgE but instead made robust IgG1/3 responses to a small number of antigens exposed on the parasite surface, highlighting their potential as vaccine antigens. Cluster analysis was performed to identify antigen clusters based on their antibody recognition profiles. Two clusters contained antigens that were preferentially recognized by IgG1/3 of PR individuals but were not major targets of IgE; these clusters included the previously described vaccine candidates Sm-TSP-2 and Sm29, as well as a panel of new antigens that have not been previously described. We have shown here the use of a high throughput immunomics approach to profile antibody responses from PR and CI individuals that has unearthed a suite of novel potentially protective and safe schistosomiasis vaccine antigens. To complement our human subjects-oriented antigen discovery approach, we are also probing arrays with sera from non-human primates that have been vaccinated with irradiated schistosome cercariae.

ELEVATED ARGINASE 1 AND LOW NITRIC OXIDE SYNTHASE 2 PBMC EXPRESSION: EVIDENCE OF ALTERNATIVE MACROPHAGE ACTIVATION IN CHILDREN WITH MALARIA

Florence Savatory

Hubert Kairuki University, Dar es salaam, United Republic of Tanzania

We demonstrated earlier that malaria infection is associated with low serum arginine levels and low expression of nitric oxide synthase2 (NOS2) leading to diminished nitric oxide (NO) production and endothelial dysfunction. We established that NO is protective in malaria. The mechanism of diminished NO production is not well understood, but it is likely to be multi-factorial. Increased metabolism of arginine by arginases and suppression of NOS2 expression likely play roles. Alternative macrophage activation (M2) is initiated by Th2 cytokines such as IL-4, IL-10, and IL-13. M2 activation is also associated with increased arginase1, decreased NOS2 and NO expression by monocytes-macrophages, and likely less resistance to malaria infection and/or malaria disease. The aim of this study was to investigate the markers for monocytes/macrophage in PBMCs from children *Plasmodium falciparum* infection. Children aged 6mo to 9 yr were recruited from Amana and Mwananyamala hospitals in Dar es Salaam, Tanzania, and categorized (modified WHO criteria) as severe malaria (SM), uncomplicated malaria (UM), or healthy control (HC). We prospectively measured PBMC mRNA for arginases 1 and 2, and NOS2 using quantitative RT-PCR. Results were analyzed using Prism 5 software and Mann-Whitney non-parametric comparison analysis. We enrolled 80 SM, 80 UM, and 48 HC participants. There was marked increase in PBMC arginase 1 mRNA in children with malaria compared to healthy controls (4.5 fold in UM and 9.3 fold in SM; $p = 0.02$ and 0.008 respectively), while NOS2 mRNA was lower in SM and UM than in HC ($p = 0.0001$) for each comparison. PBMC arginase 2 mRNA was lower in SM compared to HC, but it was not statistically significant ($p = 0.89$). In conclusion, malaria infection in children is associated with increased arginase 1, and decreased NOS2 and arginase 2 mRNA expressions. This is characteristic of alternative macrophage activation and may partly explain the low serum arginine and diminished NO production in malaria. Assessment of arginase activity in PBMCs (and purified mononuclear phagocytes) during malaria infection is warranted to fully establish the role of alternatively activated monocytes-macrophages in the hypoarginaemia observed during the malaria infection.

IMBALANCE OF INFLAMMATORY AND ANGIOGENIC FACTORS IN EARLY PREGNANCY ARE ASSOCIATED WITH PRETERM BIRTH IN A PROSPECTIVE COHORT OF MALARIA-EXPOSED TANZANIAN WOMEN

Chloe E. McDonald¹, Anne Marie Darling², Andrea L. Conroy¹, Kyla Hayford¹, Nimerta Rajwans¹, Said Aboud³, Willy Urassa³, Wafaie Fawzi², Kevin C. Kain¹

¹University of Toronto, Toronto, ON, Canada, ²Harvard University, Boston, MA, United States, ³Muhimbili University of Health and Allied Sciences, Dar es Salaam, United Republic of Tanzania

Malaria in pregnancy is associated with several adverse birth outcomes including preterm birth (PTB). PTB is now the leading cause of perinatal mortality globally, however there are currently no diagnostic tools to predict pregnancies at risk of PTB. Based on the hypothesis that altered placental angiogenesis and inflammation early in pregnancy lead to PTB, we examined if levels of inflammatory and angiogenic mediators, measured early in pregnancy (< 27 weeks gestation), were predictive of PTB in a cohort of women living in a region of high malaria transmission. Plasma samples were collected from a prospective cohort of 432 primigravid women at enrollment (12-27 weeks gestation). A total 63 women subsequently delivered preterm (< 37 weeks gestation). Levels of 18 biomarkers reflective of angiogenic and/or inflammatory pathways (Ang-1, Ang-2, Ang-L3, VEGF, sFLT-1, sTNFR2, PIGF, MIP-1 β ,

MCP-1, Leptin, IL-1 β , IL-18 BP, sICAM-1, FAC-D, sEndoglin, CRP, CHI3L1, C5a) were analyzed by ELISA. Plasma levels of PIGF ($P=0.04$), IL-18 BP ($P=0.002$), sICAM-1 ($P=0.03$), sEndoglin ($P=0.0005$), CHI3L1 ($P=0.002$), sTNFR2 ($P=0.05$) were higher at enrollment in women who subsequently experienced PTB compared to women who delivered at term. Based on multiple analytic methods, plasma levels of IL-18BP, CHI3L1 and sEndoglin were elevated at enrollment, in women who went on to deliver preterm. Combinatorial strategies were applied in an attempt to improve predictive accuracy. Combining biomarker data (sICAM-1 and CHI3L1) with clinical and demographic data improved our predictive model of PTB over that possible with clinical data alone ($P=0.0002$). In conclusion, in this cohort of Tanzanian women, levels of angiogenic and inflammatory mediators measured early in pregnancy, were associated with subsequent PTB. These proteins provide insight into the underlying mechanism of PTB and may have clinical utility as early biomarkers of preterm delivery. Given the high rates of PTB in malaria endemic regions, there is a critical need to develop early diagnostic tools to identify pregnancies at risk of PTB.

PLACENTAL MALARIA INDUCES EXCESSIVE VASCULOGENESIS

Tara C. Bracken¹, Samantha Burton¹, Ashley McMichael¹, Carlos Abramowsky², Simon Owino¹, Julie Moore¹

¹University of Georgia, Athens, GA, United States, ²Emory University School of Medicine, Atlanta, GA, United States

Placental malaria (PM) results from sequestration of *Plasmodium falciparum*-infected erythrocytes and the resulting inflammatory responses in the maternal placental blood space. PM induces maternal anemia, preterm birth, low birth weight, or stillbirth, especially in primigravidae. PM may also promote local hypoperfusion or hypoxia, inducing neovasculogenesis in the fetal placental compartment. Excessive vasculogenesis can result in chorangiomas (CHOR), defined as at least 10 vascular channels (VC) in at least 10 terminal villi in 10 low power microscopic fields in three discreet regions of the placenta. CHOR is rare but is enhanced in preeclampsia and diabetes and is associated with neonatal morbidity and mortality. To determine the extent to which PM induces CHOR, placentae were collected from 18 consenting primigravidae at two public hospitals in Kisumu, Kenya. Malaria status and PM chronicity were estimated by microscopic examination of placental blood smears and PCR and by placental histology. Patients were separated into the following groups: uninfected (UN, n=2), active/active chronic (A/AC, n=9) infection, and past/past chronic infection (P/PC, n=7). Thin sections from three fixed placental tissue sections were hematoxylin and eosin-stained, and thirty micrographic images at 200X magnification (to approximate ten low power fields at 100x) were captured from each section. Number of villi and VC therein were counted. Whereas UN and P/PC placentae were equivalent, A/AC placentae had statistically significantly higher median numbers of VC/villus ($P<0.0001$). Moreover, the latter group also had a significantly higher percentage of villi with ten or more VC relative to the other two groups ($27.2\pm 1.6\%$ versus $20.5\pm 0.8\%$ (UN) and $20.7\pm 2.0\%$ (P/PC), $P=0.0355$). Further analysis of these samples is underway to evaluate whether these samples meet the clinical definition of CHOR and associations with birth outcomes. In addition, assessment of markers of angiogenesis promises to provide insight into the molecular mechanisms underlying this phenomenon in PM.

1494

RETINAL MICROVASCULAR DYSFUNCTION IN PEDIATRIC CEREBRAL MALARIA IS ASSOCIATED WITH DEATH AND NEUROLOGICAL SEQUELAE

Ian J. MacCormick¹, Simon J. Glover², Nicholas A. Beare³, Gabriela Czanner³, Macpherson Mallewa¹, Terrie T. Taylor⁴, Malcolm E. Molyneux¹, Simon P. Harding³

¹Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Queen Elizabeth Central Hospital, College of Medicine, Blantyre, Malawi, ²Department Ophthalmology, Addenbrooke's Hospital, Cambridge, United Kingdom, ³Department of Eye and Vision Science, University of Liverpool, Liverpool, United Kingdom, ⁴Blantyre Malaria Project, University of Malawi College of Medicine, Blantyre, Malawi

Malarial retinopathy (MR) appears to reflect brain pathogenesis in pediatric cerebral malaria (CM), since it is related to mortality and highly predictive of brain histopathology. MR is associated with abnormal fluorescein angiography (FA), but mortality associated with these abnormalities is unknown. We aimed to characterize FA abnormalities and their relationship to clinical outcomes. Two ophthalmologists graded admission angiograms in 170 consecutive patients with pediatric CM from 2006 to 2010 (WHO criteria, including retinopathy negative cases). Variation between eyes was assessed using Cohen's kappa statistic. Associations between FA abnormalities, mortality, and presence of neuro-disability on discharge were assessed using left eye data and Fisher's exact test. In our series 118 survived, 25 survived with neuro-disability, and 27 died. All FA signs were consistent between right and left eyes. Frequencies of features were: Capillary non-perfusion (CNP), macular 82%, peripheral 84%; Intravascular filling defect (by vessel type): large 38%, small 14%, occluded 22%; Vessel leak: small macular 56%, small peripheral 49%, mid/large 16%, disc 52%. Severity of macular CNP ($p=0.02$) and presence of peripheral small vessel leakage ($p=0.03$) were significantly associated with death and neurological disability; peripheral CNP ($p=0.45$), and macular small vessel leakage were not ($p=0.09$). This is the largest analysis of retinal angiography in pediatric CM to date. Retinal CNP is very common. Severity of macular CNP, and the presence of fluorescein leakage from small peripheral retinal vessels are associated with death and neuro-disability. CNP indicates ischemia and matches areas of retinal whitening seen clinically. This result is consistent with a known association between macular whitening and death. FA leakage results from breakdown of the blood-retinal barrier, which is similar to the blood-brain barrier. Our results suggest that central nervous system ischemia and leakage across blood-tissue barriers may be important contributors to the severity of pediatric CM.

1495

FATAL PEDIATRIC CEREBRAL MALARIA IS ASSOCIATED WITH INTRAVASCULAR INFLAMMATION AND COAGULATION THAT IS EXACERBATED BY HIV-1 CO-INFECTION

Sarah Hochman¹, Theresa Madaline², Karl Seydel³, Terrie Taylor³, Danny Milner⁴, Sunhee Lee¹, Kami Kim¹

¹Albert Einstein College of Medicine of Yeshiva University, Bronx, NY, United States, ²Montefiore Medical Center, Bronx, NY, United States, ³Michigan State University, East Lansing, MI, United States, ⁴The Brigham and Women's Hospital, Boston, MA, United States

Most malaria deaths occur in sub-Saharan African children and are due to various severe malaria syndromes, including cerebral malaria (CM). In Malawi, the overall prevalence of HIV-1 is 10%, with lower seroprevalence in children. The entire population is at risk for malaria. High rates of malaria/HIV co-infection are likely but effects of HIV on CM pathogenesis and outcome are unknown. The Blantyre Malaria Project (BMP) has found 3 patterns of brain pathology in children who met clinical criteria for CM: sequestration alone (CM1), sequestration plus intra- and peri-vascular pathology (CM2) and no sequestration (CM3). In the BMP cohort, the HIV+ rate is 13% overall and 20% in autopsied patients. 60% of autopsies

with the CM1 pattern are HIV+ compared to 18% with CM2 and 6% with CM3. To determine whether HIV co-infection affects the pathophysiology of CM, we performed immunohistochemistry on brain tissue from autopsied patients with clinically-defined CM. We examined 10 cases with the CM1 pattern, 10 with CM2 and 10 with CM3 or coma of other cause (COC). Five from each group were HIV+. Brain sections were labeled for HIV-1 p24, ionized calcium binding adapter molecule 1 (Iba1), a marker for microglia and monocytes, and CD61, a platelet marker. No HIV-1 p24 was seen. We observed intravascular Iba1+ monocytes containing hemozoin that completely filled small vessels and adhered to the walls of larger vessels, accompanied by platelet clumps. This was significantly increased in CM1/2 cases compared with CM3/COC cases and was significantly increased in HIV+ CM1/2 cases compared to HIV- CM1/2 cases. Most HIV+ CM1/2 cases had mild immunosuppression by WHO HIV clinical staging and the total lymphocyte counts of HIV+ CM1/2 cases were similar to those of HIV- CM1/2 cases. HIV+ CM1/2 cases were significantly older than HIV- CM1/2 cases. We hypothesize that the intravascular inflammation and coagulation seen in CM autopsies contribute to the pathogenesis of pediatric CM and that dysregulation of these processes in HIV infection contribute to CM mortality.

1496

MALARIA PIGMENT (HEMOZOIN) AND EXTRAVASATED FIBRINOGEN ARE ASSOCIATED WITH RETINAL VESSEL LEAKAGE AND HEMORRHAGES IN MALAWIAN CHILDREN WITH CEREBRAL MALARIA

Valentina Barrera¹, Paul S. Hiscott¹, Nick A. Beare², Alister G. Craig³, Valerie A. White⁴, Ian J. MacCormick⁵, Simon J. Glover⁶, Terrie E. Taylor⁷, Malcolm E. Molyneux⁵, Simon P. Harding¹

¹Department of Eye and Vision Science, University of Liverpool, Liverpool, United Kingdom, ²St. Paul's Eye Unit, Royal Liverpool University Hospital, Liverpool, United Kingdom, ³Liverpool School of Tropical Medicine, Liverpool, United Kingdom, ⁴Department of Pathology and Laboratory Medicine and Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, BC, Canada, ⁵Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Queen Elizabeth Central Hospital, College of Medicine, Blantyre, Malawi, ⁶Department Ophthalmology, Addenbrooke's Hospital, Cambridge, United Kingdom, ⁷Blantyre Malaria Project, University of Malawi College of Medicine, Blantyre, Malawi

Malarial retinopathy (MR) distinguishes cerebral malaria (CM) from non-malarial causes of coma. White-centered retinal hemorrhages are a common clinical feature and vessel leakage due to blood-retina barrier breakdown is found angiographically. We conducted a *post mortem* clinicopathological study to localize features of microvascular pathology affecting neural retina in Malawian children. Histopathological analyses were carried out on 7 cases: 5 cases with clinically defined CM during life showed MR features, and 2 patients with non-malaria comas had no evidence of MR. Retinal microvascular pathology was assessed by presence of: i) extraerythrocytic hemozoin (HZ) in retinal capillaries and venules, on the basis of hematoxylin-eosin staining (H&E); ii) perivascular leakage, with anti-fibrinogen (FGN) and anti-albumin immunohistochemistry (IHC); iii) retinal hemorrhages, with H&E and specific IHC markers (CD45 for inflammatory cells; collagen, smooth muscle actin, CD34 for vessels remnants). The MR cases were classified in two groups: one case had 16% vessels with HZ (Group 1), and four cases showed HZ in a median of 49% (min-max 25-82%) vessels (Group 2). Group 1 showed patchy focal leakage only in the retinal venules with HZ, and no hemorrhages. Each case in Group 2 presented ≥ 5 retinal hemorrhages, characterized by a white-center of FGN which accumulated in the perivascular space together with HZ and inflammatory cells. In the non-MR controls HZ was absent, and one case had retinal hemorrhages secondary to head injury and intracranial hemorrhage (Terson syndrome). HZ was found associated with features of retinal vascular pathology in severe MR cases, concurring with evidence of CM vascular pathology in the brain such as ring hemorrhages. Extravasated FGN from venules with HZ, as well as its presence in the center of retinal hemorrhages, suggest leakage can evolve with disruption

of retinal layers. Further studies on a potential temporal link between the two features can help us to define consequences of blood retinal barrier breakdown in MR.

1497

NON-INVASIVE PULSE OXIMETRY TO PREDICT MORTALITY IN AFRICAN CHILDREN WITH MALARIA

Andrea L. Conroy¹, Michael Hawkes¹, Chandy C. John², Sophie Namasopo³, Robert O. Opoka⁴, Kevin C. Kain¹

¹University of Toronto, Toronto, ON, Canada, ²University of Minnesota, Minneapolis, MN, United States, ³Jinja Regional Referral Hospital, Jinja, Uganda, ⁴Makerere University, Kampala, Uganda

Between February 2012 and April 2013 we enrolled 1677 children in a prospective observational study of children 2 months to 5 years admitted to Jinja Regional Referral hospital with a history of fever or an axillary temperature >37.5°C and known disease outcomes. The mean age of children enrolled was 1.65 years old, and malaria was the most frequent reason for admission with 76% of children having a diagnosis of malaria based on microscopy and/or positive 3-band RDT (pLDH/HRP2). The mortality rate for children admitted with malaria was 3.1%. We evaluated whether non-invasive pulse oximetry would predict disease outcome in malaria and compared the findings to venous lactate, an established prognostic marker in malaria. We used receiver operator characteristic (ROC) curves to assess the predictive ability of the biomarkers. The area under the curve (AUC) for the oxygen saturation (SpO₂) was 0.69 (95% CI, 0.59-0.80; p<0.0001), and a SpO₂ less than 92% was 97% sensitive and 37% specific in predicting mortality. In addition to SpO₂, the Masimo Pulse CO-oximeter has the capacity to measure the perfusion index (PI), which is the ratio of pulsatile blood flow to non-pulsatile static blood flow in peripheral tissue. The PI is a more sensitive and objective measure of peripheral perfusion than measuring capillary refill. The PI measured on children's finger tips or toes had an AUC of 0.68 (0.57-0.78, p<0.0001), and a PI less than 0.20 was 98% sensitive and 17% specific in predicting mortality. Initiation of appropriate life-saving measures (oxygen administration, treatment for shock) in children with low SpO₂ or a low PI resulted in marked patient improvement. Venous lactate ≥5.5mmol/L had an AUC of 0.80 (95% CI, 0.71-0.90; p<0.0001) and a sensitivity and specificity of 81% and 77%. These data suggest that pulse oximetry alongside assessment of venous lactate may be useful in the triage and treatment of children with severe malaria. Additional advantages in pulse oximetry are low operating costs and real-time patient monitoring.

1498

A NOVEL, KINETOPLASTID-SPECIFIC cAMP SIGNALING PATHWAY - A PROMISING DRUG TARGET

Sabine Bachmaier¹, Matthew K. Gould², Juma A. Ali², Sam Alsford³, Jane Munday², David Horn³, Harry P. de Koning², Michael Boshart¹

¹University of Munich (LMU), Biocenter, Section Genetics, Martinsried, Germany, ²Institute of Infection, Immunity and Inflammation, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, United Kingdom, ³Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom

The signaling molecule cAMP plays crucial regulatory roles in almost all eukaryotic cells. In *T.brucei*, the genetic or pharmacological manipulation of the intracellular cAMP concentration results in severe cytokinesis phenotypes with subsequent cell death. Consequently, the cAMP-specific phosphodiesterases have been validated as excellent drug targets. However, the *T. brucei* orthologue of the major downstream target of cAMP, the cAMP-dependent protein kinase (PKA), is not activated by cAMP, nor have homologues of other known mammalian cAMP effectors been identified. We thus used genome-wide RNAi library screening to select cells resistant to Cpd A, a novel and highly specific PDE inhibitor, which kills bloodstream trypanosomes via elevated intracellular cAMP.

Four candidate genes (CARP1-4: cyclic AMP response proteins) were identified, whose depletion confers different degrees of resistance to Cpd A. CARP1, a protein unique to kinetoplastid parasites has two predicted cNMP binding domains, and its depletion resulted in up to 200-fold Cpd A resistance. We suggest that this protein is a primary cAMP sensor and CARP2-4 proteins may be components of a novel cAMP signaling pathway. Binding of cAMP to CARP1, physical and genetic interactions among the CARP proteins, and their subcellular localisation are under investigation. We propose the novel kinetoplastid-specific cAMP signaling cascade as promising new drug target for Human African Trypanosomiasis and possibly other kinetoplastid diseases.

1499

CHARACTERIZATION OF THE SMALL PROTEOME OF *TRYPANOSOMA BRUCEI*

Megan Ericson¹, Michael Janes¹, Falk Butter², Samson Obado³, Michael Rout³, Matthias Mann², Elisabetta Ullu¹, Christian Tschudi¹

¹Yale University, New Haven, CT, United States, ²Max Planck Institute for Biochemistry, Martinsried, Germany, ³Rockefeller University, New York, NY, United States

Advances in genomics research are providing new avenues to a more holistic understanding of pathogens. An RNA-Seq transcriptome study from our lab identified 1,114 novel transcripts in *Trypanosoma brucei* of which 993 have at least one potential ORF. The majority fit into the category of short ORFs (sORFs), since the predicted protein is between 25 and 100 amino acids in size. Mining mass spectrometry data sets revealed 42 novel transcripts that encode a sORF matching to at least one unique peptide, suggesting that these proteins are expressed. Thus, the trypanosome proteome appears larger than previously believed. To begin to address the possible function of small proteins in *T. brucei*, all 42 novel transcripts were down-regulated by RNAi and 7 were determined to be essential in procyclic trypanosomes. Each lethal phenotype was rescued by co-expressing an RNAi-resistant construct, further validating the significance of these small proteins. The 7 essential sORFs are only found in trypanosomatids: five are widespread, while two are specific to African trypanosomes. For example, the essential protein encoded by Tb10.NT87 is 64 amino acids long and localizes to the matrix of the mitochondria, as shown by immuno EM, and a karyopherin-like protein has been identified as a potential interacting partner. On the other hand, Tb11.NT29 encodes 62 amino acids with a predicted trans-membrane domain and is localized on the surface of procyclic- and bloodstream-form trypanosomes. In addition, essential small proteins localize to the nucleolus, cytoplasm, and a perinuclear compartment of the cell, highlighting the diverse biological roles they are likely to play. Experiments are in progress to assess the essentiality in bloodstream form trypanosomes and to identify interacting partners.

1500

FUNCTIONAL VALIDATION OF HOST METABOLIC PATHWAYS AS CRITICAL REGULATORS OF *TRYPANOSOMA CRUZI* AMASTIGOTE GROWTH IN HUMAN CARDIOMYOCYTES

Kacey Caradonna, Sheena Shah-Simpson, Barbara Burleigh
Harvard School of Public Health, Boston, MA, United States

The intracellular amastigote stage of *Trypanosoma cruzi* is a critical target for vaccine and drug development for the prevention and treatment of human Chagas' disease - the leading cause of infectious cardiomyopathy. Despite the importance of amastigotes in infection and disease, we have a limited understanding of host factors that contribute to the growth and survival of these parasites. In a recent genome-wide RNA interference (RNAi) screen, host metabolic networks centered around energy production, nucleotide metabolism, pteridine biosynthesis, and fatty acid oxidation were identified as key processes that support *T. cruzi* infection in HeLa cells (Caradonna et al. 2013. Cell Host & Microbe 13

108-117). As a more relevant *in vitro* infection model, we are exploiting human induced pluripotent stem cell (iPSC)-derived cardiomyocytes for functional validation studies. iPSC- cardiomyocytes are transcriptionally and electrophysiologically similar to adult cardiomyocytes and amenable to high-throughput RNAi screening applications. Using this system, a number of 'hits' that originally surfaced in our RNAi screen have now been validated in cardiomyocytes, including pyruvate dehydrogenase kinase 4 (PDK4). PDK4 regulates the fuel utilization balance in mammalian cells where depletion results in reduced fatty acid oxidation and reduced parasite growth. Coupling host gene knockdown studies with sensitive extracellular flux measurements in live cardiomyocytes has allowed us to confirm the metabolic phenotypes associated with targeted host gene knockdown. We are currently exploiting this experimental system to elucidate the contribution of host lipid metabolism to *T. cruzi* amastigote growth and survival. The primary objective of this study is to gain mechanistic insight into the relationship between host metabolism and *T. cruzi* amastigote growth. This knowledge is fundamental to a broader understanding of intracellular parasitism and will open the door to potential alternative interventions.

1501

ROLE OF TLR9 SIGNALING IN EXPERIMENTAL *LEISHMANIA BRAZILIENSIS* INFECTION

Tiffany Weinkopf¹, Anita Mariotto², Gregoire Simon², Yazmin Hauyon-La Torre², Floriane Auderset², Steffen Schuster², Haroun Zanger³, Nicolas Fasel³, Aldina Barral⁴, Fabienne Tacchini-Cottier²

¹Department of Biochemistry, World Health Organization-Immunology Research and Training Center, University of Lausanne, Epalinges, Switzerland, ²Department of Biochemistry, University of Lausanne, Epalinges, Switzerland, ³Centro de Pesquisas Goncalo Moniz, Fundacao Oswaldo Cruz, (FIOCRUZ) and Faculdade de Medicina, Universidade Federal da Bahia, Salvador, Brazil

Infection with *Leishmania braziliensis* causes cutaneous or mucocutaneous leishmaniasis in humans. TLR9 expression has been found in granulomas of lesions in *L. braziliensis*-infected individuals. *L. braziliensis* inoculation in mice induces very small lesions that are self-healing whereas deficiency in the TLR adaptor molecule, MyD88, render mice susceptible to infection. The TLR receptor involved has not been identified, prompting us to investigate if TLR9 triggering by the parasite contributes to the strong resistance to infection observed in *L. braziliensis*-inoculated mice. The parasites activated wild-type (WT) dendritic cells (DCs) *in vitro*, but not DCs derived from TLR9-/- mice. TLR9-/- mice inoculated with *L. braziliensis* exhibited a transient susceptibility characterized by increased lesion size and parasite burden compared to WT mice. Surprisingly, elevated levels of IFN γ were measured at the site of infection and in draining lymph node T cells of TLR9-/- mice at the peak of susceptibility, suggesting that unlike observations *in vitro*, the parasite could induce DC activation leading to the development of Th1 cells in absence of TLR9 expression. Taken together these data show that TLR9 signaling is important for the early control of lesion development and parasite burden, but it is dispensable for the differentiation of Th1 cells secreting IFN γ , and that the high levels of this cytokine are not sufficient to control early parasite replication following *L. braziliensis* infection.

1502

DYNAMICS OF APICOMPLEXAN INNER MEMBRANE COMPLEX

Dinkorma Ouologuem, David Roos

University of Pennsylvania, Philadelphia, PA, United States

Unlike most cells, which divide by binary fission, protozoa in the phylum apicomplexa divide by a distinctive process in which multiple daughters are constructed within the mother (schizogony, endodyogeny, etc), using a membrane-cytoskeletal scaffolding known as the Inner Membrane Complex (IMC). The IMC is closely associated with the plasma membrane

during interphase, but new daughters develop within the cytoplasm, establishing new IMCs. Daughter IMCs elongate rapidly, partitioning subcellular compartments according to a strict schedule. Newly assembled daughters ultimately emerge from the mother, picking up the maternal plasma membrane, and leaving behind vestiges of the maternal cell that were not incorporated into the daughters. While the maternal plasma membrane remains intact throughout this process the maternal IMC disappears -- is it degraded, or recycled to form the daughter IMC? Exploiting a fluorescently tagged integral membrane protein marker for the IMC (GAP40), we have used live cell imaging, photobleaching-recovery (FRAP), and mEos2 photoactivation to monitor the dynamics of IMC biogenesis and turnover during the replication of *Toxoplasma gondii* tachyzoites. We demonstrate that formation of the IMC involves two distinct steps: de novo assembly during daughter IMC elongation within the mother cell, followed by emergence from the mother cell and further maturation via recycling of the maternal IMC membrane.

1503

PLASMODIUM FALCIPARUM CDC2-RELATED PROTEIN KINASE (CRK) 4 REGULATES DNASEGREGATION AND THE ONSET OF BLOOD-STAGE SCHIZOGONY

Markus Ganter¹, Jeffrey D. Dvorin², Christian Flueck³, Jing Yang¹, David A. Baker³, Manoj Duraisingh¹

¹Harvard School of Public Health, Boston, MA, United States, ²Boston Children's Hospital, Division of Infectious Diseases, Boston, MA, United States, ³London School of Hygiene & Tropical Medicine, London, United Kingdom

A hallmark of Plasmodium life-cycle progression is a sequence of invasive and replicative stages. Intrahepatic- and intraerythrocytic-proliferation is achieved through schizogony, where a multinucleated cell is formed after which daughter parasites bud off the mother cell. However, the regulatory proteins involved in schizogony are largely unknown. Employing the inducible destabilization domain system in a loss-of-function knockdown screen of schizont-stage kinases, we identified the *P. falciparum* cdc2-related protein kinase (PfCRK) 4 as essential for proliferation. Depletion of PfCRK4 leads to a complete block in early schizogony at a DNA-content of approx. 6N, which is reversible within eight hours. The block at 6N is similar to what is observed following treatment with the anti-folate drug WR99210, which might be indicative of a general cell cycle checkpoint at 6N. Despite several rounds of DNA replication, analysis by microscopy revealed that PfCRK4-knockdown parasites are unable to segregate their chromosomes. This defect is likely due to an impaired division of the spindle pole body in PfCRK4 depleted parasites. Among apicomplexan parasites, CRK4 is uniquely found in Plasmodium spp., and we provide evidence that PfCRK4 is a key regulator at the onset of schizogony.

1504

TLR7-ELICITED REGULATORY B CELLS USE IL-10 TO SUPPRESS AIRWAY INFLAMMATION THROUGH INDUCTION OF CD4+FOXP3+ T CELLS

Adnan Khan¹, Sylvie Amu¹, Sean P. Saunders¹, Casey Weaver², Tim Sparwasser³, Orla Sheils⁴, Padraic. G. Fallon¹

¹Trinity Biomedical Sciences Institute, School of Medicine, Trinity College, Dublin, Ireland, ²Department of Pathology, University of Alabama, Birmingham, AL, United States, ³Institute of Infection Immunology, TWINCORE, Centre for Experimental and Clinical, Hanover, Germany, ⁴Department of Histopathology, Trinity College Dublin, Sir Patrick Duns Research, Dublin, Ireland

Helminths are potent modulators of the immune system using a diverse range of mechanisms. In recent times, a role for helminth-induced regulatory CD19+CD1dhi B cells (Breg) has been identified as regulators of inflammation in mouse models. Using, microarray technology we have analyzed the gene profiles of *Schistosoma mansoni*-elicited Breg. With respect to innate activation of these cells, toll-like receptor 7 (TLR7)

was a significantly upregulated pathway of interest. The use of TLR7 ligands both *in vitro* and *in vivo* demonstrated the generation of Breg - comparable to helminth-elicited Breg - that produced copious amounts of the immunosuppressive cytokine IL-10. In a mouse model of allergic lung inflammation the use of either TLR7 ligands to induce Breg or the adoptive transfer of *in vitro* generated Breg demonstrated a reduction in airway inflammation and an improvement in lung function. Previously, we have shown how helminth-induced Breg can suppress pulmonary inflammation via CD4+FoxP3+ T cells. Here, we have investigated if TLR7-elicited Breg suppresses airway inflammation via CD4+FoxP3+ T cells and whether this effect is dependent on IL-10. Our work demonstrates how deciphering mechanisms by which helminths modulate the immune system can yield specific targets of therapeutic interest.

1505

THE ROLE OF EPIDERMAL KERATINOCYTES IN THE CUTANEOUS IMMUNE RESPONSE TO *SCHISTOSOME CERCARIAE* AND THEIR EXCRETORY/SECRETORY ANTIGENS

Claire D. Bourke¹, Adrian P. Mountford²

Centre for Immunology and Infection, University of York, York, United Kingdom

The epidermis is the site of the initial interaction between schistosome parasites and their mammalian host. During invasion schistosome larvae (cercariae) actively penetrate cutaneous tissue via mechanical damage and the release of excretory/secretory (E/S) products containing proteolytic enzymes and glycans. Invasion promotes angiogenesis and differentiation of 'wound healing' leukocytes in the dermis but it is unclear how these events are orchestrated. Since epidermal keratinocytes are innate sensors of cutaneous wounding, we hypothesised that these cells become activated early during schistosome infection leading to changes in the cutaneous immune responses. C57BL/6 mice were exposed to live *Schistosoma mansoni* cercariae via the pinna and dermal and epidermal cells were isolated from the site of infection at 6h, 24h and 96h post-infection. Epidermal non-haematopoietic (CD45-) cells were then phenotyped *ex vivo* via flow cytometry to identify keratinocyte sub-populations. Relative to un-infected skin, a population of epidermal keratinocytes (CD45-CD326-CD34+) was found to increase following infection. The expansion of this population coincided with expression of markers associated with keratinocyte activation and wound healing in skin explants. Cultures of primary murine epidermal keratinocyte also demonstrated an activated response upon exposure to cercariae E/S material *in vitro*. The functional relevance of changes in keratinocyte sub-populations in the epidermis and their activation state was explored via analysis of parallel changes in dermis-infiltrating antigen presenting cells and tissue inflammation. These results suggest that cutaneous non-haematopoietic cells, particularly keratinocytes, may be important mediators of the early innate immune responses to schistosomiasis *in situ*.

1506

LECTIN AND C2-KINASE SIGNALING REGULATE TROGOCYTOSIS-LIKE INGESTION AND HOST CELL KILLING BY *ENTAMOEBIA HISTOLYTICA*

Katherine Ralston¹, Michael D. Solga², Nicole M. Mackey-Lawrence², William A. Petri, Jr.²

University of Virginia, Charlottesville, VA, United States

Entamoeba histolytica is the causative agent of amoebiasis, a diarrheal disease that is a major source of morbidity and mortality in the developing world. Pathogenesis is associated with profound tissue destruction, manifesting as intestinal ulceration or extraintestinal abscesses. Parasite cytotoxic activity is central to tissue destruction, but the mechanism for killing of host cells was unknown. Recently, by employing live confocal fluorescence microscopy, we discovered that amoebae kill by biting off and ingesting distinct pieces of living human cells. The process is reminiscent of trogocytosis (Greek trogo-, nibble) between immune cells. Amoebic

trogocytosis initiates within one minute of host cell contact and precedes cell death, as assessed by permeabilization and DNA fragmentation. By using imaging flow cytometry to simultaneously quantify ingestion and killing, we find that pharmacological inhibitors of trogocytosis reduce host cell death in a dose-dependent manner. Trogocytosis is relevant to disease pathogenesis, since we demonstrated using live two-photon microscopy that trogocytosis occurs during invasion of colon explants from fluorescent-membrane mice. We are currently employing dominant negative mutants and recently developed gene knockdown approaches in *E. histolytica*, in order to define the pathways regulating trogocytosis. Interestingly, a C2 domain-containing protein kinase, EhC2PK, is required for both trogocytosis and conventional phagocytosis in *E. histolytica*, suggesting that some aspects of conventional phagocytic machinery may be common to trogocytosis. We are using these and other trogocytosis mutants as valuable tools to further dissect tissue invasion and destruction in animal models of infection. Finally, it is notable that the closely related parasite *E. dispar* is also capable of trogocytosis, and it has been suggested that trogocytosis occurs in *Naegleria fowleri*. Therefore, not only do these studies change the existing paradigms for cell killing and tissue destruction in amoebiasis, they also suggest an ancient origin of trogocytosis as a form of intercellular exchange.

The number(s) following author name refers to the abstract number.

A

- Abadie, Ricardo 710
 Abakume, Philip T. 147
 Abanyie, Francisca **1451**
 Abariga, Samuel A. **1093**
 Abass, Kabiru M. 88
 Abatih, Emmanuel 560
 Abd El Wahed, Ahmed **921**
 Abdalal, Shaymaa 640
 Abdallah, Joseph F. 307
 Abdel Fadeel, Moustafa 1185
 Abdeladhim, Maha 727
 Abdullayev, Rakif **742**
 Abebe, Rediet 762
 Abedin, Jaynal 1404
 Abeynayake, Janaki 115
 Abikoye, Olatayo O. 730
 Ablordey, Anthony 83
 Aboagye-Antwi, Fred 381
 Aboe, Agatha 31
 Abong'o, Bernard O. 36, **868**
 Abot, Steve 1437, 226
 Aboud, Said 1492
 Abraham, David 1486
 Abramowsky, Carlos 1493
 Abrão, Emiliana P. 596
 Abreu, Cláudia B. 1408
 Abreu, Mery N. S. A. 488
 Abuaku, Benjamin 507
 AbuBakar, Sazaly **1056, 28**
 Abugri, James 994
 Aceituno, Anna M. F. **679**
 Aceng, Ruth 910
 Acevedo, Monica **145**
 Acevedo, Veronica 93
 Achan, Jane 181, 370, 502, 542, 557
 Acharya, Pragyana **633**
 Achee, Nicole 1342, 1355, 1464, 567, 62, 871
 Achidi, Eric A. 363
 Achilla, Rachel 444
 Achtman, Ariel H. **1198**
 Ackerman, Hans 1013
 Acosta, Janet 789
 Acosta, Luz P. 425, 564, 1000, 1003, 1436
 Acosta, Monica M. 1299
 Acosta-Serrano, Alvaro 778
 ACT Asia Baseline Study Group, on behalf of WWARN 1193
 Adadé, Kangni 1475
 Adam, Ishag 630
 Adams, David P. **172, 247, 717, 885, 705**
 Adams, Emily 778
 Adams, John H. 669
 Adams, Matthew 1266, 328, 825
 Adams, Martin 742
 Adau, Vanessa 1250A
 Addiss, David 276, 30, 1237
 Addo-Yobo, Joseph 737
 Addy, Ebenezer T. 253
 Adedoyin, Olanrewaju T. 730
 Adegbe, Emmanuel 1325
 Adeginka, Akim 251
 Adelman, Zachary N. 470
 Ademowo, George O. **1303**
 Ademowo, Olusegun 1261
 Adenis, Antoine A. A. **64**
 Ader, Flavie 993
 Adesina-Adewole, Bukola 1261
 Adewole, Isaac F. 1261
 Adeyemi, Isaac O. 699
 Adeyemi, Mosunmola L. 1391
 Adeyinka, Abimbola 646
 Adhish, Vivek S. 1094
 Adima, Félix 1380
 Adisakwattana, Poom **272**
 Adjalley, Sophie H. 372
 Adjei, George 796
 Adjuik, Martin 75, 857
 Admasu, Kesetebirhan **1311**
 Adoke, Yeka 177, 199
 Adolf, Karchmer W. 728
 Adu-Sarkodie, Yaw 761
 Aebig, Joan 1155, 930
 Affolabi, Dissou 1177, 84
 Afolabi, Muhammed O. **138**
 Afrane, Yaw 336
 Agaba, Bosco 204
 Agaba, Shifra 1190
 Agbayani, Nestor A. **1099**
 Ager, Arba 46
 Agler, Anne H. 1250
 Agomo, Chimere O. 730
 Agongo, Godfred 994
 Agudelo Garcia, Olga M. **196**
 Aguero, Maria J. 130, 131
 Aguiar, Joao 1148, 1148, 1313, 1153
 Aguiar, Julia 84
 Aguilar, Hector 954
 Aguilar, Patricia 1390
 Aguilar, Ruth 1198
 Aguinaga, Rosita E. 74
 Agwang, Constance **183**
 Ahamed, Syed F. 405
 Ahluwalia, Jaspal 1069
 Ahmad, Abdullahi 1308
 Ahmed, Fayaz 1066
 Ahmed, Jalal Uddin 1165
 Ahmed, Makhdum **1404**
 Ahmed, Manjang 1483
 Ahmed, Safir Uddin 1165
 Ahouidi, Ambroise D. 354, 42
 Ahyong, Vida 811
 Aibana, Omowunmi **1037**
 Aidoo, Michael **3, 798**
 Aikins, Moses K. S. 75
 Ainslie, Kristy M. **1171, 303, 722**
 Ainslie, Rob 1331
 Airs, Paul 942
 Aïssata, Barry 503
 Ajariyakhajorn, Chuanpis 443
 Ajisejiri, Simeon 435
 Ajumobi, Olufemi O. **330, 730**
 Akama, Tsutomu 1424, **301**
 Ake, Malakai 1237
 Akech, Sam 456
 Akhund, Tauseef 1066
 Akhvlediani, Nino 1185
 Akhvlediani, Tamar **1185**
 Akhwale, Willis 970
 Akinkunmi, Ezekiel O. **699**
 Akintonwa, Alade 1228
 Akinyede, Akinwumi A. **1228, 646**
 Akinyi, Sheila 1264, 1264, **307**
 Akol, Anne M. 1109, 388
 Akom, Eniko 213, 317, **847**
 Akpakli, Jonas 75
 Akpan, Henry 435
 Akrestrom, Bo 158
 Aktar, Amena 955
 Akter, Jasmin 506, 864
 Akter, Shirina 940
 Akullian, Adam 140
 Akuoko, Osei K. **379**
 Akuoko, Victor 87
 Akurut, Hellen 1284
 Akweongo, Patricia 75
 Akyeampong, Andrea 1154, 1159
 AL Dose Impact Study Group, on behalf of WWARN 654
 Al Hujaili, Abdullah D. **892**
 Al Salem, Waleed S. **778**
 Al-Delaimy, Ahmed K. **755, 897**
 Al-mafazy, Abdul-wahiyd 1141
 Al-Mamun, Abdullah 1404
 Al-Mekhlafi, Hesham M. 755, **897**
 Al-Sabaa, Howaida A. H. F. 892
 Alabaster, Amy 976
 Alabi, Adekunle D. 730
 Alabi, Abraham S. 1367
 Alaii, Jane A. 36
 Alam, Mohammad Shafiul 506, 864
 Alam, Md. Murshid 955
 Alam, Zakia 141
 Alamgir, A.S.M. 442
 Alano, Pietro **45**
 Alarcon, Jorge 1341
 Alarcon-Chaidez, Francisco 477
 Alaro, James R. 1157, **665**
 Alavi, Isidoro 296
 Alba, Milena 1250A
 Albarino, Cesar 910
 Albers, Anna 1187
 Aldridge, Robert C. 866
 Aldstadt, Jared 117
 Alemayehu, Saba 316
 Alemtaye, Genetu 1472
 Alemu, Wondimagegnehu 957
 Alera, Maria T. 1061
 Aleva, Andrea 912
 Alexander, Neal 1363, 35
 Alexandrino, Jacilara 786
 Alfonso-Parra, Catalina **473**
 Ali, Abdullah 1141, 829
 Ali, Asad **1368, 413, 1066**
 Ali, Doreen 1132, 1136, 1252, 1268, 211, 212, 455, 500, 859
 Ali, Juma A. M. 1498
 Ali, Mohammad 701
 Ali, Mohammed 958
 Ali, Omar 1008
 Alia, Miriam 1380
 Alidina, Zainab **1133**
 Alifrangis, Michael 830, 850
 Aliota, Matthew T. 12
 Alike, Matilde 634
 Alisheke, Lutango 1078
 Aliyeva, Saida 742
 Alkaitis, Matthew 1013
 Alkan, Cigdem 1471
 Allen, Elizabeth 1230
 Allen, Judith E. 1486
 Allen, Koya C. **739**
 Alley, M.R.K. 811
 Allian, Fatima 835
 Almedia, Marcio 954
 Alo, Francesco 1371
 Alonso, Pedro L. 1198
 Alout, Haoues **383**
 Alphey, Luke **402**
 Alphonsus, Kal 1454
 Alsford, Sam 1498
 Altamiranda, Mariano **397**
 Althoefer, Kaspar 621
 Althouse, Benjamin M. **1385, 605, 1058**
 Alumbasi, Lubomira T. **348**
 Aluthge Dona, Dulshara S. A. **353**
 Alvarado, Gilbert 721
 Alvarado, Luisa I. 558, **608**
 Alvarado, Margarita 1378
 Álvarez, Álvaro 1105, 795
 Alvarez, Carlos 358
 Alvarez, Liliana 554
 Alvarez, Maricruz 277
 Alvarez-Martinez, Miriam J. 468
 Alvaro Alvarez, Celeste 1361
 Aly, Ahmed S. I. **640**
 Alzahrani, Mohamed 778
 Amador, Manuel 872, 93
 Amankwah, Seth 308
 Amarsinghe, Ananda 588, 595
 Amaratunga, Chanaki 1362, 5, 669
 Amarista, Manuel A. 130
 Amaya, Moushimi **434**
 Amaya-Larios, Irma Y. 604
 Amazigo, Uche V. 1238
 Ambuel, Yuping 609
 Amenga-Etego, Seeba 459
 Amidou, Samie 1406

The number(s) following author name refers to the abstract number.

- Amlaga, Kwame C. 1475
 Ammah, Naa O. 292, **771**
 Amoako, Nicholas 994
 Amoin, Naomi B. 1061, 580, 79
 Amos, Ben 1194, 556
 Amour, Caroline 1410
 Amoussouhoui, Arnaud 1085
 Amouzou, Agbessi 624, 935
 Ampofo, Joseph 685
 Ampofo, William K. 1388
 Ampuero, Julia S. 410, **618**
 Amu, Sylvie 1504
 Amuri, Mbaraka 922
 Amza, Abdou 285
 An, Lingling 1361
 Anagonou, Esai 85
 Anand, Namrata **804**
 Anar, Burcu 927
 Ancca-Juarez, Jenny 781
 Andagal, Ben **849**
 Anders, Robin F. 40, 662
 Andersen, Hanne 962
 Anderson, Charles 1155
 Anderson, Jennifer M. 1362, 153, 665
 Anderson, IV, John D. 1084, **1087**
 Anderson, Leonard 171
 Anderson, Leticia **901**
 Anderson, Michelle 470
 Anderson, Roy M. 495, 1026
 Anderson, Sheri L. 878
 Anderson, Timothy J. C. 954
 Andersson, Neil 123
 Andersson, Sarah 1076, 1077, 619, **80**
 Andiego, Kennedy 562, 563
 Andrade, Christy C. 1466
 Andrade, Marai Sandra 791
 Andrade, Rosa M. 22
 Andreadis, Theodore G. **1383**
 Andrews, Ross 754
 Andriani, Grasiella 1421
 Añez, Germán **118**, 1216
 Angeles, Jose Ma. M. **950**
 Angov, Evelina 1157
 Angulo, Iñigo 44
 Angulo, Noelia 531, 533, **789**, 788
 Angus, Brian J. 428
 Anh, Dang Duc 1067, 1072
 Anh, Nguyet L. 50
 Ani, Samuel C. 1224
 Anicet, Ouedraogo G. 687
 Anishchenko, Michael 1209, 1466
 Anku, Benjamin 87
 Annon, Lawrence **761**
 Ansari, Aftab A. 134
 Anstey, Nicholas M. 334, 4, 461, 635, **995**, 1098, 1251
 Anthony, Kodzo A. 1475, **288**, **289**
 Antigoni, Juana 410
 Antonelli, Tim 572
 Antonia, Alejandro L. 505, **858**
 Antonio, Martin 1079
 Antonio-Nkondjio, Christophe 1111, 1115
 Anugweje, Kenneth C. 802
 Anwar, Asif 818
 Anyan, William K. 292
 Anyona, Samuel 361, 657, **658**
 Ao, Trong T. H. **466**
 Apaza, Sonia 1387
 Apiwattanakul, Nopporn 134
 Apolaya, Moises 1372
 Appawu, Maxwell 367, 394, 381
 Apperson, Charles S. 517, 743
 Appleby, Laura J. 483, 489
 Apte, Simon H. 47
 Aqqad, Maha 86
 Arabi, Mouhaman **680**
 Aragam, Nash 824
 Arama, Charles 484
 Arana, Yanina 531, 533
 Aranda, Maria 608
 Arango, Eliana 1158, 1158
 Araújo, Emanuele T. S. 1052
 Araújo, Felipe 1197
 Araujo, Maria Ilma A. S. **427**
 Araujo, M. S. M. 274
 Araujo Fiuza, Jacqueline 1242
 Archuletta, Sophia 515
 Ardjosentono, Marjorie 1310
 Arenas, Giovana 1372
 Arens, Theo 220
 Arevalo, Jorge 1249, 1250A, 302
 Arévalo-Herrera, Myriam 6, 795, 931, 1105, 1156, 1162, 1300, 216
 Argy, Nicolas **1097**
 Arias, Luis M. 1024
 Arias, Luzlexis 130
 Arifuzzaman, Md. 955
 Arimatsu, Yuji 419
 Arinaitwe, Emmanuel 1121, 1121, 181, 195, 204, 344, 37, 504
 Arinola, Olatubosun G. 1303
 Aristizabal, Beatriz 196
 Ariyoshi, Koya 729
 Arjyal, Amit 1449
 Arlian, Larry 100
 Armah, George 685
 Armstrong, Christopher 926
 Armstrong, Janice 549
 Armstrong, Jillian 734
 Armstrong, Philip M. 1383, 1389
 Armstrong, Stuart D. 16, 21
 Arndt, Michael B. **1025**
 Arnold, Brendan J. 314
 Arnold, Fred 863
 Aroian, Raffi V. 278
 Aronson, Judith F. 477
 Aronson, Naomi **727**
 Arora, Narendra K. 1094, 1074
 Arostegui, Jorge 123
 Arque, Eulogia 269, 414
 Arriola, Carmen S. 532
 Arrospide, Nancy 307, 358
 Arroyo, Maria Isabel 1158, 1158
 Arruda, Rayanne 1197
 Arsanok, Montri 243
 Artiles, Karen 1403
 Artimovich, Elena M. **1267**
 Arumugam, Sridhar **1486**
 Arumugam, Thangavelu U. 1315, 222
 Arvelo, Wences 1481, 277, 466
 Aryan, Azadeh **474**
 Arze, Cesar 328
 Asada, Masahito 950
 Asafu-Adjaye, Andy **381**
 Asan-Ampah, Kobina 87
 ASAQ Dosing Impact Study Group, on behalf of WWARN 971
 Ashley, Elizabeth A. 822
 Asiedu, Kingsley 961
 Asiegbu, Vivian 1272
 Asih, Puji B. 1365
 Asito, Amolo S. **198**
 Aslan, Hamide 727
 Asri, Sukarno 835
 Assadou, Mahamadoun H. 929
 Assawariyathipat, Thanawat 243
 Assefa, Ashenafi 1311, **332**
 Assefa, Berhane 1369
 Assefa, Samuel 641
 Assi, Sulaf 621
 Assogba, Benoit Assogba 1346
 Assomo Ndemba, Peguy 539
 Astatkie, Ayalew **149**
 Astete, Helvio 517, 518, 983
 Astupiña Figueroa, Elizabeth S. **230**
 Atashili, Julius 363
 Atamba, Pennabe E. **194**
 Atemie, Kalada J. J. 972
 Athrey, Giridhar **1345**, **472**
 Atieli, Harrysone E. **377**
 Atkinson, Peter M. 280, 479
 Atshabar, B B. 908
 Attah, Simon K. 1413
 Attaher, Oumar 186, 457, 853
 Atuncha, Vincent O. 36
 Atwal, Sharan 1429
 Auderset, Floriane 1501
 Auguste, Albert J. **1389**
 Auma, Mary A. **236**
 Avendaño, Adrián 721
 Avendaño, Natali 1108
 Avery, Vicky M. 372
 Avila, Frank W. 473
 Avila, Patricia 1372
 Awah, Paschal K. 1085
 Awandare, Gordon A. **994**
 Awinda, George 355
 Awini, Elizabeth 75
 Awiti, Alphonse 563
 Awodele, Olufunso 1228, 646
 Awono-Ambene, Parfait 1111
 Ayala, Diego 1113
 Ayala, Eduardo R. **233**
 Ayebazibwe, Nicholas 1044, 1451
 Ayeh-Kumi, Patrick 422, 886
 Ayers, Tracy 1033, 957
 Ayi, Irene 142, 292, 422, **70**, 886
 Ayi, Kodjo **990**
 Aymukhametova, A C. 908
 Aynalem, Getahun 3
 Ayode, Desta A. **279**
 Azam, Iqbal 413
 Aziz, Fatima 413
 Aznar, Christine 64
 Azares, Edlen 114
 Azziz-Baumgartner, Eduardo 1375, 462, 466

B

- Ba, Fatou 938
 Ba, Mady 1281, 545, 798, 938
 Ba, Mamadou S. **548**, 655
 Ba-Diallo, Awa 1225
 Babakhanyan, Anna **41**
 Babayan, Simon A. 1486, **963**
 Baber, Ibrahimia 929
 Babineau, Denise 487
 Babu, Subash 966
 Bacay, Brian 793
 Bacellar, Olivia 786
 Bachelder, Eric M. 1171, 303, 722
 Bachmaier, Sabine **1498**
 Bacon, David J. 307, 358
 Badanicova, Kristina 349
 Badiane, Aida S. 268
 Badu, Kingsley **396**
 Baggett, Henry C. 407
 Bah, Germanus S. 21
 Bahia, Ana C. 981
 Bai, Liang 366
 Baiden, Frank **201**, **459**, **796**
 Baidjoe, Amrish 520
 Bailey, Jeffrey A. 1101, 1104
 Bailey, Robin L. 285, 1230
 Baird, J. Kevin 175
 Baiwog, Francesca 1291
 Bakajika, Didier 1413, 253
 Baker, Charlotte 989
 Baker, David A. 1503
 Baker, Julia M. 413
 Baker, Kelly K. **685**
 Baker, Mark 48
 Baker, Stephen 1479
 Bakone, M. 1238
 Balajee, Arunmozhi 731, 1186
 Balard, Yves 1418
 Balasundaram, Susheela 66
 Balazova, Miriam 176

The number(s) following author name refers to the abstract number.

- Baldé, Mamadou C. 1444
 Baldet, Thierry 1344, 1364
 Baldeviano, G. Christian 1309, 358, **1120**, **1120**, **1128**, 1192, 509, 1123, 342, 726
 Baldini, Francesco 946
 Bales, Jacquelyn M. 907
 Baliilo, Marcel 740
 Balinandi, Stephen 1379, 1380, 910
 Baliraine, Frederick N. 821
 Ballard, Ronald 961
 Ballard, Sarah B. **1387**, **431**
 Ballesteros, Sebastien 919
 Ballou, W. Ripley 1443
 Balmaseda, Angel 115, 121, 123, 125, 1403, 9, 985
 Balogun, Muhammad S. 435
 Bamadio, Modibo 975
 Bamani, Sanoussi 1235
 Banda, Benjamin 624
 Banda, Tamara **103**, 447
 Banerjee, Rajdeep 24, 663
 Baneth, Gad 749
 Bangali, Mannan 1165
 Bangiolo, Lois 976
 Bangirana, Paul **1450**
 Baniecki, Mary Lynn 7
 Bannister, Thomas 1021
 Bansil, Pooja 1275
 Banu, Nuzhat N. 442
 Baratti-Mayer, Denise 1200
 Barber, Bridget E. 334, **635**, 995, 1251
 Barbosa, Andrea B. 1199
 Barboza, Jose Luis 518
 Barbu, Corentin M. **1420**, 773
 Barelli, C. S. G. A. 274
 Baresel, Paul 1089, 1090
 Baric, Ralph S. 1399
 Barillas-Mury, Carolina 976, 977
 Baring, Elisa **284**
 Barker, Christopher M. 869
 Barnabé, Christian 1246
 Barnes, Karen I. 1144
 Barnes, Kayla G. **1107**, 691
 Barnes, Samantha J. 669
 Barnes, Trevor 598
 Barnett, Elizabeth D. 724, 728
 Barnwell, John W. 1264, 1264, 307, 317, 1319, 1319, 996
 Baro, Nicholas 644
 Barogui, Yves 85
 Barongo, Aileen K. **1163**
 Barral, Aldina 1501
 Barranco, Elizabeth 515
 Barras, Jamie 621
 Barrera, Roberto 112, 872, **93**
 Barrera, Valentina **1496**, **155**
 Barreto, Andreia S. 427
 Barringer, III, George 97
 Barrios, Cindy 1180
 Barron, Alexander **1122**
 Barrón, Eduardo 230
 Barry, Amadou **457**, 853
 Bart, Stephen M. 491
 Bartholomay, Lyric 942
 Bartlett-Healy, Kristen 571
 Bartz, Faith E. 679
 Basáñez, Maria-Gloria 15, 32, 848, 1049
 Bashin, Michelle 1374
 Basnyat, Buddha 1449
 Basri, Hasan 175
 Bass, Jennifer 740
 Bassat, Quique 49
 Basso, Annalisa 954
 Bast, Joshua 920
 Bastiaens, Guido J. H. **220**, 450, 503
 Bastien, Patrick 1418
 Basu, Sanjay **470**
 Batcho, Wilfrid 1237
 Bates, Paul A. 90
 Bathily, Aboudramane 1125, 451
 Batsa Debrah, Linda **1187**
 Batzloff, Michael 449
 Bauch, Julie A. **832**
 Bauleni, Andy 1132, 1136, 1428, 150, 211, 212
 Baum, Elisabeth **670**
 Baus, Esteban G. 777
 Bausch, Daniel G. 1372, 1375, 1381, 1384, 1387, 431, 445, 467, 703
 Bautista, Marcos C. 1185
 Bautista, Ronald 1102
 Baxter, Peter 280
 Bayoh, Nabie 1329, 519
 Bazan, Isabel 983
 Be, Hien V. 50
 Beach, Michael 883
 Beal, Katherine 857
 Beane, Jennifer E. 1468
 Bearden, Scott W. 476
 Beare, Nicholas A. V. 1494, 1496, 155, 638
 Beatty, P. R. 122
 Beatty, Wendy L. 18
 Beaty, Barry 1462, 9, **942**
 Beaty, Meaghan 1462
 Beauharnais, Catherine C. **653**
 Beavogui, Abdoul Habib 323
 Beck, Hans-Peter 1257
 Becker, Luke B. 1040
 Becker, Stephen 1079
 Becker, Tim 1187
 Beckett, Anne G. **68**
 Bedoya-Vidal, Sebastian 672
 Beebe, Nigel W. 523, 876
 Beech, Robin N. 1435
 Beeson, James G. 1291, **1442**, 40, 662, 667
 Beg, Mohammad Asim 154, 319
 Begum, Farzana 958
 Begum, Sharmin 1079, 1410
 Behrens, Ron 1332
 Bei, Amy K. 320, 354, **42**, 327
 Bejtullahu, Armand 910
 Béliard, Sabine **1367**
 Belem, Adrien Marie Gaston 783, 783
 Belinskaya, Tatyana 719
 Bell, David 538, 836, 1286
 Belli, Alejandro 123
 Bello, Betsy **1358**, **1366**
 Bello, Felio J. **94**, **95**, **96**
 Belloni, Virginia 475
 Belmonte, Arnel 1437, 226
 Belmonte, Maria 1437, 226
 Beltran, Manuela 112, 584
 Belyaev, A. I. 908
 Benacer, Douadi **238**
 Benavente, Luis 1253
 Benavides, Yoldi 795
 Benavidez, Yoldi 1105
 Benbow, Eric 85
 Benca, George 1219, 176
 Benca, Juraj 409, 769
 Bendezú, Jorge 307, 1102, 1323
 Benedetti, Paolo 1222
 Benefit, Brenda 1058, 1385
 Benítez, Washington 490
 Benjamen, Abel 250
 Bennett, Adam 1276, 1295, 1426, **500**, 859, 862
 Bennett, Jason W. 226, **973**, 180
 Bennuru, Sasisekhar **1417**, 19
 Benoit, Stephen 1481, 554
 Benson, Scott 706
 Berdougo, Eli 602
 Bergeron, Eric 1380
 Bergman, Lawrence W. 1322
 Bergren, Nicholas A. **439**
 Berhane, Yemane 1295, 1311, 149
 Berkvens, Dirk 922
 Berman, Josh **296**
 Bern, Caryn 1020, 734, 780
 Bernal, Maruja 1179, 710
 Bernart, Chris 1481, 466
 Bernhardt, Scott A. 101
 Berrie, Eleanor 932
 Berriman, Matthew 954
 Berry, Neil G. 266, 926
 Bertelsen, Nathan **78**
 Berthe, Sara R. **207**
 Berthé, Zana 1235
 Bertin, Gwladys 1097
 Bertsch, David 559
 Betancourt-Cravioto, Miguel 1062
 Bethel, Laura M. 907
 Bethell, Delia 506, 822, 328
 Bethony, Jeffrey M. 1489, 1490, 759
 Bett, Andrew 516
 Bettger, Theresa 182
 Betuela, Inoni 1257
 Bevan, Michael J. 184, 185
 Beyeler, Naomi 1086, 1307
 Beyenbach, Klaus W. 1110
 Bezares, Erskin 989
 Bhandary, Binny **693**
 Bhasker, Khondaker R. H. 1422
 Bhatia, Deepak D. 702
 Bhatnagar, Julu 133
 Bhatt, Samir 104, **1297**, 1298, 1418
 Bhattacharya, Parna **1244**
 Bhattacharyya, Tapan 71
 Bhattarai, Achuyt 500, 859
 Bhattarai, Rachana **534**
 Bhuiyan, Taufiqur R. 955, 701
 Bhutta, Zulfiqar 1066, 1368
 Bichaud, Laurence 1191, 1471
 Bickersmith, Sara A. 1359
 Bickmen Tchana, Steve 1411, 1412
 Bid, Rhiannon **35**
 Bienvenu, Anne-Lise 794, 810
 Bieri, Franziska A. **1239**
 Biggerstaff, Brad 582, 584
 Biggs, Holly M. **249**, **556**
 Bigira, Victor 370, 502, 504, 542
 Bihary, Richard F. 1254
 Bijker, Else M. 220, 450, 453
 Bijker, Kasper 131
 Biligui, Sylvestre 1012, 993
 Billingsley, Peter F. 220, 223, 979, 1437
 Billker, Oliver 927
 Billman, Zachary P. 184, **185**
 Billo, Mounkaila 2
 Bimi, Langbong 142
 Biney, Ekow 1253
 Biney, Ellen J. 90
 Bingham, Andrea M. **909**
 Binka, Fred 75
 Birbeck, Gretchen L. 245
 Bird, Brian 1380
 Biritwum, Nana-Kwadwo A. D. 32, **1048**
 Birkan, Melisa 893
 Birrell, Geoffrey 46
 Bisanzio, Donal 869, 984
 Biselli, Joice 132
 Biswas, Hope 9
 Biswas, Sumi **1152**, 928
 Björkman, Anders 543, 822, 829, 1096
 Black, Christine 1064
 Black, Robert E. 1409, 935
 Black, IV, William C. 60, 101, 1338, 1347, 1462
 Blackstock, Anna J. 1034, 277
 Blagborough, Andrew **497**, 928
 Blair, Carol 9
 Blaney, David 1170, 1189
 Blankenship, D'Arbra 1195, 1254
 Blanton, Curtis 741
 Blau, Dianna 133

The number(s) following author name refers to the abstract number.

- Blay, Emmanuel A. **142**, 886
 Blazes, David L. 1387
 Blinkhorn, Richard Jr. 411
 Block, Karla 113
 Blouin, Brittany 758
 Blumberg, Benjamin J. **97**
 Boaeleart, Marleen 775
 Boakye, Daniel A. 380, 394, 70, 90, 292, 422, 367
 Boatin, Boakye A. 1475
 Boaz, Mark 593
 Bobogare, Albino 828
 Bockarie, Moses J. 1042, 1045, 1234, 1254, 1453, 262, 282, 400
 Boddey, Justin 1100
 Bodhidatta, Ladaporn 1406
 Boegler, Karen A. 476
 Boettcher, Molly G. 1207
 Bogaardt, Carlijn 1215
 Boggild, Andrea K. **1250A**, **799**
 Bogich, Tiffany L. **919**
 Bohidatta, Ladaporn 1079
 Boisen, Nadia 1407
 Boissière, Anne 387
 Boivin, Michael 235, 1450
 Bojang, Kalifa A. 138
 Bolay, Fatorma K. 1039
 Boley, Matthew 893
 Bolling, Bethany G. **1356**
 Bolton, Jessica S. **1153**, 1313
 Bomans, Pieter 1177
 Bona, Ernesto 835
 Bona, Roberta 45
 Bonaparte, Matthew 599
 Bonawitz, Rachael E. **1**
 Boncy, Jacques 1186, 1264, 1264, 317, 731, 738
 Bond, Meaghan **528**
 Bond, Vincent C. 629
 Bonet Gorbea, Mariano 760
 Bongio, Nicholas 924
 Bonku, Edward **857**
 Bonnach, Ch. 769
 Bonney, Joseph H. K. 1388
 Bonnot, Guillaume 810
 Booker, Michael 925
 Boon, Nele 560
 Bopda, Jean 1043, 1046, 1411, 1412, 15, 757
 Bopp, Cheryl 957
 Borg, Natalie A. 498
 Borghini-Fuhrer, Isabelle 645
 Borin, Khieu 412
 Borrini Mayori, Katty 304
 Borrmann, Steffen 822, 969
 Borse, Rebekah H. 1035
 Borteb, Hassan 1171
 Bosco-Lauth, Angela 1466
 Bose, Kuthaje S. 1041
 Bosh, Irene 610
 Boshart, Michael 1498
 Bosio, Chris 60
 Bosompem, Kwabena M. 771, 952
 Botchway, Felix A. **308**
 Bouchrik, Mourad 794
 Boudova, Sarah **865**
 Bougma, Roland Windtare 1232
 Boukheng, Thavrin 202
 Boulanger, Lucy 3
 Boulay, Marc **1331**
 Boum, Il, Yap 236, 736
 Bouraima, Mouawiyatou 288, 289
 Bourguinat, Catherine **15**
 Bourke, Claire D. **1505**, **483**, 489
 Bousema, Teun 1327, 1429, 1430, **503**, 520
 Boussinesq, Michel 1043, 1046, 15, 264, 757
 Bouyer, Donald H. 1164, 716, 746
 Bowen, Katherine 189, 193, 37
 Bowen, Richard A. 1466
 Bowles, Cayley **1480**
 Bowman, Deidra J. **856**
 Bowman, Natalie M. **855**
 Boyd, Alexis **1432**
 Boyd, Scott 1403
 Boye, Cheikh S. B. 1202
 Boyer, Micah 1085
 Boyle, Michelle J. **40**, 662
 Bozdech, Zbynek 1125, 156, 162
 Bozo, Ricardo W. 734
 Bozo-Gutierrez, Ricardo W. 1020
 Bracken, Tara C. **1493**
 Brackman, Deanna J. 303
 Brackney, Doug E. 1468, 941
 Brady, Lauren M. 191
 Brady, Oliver **104**
 Braga, Cássio 1197
 Brana, Athos M. 1088
 Branco, Fernando L. C. C. 1088
 Branda, Cesar 710
 Brandao-Filho, Sinval P. 791
 Brasseur, Philippe 205
 Bratschi, Martin W. 1173
 Brault, Aaron C. 1209, **1466**, 1467
 Breart, Gerard 987
 Breiman, Rob 1396, 1405
 Brenière, Simone F. 1246
 Brentlinger, Paula E. **69**
 Brenyah, Ruth C. **1302**
 Bretz, David 1365
 Brewoo, Joseph N. **514**, 601, 609
 Briand, Valérie 1097
 Bricaire, François 993
 Briceño, Ireneo 1355
 Brickley, Elizabeth B. **190**
 Bridges, Daniel 1280, 1339
 Brienen, Eric A. T. 490
 Briggs, Melissa 1136, **211**, **212**
 Brindley, Paul J. **1489**, 416, 896, 420A
 Brinkerhoff, Robert 480
 Briolant, Sébastien 873
 Britch, Seth C. 866
 Brito, Miguel **430**
 Britton, Sumudu **834**
 Brock, Aleisha R. **508**
 Brockley, Sarah 1155
 Brockschmidt, Felix 1187
 Brockstedt, Dirk G. 1438
 Brodin, David 1096
 Brogdon, William 1461
 Bron, Christophe 112
 Broncano, Nely 1027, 891, 912
 Bronowski, Christina 265
 Bronzan, Rachel 288, 289, **1475**
 Brooker, Simon 1284, 1293, 30, 495, 975, 1448, 1474
 Brooks, David 1056
 Brooks, W. Abdullah 106
 Brough, Doug L. 1148, 1148
 Brown, Andrea 207
 Brown, Allison C. 1033
 Brown, Charles A. 380, 886
 Brown, Joelle 1277
 Brown, Robert W. 1254
 Brownstein, John 625, 1418
 Bruce, Jane 459
 Bruce, Nigel G. **1374**
 Bruder, Joseph T. **1148**, **1148**, 226
 Brumeanu, Teodor-Doru 1154, 1159
 Brun, Reto 301
 Brunette, Gary 1445
 Brunetti, Enrico 1222, **231**, **535**, **537**, **756**
 Brunkard, Joan 957
 Bruno, Antonella 756
 Bryan, Julie 293
 Bryan, Joe P. 466, 1481
 Bryan, Owen L. **597**
 Bryant, Juliet E. **50**
 Bryce, Jennifer 622, 624, 935
 Bu, Wei 1424
 Buathong, Nillawan 1324, 806
 Bucala, Richard 72
 Bucheton, Bruno 783
 Buckee, Caroline O. 335
 Buckeridge, David 860
 Buckner, Frederick S. **1021**
 Buddhari, Darunee **117**
 Budge, Philip J. **911**, 1377
 Budke, Christine M. 534
 Buekens, Pierre 1248, 987
 Buene, Manuel 69
 Buff, Ann M. **551**, **628**, 851
 Buffet, Pierre Antoine 1012, 993
 Bugoro, Hugo 523
 Bukirwa, Hasifa 173
 Bulimo, Wallace 1369, 444
 Bull, Peter 631, 667
 Bumoko, Guy Makila Mabe **235**
 Bunawan, Nur C. 627
 Bunzali, Yusuph 684
 Burdiladze, R. 418
 Burga, Rosa 1178, 709
 Burgess, Steven 1269
 Burgess, Timothy 113, 733
 Burke, Donald 510, 511
 Burkett-Cadena, Nathan D. 909
 Burkhard, Peter 1439
 Burkhardt, Martin 930
 Burkot, Thomas R. 1283, 399, 523
 Burnleigh, Barbara 1500
 Burns, Jr., James M. **1157**
 Burns, Matthew 1339
 Burri, Christian **652**
 Burrows, Jeremy 1273
 Burrus, Roxanne G. 1341
 Burton, Samantha 1493
 Burton, Timothy A. 1351, 383
 Bushell, Ellen S. C. 927
 Bushman, Mary **507**
 Bustinduy, Amaya L. 103, 447
 Buteau, Josiane 1186, 317
 Butter, Falk 1499
 Butterworth, Alice S. **47**
 Button-Simons, Katrina A. 1099
 Buultjens, Andrew 83
 Byakika, Pauline 557
 Byass, Peter 1340
 Bygbjerg, Ib C. 830, 850
 Byrd, Brian D. 866
 Byrd, John 1023

C

- Cabada, Miguel M. **269**, **414**, 415
 Cabello, Ines 789
 Cabello de Quintana, Maritza 131
 Cabezas, Cesar 358
 Cabrera, Ana **351**
 Cabrera, Mynthia 1434
 Cabrera, Whitney 226
 Cabrera-Mora, Monica L. 637
 Caccone, Agalgisa 1345
 Caffrey, Conor R. 1435
 Caicedo, Paola A. C. **1363**
 Cairo, Hedley 1262, **1310**
 Calcina, Juan F. 230, 532
 Calderón, Alfonso 1180
 Calderón, Maritza 356
 Calderón-Arguedas, Ólger 721, 747
 Calderwood, Stephen B. 955, 959
 Callahan, Larry 725
 Calle, Gabriela 1341
 Calzada, Jose 644
 Cama, Vitaliano 1044, 1451
 Camacho, Daria 130, 131
 Camara, Daouda 323
 Camara, Gnepou 323
 Camara, Mamadou 783
 Camara, Siriman 209

The number(s) following author name refers to the abstract number.

- Camara-Mejia, Javier 102
 Camarda, Grazia 45
 Campbell, Corey 60, 1468
 Campbell, James I. 1479
 Campbell, Judith R. 248
 Campbell, Lindsay 579
 Campbell, Shelley 910, 1379
 Campino, Susana 641
 Campo, Brice 648
 Camponova, Flavia 1285
 Campos, Karen 1120, 1120, 1309
 Campos, Rhanderson G. 1088
 Campos, Tais 1022
 Campos Ponce, Maiza 496, 760
 Canal, Enrique 1179, 1384
 Canales, Marco 287, 490, 752, 753
 Canavati de la Torre, Sara E. 202
 Cancino, Marcela 6
 Candido, Renata R. F. 951
 Cannon, Deborah 1380, 1379
 Cano, Jorge 1453, 262
 Cantey, Paul T. 1044, 1451
 Cantilena, Louis 806
 Cao, Jun 1276, 1278, 366
 Cao, Xiaohang 954
 Cao, Yuanyuan 1278
 Capewell, Paul 783
 Capian, Nicolas 524
 Capobianco, Marcela P. 671
 Cara, Andrea 45
 Carabali, Mabel 1067, 1072, 588, 595
 Carabin, Hélène 534, 565, 856
 Caradonna, Kacey 1500
 Caranci, Angela 567
 Cardoso, Fernanda 1490
 Cardoso, Luciana S. 427
 Carias, Lenore L. 669
 Caridha, Diana P. 359, 180
 Carinci, Romuald 873
 Carles, Gabriel 987
 Carlin, Bobbi 1053
 Carlson, Jonathan 942
 Carlton, Elizabeth J. 1031
 Carme, Bernard 64
 Carmical, J. Russ 477
 Carmichael, Rory D. 1018
 Carmolli, Marya P. 512
 Carmona-Fonseca, Jaime 1127, 196
 Carn, Gwénaëlle 813
 Carneiro, Pedro Paulo 786
 Caro, Valerie 392
 Caroline, Amy L. 907
 Caropresi, Liliana 1024
 Carpio, Victor H. 187
 Carranza, Marco 747
 Carrasco, Hernan J. 71
 Carrera, Claudia 1130
 Carrera, Jean P. C. 55, 127
 Carrión, Rebeca 618
 Carrion Navarro, Oscar 304
 Carrique-Mas, Juan 50
 Carro, Ana C. 105
 Carroll, Darin S. 51
 Carroll, Ryan 159, 160
 Carter, Darrick 930
 Carter, Nick S. 42B
 Carvalho, Edgar 427, 786
 Carvalho, Lucas P. 1022
 Carvalho, Marilia S. 524
 Carvalho-Queiroz, Claudia 954
 Casale, Patricia O. A. 221
 Casapia, Martin 758
 Casares, Sofia 1154, 1159, 933
 Case, Kristin 706
 Casimiro, Danilo R. 1155
 Cassiano, Gustavo C. 671
 Cassin, Jessica W. 1296
 Castellanos, Angélica 1156, 216
 Castellanos-Gonzalez, Alejandro 23, 27
 Castilho, Tiago 72
 Castillo, Leticia 466
 Castillo, Roger M. 448
 Castillo Neyra, Ricardo 781
 Castrillon, Carlos 197, 302
 Castro, Yagahira E. 1423
 Castro Noriega, Maria d. 295
 Castro-Jorge, Luiza A. 596
 Cathérine, Blais 687
 Cattaneo, Federico 231, 535
 Catteruccia, Flaminia 946
 Caudill, Andrew 913
 Caughlin, Trevor 842
 Caulfield, Laura E. 1095
 Caumes, Eric 993
 Cavasini, Carlos 1197
 Caws, Maxine 406
 Cayotopa, Athaid 1197
 Ccopa, Fredy 531, 533
 Cedillo Barron, Leticia 597
 Celis, Juan C. 1309
 Cerami, Carla 1016, 1318
 Cespedes, Nora 1156, 216
 Cevallos, William 1031
 Cevenini, Luca 45
 Cevini, Claudia 756
 Chackerian, Bryce 129, 583
 Chacon, Rafael 466, 1183
 Chai, Jong-Yil 889
 Chai, Jee-Won 889
 Chakraborty, Poulomy 1084
 Chakravarty, Jaya 291, 785
 Chakravarty, Sumana 228, 229, 979, 1437, 1438, 223
 Chalira, Alfred 211, 212, 1136
 Chalker, John 77
 Chaluluka, Ebbie 505
 Chalwe, Victor 324
 Cham, Mamady 1483
 Chambers, Matthew S. 1069
 Chan, Adeline 1305
 Chan, Ernest 1319, 1319, 574, 996
 Chan, Jo-Anne 667
 Chan, Lai Yue 420A
 Chancey, Caren 1216, 1217
 Chanda, Pascalina 653
 Chandani, Yasmin 1076, 1077, 619, 80
 Chandler, Clare 1259, 1260
 Chand, Krisin 175
 Chandra, Elizabeth M. 792
 Chandra, Richa 814
 Chandramohan, Daniel 1327, 138, 1429, 201, 459, 796
 Chandrasekaran, Vedachalam 966
 Chang, Hsiao-Han 544, 644
 Chang, LeeJah 1437
 Chang, Li-Yen 28
 Chang, Michelle 1264, 1264, 213, 847
 Chang, Serena 1012
 Changano, Veronica 1179
 Chann, Soklyda 1324, 806
 Chanthaseng, Phongsavay 1083
 Chanthavanich, Pornthep 1067, 1072, 588, 595
 Chantry, Mathilde 302
 Chao, Chien-Chung 719
 Charland, Katia 860
 Charlebois, Edwin 181
 Charles, Jhanshi 1074
 Charrel, Remi N. 1191, 1471, 736
 Chase, Amanda J. 1401
 Chatterjee, Soumya 255, 968
 Chaurasia, Ankita 775
 Chavchich, Marina 359, 46
 Chaves, Luis F. 543, 704
 Chavez, Carlos 133
 Cheah, Phaik Yeong 616
 Cheah, Phaikyeoung 649
 Checkley, William 1095, 1409
 Cheikh, Sokhna 378
 Chen, Arlene 956
 Chen, Cheng Y. 961
 Chen, Ching-I 1209
 Chen, John 41
 Chen, Jun-Hu 350
 Chen, Jingyang 633
 Chen, Lin H. 724, 728
 Chen, Ping 1148, 1148
 Chen, Runsheng 1004
 Chen, Tai Ho 114
 Chen, Tien-Huang 589
 Chen, Wei-June 589
 Chen, Xiaowei 1004
 Chen, Yang 690, 696
 Chen, Yao-Shen 275
 Chen, Yik 40
 Chenais, Naig 1285
 Cheng, Ling 1003, 1149, 1149, 227, 452
 Cheng, Qin 359, 828
 Cheng, Rubing 127
 Cheng, Yang 350, 352
 Chenoweth, Stephen F. 876
 Chepkorir, Edith 592, 917, 920
 Chere, Belete T. 792
 Cherif, Mahamoud S. 656
 Chertow, Jessica H. 1013
 Chesnais, Cédric B. 1043, 1046, 757
 Chesson, Joanne 667
 Cheung, Carol Y. 8
 Chevalier, Frederic 954
 Chi, Kai-Hua 961
 Chiaravalloti Neto, Francisco 1206
 Chibale, Kelly 815
 Chibsa, Sheleme 1311
 Chichester, Jessica 1155
 Chico, Martha 1027, 891, 912
 Chidiebere, Osuorah Donatus 1483
 Chigusa, Yuichi 950
 Chijioko-Nwauche, Ifeyinwa N. 802, 972
 Chikawe, Maria 1233, 1456
 Chile, Nancy 531, 533
 Chilingulo, Cowles 800
 Chimbanga, Emmanuel 622
 Chimpanga, Boniface 80
 Chimuna, Tiyese 622, 624
 Chin, Stephanie A. 285
 Chinha, Omayra 107, 145
 Chinchilla, Blanca 1481
 Ching, Wei-Mei 719
 Chinkhumba, Jobiba 1136, 211, 212
 Chinnawirotpisan, Piyawan 126, 441
 Chiadini, Peter 1286, 1332
 Chipenda, Henrique 326
 Chipeta, James 561, 898, 900
 Chippaux, Jean-Philippe 1444
 Chisha, Zunda 1280
 Chitadze, Nazibrola 1169
 Chitnis, Chetan E. 932, 1442
 Chitnis, Nakul 1047, 1282, 520, 869
 Chitongo, Paradzai 486
 Chittaganpitch, Malinee 407
 Chittham, Wachiraphan 391, 395
 Chitundu, Helen 898, 900
 Chiu, Charles Y. 905
 Chizhikov, Vladimir 1217
 Choi, Jeong 780
 Choi, Ryan 23
 Chokephaibulkit, Kulkanya 134
 Chou, Yiing-Jenq 329
 Chou Chu, Lily 781
 Choudhury, Tanveer A. 1419
 Chour, Char Meng 806
 Chourasia, Ankita 785
 Chowdhury, Fahima 701, 955, 958
 Chowdhury, Imtiaz A. 442
 Chris, Bernart 554

The number(s) following author name refers to the abstract number.

- Chris, Drakeley 1429
 Christen, Jayne M. **583**
 Christensen, Bryan 1374
 Christian, Elizabeth 594, 598, 602
 Chu, Brian 1232
 Chu, Brian K. **1237**
 Chuang, Ilin 226
 Chuansumrit, Ampaiwan 134
 Chukwuocha, Uchechukwu **200**
 Chunara, Rumi 625
 Chung, Wendy 219
 Chuor, Char Meng 1324
 Chuquiyauri, Raúl 356
 Churcher, Thomas S. 1049, 32, 928, 497
 Chusri, Sarunyou 126
 Chuxnum, Teerasak 718
 Cicéron, Liliane 993, 1012
 Cimino, Ruben 1024
 Cioli, Donato 954
 Ciota, Alexander T. 11, 1212, **1465**
 Cirillo, Daniela M. 1371
 Cisse, Badara 548, 655, 772
 Cisse, Kadidia 186
 Cisse, Moustapha 1281, 545, 798
 Claessens, Antoine 1005, 1012
 Clare, Rachel 266
 Clark, Carolyn 255
 Clark, Eva H. 780, **1020**
 Clark, Gary G. 571
 Clark, Jeffrey N. **260**
 Clark, Jeffrey W. **62**
 Clark, Jesse 1174
 Clark, Martha A. **1016**, 1318
 Clark, Taane 641, 328, 333
 Clark, Tamara D. 181, 370, 502, 542
 Clarke, Sian E. 1146, 1259, 1260, **975**
 Clavell, Luis 989
 Clayton, Amanda 572
 Clayton, April M. 97
 Clem, Rollie J. **689**, **689A**, 693
 Clemens, John 701, 958
 Clements, Archie 479, 565, 754, 281
 Clements, James 1092
 Clennon, Julie 85
 Clerk, Christine 1256
 Coalson, Jenna E. **1292**, 1428
 Coates, Craig 1118
 Cochero, Suljey 1349
 Codeço, Claudia 1197
 Coelho, Paulo Marcos Z. 1196
 Coffeng, Luc E. **1238**
 Cohee, Lauren 865, 1428
 Cohen, Justin 1141, 1142, 862, 1145
 Cohuet, Anna 1113, 1330, 867, 928
 Coimbra, Terezinha L. Moraes. 1206
 Coker, Richard 412
 Colacicco-Mayhugh, Michelle G. 871
 Colaco, Rajeev 1133, 210
 Colares, Jeová K. B. 1052, 611
 Colborn, James M. **1305**
 Coleman, Jane **385**
 Coleman, Michael 1107
 Coler, Rhea N. 1422
 Coller, Beth-Ann **516**
 Collins, Frank 1365, 575, 1283
 Coloma, Josefina 123
 Colombo, Tatiana 132
 Colquhoun, David R. 1106
 Colwell, Rita 956
 Comfort, Alison B. **1279**, **541**
 Conceição, Luciana M. 671
 Condit, William C. 1254
 Condori Pino, Carlos 304
 Cong, Yi 706
 Congpuong, Kanungnit 831, 843
 Conn, Jan E. 1114, 1359, 397
 Conrad, Melissa D. **504**, 821
 Conroy, Andrea L. 1492, **1497**
 Constant, Edi Constant 1346
 Conti, Simon 1488, 997
 Contreras, Carmen Lucia 466
 Contreras, Ingrid 446, 554
 Conway, David J. 994
 Cook, Darren 1433, 20, 267, 266
 Cool, David R. 100
 Cooper, Philip **1027**, 891, 912
 Cooper, Robert D. 523
 Cooper, Roland A. 1269, 1271, 817
 Cope, Jennifer 883
 Copeland, Carmen M. D. **629**
 Coppellotti, Olimpia 386
 Corbett, Kizzmekia S. **1397**
 Cordova Rojas, Marisol 294
 Cornejo, Marilhia 287, 752, 753
 Cornel, Anthony 61
 Cornelia, Sylvie 390
 Cornelio, Elia 107, 145
 Corona, Teresa 534
 Corradin, Giampietro 1156, 216
 Corrah, Tumani 1483
 Correa, Dolores 1065
 Correa, Margarita M. 1108, 397
 Correa-Oliveira, Rodrigo 424, 759, 1241, 488, 429
 Corredor, Mauricio 1127
 Cortés, Jesus A. 94
 Cortese, Joseph F. 1010
 Cosmas, Leonard 1028
 Cosme, Luciano 472, **1118**
 Costa, Federico **1484**, 524
 Costa, Justin **555**
 Costa Martins, André Guilherme 71
 Costales, Jaime A. **74**
 Cotton, Rachel N. 968
 Coulibaly, Boubacar 794
 Coulibaly, Cheick A. 99
 Coulibaly, Drissa 1443
 Coulibaly, Mamadou B. **1348**, 929
 Coulibaly, Michel E. 967
 Coulibaly, Nianégué 794
 Coulibaly, Seydou 765
 Coulibaly, Sidi 1235
 Coulibaly, Yaya Ibrahim 765
 Coulibaly, Yaya I. **400**, 967, **99**
 Coulombier, Denis 1215
 Counihan, Helen 1190, 136
 Couppié, Pierre 64
 Coursen, Jill 451
 Courtin, Fabrice 772
 Cousin, Carolyn 902
 Covaleda, Lina 1390
 Cowman, Alan F. 1442, 667, 222
 Cox, Daniel 191
 Cox, Jonathan 1430, 520
 Cox, Momodou 916
 Coyle, Christina 751
 Craig, Alister G. 1496, 155
 Craig, Allen S. 1279, 324, 385, 541
 Crandfield, Michael 642
 Cranfield, Michael 643
 Cravioto, Alejandro 701, 958
 Crawford, Thomas C. 1020, 780
 Crespo-Ortiz, Maria P. 1263, 1263
 Crevat, Denis 591
 Crompton, Peter D. 1125, 1126, 1129, 1440, 344, 451, 1123
 Crosnier, Cecile 451
 Cross, Nadia 662
 Crowe, James 13
 Crowley, Kathryn 1233
 Crownover, Penelope 814
 Crump, John A. 249, 556
 Cruz, Maria 302
 Cruz, Mary 296
 Cruz-Chan, Vladimir 566
 Csajka, Chantal 813
 Cserti-Gazdewich, Christine 1011, 164
 Cuéllar, Victoria 277
 Cui, Li-Wang 350
 Culleton, Richard 338
 Cummings, Derek A. T. **1058**, 1385, 510, 511, 605
 Cummings, Hannah 1019
 Cummings, Michael P. 328
 Cundill, Bonnie 1260
 Cuong, Nguyen V. 50
 Curaca, Viviana 145
 Currie, Bart 493
 Currie, Cameron 261
 Curry, Heather 1171
 Curtis, Kurt C. 1039, 420
 Cybulski, James S. **1092**
 Czanner, Gabriela 1494
 Czesny, Beata 1008

D

- D'Alessandro, Umberto 1272, 1483, 49, 861, 1312, 1308, 138
 D'Ortenzio, Eric 390
 Da, Dari F. 1330, **928**
 da Silva, Alexandre 883
 da Silva, Flavia Dias Coelho 464
 da Silva, Maria Fernanda L. 791
 da Silva-Nunes, Mônica **1088**, 1197
 Dabiré, Roch K. 386, 1346, 1463, 1344, **1364**
 Dabo, Abdoulaye 484
 Dacuma, Mary Grace **835**
 Dadzie, Samuel K. 394, 367
 Dafee, Foday 957
 Dahal, Kumud **1243**
 Dahal, Prabin **1193**
 Dahir, Saidi 53
 Dahlström Otienoburu, Sabina 214, **647**
 Dahlui, M. 1063
 Dai, Minxian 1103
 Dakshinamoorthy, Gajalakshmi **962**
 Dale, Helen 613
 Daley, Daniel A. 1269, 1271
 Dallah, Fadi 987
 DallaPiazza, Michelle 78
 Daly, Thomas M. 1322
 Dama, Souleymane 1096, **660**
 Dambach, Peter 988
 Damon, Inger K. 51, 740
 Damonte, Elsa B. 105
 Dangol, Sabina 1449
 Dangy, Jean-Pierre 1173
 Daniel, Elsa Paula S. Kaingona. 326
 Daniel-Ribeiro, Claudio Tadeu 326
 Daniels, Rachel F. 320, 354, 42, 327, **544**, 644, 7
 Danko, Janine 113
 Danlami, Mohammed Bashar 1056
 Dann, Sara M. 27
 Daou, Modibo 1443, 484
 Dara, Antoine 1096
 Dara, Charles 451
 Darby, Alistair C. 16
 Dario Velez, Ivan 128
 Darlaba, Maxwell 75
 Darling, Anne Marie 1492
 Darra, Charles 1125
 Darrick, Carter 1439
 Darwin, Lincoln S. 626
 Das, Manoj K. D. **340**
 Das, Smita **1352**
 Das, Sumon K. 1188

The number(s) following author name refers to the abstract number.

- Dasgupta, Debleena 1439
 Daszak, Peter 440, 52, 915
 Datagni, Michel G. 1475
 Date, Kashmira A. **1036**
 Dauner, Allison 1059, **113**
 Davenport, Dwann **1242**
 Davenport, Gregory 361, 657, 658
 Davey, Gail 135, 1448, 279, 280
 David, Renault 687
 Davide-Smith, Margaret 33
 Davidson, Edgar 602
 Davies, D. Huw **1123**, 1125, 1440, 1128, 197
 Davis, Justin K. 517
 Davis, Richard E. **786**
 Davis, Stephanie M. 1028, **998**
 Dawlat Khan, A K. M. 940
 Dawson, Nikiah 930
 Day, Nicholas P. 649, 1479
 Dayan, Gustavo 591
 Days, Emily 1110
 de Alwis, Ruklanthi **1054**, 13, 1399
 de Araújo, Fernanda F. 1241
 de Cassan, Simone C. 932
 de Castro Guimaraes, Ana 1433, 20, 267
 De Filippis, Ana Maria 109
 de Gier, Brechje 496
 De Heer, Hendrick D. 279
 de Jong, Bouke 1177, 84
 de Jong, Katja 1479
 de Koning, Harry P. 1498
 De La Cruz, Anna 1086, 1307
 de la Rosa, Olimpia 1380
 de Lamballerie, Xavier 1191, 1471
 De las Salas Ali, Jorge Luis 1358
 De los Santos, Maxy **1192**
 de los Santos, Tala 17, 263
 de Mast, Quirijn 220
 de Medeiros, L. L. 82
 De Meeûs, Thierry 783
 de Morais, Luis 69
 De Muylder, Geraldine 774
 de Roode, Jacobus 507
 de Silva, Aravinda 13, 514, 1054, 1397, 1399
 De Silva, Aruna Dharshan 607
 de Silva, Dharshan 1397
 de Silva, Nilanthi R. 1029, 1473
 De Silvestri, Annalisa 231
 de Vlas, Sake J. 1238
 Debes, Amanda K. 1169
 Debes, Jose 273
 Debnath, Anjan **22**
 Debrah, Alexander Y. 1187
 deBruyn, Becky S. 59
 Dechering, Koen **816**
 DeClerck, Hilde 910
 Decosterd, Laurent A. 813
 Deenonpoe, Raksawan 1489
 Deewatthanawong, Prasit 473
 Degefie, Tedbabe 935
 DeGroot, Anne S. 256
 DeHecq, Jean-Sébastien 390
 Deissler, Robert J. 1254
 Deitz, Kevin 1345
 Delcambre, Gretchen H. **1213**
 Delfino, Breno M. 1088
 Delgado, Christopher 1312
 Delgado, Yosnaida 131
 Delisle, Hélène 144
 Delmini, Rupert 459
 Delorey, Mark 872
 Deloron, Philippe 1097
 Demanou, Maurice 264
 Demas, Allison **1317**, **1317**
 Dembélé, Demba 823, 1096, 1274, 323
 Dembele, Issiaka 765
 Dembele, Massitan 400
 Deme, Awa Bineta **309**
 Deming, Michael 1416
 Demissie, Meaza 149
 Dendukuri, Nandini 1376
 Deng, Bingbing 224
 Deng, Haiyan 818
 Dengue v. Under-Reporting Initiative 1062
 Denham, Steven 1462
 Denlinger, David S. **101**
 Dennison, Nathan **1112**
 Dent, Arlene 1089, 1090, 1122, **664**, 936
 Dent, Joseph A. 1435
 Denton, Jerod S. 1110
 Deogratias, Damas 1233, 31
 Depaquit, Jerome 1471
 Derado, Gordana 277
 Derby, Kiersten S. **700**
 Deribe, Kebede 135, **1448**
 DeRisi, Joseph L. 811
 Derman, Alan 278
 DeRocher, Amy E. 23
 Derrick, Deborah **1081**
 Derrick, Steven 218
 Derriennic, Yann 1279, 541
 Dery, Gilbert 1253
 Deryabin, P N. **908**
 Desai, Meghna **851**
 Deseda, Carmen C. 1189
 Desewu, Kwame 90
 Deshpande, Bhushan 1445
 DeSimone, Joseph D. 942
 Desir, Luccene 1038
 Desormeaux, Anne Marie 112, **731**
 Desrochers, Rachelle 1070
 Desrosiers, Joseph 256
 Desruisseaux, Mahalia S. 1103, 639, 152
 Detjen, Anne K. 1376
 Devi, Pushpa 702
 Devine, Gregor J. 881, **1464**
 Dey, Ranadhir **1019**, 1242, 1244
 Deye, Gregory 180, 973
 Dhabangi, Aggrey 1011, 164
 Dhanalaxmi, C. Mohan 1074
 Dhanasekaran, Govindarajan 516
 Dhar Chowdhury, Parnali **106**
 Dhingra, Satish K. 1265
 Di Caro, Antonio 615
 Dia, Ibrahimia 1113
 Dia, Seydou 1125, 451
 Diabaté, Abdoulaye 1344, 1364, 386
 Diagne-Samb, Habsa 1225
 Diakité, Mamadou 1012
 Diakite, Mahamadou 665, 822, 99, 153, 1308
 Diakitè, Seidina A. S. 153, 1012
 Diallo, Abdoulbaki 457, 853
 Diallo, Abdallah 99, 967
 Diallo, Boubacar 765
 Diallo, Boubakar 818
 Diallo, Diawo 1058, 1385
 Diallo, Ibrahimia **798**, 938
 Diallo, Mawlouth 1058, 1385
 Diallo, Seydou 268
 Diallo, Saliou 323
 Diamond, Michael S. 1398
 Diancourt, Laure 392
 Diarra, Ayouba 818
 Diarra, Bakary 186
 Diarra, Issa 1443, 484
 Diarra, Seybou 975
 Diarra, Souleymane 457, 853
 Dias, Tamiris T. **1204**
 Diatta, Georges **482**
 Diaw, Mamadou Moustapha 938
 Diawara, Elisateh Yawa **323**
 Diawara, Sory I. 1308
 Diaz, Andrea 94
 Diaz, Elia 1178
 Diaz, Yamilka Y. **127**
 Diaz-Pinto, Hector 989
 Diaz-Virreta, Ana 1390
 Dickerson, Aimee 206
 Dickinson-Copeland, Carmen 357
 Dicko, Alassane 186, 457, 853
 Dicko, Ilo 400, 765
 Dicko, Yahia 457, 853
 Dickson, Emmanuel A. **682**
 Dickson, Emmanuel K. 994
 Dickson Goss, Laura **60**
 Dida, Gabriel O. 1336
 Diedhiou, Cyrille K. 354
 Diemert, David **759**
 Dieng, Therese 772
 Dieng Sow, Gnagna 545
 Dietze, Reynaldo 464
 Dieye, Baba 1270, 1270, **320**, 327, 354
 Dièye, Tandakha N. 42, 560
 Dieye, Yakou 545
 Diffenbaugh, Noah S. 870
 Diggle, Peter J. 1484, 331, 524
 Diggs, Carter 226, 1443
 Dikoume Mbongo, Adolphe 539
 Dillon, Brian E. 187
 Dimaano, Efren 729
 Dimalibot, Judeline 835
 Dimatatac, Frederico 586
 Dimopoulos, George 1112, 1357, 1363, 569, 688, 690, 695, 696, 97, 981
 DiNardo, Andrew R. **1376**
 Dineen, Brendan 741
 Dinglasan, Rhoel R. 1106, 1258, 924, 1100, 498
 Diniz, Renata 759
 Dione, Michel 1079
 Diongue, Khadim 268
 Diop, Aissatou 938
 Diop, Ismaila L. 208
 Diop, Ousmane 1058, 1385
 Diouf, Ababacar 1157, 224, 42, 451, 665
 Diouf, Mame Birame 1281
 Diouf, Mamadou Lamine **499**
 DiPetrello, Christen 923
 Dissanayake, Gunewardena 1311
 Diuk-Wasser, Maria **478**, **480**, 748
 Divala, Titus H. **240**
 Dixit, Amruta **530**
 Dixit, Vaishali P. 1403
 Djato, Touka M. 1475
 Djibril, Naguibou M. **768**
 Djimde, Abdoulaye A. 323, 823, 822, 1096, 1274
 Djogbenou, Luc 376, **1346**
 Djouaka, Rousseau 1459
 Do, Rose 780
 Dō kaya, Mert 1123
 Doak, Colleen M. 496
 Dobson, Andrew P. 947
 Dodd, Benjamin 1468
 Dodd, Kimberly 910
 Dodean, Rosie 1271, 817
 Dodoli, Wilfred 211, 212, 1136
 Dodson, Brittany 11
 Dodson, Brittany L. **1214**
 Doerig, Christian 1008
 Dogbe, Kokou-Sika 288, 289
 Doggett, J. Stone 820
 Dogovski, Con 1263, 1263
 Doha, Said A. 579
 Doker, Thomas J. **1189**
 Dokladny, Karol 361
 Dolenz, Charlotte **862**
 Dolo, Housseini 967
 Domanico, Paul 1226, 1229
 Dombo, Ogobara K. 1125
 Domingo, Gonzalo J. 1275, 17, 263
 Dompok, Albert 761
 Dondorp, Arjen 328, 506, 649, 1479, 635, 822

The number(s) following author name refers to the abstract number.

- Donegan, Sarah 1272
 Dong, Chen 811
 Dong, Yuemei 690, **696**
 Dongmo, Francois T. 194
 Dongus, Stefan 881
 Donnell, Robert 86
 Donnelly, Martin J. 1346, 1458, 1460
 Dool, Pieter 483
 Doolan, Denise L. 1148, 1148, 1490
 Doranz, Benjamin J. 594, 598, **602**
 Doritchamou, Justin 1158, 1158
 Dorkenoo, Ameyo M. 1237
 Dorkenoo, Monique A. 1475
 Dorn, Patricia 578
 Dornakova, Veronika 304
 Dorsey, Grant 1121, 1121, 1306, 181, 189, 193, 195, 204, 344, 37, 370, 502, 504, 538, 836, 860
 dos Santos, Balbino L. 524
 Dos santos, Flavia **109**
 dos Santos Lima, Valdirene 71
 Dotsey, Emmanuel Y. **1440**
 Dotson, Ellen 501
 Doucoure, Souleymane 390
 Douglas, Nicholas M. 461
 Douglass, Janet **252**
 Doumbia, Sidy 1348
 Doumbia, Saibou **153**, 665
 Doumbia, Seydou O. **1308**, 1348, 818, 99
 Doumbia, Salif S. 400
 Doumbo, Ogobara K. 1126, 1443, 484, 974, 1096, 323, 823, 929
 Doumbo, Safiatou 1125, 1126, 451
 Doumbouya, Mory 153
 Doumtabe, Didier 1125, 1126, 451
 Dowd, Kimberly A. 1402, 513, **1398**
 Dowler, Megan 1154, 1159
 Downing, Louise 1207
 Downs, Jennifer A. 490
 Downs, Philip 1477, **33**
 Doyle, Jamie R. 1360
 Doyle, Stephen 15
 Dozie, Ikechukwu 200
 Drake, Tom 412
 Drakeley, Chris 1121, 1121, 1284, 1430, 195, 503, 543, 641, 1431, 344
 Draper, Simon J. 1152, 932
 Drobot, Michael A. 106
 Drew, Clifton 133
 Drew, Mark E. 1320
 Dreyer, Anita 1173
 Drietz, Matt 515
 Driguez, Patrick 1490
 Driss, Adel 357
 Drolet, Barbara **92**
 Duah, Nancy O. 507
 Dubensky, Jr., Thomas W. 1438
 Dubot-Pérès, Audrey 390
 Dubovsky, Jason 1023
 Duda, Kirsten 1418
 Duffull, Stephen B. 822
 Duffy, Michael 667
 Duffy, Patrick E. 1149, 1149, 1150, 1155, 227, 228, 452, 457, 853, 930, 1147, 1147, 186, 190, 633, 929
 Duffy, Sandra 372
 Dufort, Elizabeth 411
 Dufour, Vanessa **1435**
 Duggal, Nisha **1467**
 Duman-Scheel, Molly 944, 945
 Dumonteil, Eric **102**, **1245**, **566**
 Duncan, Robert 1019, 1242
 Dunn, Matthew 56
 Duombo, Ogobara K. 451
 Duong, An D. **406**
 Duong, Socheat 827
 Duparc, Stephan 42B, 48, 645, 175
 Duplessis, Chris 90
 Dupnik, Kathryn **82**
 Dupouey, Julien 1191
 Duraisingh, Manoj 1503
 Durand, Lizette O. **1375**
 Durand, Salomon 1120, 1120, 1128, 1192, 1309, 342, 358, 509
 Durbin, Anna P. 1402, **512**, 513, 605, 606
 Duris, M. 348
 Durvasula, Ravi 1017, 576
 Dusfour, Isabelle **384**, 873
 Duthie, Malcolm S. 1422
 Dutta, Sheetij 1443
 Duy, Pham T. 1479
 Dvorin, Jeffrey 923, 1503
 Dyck, David 1075
 Dyer, Naomi 778
 Dyson, Hugh E. 1169
 Dzinjalalama, Fraction K. 1267
- E**
- Eappen, Abraham 229, 979
 Earle, Duncan 1280, 545
 Easom, Eric E. 301, 648, 1424, 811
 Eastman, Richard 992
 Easton, Alice 495
 Ebel, Gregory D. 1468, 941
 Eberhard, Mark 1044, 1451
 Eberhart, Christina 1021
 Ebondo Ngoie, Symphorien 652
 Ebong, Omotayo O. 802
 Ebusu, Charles 1121, 1121, 189, 193
 Eccles-James, Ijeoma 189, 193, 37
 Echazu, Adriana **1024**
 Echevarria, Juan 1220
 Eckhoff, Philip A. **1283**, 1301, 546
 Eckmann, Lars 22
 Eddyani, Miriam 1177, 83, **84**
 Edgel, Kimberly A. 1120, 1120, 1123, 1192, 1309, 358, 509, 726, 1128
 Edi, Constant **376**
 Edillo, Frances E. **1061**, **580**, 79
 Edozieh, Kate U. 730
 Edstein, Michael D. 46
 Eduardo, Eduardo Valencia 1423
 Edwards, Carolyn 1400
 Edwards, Kathryn M. 911, 1377
 Edwards, Nick J. 932
 Edwards, Tansy **1230**
 Egurrola, Jorge 1067, 1072, 128, 588, 595
 Egwang, Thomas 183
 Ehلمان, Daniel 1372
 Ehrbar, Dylan J. 1212, 1465, 11
 Ehrler, Lindsey 1147, 1147
 Eibach, Daniel 794
 Eichinger, Daniel 884
 Eigege, Abel 1454
 Eigsti, Renee L. **790**
 Eisele, Thomas 1253, 1295, 1425, 859, **1426**, 500
 Eisen, Lars 1462, 568, 9
 Eisen, Rebecca J. 1064, 476
 Eisenberg, Joseph N. S. 1031, 676, 960
 Eisenberg, Marisa C. 707
 Ekasari, Tyas 175
 Ekawati, Lenny 175
 Ekberg, Greg 1148, 1148
 Ekenna, Uche 1133, 210, 550
 Ekiyor, Christopher P. 200
 El Arifeen, Shams 937
 El-Deeb, Ibrahim 449
 El-Hassan, Ahmed 784
 El-Sawaf, Bahira M. 579
 Elagib, Atif A. **158**
 Elanga Ndille, Emmanuel **390**
 Elbashir, Haggar 630
 Elbashir, Mustafa 158, 630
 Elbeshbishi, Yara 1161
 Elder, John P. 983
 Elemi, Iwasam 1272
 Elguea, Carlos 528
 Elhelu, Oumsalama **902**
 Elias, Sean C. 932
 Elisa, Sicuri 617
 Elisha, Anisha 961
 Elizondo, Douglas 121
 Elliott, Alison 1284
 Elliott, Suzanne 48
 Ellis, Alicia M. 983
 Ellis, Brian 278
 Ellis, Crystal N. **959**
 Ellis, Esther M. **112**, 1189, 584, **989**
 Ellis, Michael 727
 Ellis, Ruth 929
 Ellner, Jerrold 464
 Elmer-DeWitt, Molly 1306
 Elphinstone, Robyn **164**
 Else, Kathryn J. 1433
 Elwoud, Dan 512
 Elyazar, Iqbal 175
 Embeke, Narcisse 1255
 Emch, Michael 858
 Emeje, Martins 168, **803**
 Emerson, Paul M. 1472
 Emmanuel, Isaac M. 550
 Emmanuel, Rossignol 738
 Emrich, Scott J. 575
 Emukule, Gideon 465
 Enama, Mary 1437
 Endeshaw, Tekola 1472
 Endy, Timothy P. 117
 Engoru, Charles E. 456
 Engwerda, Christian 449
 Enquesselasse, Fikre 1448
 Ephraim, Richard D. 1302
 Epstein, Jonathan H. 52
 Epstein, Judith 1160, 1161, 1437, 226
 Erasmo, Jonathan N. V. 580
 Erath, Jessey L. **1421**
 Erdman, Laura K. 1011
 Erhart, Annette 1312, 49, 861
 Erickson, Bobbie R. 1379, 1380
 Ericson, Megan **1499**
 Errea, Renato 287, 752, 753
 Erskine, Marcy 1070
 Erume, Joseph 183
 Eryando, Tris 675
 Esan, M. 646
 Escalante, Ananias A. 1267, 1299, 1300, 642, **643**, 353
 Escher, Elisabeth 1472
 Escobedo-Vargas, Karin 1135
 Eskin, Eleazar 61
 Espada, Liz 1341
 Espejo, Victoria 410
 Espetia, Susan 1387
 Espina, Luz M. 118
 Espinoza, Nereyda 711
 Espósito, Danillo L. A. 596
 Esquelin, Ines 515
 Essandoh, John **1343**, 1346
 Estanislau, Cesar A. Maximiano. **681**
 Estanislau, Juliana d. Silva. Gomes. **1241**
 Esterhuizen, Johan 943
 Esterman, Adrian 508
 Estevez, Virginia 1215
 Estevez-Lao, Tania Y. 1110
 Estrich, Cameron G. **404**

The number(s) following author name refers to the abstract number.

- Eswarappa, Meghana 125
 Etienne, Lesly 112
 Etogo Ondigui, Bienvenu 1411
 Evans, Darin **1454**
 Evans, Holly **964**
 Existe, Alexandre 213, 847
 Eyako, Wurapa 1369
 Eyase, Fredrick 592, 970
 Ezedinachi, Emmanuel 1272
 Ezeigwe, Nnenna M. 730
 Ezirim, Chinwe T. 802
- F**
- Fabris, Clara 386
 Fair, Joseph N. 905
 Fairhurst, Rick M. 1362, 153, 360, 5, 506, 665, 669, 822, 1012
 Faith, Sitnah H. 1033
 Faiz, Md. Abul 1479
 Faizullahoy, Adnan 1005
 Fakoli, Lawrence 1039
 Fakoya, A. 646
 Falade, Catherine O. **1261**, 1303
 Falcone, Franco 424
 Falk, Hendrik 1198
 Fall, Fatou Ba 798
 Fall-Niang, Mame Yacine 1225
 Fallon, Pdraic. G. 1504
 Fan, Erkang 1021, 23, 27
 Fan, Zhang 706
 Fancony, Claudia 281
 Fanello, Caterina I. **649**
 Fang, Huang 506, 864
 Fansiri, Thanyalak 391, **392**
 Fantahun, Mistire 762
 Fanthome, Amber 20
 Farag, Tamer 1405
 Farajollahi, Ary 571
 Fares, Rafaelle C. Gomes. 1241
 Farias, Helena M. C. 1484
 Farmakiotis, Dimitrios 248
 Farrar, Jeremy 14, 1449, 1482, 1485, 406, 919, 175
 Farrell, Margaret 1185
 Farris, Christina 744
 Faruque, A. S. G. 1188, 704
 Fasabi, Manuel 356
 Fasel, Nicolas 1501
 Fataki, Olivier T. A. **343**
 Faulx, Dunia 263
 Faust, Christina **205**
 Fawzi, Wafaie 1492
 Fay, Michael P. 929, 930
 Faye, Adama 765
 Faye, Babacar 1137, 268, 548, 655, 772, 798
 Faye, Oumar 921
 Faye, Ousmane 499, 501
 Fayomi, Benjamin 1253
 Feachem, Richard G. A.. 1276
 Feeney, Margaret 189, 193, 37
- Feghali, Karla C. 316
 Feitosa, Ana L. P. 596
 Feldmann, Heinz 913
 Felger, Ingrid 1156, **1257**, 216
 Felgner, J. 223
 Felgner, Philip 1123, 1128, 1490, 197, 223, 664, 670, 1125, 1440, 344, 454
 Felix, Gilberto 872, 93
 Felling, Barbara 1076, 1077, 619, 80
 Felzemburgh, Ridalva D. M. 524
 Feng, Gaoqian **662**
 Feng, Zheng 896
 Fenton, Andy 1068
 Ferdig, Michael T. 1006, 1099, 328, 506, 864
 Ferguson, Heather 61
 Ferguson, Neil M. **1470**
 Fernandes, Jamille 427
 Fernandes, José 318
 Fernandes, Marconi 759
 Fernandez, Antonio 1020, 780
 Fernandez, Jorge 1372
 Fernández, Regina R. 618
 Fernandez, Stefan 120, 126, 441, 443, 614
 Fernandez-Arias, Cristina **1014**
 Fernandez-Salas, Ildefonso 123, 986, 597
 Fernando, Anira N. 607
 Ferrari, Giovanfrancesco 652
 Ferreira, Marcelo 7
 Ferreira, Pedro Eduardo 829
 Ferreira-da-Cruz, Maria de Fatima **326**
 Ferro, Cristina 1358
 Ferro, Santiago 6
 Ferrufino, Lisbeth 734, 780
 Ferruti, Paolo 498
 Fichet-Calvet, Elisabeth 1388
 Fidock, David A. 1265, 1273, 372, 45, 811
 Fieck, Annabeth 1017
 Fields, Barry 1396, 592
 Figueroa, Carlos A. **1381**
 Filgueira Júnior, José 1197
 Filho, Fernando A. X. M. 1052
 Filho, José Q. 1407, 1408
 Filler, Scott 204
 Filler, Scott J. 324
 Fillinger, Ulrike 374
 Finch, Casey 478
 Fine, Jason 743
 Finkelstein, Julia L. **1089**, 1090, 405
 Finn, Tim 1253
 Finn, Tyler 516
 Fiore, Jacqueline 1428
 Fire, Andrew Z. 1403
 Firestone, Cai-Yen 1469
 Fischer, Kerstin **18**
 Fischer, Marc A. 1445, 1203
- Fischer, Peter U. 1039, 1046, 18, 420, 757
 Fitch, Christina E. **627**
 Fitter, David L. 1035
 Fiuza, Jacqueline 1247
 Flannery, Erika L. **808**
 Fleckenstein, Lawrence 645
 Flegg, Jennifer A. **822**, 830, **854**
 Fleischmann, Erna 615
 Flisser, Ana **1065**, 534
 Floeter-Winter, Lucile M. 791
 Florence, Salvatore 1098, 4
 Florentini, Edgar A. **788**, 789
 Flores, Adriana E. 1349
 Flores, Julian 1410
 Flores Franco, Jorge Luis 780
 Flores Leon, Amilcar A. **294**
 Flores-Mendoza, Carmen 1135, **1341**
 Flores-Rivera, Jose 534
 Florey, Lia 1311, 500, **859**, **863**
 Florez, Janeth 610
 Florez Rivadeneira, Zulibeth 1349
 Flueck, Christian 1503
 Flueckiger, Rebecca M. 1075
 Fofana, Abdrahamane 1117
 Fofana, Bakari 1096
 Folley, Anne E. 896
 Folsom-O'Keefe, Corrine 478, 480
 Fong, Rachel 594, 598
 Fongoro, Sahare 818
 Fonseca, Benedito A. L. **596**, 612
 Fonseca, Dina 571
 Fontaine, Albin 392
 Fontenille, Didier 1113
 Fontes, Cor Jesus F. 1199
 Fontes, Raissa M. 1052, 611
 Forbush, Melissa **1269**
 Ford, Byron D. 171
 Ford, Gavin W. **1181**
 Ford, Louise **266**
 Forero, David 795, 1162
 Forquer, Isaac P. 43, 820, 817
 Forrester, Naomi L. 1389
 Forshaw, Adam **576**
 Forshey, Brett M. 448, 581, 983
 Forst, Steven 261
 Fortes, Filomeno 1305, 326
 Fournet, Florence 390
 Fowkes, Freya J. I. **1291**, 1442, 667
 Fox, Anna M. W. 27
 Fox, Ellen C. Mueller. **257**
 Fox, James 1410
 Fox, LeAnne 1028, 1416, 998
 Foy, Brian D. 1351, 383, 941, 978
 Fozo, Elizabeth 86
 Fraga, Deborah 524
 Fraga, Valéria D. 671
 Franca-Koh, Ana C. 1334
 Francis, Filbert 1427
- Franco, Leticia **603**
 Françoise, Kátia S. 221
 Frando, Andrew 116
 Frank, Matthias 1367
 Franke, Molly F. 463, 1037
 Franklin, Hannah 135, **143**
 Frantz, Doug E. 954
 Fraser, Jamie 113, 733
 Frederic, Simard 687
 Freed, T. Zach 1350
 Freeman, Brandi D. 1103
 Freeman, Matthew C. 712
 Freeman, Nicole 1186, 731, 738
 Freilich, Daniel 1161
 Freire, Janaina 759
 Fremont, Daved 1398
 Frempong, Kwadwo K. 292, 367
 Frempong, Naa Adjeley **422**
 French, Michael D. **1240**
 French Artesunate Study Group 993
 Frentiu, Francesca D. 876
 Freund, Yvonne R. **1424**, 301, 648, 811
 Frevert, Ute 1434
 Freyman, Kimberly 1353, **1354**
 Fried, Michal 186, 190, 457, 633, 853
 Fried, Michel 227, 452, 1149, 1149, 1150
 Friedman, Eleanor **987**
 Friedman, Jennifer F. 1000, 1002, 1003, 1149, 1149, 1150, 1436, **227**, 452
 Frieze, Kathryn M. **129**
 Fröberg, Gabrielle **829**
 Fryauff, David 1439
 Fu, Chi-Ling 1001, 997
 Fuehrer, Hans-Peter 328
 Fujiwara, Ricardo T. F. 488
 Fukuda, Mark 328
 Fukuno, Mai 793
 Fukushima, Masako 1479
 Fuller, James A. **676**
 Fumador, Senyo Kofi 886
 Fung, Isaac Chun Hai **1035**, **139**
 Funk, Theresa 1147, 1147
 Funkhouser, Sheana W. 743
 Furini, Adriana A. C. 671
 Fyfe, Janet A. M. 83
- G**
- Gaba, Mukul 1074, 1094
 Gabert, Rose 1279, 541
 Gaborit, Pascal 873
 Gabriel, Martin 615
 Gabrieli, Paolo 946
 Gabryszewski, Stanislaw J. **1265**
 Gadalla, Nahla 1429
 Gadea, Nilda 1174, 1227
 Gadiaga, Aida 938

The number(s) following author name refers to the abstract number.

- Gaeddart, Mary 464
 Gaff, Holly 573
 Gagaring, Kerstin 808
 Gage, Kenneth L. 476
 Gagova, Iveta 348
 Gailhardou, Sophia 591
 Gaines, David 573
 Galal, Nahla M. 271
 Galarza, Ivonne 558, 608
 Galdos-Cardenas, Gerson 1020, 734, 780
 Galeana-Hernández, Marisol 604
 Galinsky, Kevin 7
 Gallardo, Maria S. 752, 753, 287
 Gallego-Delgado, Julio 634
 Gallinsky, Kevin 1010
 Gallo, Kerry 276
 Galloway, Renee 133, 558, 249, 238
 Galvão, J. G. V. 82
 Gamboa, Dina 281
 Gamboa, Dionicia 1102, 1124, 1130, 1131, 1323, 197, 307, 356, 39
 Gamo Benito, Francisco Javier 925, 44, 648
 Gan, Victor C. 111, 124, 553, 586, 587, 8
 Gandarilla, Omar 780
 Ganesan, Anuradha 733
 Ganeshan, Harini 1437, 226
 Gankpala, Lincoln 1039
 Ganley-Leal, Lisa M. 1000
 Gannavaram, Sreenivas 1244, 1247
 Ganter, Markus 1503
 Gao, Qi 1276, 1278, 350, 366
 Gaona, María A. 94
 Garcia, Andres J. 984
 García, Cybele C. 105
 Garcia, E. S. 274
 Garcia, Hugo 232, 531, 533
 García, Haydee 989
 Garcia, Hector H. 532
 Garcia, Josefina 410
 García, Lineth 71
 Garcia, Patricia 528
 Garcia, Santos 679
 García Cordero, Julio 597
 Garcia-Bustos, Jose 1008
 García-Gubern, Carlos 558
 Garcia-Jasso, Carlos 415
 Garcia-Rejon, Julian 1462
 Garcia-Sastre, Adolfo 1390
 Gardiner, Don L. 47
 Gardner, Christina L. 56
 Gargano, Julia 883
 Garner, Paul 1272
 Garske, Tini 1470, 458
 Garver, Lindsey S. 976
 Garzoni, Luciana R. 1241
 Gass, Katherine 1237
 Gasser, Robin 492
 Gastanaduy, Paul 554, 613, 703, 237, 446
 Gati, Stephanie B. 1373
 Gatti, Simona 756
 Gaugler, Randy 571
 Gautam, Shalini 73
 Gavidia, César M. 230, 532, 533, 98
 Gaydon, Jane 48
 Gaye, Oumar 1137, 548, 655
 Gaye, Omar 772
 Gaye, Seynabou 938
 Gaye-Diallo, Aissatou 1225
 Gaynor, Bruce D. 285
 Gaze, Soraya 1490
 Gazzinelli, Andrea 283, 424, 429, 488
 Gazzinelli, Flavia 283
 Gazzinelli, Maria Flávia 732, 759
 Ge, Min 648
 Ge, Xiaopeng 661
 Geary, Timothy G. 1435
 Gebre-Michael, Teshome 749
 Gebreyesus, Tsega 279
 Gee, Jay E. 1189
 Gegerfelt, Agneta v. 962
 Geiger, Jennifer A. 23
 Gelaw, Solomon 619
 Gelaye, Woyneshet 1472
 Gelderblom, Huub C. 30
 Gentile, James 1283
 George, Dylan B. 1418
 George, Elizabeth Rusell 456
 George, Kasim 979
 George, Phillip 469
 George, Parakkal Jovvian 966
 George, Sarah L. 514
 Geraci, Nicholas S. 1018
 Gerard, Craig 1011
 Gerard, Joseph 700
 Gerbasi, Robert 1154
 Gerbasi, Vincent R. 1439, 1313
 Gerbi, Gemechu 741
 Geromanos, Scott 215
 Gerrin, Carol D. 885
 Gershman, Mark D. 1445
 Gesase, Samuel 170, 1327
 Getachew, Dawit 619
 Gething, Peter W. 104, 1297, 801, 1298, 497
 Getso, Kabiru I. 435
 Geubbels, Eveline 922
 Ghaffar, Atif 640
 Ghani, Azra C. 458, 735, 497, 848
 Ghansah, Anita 142, 70, 886
 Ghedin, Elodie 1382
 Gherzi, Bruno M. 1384, 445
 Ghose, Aniruddha 1479
 Ghosh, Anil K. 924
 Gibbons, Arideth 1379
 Gibbons, Ardith 910
 Gibbons, Robert V. 117, 443
 Gibson, Gabriella 1364
 Gicheru, Nimmo 1442
 Gidado, Saheed O. 435
 Gidwani, Kamlesh 775
 Gikunju, Stella 1396
 Gil, Ana I. 911, 1377
 Gil, José Pedro 829, 1096
 Gilbreath, Thomas 1361
 Gildengorin, Ginny 103, 447, 53, 934
 Gill, Christina 16
 Gilles, Jérémie 1364
 Gillespie, John R. 1021
 Gilliland, Jr., Theron 1059
 Gillingwater, Kirsten 1424, 301
 Gilman, Robert H. 1020, 1387, 1409, 1423, 356, 431, 532, 734, 781, 788, 230, 531, 533, 780, 789
 Gilmore, Dana 727
 Gilroy, Kate 622
 Gimnig, John E. 1329, 1431, 519, 852, 1288, 455
 Giordani, Maria Teresa 1222
 Giorgi, Emanuele 331
 Giovannoni, Federico 105
 Giraldo-Calderon, Gloria I. 575
 Girerd-Chambaz, Yves 593
 Girgis, Natasha M. 1434
 Giri, Abhisek 1449
 Girling, Gareth 927
 Girod, Romain 873
 Gitau, Evelyn N. 241
 Githeko, Andrew 336, 460
 Githure, John I. 1119
 Givens, Matthew 1321
 Glaser, Elizabeth 1329, 1337
 Glaser, Robert L. 401
 Glass Elrod, Mindy 1189, 558
 Glenn, Travis 913
 Glover, Simon J. 1494, 1496, 155, 638
 Gnidehou, Sedami 1158, 1158
 Go, Chi-Jong 586
 Gobert, Geoffrey 949, 999
 Goblirsch, Sam 1222
 Goenaga Olaya, Sergio 1349
 Goettsch, Brittany 530
 Goez-Rivillas, Yenny 1164
 Goheen, Morgan M. 1016, 1318
 Goita, Seydou 1235
 Gokhale, Makarand 76
 Golden, Allison 17, 263
 Golden, Hannah E. 1439
 Goldman, Ira 317
 Goldstick, Jason 1031
 Gollogly, Jim 1181
 Gomes, Regis 727
 Gomes, Santana 754
 Gomez, Guillermo 777
 Gomez, Giovan F. 1108
 Gomez, Jorge 410
 Gomez, Patricia P. 206
 Gómez Camargo, Doris 1349
 Gomez de la Torre, Juan Carlos 1179
 Gomez-Puerta, Luis A. 98, 232, 532
 Goncalves, Bronner P. A. 190
 Gondorf, Fabian 965
 Gong, Bin 1164, 716
 Gongalves, Bronner 929
 Gonzal, Analisa 1000, 1003
 Gonzales, Carlos 1454
 Gonzales-Gustavson, Eloy 232
 Gonzalez, Armando E. 532, 98, 232, 531
 Gonzalez, Andrea L. 872
 González, Gladys 558
 González, Iveth J. 538, 836, 1286
 Gonzalez, Karla N. 116
 González, Liza 989
 González, Ranulfo 1108
 Gonzalez Reiche, Ana S. 1392
 Gonzalo-Rodriguez, Jonathan 672
 Good, Michael 449
 Goodhew, Brook 34, 35, 481
 Goodman, Anna L. 932
 Goodrich, Mary 415
 Goodrich-Blair, Heidi 261
 Goodson, Holly 620
 Goodson, James 1070
 Gorbet, Geoffrey N. 564
 Gordon, Aubree 985
 Gordon, Catherine A. 564
 Gordon, Gilad S. 1053, 515
 Gordon, Susan 1414, 252
 Gori, Elizabeth 486
 Gosi, Panita 1104, 1321, 1324, 243
 Gosling, Roly 1276, 1277, 1327, 1429, 538, 836
 Gotia, Hanzel T. 894
 Goto, Yasuyuki 950
 Goutzou, Eduardo 1220
 Gouagna, Louis-Clement 1364
 Gould, Matthew K. 1498
 Gounoue, Raceline 1411, 1412
 Goupil, Louise S. 421
 Gower, Laura 1231, 31
 Gracia, Lineth 296
 Graeff Teixeira, Carlos 951
 Graf, Paul C. F. 358
 Graff, Joel W. 790
 Graham, Andrea L. 947
 Graham, Barney 1437
 Graham, Brittany 415
 Graham, Christine B. 476
 Graham, David 1100, 1258
 Grahek, Shannon 759
 Grandez-Castillo, Gustavo 672
 Grandez-Urbina, J. A. 672
 Granger, Donald L. 1098, 4
 Grant, Alison D. 66
 Grant, Dorsey 542
 Grant, Warwick 15

The number(s) following author name refers to the abstract number.

- Gratz, Jean 1079, 1406, 1410
 Graumans, Wouter 220
 Graves, Patricia 252, 1040
 Graves, Shawna F. **1443**
 Gray, Darren 565, 754, 1239, 564
 Gray, Marion 1414
 Gray, Meg 978, 1351
 Green, Justin 42A, **42B**
 Greenberg, Robert M. 428, **953**
 Greenhouse, Bryan 1121, 1121, 1286, 1306, 1429, 195, 344, 538, 836
 Greenwood, Brian 1429
 Gregoricus, Nicole 912
 Gregory, Christopher 582
 Gregory, Michael 709
 Greiman, Stephen E. **948**
 Greisman, Laura **1182**
 Grenfell, Bryan 1373, 1480, 205, 919
 Gresh, Lionel 115, 121, 9, 985
 Gresty, Karryn 359, 828
 Grieco, John P. 521, 567, 62, 1342, 871, 1355
 Griffin, Marie R. 911, 1377
 Griffin, Paul 48, 219
 Griffing, Sean M. 307
 Griffith, Kevin 1064
 Griffiths, Emily C. **1068**
 Grigg, Matthew J. **1251**, 334, 635, 995
 Grijalva, Carlos G. 911, **1377**
 Grijalva, Mario J. **777**
 Grimberg, Brian T. 1254
 Grinev, Andriyan 1216, **1217**
 Grinstein, Sergio 351
 Grobusch, Martin P. 1367, 251, 318, 494, 67
 Grogan, Caroline 1078, 653
 Gromowski, Gregory D. **1469**
 Grubaugh, Nathan D. **941**
 Grunwald, Jr., William C. 100
 Guagliardo, Sarah Anne **518**
 Gubler, Duane J. 1062, 1340
 Guelbeogo, Moussa 503, 1463, 1463
 Guenther, Tanya 622, 624
 Guerbois, Mathilde 1058, 1385
 Guerin, Philippe J. 214, 822, 830
 Guerra, Eduardo 131
 Guerra, Marta A. 1189
 Guerrant, Richard L. 1407, 1408, 1409
 Guerrero-Jimenez, Darwin F. 777
 Guerry, Patricia 709
 Guevara, Carolina 342
 Gueye, Aly **345**, 772
 Gueye, Alioune Badara 798, 938
 Gueye, Debbie 499
 Gueye, Serigne M. 1415
 Guhl, Felipe 71
 Guidi, Alessandra 954
 Guidi, Monia 813
- Guillard, Eliana 1024
 Guillaumot, Laurent 384
 Guimarães, André L. O. 611
 Guimarães, Maria 1197
 Guindo, Agnes 929
 Guindo, Boubacar **650**
 Guirou, Etienne A. 974
 Gulce Iz, Sultan 1123
 Gunasekera, Anusha 220
 Gunawardena, Nipul K. **1029**, 1473
 Gunawardena, Sharmini 1473
 Gundogan, Fusun 1000, 1002
 Gundra, Uma M. 1434
 Gunn, John S. 1171
 Günther, Stephan 615
 Guo, Denghui 648, 811
 Guo, Fengying 1239
 Guo, Qin 1439
 Gupta, Gaurav 303
 Gurley, Emily S. 1073, 1203, 1404, 237, 440, 442, 462, 52, 915, 940
 Gürüz, Yüksel 1123
 Gusa, Christina M. 628
 Gushu, Montfort B. 800
 Gut, Jiri 811
 Gutierrez, Gamaliel 121, 985
 Gutierrez, Herlinda 269, 414
 Gutierrez, Jorge 558
 Gutierrez, Juan B. 1105, 795
 Gutierrez, Lucia 951
 Gutierrez, Sonia 358
 Gutman, Julie **1268**, 210, 1252
 Gutteridge, Clare E. 359
 Guy, Kiplin 293
 Guzman, Diamelis 131
 Guzman, Hilda 1356, 1382
 Guzman, Humberto O. 1088
 Guzmán, María G. 1062
 Guzman, Rene 713
 Guzmán, Yahaira 608
 Gwadz, Robert W. 1362
 Gyapong, Margaret 75
 Gyorkos, Theresa W. **758**
- H**
- Ha, Do Q. **1201**
 Ha, Kwon-Soo 352
 Haberling, Dana L. 1189
 Habib, Fawzia A. 892
 Habib, Muhammad Atif H. **438**
 Habluetzel, Annette 1330, 386
 Haddad, Danny 30
 Haddock, Elaine 913
 Hadi, Mohamad 1165
 Hadiwidjojo, Sri 1313
 Hagan, Jose E. 1484, **524**
 Hahn, Thomas 349
 Haigney, Mark 806
 Haile, Ashley 976
- Haile, Melatwork 209
 Hailemariam, Aferwork 1456
 Hailemicheal, Yirgalem 762
 Hailu, Asrat 1448, 749
 Halasa, Yara A. 1074, 1094, **571**, 580, 79, 1061, 1063
 Halbert, Jean 1008
 Hale, DeVon C. 706
 Haley, Bradd 956
 Hall, Eric 713
 Halldin, Cara 574
 Hallett, Rachel 835
 Halleux, Christine M. 1413, 253
 Halliday, Alice 1433
 Halpin, Rebecca A. 1389
 Halsey, Eric S. 128, 342, 410, 448, 509, 517, 581, 618, **726**, 983
 Halstead, Scott B. 1062, 605, 1400
 Halton, Kate 565
 Hamadani, Jena D. 462
 Hamainza, Busiku 1, 1143, 1280, 1295, 1301, 1425, 385, 540, 541, 546
 Hamazakaza, Petan 541
 Hamed, Kamal 174, 841
 Hamel, Mary J. 1329, 1431, 851
 Hamer, Davidson H. 1, 1078, 1143, 653, 724, 728
 Hamianza, Busiku 1426
 Hamilton, Elizabeth J. 544, 327
 Hamilton, Robert B. **800**
 Hamilton, William L. **1005**
 Han, Eun-Taek 1315, 350, 352
 Han, George S. **582**, **584**
 Han, Jin-Hee 350
 Han, Kay Thwe 1266, 506, 864
 Han, Sarah 61
 Hanczaruk, Bozena 1403
 Handzel, Thomas 741
 Hanf, Matthieu 64
 Hang, Jun 448
 Hanisch, Benjamin R. **632**
 Hanley, Kathryn A. 1385, 605, 1058
 Hanna, Luke E. 966
 Hanscheid, Thomas 318
 Hansen, Elsa 862
 Hansen, Kristian S. **1146**, 1259, 1260
 Hanson, Bill 1438
 Hanson, Christopher T. 1469
 Hao, Nguyen Van 14
 Hao, Ying 552, 553, 586
 Haque, Emdad 106
 Haque, Farhana **442**
 Haque, Rashidul 1079, 1406, 1410, 462
 Harahap, Alida 157
 Harding, Simon P. 1494, 1496, 155, **638**
 Harding-Esch, Emma 1230
 Harn, Donald A. 1196, 564
- Harrell, Emma J. 42B
 Harrington, Laura C. 473, **63**
 Harris, Caroline 881
 Harris, Eva 103, 1054, 1062, **11**, 115, 116, 12, **121**, **122**, **123**, 125, 13, 1403, 9, **985**
 Harris, Jason B. 955, 959
 Harrison, Bruce A. 866
 Harrison, Thomas 941, 1468
 Harrison, Wendy 1240
 Hart, John 1230
 Hart, P. J. 954
 Hart, Robert J. 640
 Hartiger, Stella M. 911
 Hartinger, Stella 1377
 Hartl, Daniel L. 544
 Hartley, Catherine S. 16
 Hartley, David M. 869
 Hartman, A. Frederick **375**
 Hartman, Amy L. **907**
 Hartzog-Storment, Molly 572
 Harun, Golam D. 940
 Harville, Emily W. 987
 Hasan, Mahtab U. 1479
 Haseeb, M.A. 1243
 Hasegawa, Tomoyuki 1315, 222
 Hashim, Ramadhan 1327
 Hashizume, Masahiro **704**
 Hasker, Epco 775
 Hast, Marisa 731, 1186
 Hatasova, Beata 409
 Hathaway, Nicholas 1101, 1104
 Hathi, Payal 1279
 Hatz, Christoph 603
 Hauck, Stephanie J. **1373**
 Hausser, Nicole L. 746
 Hauyon-La Torre, Yazmin 1501
 Havlir, Diane V. 370, 502, 181, 542
 Havt, Alexandre 1406, 1407, 1408
 Hawela, Moonga 540
 Hawes, Stephen 423
 Hawkes, Michael 1497
 Hawkins, Kenneth 1256
 Hawley, William A. 1365
 Hay, J. 908
 Hay, Simon I. 104, 1418
 Hayden, Mary 568, **1064**
 Hayden, Tonya 307
 Hayford, Kyla 1492
 Haynes, J. David 215
 Hazel, Elizabeth 622, **624**, 935
 Healy, Sean 571
 Healy, Sara 929
 Heaton, Alexis 1077
 Heavin, Jessica 226
 Heerman, Matt 576
 Heffelfinger, James D. 1404, 237, 440, 940
 Heffernan, Gavin 46
 Hegde, Sonia T. **1481**, **915**
 Heidenreich, Doris 921

The number(s) following author name refers to the abstract number.

- Heimbaugh, Chelsea 103
 Heinrich, Norbert 1371
 Heinze, Dar M. 477, 746
 Heise, Mark 103
 Heisey, Daniel A. R. 118, 1216
 Heitzinger, Kristen **711, 713**
 Helb, Danica **344**
 Helegbe, Gideon K. **656**
 Heller, Tom 1222
 Hemingway, Janet 1107
 Hemme, Ryan R. 1038, 872, 112
 Hemphill, Andrew 23
 Henao-Martínez, Andrés F. **1250**
 Henderson, Elizabeth 558
 Hendricks, Brian 1353, 1354
 Hendrix, Craig W. 974
 Hennessee, Ian P. **208**
 Henning, Tyler C. **398**
 Henttonen, Heikki 50
 Hepburn, Mathew J. 1169, 1185
 Heppner, D. Grey 1443
 Herbet, Gaetan 810
 Heredia, Viviana 1024
 Heringer da Silva, Manoela 109
 Herlihy, Julie M. 1078
 Herman, Jonathan D. **1010**
 Hermance, Meghan E. **746, 877**
 Hermsen, Cornelus C. 220, 450, 454
 Hermsen, Rob 453
 Hernandez, Carlos 123
 Hernandez, Fidel de la Cruz 1065
 Hernandez, Filiberto 1255
 Hernandez, Leda 565
 Herold, Christine 1187
 Herrera, Claudia P. **1246, 1248, 570**
 Herrera, Raul 930
 Herrera, Sócrates 1105, 1156, 1162, 1286, 1300, 216, 6, 795, 931
 Herrera, Victor Mauricio 610
 Herrerros, Esperanza 44
 Herrick, Jessica A. **1411, 254, 254, 1412**
 Hershey, Christine 1311, 500, 859, 1305
 Hertz, Julian T. 249
 Hess, Jessica 1486
 Hester, Jim 1319, 1319
 Hester, James 259
 Hetzel, Manuel W. 1289, 797
 Heu, Chan **745**
 Hewson, R. 908
 Hickey, Bradley 1160, **1161**
 Hickey, Patrick W. 555
 Hien, François de Sales D. 1364
 Hien, Tran Tinh 14, 328
 Higgins, Sarah J. **1015**
 Higgs, Stephen 1210, 1211, 877
 Hii, Jeffrey 828
 Hilaire, Johanne 1037
 Hildenwall, Helena **1194, 801**
- Hildreth, Stephen 599
 Hill, Adrian V. S. 1152, 932, 928
 Hill, Fergal 1152
 Hill, Vincent 883, 956
 Hills, Susan 1203, 1445
 Hillyer, Julián F. 1110
 Hinnebusch, B. Joseph 476
 Hinrichs, David J. 43, 820, 817
 Hirayama, Kenji 656
 Hiscott, Paul S. 1496, 155
 Hiscox, Alexandra 1287
 Hittner, James 361, 657
 Hjelle, Brian 129, 583
 Hlabaw, Ohnmar **1138, 1335**
 Ho Dang Trung, Nghia **1482, 1485**
 Hoang, Ky V. 1171
 Hoang, Thanh Hang 1485
 Hochman, Sarah **1495**
 Hodder, Peter 1021
 Hodges, James S. 1450
 Hodges, Theresa 1345, 472
 Hoerauf, Achim 1187, 965
 Hoffman, Stephen L. 1285, 1438, 220, 228, 229, 979, 1437, 223, 449
 Hoffmaster, Alex 1189
 Hol, Wim G. 1021
 Holding, Penny A. 936
 Holland, Martin 35
 Holland, Nicole 1446
 Hollingdale, Michael 226
 Hollingsworth, Deirdre 1026, 1240, **495**
 Holloman, Marsha 725
 Holloway, Cassandra 276
 Holloway, Kathleen A. 77
 Holmes, Chris 830
 Holmes, Edward C. 1382
 Holowka, Thomas **72**
 Holt, Deborah 493
 Homa, Gadissa 619
 Homaíra, Nusrat 462
 Homan, Tobias 1287
 Honeycutt, Jared 1488, 997
 Hoonchaiyaphum, Thirasak 321, 864
 Hopkins, Adrian 30
 Hopkins, Corey R. 1110
 Hopkins, Mary Ann 78
 Hoppe Cotte, Annett 1070
 Horiuchi, Kalanthe 582, 584
 Horn, David 1498
 Horton, Dan 870
 Horton, Lindsey 1374
 Hoshi, Maria Isabel **356**
 Hoshi, Tomonori **368**
 Hossain, Ilias 1483
 Hossain, M. Jahangir 1073, 1203, **1483, 915**
 Hossain, Md. Amir 1479
 Hossain, Shaikh A. Shahed **1165**
 Hosseini, Parvizez 914
- Hotez, Peter 759, 1447
 Houezo, Jean Gabin 84
 Houpt, Eric 1079, 1406, 1410, 573, 462
 Houston, James 613
 Houzé, Sandrine 1097, 993
 Howard, Hayford 1413, 253
 Howard, Randall F. 1439, 930
 Howell, Katherine 667
 Howie, Stephen 1483
 Hsiang, Michelle S. **1276, 538, 836, 1286**
 Hsieh, Michael **1001, 1488, 997**
 Hsieh, Yi-Ju 1001
 Hu, Branda **599**
 Hu, Min **492**
 Hu, Wei 896
 Hu, Xiaobang 471
 Hu, Xiao 800
 Hu, Yan **278**
 Huang, Chiung Yu 451
 Huang, Fusheng 389
 Huang, Fang **825**
 Huang, Huiqi 8
 Huang, Jun 1437, 226
 Huang, Laurence 468
 Huang, Ning 689A
 Huang, Wenlin 23
 Huang, Yan-Jang S. **1210, 1211**
 Huang, Zhuojie 842
 Huayanay-Repetto, Anibal 1135
 Huber, Curtis 1264, 1264, 317
 Hubert, Veronique 1097
 Hübner, Marc P. **965**
 Hue Tai, Luong Thi 14
 Hueb, Marcia **1199**
 Huebner, Marc P. 257
 Huerta, Daniel 278
 Huezo, Stephanie 817, **1271**
 Hufert, Frank T. 921
 Hughes, Grant L. 1214
 Hughes, Molly 1066, 1368
 Hugo, Pierre 652
 Hummer, Kelly 727
 Humphreys, Georgina S. 214
 Hun, Laya 1168, 721, 747
 Hung, Christopher 1123, 1125, 1128, 1440, 223, 454, 664
 Hunja, Carol W. **338**
 Hunsawong, Taweewun **614**
 Hunsperger, Elizabeth 112, 114, 558, 584, 608, 989, 133, 872
 Hunte, Tai 883
 Hunter, Christopher A. 953
 Huq, Anwar 956
 Hurliman, Michele 1053, 515
 Hurwitz, Ivy **1017, 576**
 Husain, Md. Ashaque 1165
 Hussem, Kittinun 443
 Huy, Nguyen T. 656
 Huynh, Jeremy P. 1399
 Huysel, Tine 560
 Huzard, Damien 1285
- Hwang, Jimee 1276, 1277, 1311
 Hynes, Noreen 512
-
- Iamsirithaworn, Sopon 117
 Ianuzzi, Michael 417
 Iashvili, N **418**
 Ibarra, Kristie **13**
 Ibekwe, Nneka 803
 Ibrahim, Sulaiman S. 1459
 Iddi Simba Khamis, Ali 1453
 Idoko, Olubukola T. O. **916**
 Idro, Richard 1450, 165, 632
 Igbeneghu, Oluwatoyin A. 699
 Iglesias, David 1227
 Ignotti, E 274
 Ikilezi, Gloria 181
 Ikumapayi, Usman N. 1483
 Ilboudo, Hamidou 783
 Ilias, Muhammad 293
 Imbert, Sebastien 993
 Imnadze, Paata 1169, 1185
 Imoukhuede, Babatunde E. 138
 Imwong, Mallika 328, 506
 Infectious Diseases Pathology Branch 133
 Inoue, Noboru 950
 inSCALE Study Group 939
 Invest, John F. 522
 Ippolito, Giuseppe 615
 Irani, Ayesha 27
 Ireri, Edmund 998
 Irungu, Lucy 880
 Irura, Zephania 592, 917
 Irving, Helen 1459, 691
 Isaac-Marquez, A P. 244
 Isayeva, S B. 908
 Ishag, Elhassan M. Elhassan. Ishag. **630**
 Ishengoma, Deus S. 1427, **170, 850**
 Ishino, Tomoko **1007, 1314, 1316**
 Islam, Ausriful 52
 Islam, Khaleda **141, 237**
 Islam, Md. Atiquel 52
 Islam, Md. S. **940**
 Ismail, Hanafy M. 1459
 Ismail, Miriam D. 1292
 Ismayilov, Afrail 742
 Ismayilova, Rita 742
 Isoe, Jun 475, 686
 Isozumi, Rie 543
 Issaly, Jean 384, 873
 Issiaka, Djibrilla 457, 853
 Italiano, Claire M. 28
 Ito, Daisuke **1315, 222, 352**
 Ito, Koichi 449
 Ittiprasert, Wannaporn 902
 Ivanov, Mykola 1394
 Ivanovich, Elizabeth **1333**
 Ivers, Louise C. 525, 68, 1037

The number(s) following author name refers to the abstract number.

Izurieta, Ricardo 1182

J
 Jabbarzadeh, Shirin 399
 Jackson, Ashley 719
 Jackson, Katherine 1403
 Jacob, Christopher G. 1266, 1296, 321, 506, 825, 864, 328
 Jacob, Melissa 293
 Jacobs-Lorena, Marcelo 924, 977
 Jacobson, Julie 140
 Jacobson, Karen R. 463
 Jacobus, David 46
 Jacobus, Laura 46
 Jacquierioz, Frederique 1309
 Jadeja, Neville 751
 Jagannathan, Prasanna 189, 193, 37
 Jahan, Assis 413
 Jahan, Nusrat 110
 Jaichapor, Boonsong 391
 Jain, Aarti 223, 454, 670, 1123, 1125, 1128
 Jain, Surendra K. 293
 Jain, Vidhan 357
 Jalloh, Binta 1304
 Jambai, Amara 957
 James, Eric R. 1285, 220, 228, 1437, 223
 Jameson, Samuel B. 1248, 570
 Jamongneau, Vincent 783
 Jampaulo, Vander O. 217
 Jamsen, Kris M. 822
 Janacki, Lalitha 1079
 Janes, Michael 1499
 Janko, Mark 858
 Jansa, Josep 1215
 Jansen, Ana M. 71
 Janssen, Saskia 1367, 251, 494, 67
 Jara, Marlene 1250A
 Jara Portocarreo, Marlene 1249
 Jarilla, Blanca 1000, 1003
 Jarman, Richard G. 117, 126, 392, 395
 Jarquin, Claudia M. 446
 Jarra, William 450
 Jasinskas, Al 664
 Jasmin, Jasmin 1103
 Jasseh, Momodou 1483
 Jauréguiberry, Stéphane 1012, 993
 Javati, Sarah 1257
 Jaykus, Lee-Ann 679
 Jean, Samuel E. 317, 847, 213
 Jean François, Trape 378
 Jelip, Jenarun 334
 Jeng, Baba 1483
 Jenkins, Adam M. 1116, 1348
 Jenkins, Bethany J. 1322
 Jenkins, Marion W. 1032

Jenks, Mary Harley 1232
 Jenne, Dieter 272
 Jensen, Silke 469
 Jentes, Emily S. 1445, 724, 728, 112
 Jeong, Wooseog 888
 Jeppsen, Samantha 706
 Jeronimo, S M. B. 82
 Jezorski, John 591
 Jhonston, Erik J. 618
 Jiang, Hongmei 1361
 Jiang, Jinjin 1361, 874, 980
 Jiang, Jinmai 300
 Jiang, Linda 468
 Jiang, Nona M. 462
 Jima, Daddi 1311, 332
 Jimenez, Sylvia 777
 Jiménez, Xyomara 608
 Jin, Xiannu 180, 182
 Jirage, Dayadevi 359
 Jiz, Mario A. L. 425, 564, 1436
 Jochim, Ryan C. 749
 Joglar, Francisco 989
 Johansson, Emily W. 801
 Johansson, Michael A. 104, 625
 Johari, Jefree 1056, 28
 John, Bernard 1098
 John, Beena 953
 John, Chandy C. 1450, 1497, 165, 632, 855
 John Moss, William 1258
 John-Stewart, Grace 1025
 Johnson, Amy 1023
 Johnson, Barbara W. 1203
 Johnson, Christian 85
 Johnson, Jacob D. 970
 Johnson, Lucas B. 978
 Johnson, Monika 1377
 Johnson, Mark D. 113, 733
 Johnson, Tammi L. 476
 Johnson, W. D. 82
 Johnston, Kelly L. 266
 Joice, Regina 1292
 Jois, Malasa 734
 Jolly, Grant 1149, 1149, 1436, 227, 452
 Jolly, Pauline 151
 Jones, Christopher M. 1463
 Jones, David G. 626, 1155
 Jones, Franca 713
 Jones, Jason E. 1254
 Jones, Malcolm K. 951, 949
 Jones, Rebecca 975
 Jones-Engel, Lisa 642
 Jones-López, Edward 464
 Jongsakul, Krisada 243
 Joof, Fatou 1270, 1270, 2
 Jordan, Heather R. W. 86
 Jordan, Jorge-Munoz 112
 Jorge, Carlolina L. 791
 Jori, Giulio 386
 Joseph, Gerard A. 1186, 738, 731
 Joshi, Swati 168

Jost, Philipp 1100
 Journal, Ito 317
 Ju, Chuan 896
 Juarez, Diana 467
 Juin, Stanley 112, 700, 731
 Jukes, Matthew C. H. 975
 Juliano, Jonathan J. 1101, 1104, 1321, 468, 743, 824, 855
 Juliao, Patricia 277
 Juliette, Ongus 1369
 Juma, Elizabeth 970
 Jumnainsong, Amonrat 1400
 Jung, Donald 645
 Jung, Hyun-Chae 889
 Junghanss, Thomas 536
 Junior, Francisco S. 1407, 1408
 Jupatanakul, Natapong 688, 981
 Justino de Almeida, Mariana 1273

K

Kaale, Eliangiringa 770
 Kaba, Stephen A. 1439
 Kabamba, Joelle 51, 740
 Kabbale, Fredrick G. 388
 Kabir, Furqan 1079
 Kabir, Mamun 1079
 Kabogo, Moses 1235
 Kabole, Ibrahim 1233, 31
 Kabona, George 1231, 1233, 31
 Kabore, Achille 1477
 Kaboré, Jacques 783
 Kabyemela, Edward 190, 633
 Kachur, Stephen P. 1139, 1140, 1276
 Kaddu, John B. 388
 Kaddumukasa, Martha A. K. 1109
 Kadvivane, Samwel 592
 Kadri, Boubacar 1235, 285
 Kaewkungwal, Jaranit 806
 Kafuko, Jessica 210, 550, 1133
 Kaharuza, Frank 1121, 1121, 344
 Kahathuduwa, Ganga 1473
 Kahle, Kristen M. 598, 602, 594
 Kahler, Amy 956
 Kahn, Maria 1275
 Kain, Kevin C. 1011, 1015, 1492, 1497, 351, 990, 164
 Kaindoa, Emanuel W. 838
 Kaiser, Maria 490
 Kaitaba, Oscar 1456
 Kajungu, Dan K. 49
 Kakande, Medi 1284
 Kakani, Evodxia 946
 Kakeeto, Stella 173
 Kakuru, Abel 181, 504
 Kakuru, Mary M. 344, 37
 Kakuru Muhindo, Mary 1121, 1121
 Kalam, Adil 1079

Kalavska, Andrea 176, 348
 Kalayjian, Benjamin 1426
 Kalemwa Mitembo, Didier 652
 Kalilani-Phiri, Linda 240, 865, 505
 Kalkoa, Morris 543
 Källander, Karin 1190, 939
 Kalnoky, Michael 1275, 263
 Kalyansundaram, Ramaswamy 962
 Kamala, Benjamin 1331
 Kamali, Maryam 1115
 Kamau, Edwin 316, 849
 Kamgno, Joseph 1411, 1412, 1417, 15, 264
 Kamhawi, Shaden 727
 Kamiza, Steve 160, 865
 Kamm, Kelly 937
 Kampmann, Beate 1483, 916
 Kampondeni, Sam D. 245, 800
 Kamugisha, Mathias 1231, 1233, 31, 1427
 Kamuliwo, Mulakwa 1280, 1339, 324, 540
 Kamwendo, Deborah 310
 Kanya, Moses 173, 177, 189, 193, 195, 204, 37, 370, 860, 1293, 181, 502, 504, 542, 557
 R. Kan, Boris 577
 Kanakabandi, Kishore 967
 Kaneko, Akira 338, 543
 Kang, Angray 1017
 Kang, Gagandeep 1406, 1409
 Kang, Seokyung 688
 Kangan, Lafortune 539
 Kano, Shigeyuki 793
 Kanoute, Moussa 186
 Kanza, Eric 1413, 253
 Kanzok, Stefan M. 924
 Kapella, B. K. 204
 Kapi, James 370, 502, 542
 Kapito-Tembo, Atupele P. 1292, 1428, 240
 Kapulu, Melissa C. 928
 Karabou, Potchoziou 288, 289
 Karanja, Diana M. S. 562, 895
 Karchmer, Adolf W. 724
 Karell, Mara A. 317
 Karema, Corine 49
 Karesh, William B. 914
 Kargbo, David 957
 Karhemere, Stomy 51, 740
 Karim, Md. R. 1479
 Karim, Zachary 361, 657
 Karin Källander, Karin 136
 Karine, Mouline 687
 Kariuki, Simon K. 1431, 520
 Karkalik, Andrej 769
 Karkey, Abhilasha 1449
 Karl, Stephan 951
 Kartchner, Laurel 1101
 Karthiga, K. S. 1094
 Karunaratne, Kumudu 115

The number(s) following author name refers to the abstract number.

- Karunaweera, Nadira D. 1473, 7
 Kas, Arnold 184
 Kasinathan, Ravi S. **428**, 953
 Kasper, Matthew R. 1375, 1384,
 445, **467**, 1179, 703
 Kassa, Moges 332
 Kassahun, Aysheshm 749
 Kassim, Sanogo 1274
 Kasteng, Frida 939
 Kasthuri, Raj S. 1016
 Kastner, Randee 1047, **1050**
 Kasubi, Mabula 481
 Katalenich, Bonnie L. 324
 Kataliko, Kambale 1413
 Katamba, Achilles 173
 Katebe-Sakala, Cecilia 385
 Kathleen, Glaser 893
 Kato, Aki 1314
 Kato, Cecilia 558
 Katsube, Riko 1314
 Katz, Lee 956
 Katz, Mark A. 1186, 700, 738,
 112, 731
 Kaufman, Michelle 1331
 Kaufmann, Sarah E. 628
 Kaufusi, Pakieli H. 1218
 Kaupa, Brown **797**
 Kawazu, Shin-ichiro 950
 Kawsar, Abdullah Al 141
 Kayentao, Kassoum 1125, 1126,
 451, 974
 Kayondo, Jonathan K. 1109
 Kazura, James W. 1122, 1455,
 259, 53, 664
 Kean, Casey 385
 Keane-Myers, A 722
 Keating, Joseph 1253, 1295,
 1308, 1425, 1426
 Kebede, Amha 1311, 332
 Kebede, Zelalem 1311, 332
 Kebela Ilunga, Benoit 51, 1380
 Keenan, John 151
 Keenan, Jeremy D. 285
 Keesen, T. S. L. 82
 Keita, Abdoul S. 153
 Keita, Moussa 1348
 Keita, Modibo **765**
 Keita, Somita 765
 Keita, Sory 99
 Keita, Yamoussa 1443
 Kekre, Mihir 1005
 Kellam, Lynda 42A
 Keller, Tracey 1010
 Kelley, James F. 1218
 Kelley, Laura 1141
 Kelly, Jane X. 1271, 43, **817**, 820
 Kelly, Lauren F. **464**
 Kelly, Rosmarie 399
 Kelly-Hope, Louise A. **1042**,
1045, 1234, 282, 262, 400
 Kemere, Jordan 1306
 Kemigisha, Elisabeth 736
 Kemme, Katherine A. 1320
 Kempaiah, Prakash 657
 Kempaiah, Prakasha **361**, 658
 Kemprai, Prakasha 1127
 Kenah, Eben 915
 Kenangalem, Enny 461
 Kendall, Emily A. **463**
 Kendjo, Eric 1012, 993
 Kengne-Ouafo, Jonas A. 15
 Kennedy, Luma 517
 Kenneth, John **405**
 Kenney, Joan L. **1209**, 1466
 Kerber, Sarah 1173
 Kerich, Gladys C. **776**
 Kersh, Gilbert 718
 Kertho, Edmund 1190, 939
 Keselman, Aleksander **882**
 Keswani, Tarun **188**
 Ketch, Guillaume 1346
 Keyloun, Katelyn R. 23, 27
 Khagayi, Sammy 851
 Khairallah, Carole 505
 Khalil, Eltahir 784
 Khalil, Insaf F. 830
 Khan, Adnan **1504**
 Khan, Ashraf Islam 701, 958
 Khan, Ashraf I. 955
 Khan, Iqbal Ansary 701, 958
 Khan, Salah Uddin 1073, **52**
 Khanam, Farhana 955
 Kharabora, Oksana 1104, 1321
 Khasewa, Joab **767**
 Khatun, Selina 141
 Khim, Nimol 1286
 Khmaladze, Ekaterine 744
 Khongtak, Patcharee 391
 Khoshi, Sareh 1337
 Khunwittya, Sarun **163**
 Khvedeliani, M 418
 Kiang, Richard 465
 Kibiki, Gibson 1429
 Kibirige, Davis **403**
 Kibuka, Afizi **557**
 Kibuka, Grace **146**
 Kibuuka, Afizi 177
 Kiechel, Jean-René **813**
 Kiggundu, Moses 204, **312**
 Kigozi, Ruth 173, 204, 860
 Kigozi, Simon P. **346**, **347**
 Kiguli, Sarah 456
 Kihombo, Aggrey 1337
 Kikuchi, Mihoko 656
 Kilembe, Bernard 1233, 1415
 Kilian, Albert 1325, **1326**
 Killeen, Gerry F. 1134
 Killingbeck, Sarah 122, 13
 Killoran, Kristin E. 1432
 Kilpatrick, A. Mark **870**
 Kim, Hani **1011**
 Kim, Kami 1495, 43
 Kim, Min Jae 889
 Kim, Soyeon 464
 Kim, Woo Ho 889
 Kim, Young Eun **1457**, 286
 Kimura, Masatsugu 543
 Kinabo, Grace D. 556
 Kinara, Stephen 370, 542, **502**
 King, Aaron A. 983
 King, Charles H. 103, 447, 487,
 53, **559**, 934
 King, Christopher L. 1122, 259,
 487, 669, 936, 1291, 934, 1195
 King, Jonathan D. **1472**
 King, Jonas G. **1100**, 1258
 King, Mallory 493
 King, Russell 1355
 Kinghorn, A. D. 244
 Kipp, Aaron M. 1220
 Kiptui, Rebecca 551
 Kiragu, Esther 631
 Kirinoki, Masashi 950
 Kirkpatrick, Beth D. 512, 606
 Kirkwood, Betty 939
 Kirumbi, Edward 1233, 31
 Kisoka, William J. 1415
 Kistnasamy, Malcolm B. 626
 Kitamura, Shinya 793
 Kitashoji, Emi **729**
 Kitron, Uriel 103, 399, 447, 518,
 983
 Kittayapong, Pattamaporn **1340**,
 988
 Kiwou, Moses 176
 Kizito, Fred F. K. **204**
 Kizza, Harriet M. 195
 Klampikaho, Alex 146
 Klarmann, Ute 1187
 Klassen, Jonathan 261
 Klei, Thomas R. 1486
 Klein, Wagner 1197
 Kleinschmidt, Immo 1345
 Kleschenko, Yuliya **1154**
 Kleschenko, Yulia 1159
 Kliks, Srisakul 1400
 Klimstra, William B. 56
 Klion, Amy D. 1411, 1412, 967,
 99, 254, 254
 Klis, Sandor-Adrian **88**
 Klobasa, Will 572
 Klonis, Nectarios 1263, 1263
 Kloos, Helmut K. 488, 283, 429
 Kloos, Zachary 1455
 Klungthong, Chonticha 126,
 441, 443
 Knap, Martijn 251
 Kniezova, Zuzana 348
 Knight, Matty 902
 Knights, Sheena 248
 Knobler, Stacey L. 413
 Knust, Barbara 1379, 1380, **910**
 Ko, Albert I. 1484, 524
 Koš álová, Tatiana 749
 Kobinger, Gary 1380
 Kobylinski, Kevin C. 1351
 Kochel, Tadeusz J. 581, 983,
 1059, 113
 Kodio, Mamoudou 765
 Koenker, Hannah 1325, 1331,
 207, **846**
 Koirala, Samir 1449
 Koita, Fanta 186
 Koita, Ousmane A. 1270, 1270,
 1308, 2, **818**
 Koizumi, Nobuo 729
 Kojiro, Maiko 729
 Kojom Foko, Loick P. 539
 Koka, Eric 1085
 Koka, Hellen 592, 920
 Kokaia, Nora **297**
 Koku, Roberta 142, 70, **886**
 Kolá ová, Iva 749
 Koller, Daphne 1403
 Kombila, Davy U. 1367
 Konaté, Drissa 153
 Konate, Lassana 1113, **501**
 Kone, Abdoulaye K. 484
 Kone, Aminatou **1096**
 Kone, Younoussou 1125, 1126,
 451
 Kong, Deok-Hoon 352
 Konongoi, Samson 592
 Kopin, Alan S. 1116, 1360
 Koporc, Kimberly M. **276**
 Koram, Kwadwo 292, 507
 Korde, Sonali 1279, 541
 Korgo, Pascal 623
 Kosek, Margaret 1406, 1410,
 709, 710
 Koskei, Edith 592, 920
 Kosoko, Ayokulehin M. 1303
 Kotloff, Karen 1405
 Kouam Kenmogne, Marc 264
 Koumare, Sekou 1274, 823
 Kouodjip Nono, Larissa 539
 Kouriba, Bourema 1443, 484
 Kovacic, Vanja **943**
 Kovalenko, V. L. **1395**
 Kowal, Ashley 385
 Kozakai, Yukiko 225, 5
 Kpeli, Grace S. 87
 Krajacich, Benjamin J. **1351**, 941,
 978
 Kramer, Laura D. 11, 12, 1212,
 1214, 1465, 870
 Krasuck, Peter 46
 Krause, Lutz 1489
 Krause, Peter J. 24, 478
 Krcmery, Gertruda 349
 Krcmery, Vladimir 1219, **176**,
 348, 349, 409, 764, 769
 Kremser, Peter G. 1367
 Kreppel, Katharina 61
 Kridaningsih, Tri Nury 879
 Krishnananthasivam, Shivankari
 607
 Krismawati, Hana **879**
 Kristensen, Peter 302
 Krkoska, Dušan 176
 Krogstad, Donald J. 1270, 1270,
 1308, 1348, 2, 818, 354

The number(s) following author name refers to the abstract number.

- Krolewiecki, Alejandro J. 1024
 Kronmann, Karl C. 1388
 Krotneva, Stanimira P. 1238
 Krudsood, Srivicha 1184, 313, 314, **315**
 Kruhlak, Michael 1244
 Krzych, Urszula 1147, 1147, 666
 Kuan, Guillermina 985
 Kublin, James G. 1267
 Kubofcik, Joseph 17
 Kucheriavenko, O. 723
 Kuchuloria, Tinatin 1169, 1185
 Kudlova, Zuzana 769
 Kuesel, Annette C. 1413, 253
 Kuhn, Richard 1398
 Kuklinski, Wojtek S. 1351
 Kukutla, Phanidhar 1361, 874, 980
 Kulkarni, Manisha 1070
 Kulkarni, Roshan 168
 Kulkova, Nada 1219, 348, 409, **764, 769**
 Kumar, Dinesh **291, 782**
 Kumar, Jessica A. **1195**
 Kumar, Krishan **215, 930**
 Kumar, Nirbhay 486
 Kumar, Rajesh 702
 Kumar, Rajiv **73**
 Kumar, Sanjai 218, 225, 24, 5, 663, 991
 Kumar, Swapna 937
 Kumar, Tripurari **702**
 Kumar, Udayan 842
 Kumaran, Paul 966
 Kumarendran, Balachandran 1029
 Kundu, Roopal 1041
 Kunene, Simon 538, 836
 Kuntawunginn, Worachet **243, 806**
 Kuo, Chi-Chien 479
 Kupelnick, Bruce 1093
 Kuri-Morales, Pablo 1062
 Kurolt, Ivan 603
 Kurtis, Jonathan D. 1000, 1002, 1003, **1149, 1149, 1436, 227, 452, 668, 923, 425**
 Kurtti, Timothy J. 745
 Kurumop, Serah F. 797
 Kusuma, Andreas **157**
 Kutima, Lydia H. K. **371**
 Kwakye-Maclean, Cynthia 87
 Kwapor, Mawolo 1413
 Kwasny, Mary 1041
 Kwiatkowski, Dominic P. 333, 1005, 328, 506
 Kwofie, Kofi D. 142, **292, 70**
 Kyaw, Myat P. 1266, 1138
 Kyaw, Thar Tun 1138, 1335
 Kyelem, Dominique 1232
 Kyle, Dennis E. 1273, 46
 Kyow, Myat P. 328
 Kyriakidou, Georgia **621**
- L**
- LaBarre, Paul 1256
 LaBeaud, A. Desiree 103, **447, 53, 934**
 LaBeaud, Angelle D. 487
 LaBrecque, Brendan 1351
 Lacerda, Marcus **42A**
 Lacuesta, Talitha L. 729
 Lafuente Monasterio, Maria Jose 925
 Laguna-Torres, V. Alberto 410
 Laha, Thewarach 416, 419, 420A
 Lai, Chih-Yun 1400
 Lainhart, William **1359**
 Laksananan, Teerasak 1340
 Lakwo, Thomson 1044
 Lal, Sham 1146, 1259, 1260
 Lalani, Tahaniyat 113, **733**
 Lalita, Paul 114
 Lalji, Shabbir 1133, 550
 Lalloo, David 1332
 Lam, Eugene 957
 Lam, Felix 1142
 Lama, Javier 1174
 Lamb, Tracey J. 191
 Lambert, Lynn 1155, 930
 Lambrechts, Louis 117, 392
 Lameyre, Valerie 177
 Lamikanra, Adebayo 699
 Lammie, Patrick 34, 481, 1232, 35, 895
 Lampaert, Emmanuel 1380
 Lampah, Daniel A. 461
 Lamptey, Isaac 87
 Lanar, David 1443, **1439, 5**
 Lanata, Claudio F. 1409, 911, 1377
 Lance Liotta, Lance 1423
 Landela, Ange L. **887**
 Landman, Keren Z. **213**
 Lang, Jean **590**
 Langa, Antonio 281
 Langat, David 592
 Langer, Christine 1442, 40, 662, 667
 Langevin, Stanley A. 1466
 Langham, Freya 1291
 Langhorne, Jean 450
 Langidrik, Justina 114
 Lanke, Kjerstin 503
 Lanteri, Charlotte 1104, 1321, 506, 806, 864, 243, 1324
 Lantican, Cecile Lantican 1083
 Lanzaro, Gregory 1117, 61
 Larbelee, Jammeh 253
 Larbi, John 771
 Largo, Francisco M. 1061, 580, 79
 Larke, Natasha 66
 LaRocque, Regina C. **1445, 959**
 Larrauri, Paola **1323, 39**
 Larsen, Christian P. **1266**
- Larsen, David 540
 Larsen, David A. **1425, 1426**
 Larson, Erik 116
 Larson, Heidi J. 138
 Larson, Peter S. **1336**
 Larsson, Catherine J. 512
 Lartey, Margaret 70
 LaRue, Nicole **1275, 17**
 Lascher, Jonathan 525
 Laserson, Kayla 1405, 851
 Lashvili, N. 297
 Lasry, Estrella 910
 Laswai, Augustine 35
 Lattanzi, Daniel R. 250
 Lau, Colleen L. **1040**
 Lau, Rachel 799
 Lauer, Peter 1438
 Laufer, Miriam K. 1267, 1292, 1296, 1428, 240, 865
 Laurens, Matthew B. 1443
 Lavoignat, Adeline 810
 Law, Charity W. 1198
 Law, Melissa 254, 254
 Lawrie, Alison M. 932
 Laws, Thomas R. 1169
 Lawyer, Phillip G. 101
 Lazarski, Christopher 1148, 1148
 Lazarus, Wilfred 1415
 Lazzarini, Thomas 627
 Le, Tan 1485
 Le Blond, Jennifer 280
 Le Cacheux, Catalina 128
 Le Menach, Arnaud 862
 Leader, Brandon T. 1275
 Leal, Grace 1389
 Lebo, Emmaculate 989
 LeClair, Norbert 504, **821**
 Ledogar, Robert 123
 Lee, Andrew H. 1265
 Lee, Bi-Yao 275
 Lee, Christopher C. K. 66
 Lee, Jung Seok 1067, **1072**
 Lee, Ji-Yeun 1403
 Lee, Kang Sung 1067, 1072, 588, 595
 Lee, Kim-Sung 111
 Lee, Linda K. 124, 553
 Lee, Ming-Chieh 530
 Lee, Ming-Min 261
 Lee, Moses 449
 Lee, Pei-Fen 479
 Lee, Seong-Kyun 350
 Lee, Sueng 975
 Lee, Sunhee 1495
 Lee, Susan Shin-Jung 275
 Lee, Tau-Hong 553
 Lee, Yoosook 1117, 61
 Lees, Rosemary S. 1364
 Lefevre, Thierry 867
 Legac, Jenny 811
 Legesse, Hailemariam 935
 Legorreta-Soberanis, José 123
 Legrand, Fanny 1411, **1412**
- Lehane, Michael J. 943
 Lehiy, Christopher 92
 Lehman, Leopold G. **539**
 Leisnham, Paul T. **1350**
 Leite, Álvaro M. 1407, 1408
 Leitsch, David 22
 Leiva, Karina P. 1120, 1120, 342
 Lek, Dysoley **827**
 Leke, Rose G. F. 192, 41
 Lekpor, Cecilia 308
 Lell, Bertrand 1367
 Leming, Matthew **471, 697**
 Lemma, Sisay D. **374**
 Lemmens, Edward E. 1438
 Lemnge, Martha 170, 850, **1427, 830**
 Lemoine, Jean Frantz 213, 847
 Lemos, Manuel 430
 Lengeler, Christian 652
 Lenhart, Audrey 1461, 983
 Leo, Yee-Sin 111, 1223, 124, 552, 553, 585, **586, 587**
 Leo, Yee S. 8
 Leon, Juan S. 679
 Leonardo, Lydia 565, 950
 Leong, Meredith L. 1438
 Lepow, Martha 411
 Leroy, Didier 816
 Lesage, Pierre-Loup 1142
 Lescano, A. Roxana 618, 342
 Lescano, Andres G. 1120, 1120, 1123, 1135, 1192, 1309, 342, 358, 509, 618, 726, 711, 1128
 Leshem, Eyal 1186, 700
 Lester, Rebecca 556
 Leung, Daniel T. **1188, 955**
 Levine, Gillian A. 140
 Levine, Myron M. 1405
 Levy, Karen 1031, 712, 960
 Levy, Michael Z. 1420, 304, 773, 781
 Lewandowski, John R. **1254**
 Lewandowski, Mark R. 1254
 Lewis, Michael D. 71
 Lewis, Rosamund F. 1470
 Leyden, Jacinta 1376
 Lezama, Percy 445
 Lezama-Davila, Claudio M. **244**
 Li, Benwen **258**
 Li, Chenxi 245
 Li, Fengwu 808
 Li, Jian 352, 38
 Li, Julin 366
 Li, Jun **698, 1119**
 Li, Liang 648
 Li, Ling J. 8
 Li, M. 223
 Li, Minglin 229, 1438
 Li, Qigui 180, 817
 Li, Robert S. 1239
 Li, Shanping 1125, 451
 Li, Shengming 1239
 Li, Tao 229, 979

The number(s) following author name refers to the abstract number.

- Li, Xing 293
 Li, Yu 51
 Li, Yuanyuan 1152
 Li, Yuesheng 1239
 Li, Yueshang 564
 Li, Yuexin 817, 820, 1271, 43
 Li Wai Suen, Connie 1198
 Liang, Li 1123, 1125, 1128, 1440, 344, **454**
 Liang, X. **223**
 Lickness, Jacquelyn 679
 Lieberman, Marya **526**, 620
 Liebman, Kelly A. **1461**
 Lietman, Thomas M. 285
 Liles, W. Conrad 990
 Liles, W. C. 1011, 1015
 Lim, Boon Huat 234
 Lim, Chae-Seung 350
 Lim, Jacqueline K. 1067, 1072, **588**, **595**
 Lim, Yvonne A. L. 755
 Lima, Aldo A. M. **1407**, **1408**
 Lima, Danielle M. **1052**, **611**
 Lima, Ila F. N. 1407, 1408
 Lima, Luciana 217
 Lima, Monique 109
 Lima, Noélia L. 1407, 1408
 Limbach, Keith 1148, 1148
 Limkittikul, Kriengsak 1067, 1072, 588, 595
 Lin, Feng-Chang 743
 Lin, Hong-En 1400
 Lin, Jessica T. **1101**, **1104**, 1321
 Lin, Tian 164
 Lin, William 276
 Lindblade, Kim A. 1288, 150, 277, **455**, 466, 852, 211, 212, 1132, 1136
 Lindh, Jenny M. 374
 Lindow, Janet C. 606
 Lindquist, Susan 1010
 Lindsay, Robbin 106
 Lindsay, Steven W. 374
 Lindseth, Maria A. 642
 Lingam, Raghu 939
 Linn, Anne 208
 Linthicum, Kenneth J. 866
 Liping, Yuan 1239
 Liskova, Anna 764
 Liss, Nathan M. 905
 Lissandrin, Raffaella 231, 535
 Litilit, Dianne 218
 Little, Francesca 1144
 Little, Stephen F. 1169
 Littrell, Megan 1, **1143**, 1301, 178, 179, 540, 545, 546
 Liu, Hui 825
 Liu, Jenny 1086, 1307, **1327**
 Liu, Jie 1410, 1079
 Liu, Mingli 151, 171
 Liu, Xia 218
 Liu, Yaobao 1276, 1278
 Liu, Yi 1403
 Liu, Yaobao 366
 Liu, Yingying 492
 Liu, Yuzhong 903, 904
 Lixian, Wu 706
 Lizarazo, Erley F. 130, 131
 Ljolje, Dragan 317
 Llamosas Chu, Monica 781
 Llanos-Cuentas, Alejandro 1250A
 Llewellyn, David 932
 Llewellyn, Martin S. 71
 Llewellyn, Stacey 754, 493
 Llinas, Manuel 1125
 Lloyd, Alun L. 983
 Lloyd, Spencer 706
 Lo, Eugenia **336**
 Lo, Youssoufa 499
 Lobato, Lucas H. 732
 Lobigs, Mario 1210
 Lobo, Neil F. 1283, 523, 1365
 Lodh, Nilanjan **952**
 Logedi, John 549, 551
 Logue, Kyle **574**
 Lok, James B. 491, 492
 Loke, P'ng **1030**, **1434**
 Lokko, Kojo 207
 Loll, Dana 1331
 Lon, Chanthap 1104, 1321, 1324, 328, 506, 806, 864
 Long, Carole A. 1152, 1157, 1315, 153, 222, 224, 42, 451, 665, 855
 Long, Kristin 103
 Long, Kanya 517
 Long, Kanya C. 983
 Long, Romnie 516
 Loo, Jennifer 1374
 Looareesuwan, Panu 315
 Looke, David 219
 Lopansri, Bert K. 1098, 1098
 Lopera-Mesa, Tatiana M. 153, 1012, 665
 Lopes, Danilo 429
 Lopez, Ana M. 1157
 López, Beatriz 277, 446, 554, 1481
 Lopez, Gerard 1028, 277
 Lopez, Maria Rene 466
 Lopez, Martha 269, 414
 Lopez, N. Judith 608
 Lopez, Silvana 1024
 Lopez-Lazaro, Luis 645
 Lopez-Perez, Mary **1105**, 1156, 1162
 Lopez-Sifuentes, Victor 1135
 Lopez-Urbina, Maria T. 98
 Lopez-Urbina, Teresa 232
 López-Vergès, Sandra 127
 Lopman, Benjamin A. 703, 912
 Lord, Cynthia C. 878
 Lorenzana, Ivette J. 600
 Lorenzi, Olga 558, 608
 Lorono-Pino, Maria 9, 1462
 Lortholary, Olivier 64
 Lotspeich-Cole, Leda 991
 Lottfy, Nadia M. 579
 Louis, Valérie R. 1340, 988
 Loukas, Alex 1490, 420A
 Lourenco, Christopher 842
 Louya, Frédéric 1043, 1046, 757
 Lovchik, Janece 512
 LoVerde, Philip T. **954**, 488
 Lowenberger, Carl 1363
 Lozano-Fuentes, Saul 1347, 1462, 568
 Lu, Ailin 1149, 1149, 227, 452
 Lu, Feng 350, 352
 Lu, Ziyue 1011
 Lubemba, William 1339
 Luby, Stephen P. 1073, 1203, 1404, 237, 440, 442, 462, 52, 915, 937, 940, 958
 Lucantoni, Leonardo 1330, **372**, 386
 Lucas, Agape 573
 Lucas, Carmen M. 1192, 342, 509, 307
 Lucas, John R. **522**
 Lucchi, Naomi W. **317**
 Lucien, Mentor B. Ali. 700
 Luckason, Gary 1053
 Luckhart, Shirley 397
 Lucyk-Maurer, Rafael 951
 Ludovisi, Serena 535
 Luft, Chris 942
 Lugli, Enrico 255
 Lugo, Ligia 1358, 1366
 Luhanga, Meshack 1136
 Luhanga, Misheck 211, 212, 500, 859
 Lukanu Ngwala, Philippe 652
 Luke, Catherine J. 512
 Luke, Nyakarahuka 910
 Luke, Thomas 1161
 Lukens, Amanda K. 354, 544, 925, 320, 327
 Lukwago, Robinson 177
 Lulembo, Oliver 385
 Lum, J. Koji 1265
 Lumsden, Joanne 1161
 Luna, C. Giannina 1387, 431, 1381, 703
 Lund, Andrea **399**
 Lunde, Torleif Markussen **1294**
 Luo, Ping 599
 Luong, Bao Ngoc 1067, 1072
 Lupiañez-Merly, Camille 989
 Lupidi, Giulio 386, 1330
 Lust, Lydia 1187
 Lustigman, Sara 1102, 1486
 Luswata, Charles 929
 Lutomiah, Joel 920
 Lutwama, Julius J. 1109, **906**, 1379
 Lwande, Olivia 917, 920
 Lwetoijera, Dickson W. **881**
 Ly, Po 202
 Lyamuya, Eligius 65, 770
 Lye, David C. 111, 1223, 124, 552, 553, 585, 586, 587, 8
 Lyke, Kirsten E. 1443, 484
 Lynch, Matthew 207

M

- Ma, Jennie Z. 462
 Mabey, David C. W. 285, 961, 1230, 35
 MacArthur, Chad 1235
 MacCormick, Ian J. C. **1494**, 1496, 155, 638
 MacDonald, Nicholas 930
 MacDonald, Vicki **1080**, **737**
 Mace, Kimberly E. 324, **847**, 317
 Macedo de Oliveira, Alexandre 307, 325
 Macete, Eusebio 1198
 Machado, Ricardo L. D. 671
 Machain-Williams, Carlos 1462
 Machalkova, Renata 769
 Macharia, Alexander 333
 Machicado, Jorge D. **287**, **752**, **753**
 MacInnis, Brownwyn 506
 Mackenzie, Charles 1415
 MacKenzie, Donna 46
 Mackenzie, Grant A. 1483
 Mackey-Lawrence, Nicole M. 1506
 Mackinnon, Margaret 156, 162, 631
 Maclean, David 775
 MacLeod, Annette 783
 Macleod, William B. 724, 728
 MacInnis, Bronwyn 328
 MacMillan, Katherine 476
 MacMillen, Zachary 1147, 1147
 Madaline, Theresa 1495
 Madanitsa, Mwayi 240, 505, 865
 Madoo, Lark 725
 Maeda, Adriana Y. 1206
 Maestre, Amanda 1127, 1158, 1158, 196
 Maestre Serrano, Ronald **1349**
 Maffi, Eva 1237
 Magalona, Sophia 1076, 619
 Magesa, Stephen M. 830, 1133
 Magessa, Stephen 550
 Maggi Ntuku, Henry 652
 Maggid, Rehema 1456
 Magill, Alan J. 307
 Magiri, Charles 1396
 Magistrado, Pamela 1317, 1317
 Magloire, Roc 112, 1186
 Magnussen, Pascal 1146, 1259, 1260, 1284
 Magola, Ruth 1236
 Maguiña, Edson 711

The number(s) following author name refers to the abstract number.

- Maguire, Jason D. 113, 733
 Mahajan, Babita 225, 5
 Mahama, Charlse I. 771
 Mahamar, Almahamoudou **186**, 457, 853
 Mahdi, Ramsan 210
 Mahdy, Mohammed A. K. 897
 Mahendradhata, Yodi 461
 Maheu-Giroux, Mathieu 758
 Mahfooz, Najmus 1320
 Mahmud, Rohela 755
 Maia, A. O. 82
 Maia, Allan R. S. 611
 Maia, Carla 749
 Maia, Claudia C. P. 283
 Maier, Alex 667
 Maiga, Hamidou **393**, 1364
 Maiga, Oumar 765
 Maikore, Ibrahim K. 730
 Maina, Martin W. **355**
 Maire, Nicolas 1287
 Maitland, Kathryn 456
 Majam, Victoria F. **225**, 5, 24, 991
 Majambere, Silas 881
 Majanja, Janet 444
 Majewski, Andrew C. 1039, 1043, 757, 1046
 Majji, Sai 1154, 1159
 Majjid, Rehema 1415
 Makange, Yusuf 1415
 Makepeace, Benjamin L. 16, 21
 Makio, Albina 592, 920
 Makiya, Michelle 1412
 Makumbi, Fredrick 136
 Makupa, William 35
 MAL-ED Network, On behalf of the 1095, 1406, 715
 Malafronte, Rosely 1197
 Malaga Chavez, Fernando S. 781
 Malaria Indicator Survey Advisory Group 332
 Maldonado, Maria 296
 Malecela, Ezekiel K. 1427
 Malecela, Mwelecele 1051, 1233, 1456, **1415**
 Malek, M. A. 1188
 Malekani, Jean 51, 740
 Malheiros, Antonio F. 274
 Malhotra, Indu **487**, 934, **936**
 Malick, Ndiaye 1483
 Mallewa, Macpherson 1494, 638
 Malone, Joseph L. 3, 1311
 Maloney, Jenny **29**
 Maly, Dustin J. 23, 27
 Mamadou Ousmane, Ndiath 378
 Mamanova, Z T. 908
 Mammadsalohov, Agarahim 742
 Mamova, Alexandra 176
 Mamun, Abdullah A. 237
 Manamperi, Nuwani H. 1029
 Manary, Micah 808
 Mancini, Francesca 946
 Mandalakas, Anna M. 1376
 Mandanda, Benson 561
 Mandara, Celine 170
 Mandefro, Yewubdar 792
 Mandike, Renata 170, 210
 Mangas, Kirstie 83
 Mangasini, Enock 31
 Mangwiro, Clement T. N. 943
 Manhart, Carolyn J. 1402
 Manhart, Lisa E. 140
 Manjgaladze, M 418
 Manji, Imran 549
 Mann, Matthias 1499
 Mann, Victoria H. 416, 896
 Mann Flueckiger, Rebecca **30**
 Manne, Jennifer **773**, 1420
 Manneh, Jainaba 1079
 Manning, Jessica 806
 Manoff, Susan 516
 Mansanguan, Chayasin 1184
 Manske, Magnus 328, 506
 Mante, Sunny 1415
 Mantel, Nathalie 593
 Mantovani, Saulo A. S. 1088, 1197
 Mappin, Bonnie 1297, 1298, 801
 Marano, Nina 741
 Marck, Klaas W. 1200
 Marcos, Luis A. 287, 752, 753
 Marcisin, Sean **180**, **182**, 817
 Marcus, Rachel **779**
 Margolis, Harold 112, 114, 133, 582, 584, 592, 625, 989, 558, 608
 Marianelli, Leonardo **273**
 Mariani, Bianca 535
 Mariappan, T. 1074
 Mariconti, Mara 537
 Marijon, Anne 810
 Marin, Catherin 931
 Marin, Juan C. 397
 Mariotto, Anita 1501
 Markon, Andre O. **612**
 Marks, Florian 249
 Marks, Michael **961**
 Marks, Morgan 1020
 Maro, Athanasia 1079
 Maro, Venance P. 249
 Marquart, Louise 48
 Marrama Rakotoarivony, Laurence **1215**
 Marsden, Clare **61**
 Marsh, Kevin 1442, 156, 162, 40, 662, 667
 Marsh, Tom 527
 Marshall, Edith 742
 Mårtensson, Andreas 822, 824, 829
 Marti, Matthias 644, 1292
 Martin, Akogbeto C. **382**
 Martin, Diana **34**, 35, 481, 1020
 Martin, Thibaud 1344
 Martinez, Christopher 1355
 Martinez, Isabel 107, 145
 Martinez, Julia 532
 Martinez-Vega, Ruth A. 604, 1062
 Martins, Antonio C. 1088, **1197**
 Martins, Yuri C. **639**
 Marube, Elizabeth 1430
 Masembe, Charles 1109
 Maserati, Roberta 756
 Masiga, Daniel 1109
 Masimirembwa, Collen M. 815
 Maskery, Brian 1067, 1072
 Maskhao, Pongsri 1340
 Mason, Carl 1079
 Masonga, Rhoda 1296
 Massae, Patric 1231, 31, 35
 Massougbody, Achille 1444
 Masuoka, Penny 567
 Matakchiero, Amy C. 1214
 Matchimakul, Pitchaya **416**
 Matee, Macey 65
 Mathanga, Don 1136, 1252, 1288, 1428, 211, 212, 455, **1132**, 1268, 1292, 150, 852
 Mathavarat, Chaiyawat 243
 Mather, Frances J. 818
 Mather, Michael 1273
 Matheson, Andy **1332**
 Matheson, Alastair I. **140**
 Mathias, Derrick K. **498**, 1106
 Mathis, Demetrius 558
 Mathur, Radhika 300
 Matias, Abrahan 1345
 Matip Mbou, Isabelle 539
 Matos, Breno 1197
 Matos, Desiree 582
 Matoso, Leonardo F. 283, 429, 488
 Matowo, Nancy S. **364**
 Mattia, Kimberly-Anne 598, 602, **594**
 Matzhanova, A M. 908
 Maude, Rapeephan R. **1479**
 Maude, Richard J. 1479
 Maung, Thae Maung 1138, 1335
 Mausch, Norman 489
 Maves, Ryan 713
 Mawejje, Henry D. 1460
 Mawole, Johnson 176
 Maxime, Jean Claude G. 250
 Maxwell, Caroline 1327
 Mayanja, Harriet 1121, 1121
 Mayanja-Kizza, Harriet 344
 Mayda, Maria 893
 Mayer, Sandra V. 1382
 Mayo-Smith, Leslie 959
 Mayta, Holger 788
 Mayxay, Mayfong 328, 506, 822
 Mazier, Dominique 1012, 993
 Mazimba, Arthur 1078, 653
 Mazitschek, Ralph 1010
 Mazzalupo, Stacy 475
 Mbabazi, Pamela S. 1236
 Mbacke Mboup, Balla 545
 Mbah, Evaristus 1085
 Mbaye, Aminata 320, 327, 354
 Mbewe, Reuben 1078
 Mbidde, Edward 1379
 Mbise, Christina 1233
 Mbo Modiri, Clarisse 1255
 Mbodj, Sidiya **1225**
 Mbogo, Loice W. 1025, 490
 Mbonye, Anthony K. 1146, **1260**
 Mboup, Souleymane 1225, 327, 354, 42, 483, 544, 560
 Mbow, Moustapha 483, 560
 Mbuchi, Margret 1396
 Mbuji, Peter 170
 Mcavin, James 243
 McBride, Colleen 279
 McCall, Philip 881, 983
 McCallum, Fiona J. 1442, 40, 662
 McCann, Robert S. **519**
 McCardle, Patrick W. 391
 McCarthy, James S. **219**, 40, **48**, 662, 754
 McCarthy, William F. 973
 McCaw, James 1263, 1263
 McCollum, Andrea M. 1380, **51**, 740
 McCormick, Benjamin J. J. 1095, 1406, **715**
 McCoy, Margaret E. 1439
 McCracken, John P. 1481, 446, 466, 554
 McCulley, Nicholas 182
 McDonald, Chloe E. R. **1492**
 McDonald, Emily A. **1000**, **1002**, **1003**
 McDonald-Fleming, Renee **968**
 McDowell, Mary A. 1018
 McElroy, Peter 210
 McElwain, Terry 527
 McFarland, Deborah 1139, 1140
 McGarvey, Stephen 565
 McGavern, Dorian 218
 McGowan, Kim R. 1403
 McGrath, Monica 1406
 McGrath, Nuala 138
 McGraw, Elizabeth A. **57**
 McGraw, Elizabeth F. 876
 McGray, Sarah 1256, 1275
 Mchembe, Mabula 1415
 McKenzie, F. Ellis 659
 McKerrow, James H. 22, 421, 774
 McKibben, Maxim J. 487
 McKinsey, Timothy A. 1250
 McLennan, John D. **148**, **677**, **678**
 McLeod-Robertson, Stephen 46
 McMahan, Timothy J. 1016
 McMahan-Pratt, Diane 72
 McManus, Donald P. 1239, 564, 1490, 565
 McMichael, Ashley 1493
 McMillan, Joseph 399
 McMorrow, Meredith 1264, 1264
 McNamara, Case W. 808

The number(s) following author name refers to the abstract number.

- McNulty, Samantha N. **420**
 McPhun, Virginia 449
 McQueen, Philip G. **659**
 McQuiston, Jennifer 558
 McWhinney, Brett 48
 Mduluzu, Takafira 483, **486**, **489**,
 561, 898, 900
 Mduma, Esto 1410
 Mead, Daniel G. 399
 Mead, Paul S. 1064
 Means, Arianna R. **140**, **423**
 Medeiros, Nayara I. 1241
 Medina, Freddy A. **1401**
 Medina, Jacqueline 131
 Medina, Juan F. 1401
 Medina, Marco A. 410
 Medrano Mercado, Nora 304
 Meek, Sylvia 1138, 1335
 Meffre, Eric R. F. 1441
 Mehlhorn, Heinz 251
 Mehlotra, Rajeev K. 1455
 Mehta, Saurabh 1089, **1090**, 405
 Mejia, Alan 531, 533
 Mejia, Aurelio 1067, 1072
 Mejia, Carolina 1423
 Mejia, Rojelio **1446**
 Mekasha, Sindew 1451
 Mekonnen, Seleshi K. M. **339**
 Melaku, Sileabatt 1472
 Melendez, Astrid X. T. O. 524
 Melendez, Victor 180, 182, 817,
 973
 Melrose, Wayne D. 1040, 1414
 Meltzer, Martin I. 1035
 Memish, Ziad 778
 Memusi, Dorothy 551
 Menacho, Gilbert S. 1020
 Ménard, Didier 1286, 1319,
 1319, 827, 996
 Mendell, Nicole L. 1164, 716
 Mendelsohn, Joshua B. **66**
 Mendes, Felisberto 490
 Mendez, Tiago 1490
 Méndez-Galván, Jorge 1062
 Mendocilla, Silvia 410
 Menéndez, Clara 1198, 458
 Meneses, Claudio 727
 Menezes, Neia P. 712
 Meng, Zhaojing 19
 Menon, Jayaram 334
 Mensah-Brown, Henrietta 994
 Mentor, Lucien Ali Ber 731, **738**
 Mentor Ali Ber, Lucien 1186
 Meny, Diana **549**
 Menzies, Dick 1376
 Menzies, Stephanie 891, 1027
 Mercado, Juan Carlos 985
 Mercado Olavarria, Chanis M.
 1189
 Mercereau-Puijalon, Odile 1319,
 1319, 996
 Mercier, Thomas 813
 Meremikwu, Martin 49, **1272**
 Merritt, Ethan A. 23
 Meschi, Silvia 615
 Meseko, Clement A. **437**
 Meshnick, Steven R. 324, 468,
 505, 743, 824, 843, 855, 858
 Messenger, Louisa A. **71**
 Messer, William B. **1399**
 Messina, Jane P. **54**
 Metcalf, Charlotte 205
 Metenou, Simon 1412, 194, **967**
 Metoxen, Alexander 471
 Meurs, Lynn 483, **560**
 Meyers, Jacob I. **978**
 Meza, Rina 1172
 Mghamba, Janneth 170
 Mgwatu, Gogadi 684
 Mharakurwa, Sungano 1258,
 1279, 541
 Michaelides, Tula 1083
 Michelin, Elisa 45
 Michelle, Chang 3
 Michelow, Ian 1149, 1149, 227,
 452
 Michoud, Frederic 1285
 Micieli, Maria V. 401
 Midzi, Nicholas 483, 486, 489
 Mier y Terán Romero, Luis 511
 Mier-y-Teran, Luis **510**
 Migchelsen, Stephanie J. 961
 Mikita, Kei **4**
 Mikolasova, Gertruda 348, **409**,
769
 Milali, Masabho P. **373**
 Miles, Michael M. 71
 Miller, Aimée 1142
 Miller, Andre 902
 Miller, Ann K. 42B
 Miller, Becky A. **1362**, 864
 Miller, Hellen C. 1365
 Miller, John M. 1, 1280, 1143,
 1295, 1301, 1425, 1426, 540,
546
 Miller, Louis H. 451
 Miller, Mark 1095, 1406
 Miller, Melanie M. 278
 Miller, Nathan P. **935**
 Milligan, Paul 548, 655
 Milne, Kathryn H. 932
 Milner, Dan 159, 160, 1495
 Milord, Marie Denise 1038
 Mimche, Patrice N. **191**
 Minakawa, Noboru 1336, 368
 Mintz, Eric D. 1034, 1186, 1405,
 738, 957
 Miotto, Olivo 328, 506
 Miotto, Paolo 1371
 Miranda, Eduardo F. 233
 Mirante, Clara 430
 Mireji, Paul O. **290**
 Mirelman, Andrew 1073
 Miro, Jose M. 468
 Misikova, Eva **349**
 Misomali, Amos 80
 Misra, P.R. 1032
 Missamou, François 1043, 1046,
 757
 Mita, Toshihiro 506, 864
 Mitchell, Kate M. 483
 Mitchell, Sara 946
 Mitprasat, Mashamon 806
 Mitra, Indrani 1059, 113
 Mitre, Edward 1432, 19, 257, 964
 Mitreva, Makedonka 420
 Miura, Kazutoyo 1152, 1157,
 1315, 222, **224**, 42, 451, 665
 Mix, Andrew 1161
 Miyamoto, Yukiko 22
 Mkocho, Harran 1231, 1233, 34,
 481
 Mkude, Sigsbert 170
 Mkwanda, Square 262, 282
 Mlambo, Godfree 486
 Mlangwa, Susan 1331
 Mmbando, Bruno 850, 1427
 Mmbando, Donan 31
 Moch, J. Kathleen 215
 Moch, Kathy 1154
 Modi, Surbhi 613
 Modrek, Sepideh 1307
 Moe, Christine L. 683, 685
 Moebius, Jacqueline **1126**
 Moffett, Daphne 112
 Mogasale, Vittal **1067**, 1072
 Mohamed, Ally 170
 Mohamed, Khadeeja M. 42B
 Mohamed, Sara 784
 Mohamed, Zeehaida 234
 Mohammed, Khlafan 1453
 Mohammed, Said 1453
 Mohan, Rathy 929
 Mohareb, Emad 1388
 Mohd Zain, Siti Nursheena 238
 Mohmmed, Ahmed 630
 Mohr, Sharif 524
 Moitra, Prasun **24**, 5
 Mokuolu, Olugbenga A. **730**
 Molaei, Goudarz 1383
 Mølbak, Kåre 1409
 Moldabekov, B 908
 Molehin, Adebayo J. **426**
 Molero, Francisca 603
 Molestina, Robert E. **893**
 Molina, Douglas M. 454, 197,
 1123, 223
 Molina, Sandra 35
 Molina-Cruz, Alvaro **976**
 Molla, Yordanos B. **280**
 Molteni, Fabrizio 210, 550
 Molyneux, David H. 1042, 1045,
 1234
 Molyneux, Elizabeth 528
 Molyneux, Gemma **265**
 Molyneux, Malcolm E. 160, 1494,
 1496, 155, 638
 Mon, Hsu H. 1266
 Monaghan, Andrew **568**, 1064
 Moncayo, Abelardo C. 1353,
 1354
 Mondal, Dinesh 1422
 Mong, Aprue 1165
 Mongkolsapaya, Juthathip 1400
 Mongkolsirichaikul, Duangrat
 443
 Monica, Acevedo 107
 Monroe, Benjamin 740
 Monroy, Eric 1167
 Montagu, Dominic 1086, 1307
 Montano, Silvia M. 1174, 1227,
 1386
 Montavon, Céline 1411, 1412
 Monte, C. Tim W. 769
 Montenieri, John A. 476
 Monterrosa Vergara, Elkin 1349
 Montgomery, Joel 1396, 592,
 1028, 1384
 Montgomery, Susan P. 562, 563
 Montoya, Alberto 325
 Montoya, Diego 287, 752, 753
 Montoya, Magelda 985
 Moon, Troy 69
 Moonah, Shannon N. 462
 Moonen, Bruno 1141, 1145, 862
 Moore, Anne 1044, 1451
 Moore, Christopher C. 236
 Moore, David 1372
 Moore, Julie 1493
 Moore, Kerryn 1291
 Moore, Sean 1064
 Moormann, Ann M. 664, 668,
 855
 Moraga-Serrano, Paula 524
 Morahan, Belinda J. **1008**
 Moraleda, Cinta 1198
 Morales, Maria 1388
 Morales-Perez, Arcadio 123
 Moreira, Andrés 721, 747
 Moreira, Clarissa M. **214**, **651**
 Morelli, Marco 1269
 Moreno, Alberto 1105, 637
 Moreno, Brechla 129
 Moreno, Darwin A. 95
 Moreno, Marta 1359
 Moretz, Samuel E. 224, 42, 665
 Morgan, Marjorie **100**
 Mori, Nicanor 1386
 Mori, Virgilio 835
 Morlais, Isabelle 1258, 387
 Morou, Evangelia 550
 Morris, Alexandra **1141**, 1142
 Morris, C. P. **19**
 Morris, Carrie A. **645**
 Morris, Jamae **883**
 Morris, Paul 257
 Morris, Sheldon 218, 991
 Morris, Thomas 584, 883
 Morrissey, Joanne 1273
 Morrison, Amy 518, 983, 517,
 581
 Morrison, Robert 190, 633, 1147

The number(s) following author name refers to the abstract number.

- Morrissey, Anne B. 556
Morton, Lindsay C. **1264**, **1264**
Moscoso, Fabiola 466
Moseley, Pope 361
Mosha, Dominic F. **167**
Mosha, F. 1051
Mosha, Fausta S. F. **65**, **770**
Mosha, Jacklin 1429
Moshi, Irene R. **839**
Mosore, Mba-Tihssommah **90**
Moss, Eli 7
Mossoko, Mathias 1380
Mota, Francisco S. 1408
Mota, Matheus J. 1052
Motoki, Maysa T. **1114**
Mott, Joshua 465
Mou, Ferdinand 1085
Mouangue, Antoine 539
Mouchet, François 390
Moudy, Robin M. 517, 570
Mounsey, Kate **493**
Mountford, Adrian P. 1505, 483
Moura, Alessandra F. 1407, 1408
Moura, Sofia 430
Mourão, Marina d. 901
Moureau, Gregory 1471, 1471
Mouri, Oussama 1012, 993
Moyle, Sarah 932
Moyo, D. 1136
Moyo, Dubulao 211, 212
Mpimbaza, Arthur 173, 204, 557
Msellem, Mwinyi I. **833**, 1141
Msibi, Patrick 538, 836
Mtande, Exton 1132, 150
Mtimuni, Angella 622
Mtove, George 1194, 456, 556
Mubiru, Denis 1190
Muchiri, Eric 487, 934, 103, 447, 53
Muchiri, Geoffrey 562
Muchunguzi, Victor 65, 770
Mudhanga, Frederick 177
Muehlenbachs, Atis 865
Mueller, Ivo 1198, 1257, 1289, 1291, 1442, 667, 797
Mueller, John 1365
Mueller, Jenny 138
Mues, Katherine E. **1416**
Mugalura, Frances E. **550**
Mugarula, Francis 210
Muhammad, Shah 1483
Muheki, Edridah **1236**
Muhindo, Bosco 66
Muhindo, Mary K. **169**, 181, 504
Muhindo, Rose 236
Muhtu, U. 1091
Muia, Alfred 1396
Muiruri, Samuel 53
Mukabana, Richard 880
Mukabana, Wolfgang R. 374
Mukemba, Jackson 1098, 4
Mukete, Arnold M. F. **363**
Mukherjee, Angana **1009**
Mukherjee, Swati 1398, **1402**
Mukundarajan, HariPriya **529**
Mukunzi, Silvanos 444, 920
Mulama, David 668
Mulama, Fridah 998
Mulangu, Félix 1380
Mulenga, Musapa 1339
Mull, Bonnie 883
Müller, Maria L. 1392
Mulligan, Robert T. 1351
Mulokozi, Abdunoor 1141
Mulvenna, Jason P. 1489, 420A, 949
Munayco, Cesar 1372
Munday, Jane 1498
Munderloh, Ulrike G. 745
Mungai, Peter L. 487, 934, 103, 447
Munishi, O. M. 249
Muniz, Pascoal T. 1088
Munoz, Beatriz 34
Muñoz, Fredy W. 446, 277, 554
Muñoz, Jorge 558, 133
Muñoz, Julian 795, **1162**
Muñoz-Jordan, Jorge 584, 989, 10, 119, 1401, 608, 986, 114
Munyua, Peninah 527
Muoki, Justus 1374
Muratova, Olga 1155, 929, 930
Murfin, Kristen E. **261**
Murnane, Darragh 621
Murphy, Jennifer L. 1033
Murphy, Sean C. **184**, 185
Murray, Kristy 1447
Murray, Megan B. 463
Murshid Hasan, S M. 940
Murusidze, M 297, 418
Musa, Ahmed 784
Musa, Kiyele 1380
Musau, Stephen 541
Mushatt, David M. 818
Muskavitch, Marc A. 1116, 1360, 1348
Musoke, Charles 1011, 164
Musokotwane, Kebby 653
Musuva, Rosemary M. **36**, 563
Mutagahywa, Joshua R. 550, 1133
Mutai, Beth K. 355
Mutalemwa, Prince 1415
Mutambu, Susan L. 486
Mutapi, Francisca 483, 486, 489
Mutebi, Edrisa 403
Mutete, Elizabeth T. 36
Muthusammy, Natarajan 1023
Mutisya, James 920
Mutombo, Boniface **545**
Mutuku, Francis M. 103, 447
Mutumbo Ndongala, Guy 51
Muturi, Alex 551
Mwanguzi, Esther 910
Muyembe, Jean Jacques 51, 1380, 235
Mwaikambo, Esther D. 1098, 4
Mwakitalu, Mbutolwe E. **1051**, 1415
Mwale-Mutengo, Mable **561**, **898**, **900**
Mwalimu, Dismas 550
Mwandama, Dyson 1132, 1252, 1268, 1288, 150, 455, 852
Mwandawiro, Charles S. 1474
Mwanga-Amumpaire, Juliet **736**, 236
Mwangi, Josphat 444
Mwangi, Thumbi **527**
Mwangoka, Grace W. **1371**
Mwangungulu, Stephen P. **840**
Mwangwa, Florence **370**, 502, 542
Mwansa, James 561, 898, 900
Mwanza, Mercie 1280
Mwema, François-Xavier 1255
Mwingira, Felistas 1257
Mwingira, Upendo J. 1231, **1233**, 1415, 1456, 31, 1235
Mwinzi, Pauline N. M. 36, 562, **563**, 895
Mwongeli, Joyce 156, 162
Mworozi, Edison A. **547**
Myers, Bennett 1148, 1148
Myers, Monica F. 1418
Myers, Nicholas M. **1071**, 526
Myles, Kevin M. 470
Mysore, Keshava 944, **945**
Mzilahowa, Themba 1288, 282, 455
- N**
- N'guessan, Raphael K. 379
N'Zonou, Pabanam 288, 289
Nachbar, Nancy 1279, 541
Nacher, Mathieu 64
Nackers, Fabienne 736
Nadjm, Behzad 556
Nadler, Kyle 1359
Nagarajan, Vijayaraj 992
Nagodavithana, Kumara C. 1452
Nagyova, Zuzana 348
Nahas, Debbie 1155
Nahrendorf, Wiebke **450**
Naigino, Rose **311**
Nair, Sethu **992**
Nakajima-Sasaki, Rie 454, 664
Nakaye, Martha 236
Nakazawa, Yoshinori 51
Nakhasi, Hira L. 1019, 1244, 1247, 1242
Nalubega, Mayimuna 189, 193
Nalusaji, Aisha 236
Naluwu, Kate 189, 193
Namara, Geoffrey 1326
Namasopo, Sophie 1497
Nambozi, Michael 324, 49
Namgay, Rinzin 837
Namirimu, Felistas N. **189**
Namountougo, Moussa **1344**
Namwanje, Harriet L. 1236
Nana Ama Amisah, Nana A. 83
Nana Djeunga, Hugues C. 15
Nanai, Alphonsina 1231, 1233, 1233, 31
Nanclares, Carolina 1380
Nandan, Deoki 1074, 1094
Nani Mudin, Rose 1062
Nanjebe, Deborah 736
Nankabirwa, Joanita 195
Nankabirwa, Joaniter I. **1293**
Nankya, Felistas 1121, 1121, 193, 37
Nankya, Florence 346
Nanyonjo, Agnes 939
Nanyonjo, Agnes M. **136**
Napier, Grant B. 1424, 301
Naples, Jean M. 952
Naquira, Cesar 781
Narahari, Saravu R. 1041
Naranjo, Nelson J. 397
Narayan, Sushma 42B
Narayanan, Aarthi 434
Nardone, Glenn 1013
Nare, Bakela 1424, 301
Nartey, Alexander A. A. **75**
Narum, David L. 5, **930**, 1155, 215
Nasci, Roger 1467
Nasidi, Abdulsalam 435
Nasr, Nabil A. 755, 897
Nasr, Sussann 204
Nasreen, Sharifa 937
Nassirou, Baido 285
Nat, Amritpal S. 417
Natalia, Evy I. 879
Natarajan, Gayathri 1019, **1023**
Nataro, James P. 1407
Nathan, Tumhamye **845**
Nathavitharana, Ruvandhi **1057**
Nation, Catherine S. 1248, 570
Nauhasseney, Honelgn 1295
Naulikha, Jacqueline 1025
Nausch, Norman 483
Nava-Aguilera, Elizabeth 123
Nayakaruhaka, Luke 1379
Nayakwadi Singer, Monica **934**
Nchinda, Godwin 1412
Ndam, Nicaise 1158, 1158
Ndao, Momar 22
Ndealilia, Senyael Swai 1079
Ndemere Musafiri, Pappy 652
Nderitu, Leonard **1396**, 592
Ndhlovu, Micky 1, 1143
Ndiaye, Agnes 938
Ndiaye, Daouda **1270**, **1270**, 2, **268**, 320, **327**, 354, 42, 544, 655, 772
Ndiaye, Jean Louis A. **655**, 1137, 268, 772, 1308, 2, 548

The number(s) following author name refers to the abstract number.

- Ndiaye, Magatte 1137
 Ndiaye, Mamadou 772
 Ndiaye, Mouhamadou 268, 320, 327, 354
 Ndiaye, Mouhamed 548, 655
 Ndiaye, Yaye Die 327
 Ndiaye, Yaya D. 1270, 1270, 320, 354
 Ndiaye, Youssoupha 548, 655, 208
 Ndiaye Dièye, Tandakha 483
 Ndiaye-Diawara, Awa 1225
 Ndibazza, Juliet **1284**
 Ndila, Caroline 333
 Ndiop, Medoune **1281**, 798, 938
 Ndir, Omar 268, 327, 354, 772
 Ndo, Cyrille 1111, 1111, 1115
 Ndour, Cheikh T. 1137
 Ndour, Moussa 938
 Ndour, Papa Alioune **1012**, 993
 Ndundu Luwawu, Jean Joseph 652
 Ndyomugenyi, Richard **1259**
 Neafsey, Daniel 7, 544
 Neal, Aaron T. **360**
 Neatherlin, John 1396, 592
 Nebie, Issa 503
 Neculai, Dante 351
 Nedosekov, Vitalii 1393, 1394
 Neelon, Brian 549
 Neesanant, Pimnapar 1079
 Neil, Kali K. **705**
 Nelwan, Erni J. 175
 Nena, Winne 296
 Nerurkar, Vivek R. 1218
 Nery, Susana V. 281, **754**
 Neto, João G. 596
 Neumayr, Andreas 603
 Nevolko, Oleg **1091**
 Newbold, Chris I. 360
 Newell, Steven 1181
 Newman, Mercy 87
 Newport, Melanie 1448, 280
 Newton, Paul N. 328, 506, 508, 822
 Neyra, Ricardo C. 773
 Nfon Priso, Jeanne D. 539
 Ng, Caroline 811
 Ng, C. W. 1063
 Ng, Ee-Ling 586, 587
 Ng, Lee-Ching 111, 586
 Nga, Tran V. T. 1479
 Ngadaya, Esther 170
 Ngapmen Yamadji, Arlette L. 539
 Ngo, Kiet A. 1465
 Ngo, Tue T. 50
 Ngo Thi, Hoa 1482
 Ngoi, Joyce M. **631**
 Ngom, Algaye 545
 Ngondi, Jeremiah 1133, 1231, 1233, 210, 31, 550
 Ngoyi, Mumba 235
 Ngsala, Billy E. 824
 Nguete, Beatrice 740
 Nguku, Patrick M. 435
 Nguyen, Chau V. V. 406
 Nguyen, Dung H. 406
 Nguyen, Hoang Mai 1485
 Nguyen, Lan T. N. 406
 Nguyen, Von **957**
 Nguyen, Vu 930
 Nguyen, Yen T. **408**
 Nguyen Van, Hong 861
 Nguyen Van, Van 861
 Ngwira, Bagrey M. M. 262
 Nhabomba, Augusto 1198
 Ni, Ziling 903, 904
 Niangaly, Amadou 1096, 1443
 Niangaly, Moussa 1125, 451
 Nichol, Stuart T. 910, 1379, 1380
 Nichter, Mark **1085**
 Nicoletti, Giovanni Jacopo 756
 Nicosia, Alfredo 932
 Niedrig, Matthias 921
 Nielsen, Carrie 1311, 500, 859
 Niemierko, Malwina 1420
 Nieto Sosa, Liliana 273
 Nieto-Sanchez, Claudia P. 777
 Nigatu, Alemayehu 619
 Nikiema, Frederic W. **322**
 Nikitova, Alina 1393, 1394
 Nikolay, Birgit **1202**, **1474**
 Nilles, Eric 114
 Nilsen, Aaron 1273, 43
 Nimo Paintsil, Shirley C. **1388**
 Nino, Laetitia 1191
 Niramitsantipong, Apinya **831**
 Nisalak, Ananda **120**, 126
 Nitatsukprasert, Chanyapat 391, **395**
 Niu, Feiyang 462
 Niu, Tianchan 869
 Nix, William A. 558
 Nixon, Christian P. 1149, 1149, 227, 452, 923
 Nixon, Christina E. **668**, **923**, 1149, 1149, 1150, 227, 452
 Njau, Joseph D. 211, **1136**, **1139**, **1140**
 Njau, Ritha 170
 Njenga, Kariuki 1369, 527
 Njenga, Sammy M. 1028, 1474
 Njeru, Ian 592
 Njie, Baba 1483
 Njie-Jobe, Jainaba 916
 Njiokou, Flobert 15
 Njiram'madzi, Jenala 528
 Njiri, James 1369, 444
 Njiru, Peter 628
 Nkuruningyi, Gyaviira 1284
 Nobre, M. L. 82
 Noecker, Cecilia A. **604**
 Noedl, Harald 328, 506, 822
 Noel, Megan 1076, 1077, 619, 80
 Nogueira, Mauricio L. **132**
 Nogueira, Rita Maria 109
 Nogueira, Rudi 1197
 Noh, Susan 527
 Nolan, Melissa S. **1447**
 Nolasco, Oscar 356
 Nold, Michael J. 215
 Nolla, Nicolas 539
 Noma, Mounkaila 1238
 Noordin, Rahmah **234**
 Norbis, Luca 1371
 Norris, Douglas E. 398, 573
 Norris, Laura C. **1117**
 Nosten, Francois 328, 506, 649, 822
 Notario, Walter 835
 Novati, Stefano 756
 Noviyanti, Rintis 157
 Novotny, Joseph M. 538, 836
 Nowak, Wojciech 383
 Nozaki, Mamoru 1007, 1314
 Nsanzabana, Christian 214, 821, **971**
 Nseye, Claudine 1380
 Nshala, Andreas 1231, 1456
 Nsohya, Sam L. 204, 821
 Nsona, Humphreys **622**, 624
 Nsubuga, Peter 65
 Ntadom, Godwin N. 730
 Ntshalintshali, Nyasatu E. N. **836**, 538
 Ntumngia, Francis B. 669
 Nuamtanong, Supaporn 272
 Nuckols, John T. 1210, 1211
 Null, Clair 685
 Nunes, Priscila 109
 Nunez, Fidel A. 760
 Nunoz, Raquel 760
 Nuriddin, Azizeh 883
 Nurmahnov, T. I. 908
 Nutman, Thomas B. 1417, 1432, 1446, 17, 19, 255, 263, 966, 968, 99, 967, 1411, 254, 254
 Nuwa, Anthony 1326
 Nwadike, Jones U. **766**
 Nwakanma, Davis 1270, 1270, 2
 Nwakwuo, Geoffrey C. 200
 Nwauche, Chijioke A. 802, 972
 Nwe, Steven 1041
 Nyabeyeu Nyabeyeu, Hervé 539
 Nyambura, Janet 444
 Nyanda, Peter 1233, 1235
 Nyandigisi, Andrew 551
 Nyange, Ally 550
 Nyarko, Alexander K. 292
 Nyarko, Joshep Harold Osei **886**
 Nyathirombo, Amos 253
 Nychyk, Serhiy 1091, **1393**, **1394**, **723**
 Nyehangane, Daniel 236, 736
 Nyeko, Richard 456
 Nygren, Benjamin L. **1034**, 1186
 Nyirenda, Oswald M. 1296
 Nylen, Susanne 73
 Nyoka, Raymond 1396
 Nyonda, Mary 156, 162
 Nyung, Myat Htut 1266
 Nyunja, Albert 592, 920
 Nyunt, Myaing M. 1266, 328, 506, **974**
 Nyunt, Myat H. 328
 Nzunza, Rosemary M. **1369**

O

- O'Brien, David 857
 O'Brochta, David A. 979
 O'Connell, Kathryn A. 178, 179
 O'Donoghue, Peter 359
 O'Gorman, Melissa 814
 O'Neill, Katelyn 689
 O'Neill, Paul M. 266, 926
 O'Neill, Scott L. 57, **58**, 876
 O'Reilly, Ciara 1405
 O'Tousa, Joseph 471, 697
 Oakley, Miranda S. 663, **991**
 Obado, Samson 1499
 Obaldia, Nicanor **644**
 Oberlies, Nicolas 260
 Oberste, Steve 558
 Oberstein, Shoshana 1044, 1451
 Obi, Emmanuel 1325
 Obidike, Ifeoma C. **168**, 803
 Obiero, Joshua M. 187
 Obiri-Danso, Kwasi 367, 394, 1388
 Obonyo, Charles 970
 Ocampo, Carlos M. 128
 Ocampo, Clara B. 1363
 Ocampo, Karen **708**
 Ocheng, David 770
 Ochieng, Caroline **592**, 920
 Ochieng, Linus 527
 Ochieng, Melvin 592
 Ochoa, Eduardo 989
 Ocholla, Steven 444
 Ochomo, Eric 519
 Ockenhouse, Christian F. 316, 973, 180
 Ocwieja, Karen E. **607**
 Odada, Peter Sumba 664
 Odagiri, Mitsunori **1032**
 Odegaard, Justin 997
 Oden, Maria 528
 Odermatt, Peter 1472
 Odero, Kennedy 1028
 Odey, Friday A. 730, 1272
 Odhiambo, Aloyce 1033
 Odhiambo, Collins O. **436**, 920
 Odhiambo, Frank O. 851
 Odhiambo, Gladys O. 36
 Odhiambo, Jane A. 1329
 Odiere, Maurice R. 36, **895**, 998
 Odom, Audrey R. **926**
 Odongo, Wycliffe 1430, 520
 Odoom, Shirley C. 90

The number(s) following author name refers to the abstract number.

- Oelnick, T. 349
 Ofula, Victor O. **917**, 592
 Ogaba, James 203
 Ogbanje, Christopher E. 203
 Ogbuehi, Ijeoma H. 802
 Ogedegbe, Olugbenga 78
 Ogobara, Doumbo 1274
 Ogola, Eric 527
 Ogundimu, Abimbola **1175**, **1391**
 Oguntimein, Oluwamurewa 725
 Ogutu, Bernhards 813, 849, **970**
 Ogutu, Michael O. 563
 Oh, Helen 515
 Ohrt, Colin 180
 Ohta, Nobuo 292, 70
 Ojo, Kayode K. **23**, 27
 Okafor, Henrietta U. 730
 Okamoto, Emi **780**
 Okany, Charles 1228
 Okebe, Joseph 1308
 Okitundu, Daniel 235
 Okoli, Charles 168
 Okorie, Patricia N. **1234**
 Okot, Charles 910
 Oktavian, Antonius 879
 Oku, Hiroyuki **793**
 Okui, Scholastica A. I. **673**
 Okunogbe, Adeyemi 1329
 Okyere, Eunice 796
 Oladejo, John 435
 Olaf, Piepenburg 1056
 Olang, George 1329
 Olanga, Evelyn A. **880**
 Olaniyan, Esther O. 699
 Olano, Juan P. 1164
 Olanratmanee, Phanthip 1340, 988
 Olayemi, Sunday 1228, 646
 Olejcekova, Petra 348
 Oliveira, Cristieli S. M. 1088
 Oliveira, Fabiano 727
 Oliveira, Guilherme 424, 901
 Oliveira, Rita 495
 Oliver, Nentwich 1056
 Olkowski, Sandra **581**
 Olliaro, Piero L. **1413**, **253**, 205
 Ollo, Da **166**
 Olobo, Joseph 183
 Olsen, Sonja J. 407
 Olupot-Olupot, Peter **456**
 Olveda, Remigo 564, 1000, 1003
 Omar, Sabah 355
 Omarov, Asef 742
 Ombeva, Amanda 1077
 Omedo, Martin O. **562**, 563
 Omer, Samia 784
 Omonisi, Abidemi E. 699
 Omore, Richard 1405
 Omoregie, Philomena I. **674**
 Onajole, Bayo 646
 Onapa, Ambrose W. 388
 Onchiri, Frankline M. **337**
 Ong'echa, John 361, 657, 658
 Ongarora, Dennis S. B. **815**
 Ongecha, John M. 970
 Ongoiba, Aissata 1125, 1126, 451
 Ongus, Juliette 917
 Onigbogi, Modupe 242
 Onigbogi, Olanrewaju O. **242**
 Onlamoon, Nattawat **134**
 Onyamboko, Marie 649
 Onyango, Kevin O. 970
 Onyesom, Innocent **805**
 Opanda, Silvanos M. **1370**
 Opaschaitat, Pattarin 718
 Opata, Michael M. **187**
 Operario, Darwin J. **1079**, **573**
 Opi, Herbert 333
 Opinya, Fredrick 1089, 1090
 Opoka, Robert O. 1450, 1497, 165, 632, 456
 Opoku, Nicholas 1413, 253
 Opot, Benjamin 444
 Oraka, Chinedu O. **1224**, **918**
 Ore, Elsa 1378
 Ore, Marianela 1372
 Oregba, Ibrahim 646
 Orellana, David 1392
 Oremo, Jared 1033
 Oriá, Reinaldo B. 1407, 1408
 Oringanje, Chioma 1272
 Orish, Verner N. **763**
 Orozco, Maria del Carmen 1323
 Orozco, Susana 122
 Orr-Gonzalez, Sachy 1155
 Ortega, Corrie 976
 Ortega-Pierres, Guadalupe 1065
 Ortiz, Eliana 1105
 Ortiz, E. C. P. 274
 Osakunor, Derick 1302
 Osbak, Kara 67
 Oscar, Roland 1264, 1264, 213, 317, 847
 Osei, Joseph H. N. 367, **394**, 70
 Osei-Atweneboana, Mike 15, 32
 Osei-Mensah, Jubin 1187
 Osier, Faith 40, 662
 Osman, Sabariah 234
 Osorio, Jorge E. **1053**, 128, 514, 515, 601, 609, 1067, 1072, 588, 595
 Osorio, Lyda 610
 Osterbauer, Beth 370, 502, 542
 Osuna, Finnley 444
 Ota, Martin 916, 138
 Otchere, Joseph 142
 Oteng, Eugene K. **1151**
 Othman, Nurulhasanah 234
 Otiang, Elkanah 527
 Otieno, Godfrey A. 970
 Otieno, Lucas 970
 Otieno, Peter 1329
 Otieno, Silas 1327
 Otoo, Nana 171
 Ototo, Ednah N. **460**
 Otshudiema, John **1255**
 Ottesen, Eric 1075, 30
 Ouattara, Maurice San 503
 Ouédraogo, Alphonse 503, 841
 Ouédraogo, André Lin 503
 Ouédraogo, Georges Anicet 1344
 Ouédraogo, Jean Bosco 1330, 1344, 322, 386, 928
 Ouédraogo, Robert K. 1330, **386**
 Ouma, Fredrick R. 895
 Oumbouke, Welbeck A. **89**
 Oundo, Joseph 917
 Ouologuem, Dinkorma **1502**
 Oury, Timothy D. 907
 Overgaard, Hans J. 1345
 Owaga, Chrispin 1430
 Owen, Katey 516
 Owino, Brian 1396
 Owino, Simon 1493
 Owusu-Agyei, Seth 201, 459, 796
 Owusu-Mireku, Evelyn 87
 Oyegbami, Banji 636
 Oyemakinde, Akin 435
 Oyieke, Florence 374
 Oyo-Ita, Angela 1272
 Pablo, Jozelyn 344, 454
 Pabon, Amara G. 1446
 Pacca, Carolina 132
 Pacheco, M. Andreína **642**, **643**, 1299, **1300**
 Pacheco, Romina 39
 Pacheco, Victor 1384
 Paddock, Christopher D. 133
 Padmanabha, Harish **1055**
 Padungtod, Pawin **718**
 Paes, Cheryl 598
 Page, Anne-Laure 736
 Page, Connie 235
 Page, Martin 1285
 Pain, Arnab 641
 Paine, Mark 550
 Paintsil, Albert 87
 Pakuta, Elizabeth 740
 Pal, Subhamoy 1059, 113
 Palaci, Moises 464
 Palacios, Aida 145
 Palmeira, M. C. A. 82
 Palmer, Guy 527
 Pan, L. 244
 Pandharkar, Trupti 300
 Pang, Junxiong, Vincent **1223**, **585**
 Pangjai, Decha 718
 Paniagua, Gloria **1167**
 Panigrahi, Pinaki 1032
 Pant, Ganesh R. **432**
 PAPA, Anna 1466
 Pape Mbacke, Sembene 378
 Papenfuss, Tracey L. 303
 Paphavee, Lertsethtakarn 1079
 Paquette, Cynthia 942
 Parakkal, Jovvian G. **270**
 Paramasivan, R. 1074
 Parameswaran, Poornima 11, **125**, **1403**
 Parameswaran, Uma 635, 1251
 Parashar, Umesh D. 237, 446, 554, 613
 Pardo-Villamizar, Carlos 4
 Paredes, Antonio 466
 Paredes, Gladys 1024
 Paredes, Maribel 710
 Parham, Robin 1226
 Parish, Alice 679
 Park, Daniel J. 544
 Park, Gregory S. 165, 632
 Park, Lois 624
 Park, Seong Hee 1226
 Parker, Ben 1410
 Parker, Michael 616
 Parobek, Christian M. **468**, 824
 Parra, Marcela **218**
 Parra-Patiño, Beatriz 610
 Parry, Christopher M. 1479
 Parsonage, Derek 22
 Parsons, Marilyn 23
 Parsons, Teresa L. 974
 Partidos, Charalambos D. 514, 601, **609**
 Partin, Kathryn M. 978
 Partridge, Andrea 1157
 Pasay, Cielo 493
 Pascale, Juan Miguel 127, 129
 Passarelli, A. Lorena 689A
 Passini, Sione S. S. 1204
 Passos, Luzia M. R. 596, 612
 Passos, Sara T. **1022**
 Pastel, Charles 725
 Pastrana-Mena, Rebecca **1106**, 498
 Patarroyo, Manuel A. 95, 96
 Patel, Jaymin C. 277, **843**
 Patel, Manish 446, 554, 613
 Patel, Pranav 921
 Patel, Viral C. 1320
 Pathmeswaran, Arunasalam 1029
 Patiño, Lilian 1378
 Patrick, Jessica M. 741
 Patrickson, John 171
 Patrocínio, Paola 424
 Pattanapanyasat, Kovit 134
 Pattaradilokrat, Sittiporn **38**, 992
 Patterson, Njogu 66
 Patterson, Noelle B. 1148, 1148
 Paul, Kishor 106
 Paul, Oluwatobi 1214
 Paul, Repon C. 1073, 1404
 Paul, Susan **1289**
 Paula, Nathalia A. 283

The number(s) following author name refers to the abstract number.

- Paula, R. C. 274
 Paulsen, Dave 1353
 Paulson, Dave 1354
 Paveenkittiporn, Wantana 407
 Pavlinac, Patricia B. 140
 Pavluck, Alex 30, 961, **1075**
 Pawlowski, Michal 528
 Paxton, Lynn 210
 Paykel, Joanna E. 514
 Payne, Ruth O. **932**
 Paz, David 294
 Paz, Jorge R. **1220**
 Paz-Soldan, Valerie A. 342, 983, 517
 Peabody, David 129, 583
 Pearce, Cedric 260
 Pearson, Mark S. **1490**
 Pech-Dzib, M Y. 244
 Peck, Roger 263, **1207**
 Pede, Ellias 1454
 Pedersen, Amy B. 1068
 Pedersen, E. M. 1051
 Pedro-Rosa, Laura 1021
 Pei, Dong 874, **980**
 Peine, Kevin J. **303**, 722
 Pemo, Dechen **837**
 Penali, Louis K. 214
 Peñaranda, Katherin **1124**
 Penilla, R. Patricia **1338**
 Pennington, Luke 997
 Penny, Melissa 1282
 Penttinen, Pasi 1215
 Pepin, Christopher 328
 Pepin, Kim 748
 Pepper, Lauren 1010
 Peprah, Dorothy 685
 Perdomo, Erick 1349
 Perea, William 1470
 Pereira, Mayne O. 221
 Pereira, Thasciany M. 1088, 1197
 Pereira Bruno, Fernando **1103**
 Perera, Liyanage P. 2180
 Perez, Daniel R. 1392
 Perez, Elizabeth **899**
 Pérez, Erika S. 1192
 Pérez, Maria Angeles 121
 Perez, Pilar 107
 Perez-Padilla, Janice 114, 1189, 558, 989
 Perez-Zarate, Cory 672
 Periago, Maria V. 759
 Perkins, Douglas 361, 657, 658, 1127, 970
 Perkins, T. Alex 869, **984**
 Perlmann, Hedvig 543
 Perng, Guey-Chuen 134
 Perry, Jillian 942
 Persson, Kristina E. M. 1442
 Peruski, Leonard F. 466, 1481
 Petchey, Owen L. 1068
 Peters, David H. 77
 Peterson, A. Townsend 579
 Peterson, E. Anne 558
 Peterson, Jennifer K. **947**
 Peterson, Stefan S. 801
 Petrella, Selma 1206
 Petri, Jr., William A. 1506, 462, 1066, 1368
 Petruccelli, Chris 1253
 Petter, Michaela 667
 Petzold, Max 801
 Peyton, David H. 1269
 Pfaff, Jennifer 598
 Pfarr, Kenneth 1187
 Pfeil, Johannes 969
 Pfeil, Sarah 447, **53**
 Pham, Hong A. 50
 Pham, Phuong T. 218, 5
 Pham Vinh, Thanh **861**
 Phann, Sut-Thang 806
 Phanse, Yashdeep 942
 Phares, Christina 1036
 Philemon, Rune 556
 Phillipe, Max 349
 Phillips, Anna E. **1476**, **1478**
 Phillips, Richard O. 88
 Phiri, Themba 1428
 Phone Kyaw, Myat 506
 Phonpakobsin, Thipwipha **443**
 Phuong, Duong Hue 14
 Phyo, Aung Pyae 328
 Pi, Wenlong **903**, 904
 Pi-Bansa, Sellase A. **367**, 394
 Pica-Mattocchia, Livia 954
 Picado, Albert 775
 Piccoli, Luca 535
 Pichugin, Alexander **1147**, **1147**
 Pickett, Gavin 361
 Picot, Stéphane **794**, **810**
 Pidtana, Kingkan 1324
 Piera, Kim A. 4
 Pierce, Kristen K. 512
 Pierce, Raymond 901
 Pierce, Susan K. 1441
 Piermarini, Peter M. 1110
 Pierson, Theodore C. 513, 1398, 1402
 Pigott, David M. **1418**
 Pike, Andrew **1357**, 695, 97
 Pike, Brian 709
 Pilat, Sandra 1198
 Pilishvili, Tamara 1374
 Pillai, Dylan R. 1101
 Pillay, Allan 961
 Pilotte, Nils 256
 Pimentel, Guillermo 1185
 Pinilla, Yudi T. 95, 96
 Pinsky, Benjamin A. 115
 Pinto, Jesus A. 1461
 Pinto, Maria T. Candido. 681
 Pintye, Jillian 423
 Pion, Sébastien D. 1046, **757**, 1043, 1417, 15, 264
 Pischel, Lauren 1149, 1149, 227, 452
 Pitaka, Freda 961
 Pitcher, Sylvie 473
 Pitts, Sidney 171
 Pitzer, Virginia 1480
 Pizango, Melita 1178
 Plattner, Jacob J. 1424, 301, 648, 811
 Platts-Mills, James **1406**, **1410**
 Plieskatt, Jordan L. 1489
 Plowe, Christopher V. 1266, 1267, 1296, 1443, 321, 328, 484, 506, 825, 864
 Pluschke, Gerd 1173, **1176**, 87
 Poespoprodjo, Jeanne R. 461
 Pogliano, Joseph 278
 Pohanka, Miroslav **1166**
 Poirier, Mathieu J. P. **1038**
 Poirot, Eugénie **1277**
 Pok, Kwoon-Yong 586
 Pokorny, Rolf 645
 Polderman, Anton M. 490
 Pollack, Henry 884
 Polley, Spencer 1286
 Polman, Katja 483, 490, **496**, 560, **760**
 Polonsky, Jonathan 910
 Poluda, David 603
 Polupan, Ivan 1393, 1394
 Poly, Frederic 709
 Ponce de Leon, Gabriel 1305
 Pond, Bob **1290**, 857
 Pond-Tor, Sunthorn 452, 1436, 668, 1000, 1003, 1150
 Pongsiri, Arissara 391
 Ponlawat, Alongkot 117, 391, 392, 395
 Ponnusamy, Loganathan 517
 Pontvianne, Jérémy 593
 Poole-Smith, B. K. **872**
 Poplett, Iain J. F. 621
 Popov, Vsevolod L. 1356, 1382
 Popper, Stephen J. 601, **606**
 Porcella, Stephen F. 215, 967
 Porco, Travis C. 285
 Porkaipandian, T. 1074
 Portaels, Françoise 83, 84
 Porter, Jessica L. 83
 Portugal, Silvia **1125**, 1126
 Postels, Douglas G. **245**
 Potchen, Michael J. 245
 Pou, Sovitj 43, 820
 Pourmand, Nader 1403
 Pova, Marinete M. 1114
 Powell, Diana S. 907
 Powell, Michael 629
 Powers, Ann 103
 Poyer, Stephen 1145, **178**, **179**
 Poyomtip, Teera 272
 Pozymniuk, A. V. 1395
 Prachumsri, Jetsumon S. 670
 Prado, Roberta O. P. **488**, 1241
 Prakash, Aishya 1416
 Prakash, Manu 1092, 529
 Prasad, Abhishek N. **1468**
 Pratlong, Francine 1418
 Premawansa, Gayani 607
 Premawansa, Sunil 607
 Prescott, Joseph 913
 Price, Ric N. **461**, **654**, 822, 508
 Prichard, Roger K. 15, 32
 Proaño, Jefferson V. 534
 Prom, Satharath 1324, 806
 Protopoff, Nattacha 550
 Prouty, Michael 1181
 Prudencio, Walter 1179
 Prudhomme O'Meara, Wendy 549
 Przysiecki, Craig 1155
 Psychas, Paul 857
 Pu, Christy 329
 Puddicombe, Babajide J. **636**
 Puddicombe, Tolulope 636
 Puffer, Bridget 594
 Puig-Ramos, Anabel 989
 Pukuta, Elisabeth 1380, 51
 Puleh, Steven S. **199**
 Pulford, Justin 1289, 797
 Pullan, Rachel L. 1448, 1474
 Pulliam, Juliet R. C. **1073**
 Pupilampu, Naiki 90
 Pyae Phyo, Aung 506
 Pybus, Brandon 180, 182, 817, 973
-
- Q**
- Qadri, Firdausi **958**, 959, 955, 1188, 701
 Qiao, Li 706
 Quakyi, Isabella 225, 5
 Quashie, Neils 507
 Queiroz, Rafaella F. G. **1196**
 Quenin-Fosu, Kwabena 87
 Quetz, Josiane S. 1408
 Quezada, Wilmer M. 307
 Quick, Robert 957, 1033
 Quicke, Kendra 191
 Quiner, Claire A. 11
 Quintanilla Calderón, Javier E. 1420
 Quintero, Gustavo E. **1180**
 Quintero, Juan Pablo 6
 Quintero, Juan P. 795
 Quispe, Antonio M. 1120, 1120, 1309
 Quispe, Carmen 1378
 Quispe-Machaca, Victor 781, 1420
 Qureshi, Ammar 42B
 Qureshi, Shahida M. 413, 1079
-
- R**
- Rabarova, Lenka 1219
 Rabi, Olawunmi R. 1303

The number(s) following author name refers to the abstract number.

- Rachmat, Agus 827
 Radhakrishnan, Anuradha 66
 Radheshyam, K. **1449**
 Radley, David 516
 Raghavan, Nithya 902
 Rahardjo, Mardi 879
 Rahman, Atiqur 959
 Rahman, Hasan A. 334
 Rahman, Mahmudur 1203, 1404, 141, 237, 440, 442, 52, 915, 940
 Rahman, Md. Anisur 937
 Rahman, Md. Arif 955
 Rahman, Md. Mostafizur 141
 Rahman, Md. Ziaur 52
 Rahman, Mustafizur 237
 Rai, Madhukar 291, 782, 785
 Raj, Dipak K. 1149, 1149, **1150**, 1436, 227, **452**, 668, 923
 Rajamanickam, Anuradha **966**
 Rajaram, Murugesan V. S. 1171
 Raju, Kanumuri S. R. 807
 Rajwans, Nimerta 1492
 Rakasz, Eva G. 609
 Ralevski, Filip 799
 Ralston, Katherine **1506**
 Ram, Pavani K. 1405, **937**
 Ramachandran, Veena **884**
 Ramadan, Mohamed A. 892
 Ramal, Cesar 1178
 Ramalho, Alanderson 1197
 Ramalho-Ortigao, Marcelo 1017, 576
 Rambeloso Zo, Jariseta **1083**
 Ramgopal, Sheila **250**
 Ramirez, Ana L. 1392
 Ramirez, Juan-David 71
 Ramirez-Hernández, Alejandro 94
 Ramirez-Sierra, Maria Jesus 1245, 566
 Ramli, Norlisah 28
 Ramos, Mariana 1179, 1372
 Ramos-Castañeda, José 1062, 604
 Ramos-Cerrillo, Blanca 1444
 Ramos-Jimenez, Javier 986, 597
 Rampton, Melanie 493
 Ramsan, Mahdi 1133, 1231, 1233, 550
 Ranade, Ranae M. 1021
 Ranaivo, Louise 1070
 Ranarivelo, Lalasoanirina 168
 Ranasinghe, Udaya S. B. **1452**, 1473
 Rancancoj, Cesar 1481
 Randolph, Ryan 1226
 Ranford-Cartwright, Lisa C. 360, 1328
 Rang, Chandary 202
 Ranson, Hilary 1463, 376
 Ranucci, Elisabetta 498
 Rao, Gouthami G. **277**
 Rao, Ramakrishna U. 1452, **1473**
 Rao, Sowmya R. 1445
 Rao, V. Bhargavi **735**
 Raphemot, Rene **1110**
 Rasgon, Jason L. 1214
 Rasmussen, Stephanie A. 1271
 Rasmussen, Zeba A. 1409, **413**
 Raso, Giovanna 1239
 Ratanawong, Pitcha 988
 Rathore, Sumit 811
 Ratshipa, Odie 613
 Ratsimbasoa, Arsène 996, 1254
 RattanadilokNaBhuket, Ponchanok 1036
 Raucinova, M. 409
 Rausch, Kelly 930
 Raviprakash, Kanakatte 113
 Raviwharman, P. **1063**
 Rawago, Fredrick 998
 Ray, Debalina **774**
 Rayan, Hanan Z. 271
 Raybaud, Benoit 1283
 Raymond, Max 1037, 525
 Rayner, Julian 1005, **927**, 215
 Raza, Afsheen **154**, **319**
 Razuri, Hugo 1375, 1384, 445, 703
 Reaves, Erik J. 1387, 431
 Rebelo, Maria **318**
 Rebollo, Maria P. **262**, 1473
 Rebollo Polo, Maria **1453**
 Reda, Ayalu A. 135
 Reddy, Michael 1345
 Reed, Douglas S. 907
 Reed, Sharon L. 22
 Reed, Steven G. 1422, 1439, 930, 216
 Reeder, John 157
 Reese, Heather 685
 Regna, Kimberly 1348, **1360**
 Regules, Jason 1154
 Rehman, Najeeb Ur 1066
 Reichard, Gregory 180, 182
 Reid, Molly C. 23, 27
 Reiling, Linda 1442, 40
 Reiman, Jennifer 449
 Reimer, Lisa 574
 Reimer, Melissa 1423
 Reiner, Jr., Robert C. **983**, 984, 581, **869**
 Reinhart, Caroline 1422
 Reis, Dener C. 283
 Reis, Mitermayer G. 1204, 1484, 524
 Reis, Renato B. 1484, 524
 Reisen, William K. 869
 Reiter, Karine 215, 930
 Reither, Klaus 1371
 Reithinger, Richard 1448
 Relman, David A. 601, 606
 Remme, Jan H.F. 1457, 286
 Remoue, Franck 390
 Remppis, Jonathan 1367
 Remy, Christine 841
 Rendell, Sara **623**
 Rendell, Victoria **734**
 Renier, Geneviève 144
 Renom, Montse 1198
 Requena, Edwin 518
 Ressenner, Roseanne 727
 Reyburn, Hugh 1194, 556
 Reyes, Lissette 277
 Reyes, Sharina 1161
 Reyes-Solis, Guadalupe 1462
 Reynolds, Mary G. 51, **740**
 Rheingans, Richard D. 1084, 1087
 Ribacke, Ulf 1317, 1317
 Ribeiro, Fernanda L. **424**
 Ribeiro, Guilherme S. 1484, 524
 Ribeiro, Paula 1435
 Ribeiro-Rodrigues, Rodrigo 464
 Ribolla, Paulo E. M. 1359
 Rice, Benjamin L. **1299**
 Richard, Stephanie A. **1095**, **1409**, 288, 289
 Richards, Allen 744
 Richards, Bethany 578
 Richards, Frank 1454
 Richards, Jack S. 1442, 662
 Richards, Stephanie L. 108, **878**
 Richards-Kortum, Rebecca 528
 Richardson, Barbra A. 1025
 Richardson, Jason 117, 392, 395
 Richardson, Monica 997
 Richesson, Douglas 733
 Richie, Nancy 226
 Richie, Thomas 1148, 1148, 1160, 1161, 1313, 1437, 226, 1153, 1154, 1159, **933**
 Richman, Adam **979**
 Richterova, Lenka **1328**
 Ricopa, Leonila 1120, 1120
 Ridl, Frances 1345
 Riewpaiboon, Arthorn 1067
 Rigamonti, Francesco 741
 Riley, Eleanor 1121, 1121, 195
 Riley, Frank 164
 Rinaldi, Francesca 231, 535
 Rinaldi, Gabriel 416, **896**
 Ringwald, Pascal 1266, 328, 506
 Rios, Maria 118, 1216, 1217
 Rios, Paul 1172
 Ripin, David 1229
 Rippon, Emily J. 1460
 Riscoe, Michael K. 1271, 1273, 43, **820**, 817
 Risha, Peter 770
 Ritter, Grant 1329
 Rivard, Robert G. 1169, 1185
 Rivas, Juan J. 721
 Rivas, Kasey L. 23, 27
 Rivas Estilla, Ana María 597, 986
 Rivera, Aidsa 133, 558
 Rivera, Irma 133
 Rivera, Pilarita T. 793, 950, 565
 Rivera, Zeyana S. 1439
 Rivera-Garcia, Brenda 1189
 Riveron, Jacob M. 1459
 Riveron Miranda, Jacob 1107, **691**
 Riveros, Maribel D. **720**
 Robb, Katharine A. **683**, 685
 Robello, Carlos 384
 Roberts, Alero A. 730
 Roberts, Elishia 916
 Robinson, Eve 1215
 Robinson, Leanne 1257
 Roca, Anna 1483
 Roca-Feltrer, Arantxa 202
 Roch, Dabire 687
 Rocha, Claudio **1179**, 1381, 1387, 431, 711, 713, 983, 1178
 Rocha, Manuel **697**
 Rocha, Manoel Otávio C. 1241
 Rocha, Mariana V. 221
 Rocha, Nivison J. 1484
 Rochford, Rosemary 1089, 1090, 819
 Rock, Fernando 811
 Rockett, Kirk A. 333
 Roda, Aldo 45
 Rodrigues, Alex M. 1199
 Rodrigues, Maria G. M. 1484
 Rodrigues, Mauricio M. 217, 221
 Rodrigues, Silvia 533
 Rodriguez, Alejandro 1027
 Rodriguez, Alfonso 1170
 Rodriguez, Ana 1014, 1421, 298, 634
 Rodriguez, Betzabe **325**
 Rodriguez, Bibiana 449
 Rodriguez, Cynthia M. **600**
 Rodríguez, Edda 133
 Rodriguez, Jairo 610
 Rodriguez, Pamela 1124, **1131**
 Rodríguez, Rosa 133
 Rodriguez, Virginia 1180
 Rodriguez-Barraquer, Isabel 510, **511**
 Roellig, Dawn 883
 Roestenberg, Meta 454
 Rogatcheva, Margarita 706
 Rogers, Alexandra R. 890
 Rogers, William O. 827
 Rogerson, Stephen J. 505, 1291
 Rogier, Eric 317
 Roguski, Katherine M. 683
 Rohousova, Iva 304
 Rojas, Ernesto 296
 Rojas, Jesus 709
 Rojas Cabrera, Ernesto 294
 Rojas Rivero, Lázara 760
 Rojas-Alvarez, Diana P. 610
 Roldan, Aleida 1481
 Rollin, Pierre 1379, 1380, 910
 Röltgen, Katharina **1173**
 Roman, Elaine **206**
 Roman Sierra, Jazmin 1189

The number(s) following author name refers to the abstract number.

- Romano, Candice 1375
 Romero, Ada 1386
 Romero, Candice 467, **703**
 Romero-Vivas, Claudia 610
 Romo, Hannah 1466
 Ronceros-Mayorga, Victor 672
 Rono, Martin 156, **162**
 Ronveaux, Olivier 1470
 Roobsoong, Wanlapa **161**
 Roos, David 1502
 Rosado-Vallado, Miguel 1245
 Rosales Chilama, Mariana **787**
 Rosanas-Urgell, Anna 1312, 861
 Roschnik, Natalie 975
 Rosenberg, Corey 1338
 Rosenthal, Philip J. 1269, 181, 195, 344, 370, 502, 504, 542, 648, 811, 821, 1306
 Roskin, Krishna 1403
 Ross, Allen G. 564
 Ross, David A. 66
 Ross, Joshua V. 508
 Ross, Leila S. **925**
 Ross-Degnan, Dennis 77
 Rossatanga, Elie G. 251, 494
 Rossi, Cindy 592, 917
 Rossignol, Emmanuel 731
 Rostal, Melinda K. **914**
 Rothman, Alan L. 117
 Rotman, Lily R. **411**
 Rotondo, Lisa 1233
 Rottman, Daniel 349
 Rouhani, Saba 975
 Rouhier, Matthew F. 1110
 Rousell, Vicki M. 42B
 Roussel, Camille 1012
 Rout, Jonathan 1416
 Rout, Michael 1499
 Rowan, Tim 1424, 301
 Rowcliffe, Kerry 46
 Rowe, Alexander K. **77**
 Rowe, Emily **124**
 Rowe, Michael D. 621
 Rowe, Samantha Y. 77
 Rowland, Mark 379
 Rowlinson, Emily 1185
 Rowton, Edgar D. 871
 Roy, Sharon L. 1028, 277
 Royal, Scott 1399
 Royals, Michael 609
 Rubach, Matthew P. **1098**
 Rubahika, Denis 204
 Rubiano-Cardona, Kelly 1162
 Rubio, Justin P. 42B
 Rucker, Joseph 598
 Rudge, James W. 412
 Rueangweerayut, Ronnatrai 42B
 Ruel, Theodore 181
 Ruf, Marie-Thérèse 1173, 1176, 87
 Ruiz Moreno, Diego 63
 Ruiz-Ortega, Marta 634
 Rujeni, Nadine 483, 489
- Ruktanonchai, Nick **842**
 Rumunu, John 375
 Rupp, Richard 1053
 Rush, A. C. 258
 Rushdi Shakri, Ahmad 932
 Russart, Nathan M. **750**
 Russell, Amy 516
 Russell, Tanya L. 1283, **523**
 Rutagwera, Marie-Reine I. 1295
 Rutta, Acleus S. M. 1427
 Rutvisuttinunt, Wiriyā **441**
 Ruwona, Tinashe B. 486
 Ryan, Edward T. 1188, 1445, 959, 955
 Ryman, Kate D. 56
- S**
- Saade, Camille A. **76**
 Saavedra, Marlon 1359
 Saavedra-Rodriguez, Karla 1338, 1347, 60, **1462**
 Sabhareon, Arunee 515
 Sabeti, Pardis 7, 544
 Sachs, Paige **521**
 Sack, R. Bradley 1409
 Sacko, Moussa 975
 Sacks, David 73, 775
 Sacks, Leonard **725**
 Sadi, Johari Y. 1427
 Sadi, Sulaiman 691
 Sadumeh, Ibrahim 1374
 Sady, Hany 897
 Saganda, Wilbrod 249
 Sagara, Isiaka 1096
 Sagara, Issaka 929
 Sage, Mike 1374
 Saghinadze, Salome 1169
 Saglib, Marianne 1000, 1003
 Sagnon, N'Fale 1463
 Saha, Amit **701**, 958
 Sahondra, Randrianasolo Bodo 490
 Sahoo, Malaya K. 115
 Sahu, Bikash R. **663**, 991
 Sahu, Rajnish 182
 Saidin, Syazwan 234
 Saito, Mayuko 1387, 197
 Sakyi, Kojo Y. **380**
 Salamat, Maria S. 565
 Salanti, Ali 1158, 1158
 Salas, Carola J. **509**
 Salawu, Oluwakanyinsola 168
 Salazar, Fabian 1027, 891, 912
 Salazar Sanchez, Renzo 304
 Salgado, Doris 610
 Salgado, Rene 500, 859
 Salgame, Padmini 464
 Saliez, Nicolas 736
 Salifu, Hassana **151**, 357
 Salihi, Magdi 630
 Saliki, Aurelien 251
- Salim, Mohammed 478
 Sall, Amadou A. 1202, 1385, 921, 1058
 Salmalvides, Frine 107
 Salmon, Charleen N. C. 677
 Salmon-Mulanovich, Gabriela 1384
 Salyer, Stephanie 112
 Sam, Sing-Sin 1056, 28
 Sam-Yellowe, Tobili 362
 Samad, Rasheda 1479
 Samake, Sibiry 99
 Samarasekera, Sandhya D. 1452
 Samb, Badara **1113**
 Samuel, P. Philip 1074
 Samuels, Aaron M. 1020
 Samy, Abdallah M. **579**
 Sanabria, Darío 133
 Sanchez, Jorge 1174, 1227
 Sanchez, Juan F. 1128, 1192, 509, 711
 Sanchez, Liz 1174
 Sanchez, Maria 1390
 Sande, John 1136, 211, 212
 Sandemann, H. 349
 Sanders, Emily 1080
 Sanders, Virginia 1424, 811, 301
 Sandi, Frank 35
 Sandiford, Simone 690, **695**
 Sandoval, Carlos 1027, 891, 912
 Sang, Edna 549
 Sang, James 628
 Sang, Rosemary 592, 917, **920**
 Sangaé, Ibrahim 928
 Sangala, Jules 1125, 451
 Sangare, Lansana 1270, 1270, 1308, 2, 818
 Sangaré, Laura R. 1025
 Sangeda, Raphael Z. 65, 770
 Sanieel, Ofelia 565
 Saniova, Beata 176
 Sanogo, Kassim 823
 Sanogo, Zana 99
 Sanou, Antoine 1463
 Santa Maria, Maria L. S. 596
 Santamaria, Ana 644
 Santana, Francisco S. 524
 Santangelo, Joseph 1053, 515
 Santara, Gaoussou 457, 853
 Santiago, Félix W. **1390**
 Santiago, Gilberto A. **119**, 1401, **986**, 114
 Santiago, Luis M. 1401
 Santolalla, Meddy L. 1120, 1120, **358**
 Santos, Andreia C. 524
 Santos, Roberto 411
 Santos, Rodrigo I. 746
 Sanz, Laura **44**, 648
 Sapozhnikov, V. I. 908
 Sarah Pisarcik, Sarah 744
 Saraiva, Roberto M. 1241
 Sardi, Francesca 535
- Sari, Men 1362
 Sariol, Carlos 515
 Sarkar, Dhiman 168, 803
 Sarpong, Doris 75
 Sarveswaran, Thaameran 526
 Sasaki, Rie 1490, 344
 Sather, Mark 818
 Satimai, Wichai 321, 506, 831, 843, 864
 Satoskar, Abhay 1023, 303, 1019, 244
 Sattabongkot, Jetsumon 1315, 350, 352
 Satter, Syed M. 1404, **237**
 Sauerwein, Robert W. 220, 450, 453, 503, 976, 454, 816
 Saunders, David 1104, 1321, 243, 328, 506, 806, 864, 1324
 Saunders, Sean P. 1504
 Sausen, Katherine 370
 Sausser, Michele 516
 Savatory, Florence **1491**
 Saville, Melanie 590
 Savioli, Lorenzo 1453
 Sawadogo, Simon P. 1364, 386
 Sawatwong, Pongpun **407**
 Sawers, Larry **1221**, 26
 Sawyer, Kelly A. 628
 Sayeed, Abdullah A. 1479
 Sazzad, Hossain M. S. 1073, **1203**, **440**, 915, 940, 52
 Scaglia, Massimo 756
 Scaraffia, Patricia Y. **475**, **686**
 Schaad, Nicolas 738
 Schafer, Ilana 1379, 910, **1380**
 Schaffner, Stephen F. 544
 Schal, Coby 517
 Scharf, Rebecca J. 462
 Schats, Remko 450, **453**
 Schatzkin, Eric **1086**, **1307**
 Schaub, Günter A. 304
 Scheele, Suzanne 23
 Schellenberg, David 735
 Schickel, Jean-Nicolas 1441
 Schiehser, Guy 46
 Schiff, Amanda 525
 Schiller, Emily 279
 Schiller, Ian 1376
 Schilperoord, Marian 66
 Schlesinger, Larry S. 1171
 Schlosser, Andreus 1197
 Schmid, Michael **116**, **12**
 Schmidt, Berit A. 1286
 Schmidt, Michael 1054
 Schmidt, Robert 165
 Schmidt Chanasit, Jonas 615
 Schmittgen, Thomas 300
 Schneider, Bradley S. 905
 Schneider, Kristan 1267
 Schock, Sara 1226
 Schoepp, Randy 592, 917, 1388
 Schofield, Louis 1198
 Scholzen, Anja 220, 450, 453

The number(s) following author name refers to the abstract number.

- Schonenberger, Klaus 1285
 Schountz, Tony **913**
 Schriewer, Alexander 1032
 Schubert, Joan 499
 Schully, Kevin L. **722**
 Schulte, Leigh **949**
 Schultsz, Constance 1482
 Schuster, Steffen 1501
 Schwach, Frank 927
 Schwanck Khilji, Sara U. **412**
 Schwartz, Alanna **1306**
 Schwartz, David A. 1250
 Schwartz, Ira B. 511
 Schwarz, Alexandra **304**
 Sciotti, Richard 182
 Scobie, Heather 1036
 Scott, Thomas W. 104, 117, 460, 517, 581, 63, 983, 984
 Screation, Gavin R 1400
 Se, Youry 1324, 328, 506, 806, 822
 Sea, Darapiseth 1324, 806
 Seaman, Jonathan 383, 1351
 Sebastian, Ellen 606
 Seck, Mame C. 268
 Seckel, Laura 81, **1082**
 Seckova, Silvia 176
 Secor, W. Evan 562, 563, 895
 Sedegah, Martha 1148, 1148, 1160, **1437**, 218, **226**
 Seder, Robert A. 223, 228, 1437
 Seemann, Torsten 83
 Segeja, Method D. 830, 850
 Segovia, Karen **1384**, 445
 Segovia, Maikell 71
 Segura, Eddy 1174
 Segura, Nidya A. 94, 95, 96
 Seim, Anders 288, 289
 Sejvar, James 1185, 1203
 Sekuloski, Silvana 219, 48
 Selby, Richmond A. 207, 1325
 Seligman, Stephen J. **1208**
 Selling, Katarina E. 801
 Selvapandiyam, Angamuthu 1019
 Selvi, S. Karthigai 1074
 Sembuche, Samuel 1427, 170
 Semnani, Roshanak T. 968
 Semrau, Katherine **1078**, 653
 Senarathna, Buddhika P. 1029
 Sene, Papa Diogoye 327
 SenguptaBanerjee, Aditi 991
 Senkoro, Kesheni 1231
 Senra, Cassia 759
 Sepulveda, Nuno **641**
 Serafini, Micaela 209
 Sereerak, Piya 419
 Serghides, Lena 1011
 Serpa, Jose A. **248**
 Serrano, Javier 133
 Serrao, Aurelio 946
 Serrato, Idalba M. 1363
 Serre, David **1319**, **1319**, 259, 574, 7, 996
 Serre, Nuria 603
 Sesay, Sanie 331
 Sethuraman, Karthik 1420
 Setiabudy, Rianto 175
 Settinayake, Sunil 1452
 Severson, David W. 59
 Seydel, Karl B. 1292, 245, 800, 1495, 160
 Seymour, Robert 1382
 Seyoum, Aklilu 1134
 Shabani, Estela **165**
 Shadomy, Sean V. 1189
 Shaffer, Jeffrey 1425
 Shaggari, Shehu 1430
 Shah, Jui 1333
 Shah, Monica 1132, 1136, 1288, 150, 211, 212, 455, 852
 Shah, Shivang 333
 Shah Muhammad, Bilquees 1483
 Shah-Simpson, Sheena 1500
 Shaha, Chandrima 300
 Shahum, Andrea **1219**, 764
 Shakarishvili, Roman 1185
 Shamsuzzaman, Abul K. Mohammad. 442
 Shanks, G. Dennis 182, 46, **844**, 1276
 Sharakhov, Igor V. 1111, 1115, 469, 59
 Sharakhova, Maria V. **1111**, 59, 59, 60
 Sharief, Abdalla H. **784**
 Sharif, Ahmad Raihan 141, 442, 940
 Sharma, Amit M. **417**
 Sharma, Namita 417
 Sharma, S. 722
 Sharp, Tyler 112, 989, **114**, 1189
 Shastri, Ghanshyam 417
 Shaw, Jeffrey J. **274**, **791**
 Shaw, Timothy I. 913
 Shehata, Magdi G. 579
 Sheils, Orla 1504
 Shelat, Anang 293
 Shelite, Thomas R. 1164, **716**
 Shepard, Donald S. **1074**, **1094**, 1329, **1337**, 571, 580, **79**, 1061, **1062**, 1063
 Sherbuk, Jacqueline 780
 Sherrill-Mix, Scott 607
 Shewchuk, Tanya 178, 179
 Shi, Ya Ping 1252, 1431
 Shieh, Hong-Ming 46
 Shieh, Wun-Ju 133
 Shields, Alicia 688
 Shieshia, Mildred 1076, 1077, **619**, 80
 Shiferaw, Miriam **741**
 Shiff, Clive J. 952
 Shikani, Henry **152**, 1103
 Shilpakar, Olita 1449
 Shimp, Jr., Richard 930
 Shin, Dongyoung 694
 Shin, Jang-Sik 645
 Shinzawa, Naoaki 1314
 Shoemaker, Trevor **1379**, 1380, 910
 Shongo, Robert 1380, 740
 Shongo Lushima, Robert 51
 Short, Sarah M. **569**
 Showalter, Julia 1087
 Shrestha, Rishav 1449
 Shu, Meng-Hooi 1056
 Shuai, Zhisheng **707**
 Shuaibu, Mohammed N. 656
 Shutes, Erin 140
 Sianongo, Sandie 561
 Siba, Peter M. 1289, 1442, 1455, 259, 667, 797, 1122, 1257, 1291, 574
 Sibley, Carol H. 214, 830
 Siby, Fanta 794
 Siciliano, Giulia 45
 Sicuri, Elisa 286
 Sidibe, Bakari 1096, 1274, 823
 Sidibe, Souleymane 1232
 Sidibe, Youssoufa 457, 853
 Siedner, Mark 236
 Sierra, Gloria M. 130, 131
 Signore, Michele 45
 Sihuincha, Moises 1120, 1120, 1178, 1192, 1309, 726
 Sikaala, Chadwick H. **1134**, **1339**
 Sikomyu, Esther 189, 193
 Silal, Sheetal P. **1144**
 Silapong, Sasikorn 1079
 Silhraova, Barbora 176, 348, 349
 Silkey, Mariabeth **1287**
 Sillah, Ansumana 1230
 Silumbe, Kafula 1301, 1425, **540**, 546
 Silva, Adriano Q. 524
 Silva, Aline 1197
 Silva, Brenda G. 1349
 Silva, Dyana A. D. 1052, 611
 Silva, Fernanda M. F. 596
 Silva, Joana C. 25, 328, 506, **894**
 Silva, Luciano K. 1204
 Silva, Manori 1029
 Silva, Marita 467
 Silva, Maria E. 1381, 1384, 1387, 431, 445, 703
 Silva, Rute C. 923
 Silva, Wilson 69
 Silva-Pereira, Rosiane 424
 Silver, Karlee L. 1015
 Silvera, Juan 1372
 Silvestrini, Francesco 45
 Sim, B. Kim Lee 1438, 229, 979, 223, 220
 Sim, Shuzhen 981
 Sima, Michal **749**
 Simam, Joan **156**, 162
 Simard, Frederic 1111, 1115, 1344, 1364
 Simaro, Perez 772
 Simasathien, Sriluck 515
 Simen, Birgitte B. 1403
 Simmons, Cameron 14
 Simmons, Graham 905
 Simon, Alistidia 31
 Simon, Gregoire 1501
 Simons, Evan 1058, 1385
 Simons, Mark P. **1172**, **1174**, **1386**, **709**, **710**
 Simonsen, P. E. 1051
 Simpson, Andrew J. 1169
 Simpson, Diane 613
 Simpson, Julie A. 1263, 1263, 1291, 461, 822
 Sims, Sharanie 1195
 Sinden, Robert E. 1152, 928, 497
 Singa, Benson 1025
 Singer, Alexandra L. **1160**
 Singer, Steven 29, 882
 Singh, Abhishek K. 775, **785**
 Singh, Neetu 73, 775
 Singh, Om Prakash 73, **775**
 Singh, Rudra P. 775
 Singh, Shailesh 629
 Singh, Shio K. 807
 Sinha, Indranil 1096
 Sinkinson, Craig A. 1182
 Sintasath, David 1138, 1335, 202
 Sintorini, Margareta M. Sintorini. **875**
 Siqueira-Neto, Jair L. 774
 Sirichaisinthop, Jeeraphat 670
 Sirikajornpan, Kanittha 120
 Sirima, Sodiomon B. 174, 809, 503
 Siripokasupkul, Raveewan 806
 Sirivichayakul, Chukiat 1067, 1072, 515, 588, 595
 Sironen, Tarja 50
 Sissako, Aliou 818
 Siwo, Geoffrey 1006
 Skarbinski, Jacek 1252, 1268
 Skern, Tim 1202
 Skinner, Danielle E. 896
 Skinner, Jeff 1125, **1129**
 Skinner-Adams, Tina S. 47
 Skipetrova, Anna 591
 Slade, Jeremiah R. 1351
 Sladeckova, Veronika 1219
 Slaney, David 508
 Slayton, Rachel B. **1033**
 Sleshi, Markos 1451
 Slotman, Michel A. 1345, 472, 1118
 Slutsker, Laurence 851
 Small, Pamela **85**, 86
 Small, Scott T. **259**
 Smartt, Chelsea T. **694**
 Smith, Barbara 385
 Smith, Cassandra 1350

The number(s) following author name refers to the abstract number.

- Smith, David L. 842, 862, 984
 Smith, Darci R. 1468
 Smith, Emily 1148, 1153
 Smith, Jared 1044
 Smith, Jeffery 214
 Smith, John A. S. 621
 Smith, Joshua 573
 Smith, Jeffery J. 1266, 321
 Smith, Meghan J. **159, 160**
 Smith, Nannette 310
 Smith, Ryan C. **977**
 Smith, Scott 13
 Smith, Stephen 385
 Smith, Thomas **1282**, 520, 1287
 Smith-Nuñez, Edward S. 1120, 1120, 1128, **1309**
 Smolinski, Mark 625
 Smout, Michael J. **420A**
 Smyth, Gordon K. 1198
 Snow, Christopher D. 978
 So, Mary 806
 Soares, Alberto M. 1407, 1408
 Soares, Irene S. 217, **221**
 Soares, R. C. 274
 Soares Magalhães, Ricardo J. **281, 565**
 Sobral, Mariana C. M. 596
 Sobsey, Mark 684
 Sobuz, Shihab Uddin 1079
 Socheat, Duong 1362, 328, 506, 822
 Socías, Eugenia 1024
 Soe, Aye Yu 1138, 1335
 Soebiyanto, Radina P. **465**
 Soenarto, Yati 461
 Sognikin, Koffi S. 1475, 288, 289
 Sogoba, Nafomon 1308
 Sogoba, Sanata 765
 Soh, Eugene 806
 Soisson, Lorraine 1443, 226
 Sokana, Oliver 961
 Sokolova, Jaroslava 1219, 348, 409, 764, 769
 Solarte, Yesid 931
 Solga, Michael D. 1506
 Soliman, Rasha H. **271**
 Solomon, Anthony 35, 1075, 961
 Solomon, Corvil 112
 Solomon, Hiwot 1311
 Solomon, Wesley **171**, 357
 Sombo, Marie-Therese 235
 Some, Fabrice A. 322
 Somethy, Sok 806
 Sonde, Hesbon 917
 Sondorp, Egbert 66
 Sonoiki, Ebere **811**
 Soong, Lynn 716, 1164
 Sopoh, Ghislain 1177, 84, 85
 Soremekun, Seyi **939**
 Sosa, Silvia M. 1392
 Sosa, Wilfredo 600
 Sotgiu, Giovanni 1371
 Soti, David 551
 Sotillo, Javier 420A
 Sotir, Mark J. 1445
 Soto, Gabriela 1372
 Soto, Giselle M. **1372**
 Soto, Jaime 296
 Soto Bravo, Aida 325
 Soto Lacouture, Hugo 1349
 Soto-Gomez, Eunice 582
 Sougoufara, Seynabou **378**
 Soulama, Issiaka **809**
 Soumaoro, Lamine 400, 967
 Sousa, Carla 109
 Sousa, Giovane R. 1241
 Sousa, Jason 180, 182, 817, 973
 Sousa-Figueiredo, José C. 281
 Souza, Natália V. 1052
 Souza, Renato P. **1206**
 Souza, Robson P. 427
 Sow, Amadou 323
 Sow, Doudou 1137, 548
 Sow, Samba O. 765
 Spangler, Maribeth 1320
 Sparwasser, Tim 1504
 Spates, Kathryn E. 1446
 Speake, Cate 1147, 1147
 Speare, Richard 1414
 Speck, Samuel H. 637
 Spence, Philip J. 450
 Speybroeck, Niko 49, 861
 Spiegel, Jerry 626
 Spiegel, Paul 66
 Spiropoulou, Christina 1380
 Spithill, Terry 449
 Spray, David C. 1103
 Spring, Michele 806
 Spurgeon, Jade 1161
 Squires, Kelly 512
 Sreenivasan, Nandini 957
 Sreng, Sokunthea 669
 Srinivasan, Prakash 215
 Sripa, Banchob 1489, 416, 419, 420A
 Sriwichai, Sabaitip 1324, 806
 Srour, Margaret L. **1200**
 Ssekitoleko, Richard 403
 Ssekitoleko, James 136, 1190, 1326
 Sserwanga, Asadu 204
 Ssewanyana, Isaac **195**, 1121
 St. Pierre, Tim 951
 St. Laurent, Brandyce 1362, **1365**
 Staedke, Sarah 195, 204, 346
 Stafford, Richard E. 1438, 229
 Stanisic, Danielle 1291, 449, 667
 Stanistreet, Debby 1374
 Stanton, Michelle C. 1042, **282**
 Staples, Edris L. **1069**
 Starzengruber, Peter 328, 506
 Starzyk, M. 409
 States, Sarah 480
 Stecca, Clara 1222
 Steel, Cathy **17**, 263
 Steen, Keith Steen 1346
 Steenland, Maria 731, 738, **1186**, 700
 Steeves, Tanner 478, 480
 Steffen, Imke **905**
 Steingart, Karen R. 1376
 Steinhardt, Laura 1132, 150, 455, **1288**
 Steinhoff, Daniel 568
 Steinmann, Peter 1047, 1050, 1457, 286
 Steketee, Richard W. 1, 1143, 1301, 1426, 540, 545, 546
 Stell, Frederick M. **1135**
 Stephens, Robin 187
 Stephenson, Rob 1140
 Stepniewska, Kasia 822
 Steritz, Matthew 1361
 Sterk, Esther 209
 Steven, Andrew 1433, 20, 266, 267
 Steven, Meschino 516
 Stevens, Eric 263
 Stevenson, Jennifer 1430, 520
 Stewart, Aisha P. 1472
 Stickles, Allison M. **1273, 43**
 Stienstra, Ymkje 88
 Stijnberg, Deborah **1262**, 1310
 Stiles, Jonathan 151, 357, 171
 Stillman, Kathryn M. 1279, 541
 Stillwaggon, Eileen 1221, **26**
 Stinchcomb, Dan T. 1053, 514, 515, 601, 609
 Stinear, Tim **83**, 84
 Stirling, Erin J. 1182
 Stock, Patricia 261
 Stock, Roberto P. 1444
 Stoddard, Steven T. 581, 983, 984
 Stoecker, Kilian **615**
 Stolk, Wilma A 286, 1238
 Stoller, Nicole E. 285
 Stoltzfus, Jonathan D. **491**, 492
 Stone, Brad C. 184
 Stone, Chris **1047**, 1050
 Stone, Heather 725
 Storti-Melo, Luciane M. 671
 Stoute, Jose A. 994
 Straimer, Judith 45
 Stramer, Susan L. 118
 Streatfield, Kim 704
 Streit, Thomas G. 1038
 Stresman, Gillian H. **1430**
 Strickman, Daniel 571
 Strode, Clare 384
 Stroher, Ute 910
 Ströher, Ute 1379, 1380, 440, 52
 Stroika, Steven 957
 Stromdahl, Ellen 573
 Stroup, Suzanne E. 573
 Strouts, Fiona R. **601**, 606
 Strunz, Eric 276
 Stuckey, Erin M. **520**
 Sturdevant, Daniel 967, 215
 Sturm-Ramirez, Katharine 1404
 Sturrock, Hugh 538, 836, **1429**
 Su, Xin-zhuan 38, 992
 Suarez, Julianne 578
 Suazo, Harold 123
 Subramanian, Savitha **1076**, 619
 Sucupira, Izis 1114
 Sudarshan, Medhavi 785
 Sudo, Moe 1316
 Sugaram, Rungniran 831, **321**, 506, 864
 Sugiarto, Paulus 461
 Sugiharto, Victor **871**
 Sugino, Yuka 1007
 Sukhshvili, Roena 744
 Sukowati, Supratman 1365
 Sullivan, David 4
 Sullivan, Richard T. **1121**, **1121**
 Suardi, S. 1365
 Sumaye, Robert D. **922**
 Sumba, Odada 1089, 1090
 Sundar, Shyam 291, 73, 775, 782, 785
 Sunduraraman, Sesh 607
 Sunintaboon, Panya 614
 Suon, Seila 1362, 669
 Sup-yeom, Joon 818
 Supali, Taniawati 490
 Suputtamongkol, Yupin 718
 Surasri, Sittidech 1324
 Surin, Johari 897
 Susanna, Dewi **675**
 Sushko, Mykola 1091
 Sutanto, Inge 175
 Sutamihardja, Awalludin 175
 Sutherland, Colin 1332, 1429, 641, 835, 972
 Sutherland, Laura J. 487, 53
 Suvada, Jose 176
 Suwannarong, Kanokwan 1082, 81
 Suzuki, Mitsuko 292
 Suzuki, Motoi 729
 Suzuki, Takashi 70
 Swai, Ndealilia 1410
 Swale, Daniel 1110
 Swayne, Sherri 598
 Swoboda, Paul 328
 Sudoyo, Herawati 175
 Sy-Ar, Mohamad 207
 Syafruddin, Din 1365
 Syed Omar, Sharifah Faridah 28
 Syll, Massamba **772**
 Sylla, Khadime 1137, **826**
 Sylla, Massamba 60, 941, 1351
 Sylla, Moussa 323
 Sytiuk, Mykola 1091
 Szabo, Ivan 348, 409
 Szein, Marcelo B. 1443, 484

T

Taberner, Patricia 508

The number(s) following author name refers to the abstract number.

- Tacchini-Cottier, Fabienne 1501
Tachibana, Mayumi 1007, 1314, **1316**
Tachibana, Shin-Ichiro 543
Tack, Danielle 740
Tadele, Getnet 279
Tadesse, Zerihun 1472
Tafesse, Mengistu 935
Tagliatalata-scafati, Orazio 1330
Taiwo, Femi 172
Tjahjono Bagus 175
Takala-Harrison, Shannon 1267, 321, 506, 825, 864, 1266, **328**
Takashima, Eizo 1314, 1315, 222, 498
Takeo, Satoru 1315, 543
Takhampunya, Ratre 391
Takken, Willem 1287, 472
Talamas, Patricia 1065
Talavera, Elanie 131
Taleo, George 543, 828
Talisuna, Ambrose O. 214, 49, **177**
Talkington, Deborah F. 1186
Tamarozzi, Francesca 231, 535, 537, 756
Tambisari, Edward 828
Tami, Adriana **130**, 131
Tamminga, Cindy 1160, 226
Tan, Asako 1006, 864
Tan, Chong-Tin 28
Tan, John C. 1018, 1269, 1271, 328, 506, 864, 992
Tan, Kim-Kee 1056
Tan, Kathrine 385
Tan, Kathrine R. **324**
Tan, Li-Kiang 111
Tan, Le V. 1449
Tan, Xiaodong 903, 904
Tanabe, Kazuyuki 543
Tandian, Cheikh M. 208
Taneja, Isha 807
Tang, Dounglas 806
Tang, Joanna 1229
Tang, Linhua 825
Tangkawattana, Sirikachorn 419
Tangnararatchakit, Kanchana 134
Tangpukdee, Noppadon 1184, **313**, 314, 315
Taniuchi, Mami 1079, 1410, 462
Tanner, Marcel 1285, 286
Tanowitz, Herbert B. 1103, 639, 751
Tanya, Vincent N. 21
Tao, Amy R. 1276
Tao, Dingyin 1100, 1106, **1258**
Tapia, Lorena 1309, 1120
Tapia-Conyer, Roberto 1062
Tappero, Jordan W. 1035, 181, 504, 1121, 344, 37
Tariq, Muhammad A. 1403
Tarning, Joel 822
Tarr, Cheryl 956
Tarr, D. Ellen K. 890
Tassi Yunga, Samuel **192**
Tassinari, Wagner S. 524
Tatem, Andrew J. 347, 842, 984
Taurines, Laetitia 810
Tawiah, Theresa 75
Taylor, Aimee R. **830**
Taylor, Alex 954
Taylor, Cameron 1311, 859, 863
Taylor, David W. 1486
Taylor, Diane W. 192, 41
Taylor, Eboni 1036
Taylor, Lizeth 1168, 721, 747
Taylor, Mark J. 1433, 20, 266, 267, 265
Taylor, Steve M. 324, 468, **505**, **824**, 858
Taylor, Terrie E. 1267, 1292, 1296, 1428, 1496, 155, 240, 245, 800, 865, 1495, 160, 638, 1494
Taylor, W. Robert 175
Taylor-Salmon, Emma 976
Tchatchu, Jean-Pierre L. 1413
Tchatchueng-Mbouguia, Jules Brice 264
Tchioffo Tsapi, Majoline **387**
Tchofa, Jose 1255
Tchouassi, Poumo David **982**
Tchouloum, Toudja 1235
Techasaensiri, Chonnamet 134
Tedioli, Fabrizio 1047, 1050, 1457, **286**, **617**
Teelen, Karina 220
Tegha, Gerald L. **310**
Teh-Poot, Christian 1245
Teimoori, Salma **419**
Teirlinck, Anne C. 450, 453
Teixeira, Clarissa 727
Teixeira, Lais H. 217
Teixeira, Marta M. 71
Teixeira-Carvalho, Andréa 1241
Teja-lisavadharm, Paktiya 806
Tejada, Abelardo 1341
Tejman-Yarden, Noa 22
Tekka, Hiwot 1311
Tekle, Afework H. 263
Tekwani, Babu 182, 293
Temiru, Afework 3
ten Asbroek, Guus 939
Teng, Crystal Y. 103, 447
Teng, Jessica E. **525**, 68, 1037
Tennekoon, Rashika N. 607
Tenorio, Antonio 603
Tenorio, Roy 197
Teoh, Boon-Teong 1056, 28
Teoh, Stephen C. B. **8**
ter Kuile, Feiko O. 458, 505
Terao, Toru 704
Terashima, Angelica 287, 752, 753
Terlouw, Dianne 331
Terry, Frances 256
Tesh, Robert B. 1356, 1382, 127
Teshale, Eyasu 741
Thaisomboonsuk, Butsaya 120, 392, 395, 443, **126**
Thakur, Kiran 4
Thangamani, Saravanan 1356, **477**, 746, **877**
Thanh, Pham V. 1312
Thapa, Sudeep D. 1449
Thein, Tun-Linn 124, **552**, 553, 1223, 585, 8, 111
Thellier, Marc 1012, 993
Thera, Mahamadou A. 1096, 1443
Theron, Danie 463
Thesing, Phillip C. 1296, 240, 865
Thi Huong Binh, Nguyen 1312
Thiam, Sylla 1281
Thiele, Elizabeth 1451
Thiem, Vu Dinh 1067, 1072
Thimasarn, Krongthong 1138, 1335
Thirion, Laurence 1191
Thiry, Etienne 922
Thiry, Georges 588, 595
Tho, Le Huu 1067, 1072
Thomas, Brent 1453, 262
Thomas, Cristina **1041**
Thomas, Dana 584
Thomas, Stephen J. 117
Thompson, Trevor A. 818
Thomson, Cynthia 515
Thomson, Dana 525
Thomson, Kerry 741
Thong, Kwai Lin 238
Thongkukiatkul, Amporn 1314, 1315
Thongyuan, Suporn 1340
Thornton, Andrew 277
Thoryk, Elizabeth 516
Thuillez, Josselin 975
Thuma, Philip 1279, 541
Thwing, Julie 1281, 501, 798, 499
Tibery, Cecilia 512
Tien, Joseph H. 707
Tiernan, Rosemary 725
Tietje, Kathleen **1256**
Tiffany, Amanda **209**
Tigoi, Caroline 917
Tihn Hien, Tran 506
Tikomaidraubuta, Kinisalote 114
Tilley, Drake H. 1172, 1174, **1178**, 1386, 1387, 431, 709, 710, 1179, 1381, 711, 713
Tilley, Leann 1263, 1263
Tillotson, Meagan 260
Timiryasova, Tatyana 599
Timmerman, Martijn 816
Timmermans, Ans 806
Timoshevskiy, Vladimir A. **59**, 60
Tine, Roger C. K. 655, **1137**, 268, 548
Tinelli, Carmine 756
Tinoco, Yeny 1375, 445, 467, 703
Tinto, Halidou 49
Tiono, Alfred B. **174**, **841**, 503
Tippalagama, Rashmi 607
Tirados, Inaki 943
Tiruppadiripuliyur, Santha K. 45
Tisch, Daniel J. **1455**, 259, 936
Tissera, Hasitha 1397
Titus, Apangu 1064
Tivura, Mathilda 459, 796
Tiwary, Puja 291, **782**
Tkach, Vasyl V. 948
Tkaczyk, Tomasz S. 528
Tobgay, Tashi 837
Toe, Hyacinthe K. **1463**
Tofail, Fahmida 462
Togo, Amadou 1274, 823
Tohnain, Koin 1085
Tokumoto, Antonio 1372
Tokunaga, Naohito 1007
Toledo, Julia 296
Tomashek, Kay M. **133**, **558**, 582, 584, 608, 112, 114, 989
Tomaz, Franciele M. M. B. 671
Tomchaney, Michael **944**
Tomson, Göran 136
Tonga, Calvin 539
Toor, Adersh J. Kaur. 702
Toossi, Zahra 1195
Tora, Ababayehu **135**, 279
Torii, Motomi 1007, **1314**, 1315, 1316, 222
Torr, Steven J. 943
Torres, Eliana F. **341**
Torres, Giselle 1401
Torres, José 133
Torres, Katherine 1102, 1124, 1130, 1131, 1440, 197, 307, **39**
Torres, Marcelo 1349
Torres, Melissa **256**
Torrico Rojas, Maricruz 294
Tortolero, Mery 131
Tosh, Donna 973
Tossa, Kokou 288, 289
Toubali, Emily **1235**
Touch, Sok 412
Toukara, Moctar 457, **853**
Toure, Mahamadou B. 1308
Touré, Sékou 823, 1274
Townes, David 1264, 1264
Townsend, Reid 420
Tozan, Yesim **969**, **988**
Tran, Duong T. 1312
Tran, Hong Chau T. **1485**
Tran, Nguyen Bao 14
Tran, Tuan M. 1125, **451**
Tran Thanh, Duong 861
Tran Tinh, Hien 1482
Traore, Aliou **1274**, **823**
Traore, Amadou S. 1348
Traore, Boubacar 1125, 1126, 344, 451, 794
Traore, Diahara 975

The number(s) following author name refers to the abstract number.

- Traore, Fatoumata Binta 765
 Traoré, Karim 153
 Traore, Lamine 818
 Traore, Moussa 457, 853
 Traore, Sekou F. 1348, 400, 99, 929
 Trapaidze, Nino **1169**
 Traub, Rebecca 754
 Tauscht, Rob 706
 Travassos da Rosa, Amelia P. A. 1382
 Travers, Tom 46
 Trenholme, Katharine R. 47, 219, 48
 Tretina, Kyle **25**
 Trexler-Green, Erin 1155
 Triana, Omar 947
 Triana, Paula 131
 Trianty, Leily 157
 Tribble, Dave 113, 733
 Trieu, Angela 1490
 Trimarsanto, Hidayat 157
 Trindade, Pamella C. A. 671
 Tripathi, Vinita **637**
 Trivedi, Surbhi B. 125
 Trivedi, Tarak K. **912**
 Trobaugh, Derek W. **56**
 Trostle, James 1031
 Trottein, Francois 489
 Trout Fryxell, Rebecca T. **1353**, 1354
 Troy, Martine 706
 Troye-Blomberg, Marita 543
 Troyo, Adriana **1168**, **721**, **747**
 Trueba, Gabriel 960
 Truman, Richard 1170
 Truong, Nguyen Tan 14
 Truscott, James **1026**, 1240, 495
 Tsai, Hung-Chin **275**
 Tsai, Isheng J. 954
 Tsai, Kun-Hsien 1060
 Tsai, Wen-Yang 1400
 Tsanova, Shota 1169
 Tschudi, Christian 1499
 Tseng, Alanna **1218**
 Tsertsvadze, Nikoloz 1169, 744
 Tsertsvadze, Tengiz 1185
 Tshala-Katumbay, Desire 235
 Tshetu, Antoinette K. 858, 649, 652
 Tsuboi, Takafumi 1007, 1314, 1315, 1316, 1442, **222**, 352, 498, 543
 Tu, Ying 293
 Tu, Zhijian 1115
 Tuah, Wilson 88
 Tucker, Matthew 899
 Tulliano, Gianfranco **298**
 Tullo, Gregory 42, 665, 153
 Tumusiime, Alex 1379, 1380, 910
 Turell, Michael J. **866**, 871
 Turiansky, George 727
 Turnbull, Lindsey B. **1006**, 1099
 Turner, Hugo C. **1049**, **32**
 Turner, Joseph D. **1433**, **20**, **267**, 483
 Turner, Joy D. **714**
 Turner, Nathan 678
 Turnsek, Maryann 956
 Turpin, Cornelius 151
 Tutterrow, Yeung 1422
 Tweyongyere, Robert **485**
 Ty, Maureen 634
 Tyagi, B.K. 1074, 1094
 Tylleskar, Thorkild 235
 Tyner, Stuart 243, 328, 506
 Tzec-Arjona, Evelyn 1245
- ## U
- Ubaida Mohien, Ceereena 1100, 1258
 Ubol, Sukathida 614
 Udagama, Preethi V. 353
 Uddin, Taher 955, 959
 Udhayakumar, Venkatachalam 1264, 1264, 307, 317, 325, 507
 Ugarte, Claudia 145
 Ugarte-Gil, Cesar 1220
 Ugwuegbulam, Cletus 42A
 Ukhovskiy, Vitalii 723
 Ukoha, Ndukwue K. **848**
 Ulloa, Armando 1353, 1354
 Ullu, Elisabetta 1499
 Umaru, John 1454
 Umbugadu, Christopher 1454
 Umeh, Ebele U. **147**
 Umeh, Joseph C. 147, **203**
 Umuro, Mamo 1396
 Un Nissa, Tayyab 1079
 Undurraga, Eduardo A. 1061, 1062
 Unicomb, Leanne 958
 Unnasch, Thomas R. 1389, 909
 Upton, Leanna 497
 Urassa, Willy 1492
 Urquiaga, Jorge 287, 752, 753
 Urrego, Daniela 148
 Usuda, Daisuke 729
 Utami, Retno A. Setya. 157
 Uthaimongkol, Nichapat 243
 Utzinger, Jürg 1472
 Uyoga, Mary A. 936
 Uyoga, Sophie **333**
 Uzelac, Aleksandra 464
- ## V
- Vaca, Maritza 912
 Vaca, Sergio 1167
 Vadla, Malathi 321
 Vahi, Ventis 961
 Vaidya, Akhil 1273, 1322, 43
 Vaillant, Michel 1413, 253
 Valbuena, Gustavo A. 1164, 716, 610
 Valdez, Melissa 263
 Valdivia, Hugo O. 342
 Valencia, Braulio M. 1250A
 Valente, Ilaria C. 1371
 Valente, Vanderson 759
 Valentim, Claudia L. L. 954
 Valentiner-Branth, Palle 1409
 Valenzuela, Carla V. 1220
 Valenzuela, Jesus 727
 Valenzuela, Jesus G. 749
 Valim, Clarissa 1270, 1270, 1428, 320, 327, 354
 Valle, Jorge 1461
 Valle, Ruben 1372
 Vallejo, Andrés **6**, 1286, 1300, **795**, **931**
 Valliant, Michel 205
 Vallur, Aarthy C. V. **1422**
 Valverde, Emilio 69
 van de Bohr, Margot 496
 van de Vegte-Bolmer, Marga 220
 van den Broeck, Frederik 560
 van den Driessche, Pauline 707
 Van den Eede, Peter 1312
 van den Ende, Stannie 1479
 van den Hurk, Andrew 876
 van der Laan, Kim 760
 van der Poll, Tom 1479, 67
 van der Vaart, Thomas 1479
 van der Ven, Andre J. A. M. 220
 Van der Vliet, Diane **591**
 van der Werf, Tjip S. 88
 van der werff, Suzanne 760
 van Dijk, Janneke H. 541, 1279
 van Dodewaard, Caitlin A. M. **108**
 Van Doorn, Rogier 1485, 919
 van Eijk, Annemieke 851
 van Gemert, Geert Jan 220, 453
 van Grinsven, Tim 220
 Van Helden, Paul 463
 Van Hong, Nguyen **1312**
 Van Kerkhove, Maria D. 1470
 van Lieshout, Lisette 1025, **490**, 453
 Van Malderen, Carine 861
 van Meer, Maurits P. A. 220
 Van Overmeir, Chantal 1312
 van Rooijen, Nico 1433
 van Schaijk, Ben C. L. 976
 Van Slyke, Greta A. **1212**, 1465
 Van Tyne, Daria 1009, 327, 544
 Van Voorhis, Wesley C. 23, 27
 Vanachayangkul, Pattaraporn **806**
 VanBlargan, Laura A. **513**
 Vancea, Adrian 733
 Vandamme, Anne-Mieke 65, 770
 Vandelannoote, Koen **1177**, 84
 Vanden Eng, Jodi **1070**, 385
 Vanlandingham, Dana L. 1210, 1211
 Vantaux, Amélie **867**
 VanTyne, Daria 320, 354
 Varadarajan, Poovazhagi 1074, 1074
 Vargas, Maria José 1403, 985
 Varghese, Ann 1233
 Vasantharoopan, Arthi **1405**
 Vasilakis, Nikos 1356, **1382**
 Vasireddy, Vamsi 178, 179
 Vasquez, Daniel 128
 Vasquez, George 287, 752, 753
 Vasquez, Gissella M. 1135, 1341
 Vassall, Anna 939
 Vaughan, Jefferson A. 750, 948
 Vaughn, Meagan F. **743**
 Vaury, Chantal 469
 Vazquez-Prokopec, Gonzalo M. 983, 984, 399, 518
 Veasey, Lee 260
 Vedovello, Danila 132
 Veenstra, Timothy D. 19
 Vega, Martha R. 610
 Vega-Rodriguez, Joel **924**
 Vegte-Bolmer, Marga 453
 Vekemans, Johan 1443
 Velandia, Myriam 96
 Velasco-Salas, Zoraida I. 130, **131**
 Velez, Ivan 1067, 1072, 588, 595, 515
 Venkatesan, Meera 1266, 214, 321, 825, 974
 Vennervald, Birgitte 1284
 Ventocilla, Julio 1120, 1120, 342
 Venugopalan, B 1063
 Vera, Farah Z. 1338
 Vera-Maloof, Farah Z. **1347**
 Verastegui, Hector 1377, 911
 Verastegui, Manuela 230, 531, 789, **533**, 788
 Vercauteren, Jurgen 65
 Verduquez, Aleida 296
 Vereecken, Kim 560, 760
 Verjovski-Almeida, Sergio 901
 Verlinde, Christophe C. L. 1021, 23
 Verma, Amit 842
 Vermund, Sten 1220
 Verotta, Luisella 498
 Vertefeuille, John 1186
 Vertus, Claude 349
 Verweij, Jaco J. 1025, 490
 Vestergaard, Lasse S. 828
 Vezenegho, Samuel **873**
 Viboud, Cecile 413
 Vicenti, Maria F. 131
 Victor, Thomas C. 463
 Victora, Cesar 624, 935
 Vicuna, Yosselin **891**, 912
 Vidadala, Rama Subba Rao 23
 Vidadala, Rao S. 27
 Vidal-Cardenas, Elisa M. **342**

The number(s) following author name refers to the abstract number.

- Vidya, C. 1074, 1094
 Vignali, Marissa 633
 Vilcarromero, Stalin 581, 726, 983
 Vilela, Karla J. 1387, 431
 Vilkova, A N. 908
 Villacorte, Elena A. 793, 950
 Villanueva, Liliana 566
 Villanueva-Meyer, Pablo 415
 Villar, Luis A. **610**
 Villarama, Benito J. 729
 Villaran, Manuel **1227**
 Villaran, Manuel V. 410
 Villaroel, Darsi 296
 Villarreal, Cuauhtemoc 1135
 Villasante, Eileen 1148, 1148, 1154, 1159, 1160, 1161, 1313, 1437, 226, 1153, 933
 Villasis, Elizabeth **1102**, 1130
 Vincenti, Maria F. 130
 Vinetz, Joseph 1102, 1123, 1124, 1128, 1130, 1131, 1323, 356, 1359, 1440, 197, 39
 Vinh Chau, Nguyen Van 14
 Vinje, Jan 912
 Vir, Vimal 702
 Visser, Leo G. 450, 453
 Vivekanada, K. 1041
 Vizcaino, Lucrecia R. 1461
 Vlková, Michaela 749
 Voge, Natalia **9**
 Vojtikevicova, Eva 769
 Volf, Petr 749
 Volkman, Sarah K. 1009, 1270, 1270, 2, 320, 354, 42, 544, 1317, 327, 644, 7
 Volkova, Evgeniya 1217
 Vontas, John 550
 Vujcic, Jelena 937
 Vujcikova, Julia 1219
 Vulule, John M. 1431, 519, 664, 851, 855
- W**
- Wachira, Cyrus 1396
 Wacira, Daniel 551, 628
 Wadaka, Mamai **687**
 Wadegu, Meshack **444**
 Wadgoankar, Raj 1243
 Wafula, Rebecca 549
 Wagacha Burton, John 66
 Waggoner, Jesse J. **115**
 Waghabi, Mariana C. 1241
 Wagman, Joseph **1342**, **1355**
 Wagstaff, Simon 265
 Wahajuddin, Wahajuddin **807**
 Wahed, Amer 528
 Wahid, Rezwanul **484**
 Waiboci, Lillian 592, 741, 1396
 Waihenya, Rebecca 355
 Waiswa, Peter 199
- Waithaka, Albina 241
 Waitumbi, John N. 355
 Wakabi, Timothy 1236
 Wakam Nobou, Sorelle 539
 Wakhule, Lilian 1396
 Waleckx, Etienne **578**
 Walker, David H. 1164, 716
 Walker, Dawn M. **1320**
 Walker, Edward D. 519
 Walker, Larry 180, 293
 Walker, Martin 1049, 32
 Walker, Patrick **458**
 Walker, Peter J. 1382
 Walker, Xaviour J. **724**, **728**
 Wallace, Derek 591, 599
 Walldorf, Jenny 865, 1292, **1428**
 Waller, Lance 85
 Walsh, Douglas 243
 Walton, Judd L. 1025, 140, 423
 Walter, Katharine **748**
 Wamala, Joseph 1379, 910
 Wamala, Samuel 189, **193**, 37, 1121
 Wamboga, Charles 1236
 Wamburu, Kabura 1396
 Wammanda, Robinson O. 730
 Wampfler, Rahel 1257
 Wamulume, Chibesa 1, 1143
 Wamulume, Sichitamba 1280
 Wandera, Bonnie 1293
 Wang, Alice **684**
 Wang, Bo **350**, 352
 Wang, Heng 1004
 Wang, Hsi-Chieh 479
 Wang, Libing 1306
 Wang, Meihui 366
 Wang, Rong 814
 Wang, Shuqi 896
 Wang, Sibao 924
 Wang, Weiming 1278
 Wang, Wei-Kung **1400**
 Wang, Xiaohong 1119
 Wang, Xiaowei 1155
 Wang, Xuelei 487
 Wang, Xiaohong 698
 Wang, Zhensheng 1004
 Wanga, Joyce A. 1153
 Wangui, Julia 444
 Wanionek, Kimberli 512
 Wanjala, Christine L. 460
 Wanji, Samuel 1417, 15
 Wannemuehler, Kathleen 1036
 Wanzira, Humphrey 504
 Warburg, Alon 749
 Ward, Abigail 1141, **1142**
 Ward, Danielle 1486
 Ward, Lauren N. 1434
 Ward, Stephen A. 266
 Wardrop, Nicola 280, **479**
 Ware, JeanAnne 1446
 Warit, Saradee 614
 Warren, H. Shaw 164
 Warren, Robin M. 463
- Wartel, T. Anh 591
 Wasike, Eric W. 371
 Wassmer, Samuel 634
 Wastling, Jonathan M. 16, 21
 Watanabe, Emi 279
 Waterman, Stephen **1170**
 Waters, Norman C. 359, 828
 Watkins, Melynda 1226, **1229**
 Watts, Douglas 1058, 1385
 Watts, Nathaniel 533
 Weakley, Allison 61
 Weaver, Abigail A. 526, **620**
 Weaver, Casey 1504
 Weaver, C. D. 1110
 Weaver, Scott C. 1385, 1389, 439, 605, 1058, 127
 Webb, Kinari 627
 Webster, Jayne 201, 459, 796
 Webster, Joanne 1240
 Webster, Sophia H. **572**
 Webster, Wendy M. 1169
 Weetman, David 1343, 1346, **1458**, 1460, 376
 Wei, Chunyan **1004**
 Weidmann, Manfred 921
 Weil, Gary J. 1039, 1043, 1046, 1452, 1473, 18, 258, 420, 757
 Weinberg, J. Brice 1098
 Weinberg, Joe B. 4
 Weinkopff, Tiffany **1501**
 Weinstein, Philip 508
 Weiss, Daniel J. 1297, **1298**
 Weiss, Louis M. 1103, 639
 Weiss, Walter R. 1439
 Wellems, Thomas 7
 Wellhausen, Jeffrey D. 1207
 Wellington, Nii 685
 Welsch, Alex 725
 Welsh-Rodriguez, Carlos 568
 Wemakoy, Okitolonda 740
 Wendler, Jason 633
 Weng, Ju Lin 576
 Wenger, Edward 546, 1283, **1301**
 Wentworth, David 1389
 Werbovetz, Karl **300**
 Wesolowski, Amy **335**
 Wesson, Dawn M. 1248, **517**, 570
 West, Dennis P. 1041
 West, Sheila 34, 285
 Wever, Claudia 1435
 Whaley, Michelle 471, 697
 Whistler, Toni 407, 718
 White, Eric S. 1003
 White, Lisa J. 1144
 White, Nicholas J. 328, 506, 649, 822, 844
 White, Valerie A. 1496, 155
 White, Jr., A. Clinton 27, 23, 269, 414, 415
 Whitehead, Stephen S. 1402, 1469, 512, 513, 606
 Whitehorn, James **14**
 Whitehurst, Nicole 1253
- Whitman, Malcolm 1010
 Whittaker, Maxine 202
 Whitty, Christopher 1332
 Wichianprasat, Pongdej **1184**
 Wickham, Kristina S. **819**
 Wickramaarchchi, Thilan 353
 Wickremasinghe, Renu 543
 Widdowson, Marc-Alain 1404, 465
 Widen, Steven 1382
 Widjaja, Susana 113
 Widness, John A. 165
 Widyatmoko, Hilarion W. 875
 Wiegand, Roger C. 925
 Wiegand, Ryan E. 1028, 1268, 324, 998, 1288, 455
 Wiens, Kirsten E. 1434
 Wiersinga, Joost W. 1479
 Wiersma, Jorien 220
 Wijayalath, Wathsala 1154, **1159**
 Wijedoru, Lalith 1479
 Wikel, Stephen 477
 Wilairatana, Polrat 313, **314**, 315
 Wilder-Smith, Annelies 1056, 1340, 552, 603, 988
 Wilding, Craig S. 1458, **1460**
 Wilkins, Kimberly 51
 William, Timothy **334**, 635, 995, 1251
 Williams, Gail 564, 565, 1239
 Williams, Jessica 528
 Williams, John V. 911, 1377
 Williams, Katherine L. 1054, 985
 Williams, Maya **128**, 448, 467
 Williams, Steven A. 256
 Williams, Thomas N. 333, 456
 Williamson, Heather 85
 Williamson, Kim C. 1008, 659
 Willilo, Ritha A. **210**, 550
 Wills, Bridget 14
 Wilschut, Jan C. 130, 131
 Wilson, Anne 1141
 Wilson, David 44
 Wilson, Kerry 626
 Wilson, L. Anthony 236
 Wilson, Mary 786
 Wilson, Mary E. 724, 728, 790
 Wilson, Mark L. 1292, 1336, 612
 Wilson, Michael D. 380, 394, 90, 367
 Wilson, Nana O. **357**, 629, 151
 Win, Lyndes 828
 Winikor, Jared 976
 Winter, Rolf 43, 817, 820
 Winters, Anna M. 1280, 1339
 Winters, Benjamin 1280, 1339
 Winzeler, Elizabeth 7, 808
 Wirth, Dyann F. 1010, 1270, 1270, 1317, 1317, 2, 320, 354, 42, 544, 925, 1009, 327, 644, 7
 Wirtz, Robert 385
 Witrick, Brian A. **717**
 Witty, Michael 1424, 301

The number(s) following author name refers to the abstract number.

Woc-Colburn, Laila 1447
 Wojcik, Oktawia 625
 Wolber, Marcel 1485
 Wolbers, Marcel 14
 Woldehanna, Sara 1083, **81**
 Wölfel, Roman 615
 Wolfner, Mariana F. 473
 Wolkon, Adam 1070, 1288, 150, 455
 Won, Kimberly Y. 1040, 895, 998
 Wondji, Charles **1459**, 691, 1107
 Wong, Jacklyn **1431**, 455, **852**
 Wong, Joshua G. X. 111, 124, 552, 553, **587**
 Wong, Kum-Thong 28
 Wong, Paolo A. 1378
 Wongarunkochakorn, Saowaluk 1324
 Wongjindanon, Nuttapong 1036
 Wongsanen, Klanarong 649
 Wood, Angela 190
 Wood, Thomas G. 1382
 Woodward, Robert 951
 Woolsey, Aaron M. **1145**
 Workman, Lesley 214
 Worlanyo, Pida 857
 Worodria, William 403
 Worrell, Caitlin M. **1028**
 Wright, Chelsea 573
 Wright, Gavin J. 451
 Wright, Karin D. 1096
 Wring, Stephen A. **1226**
 Wu, Baolin 1119
 Wu, Hai-Wei 1149, 1149, 1150, **1436**, 227, 452
 Wu, Jian 992
 Wu, Shuenn-Jue 1059, 113
 Wu, Yi-Chieh 1400
 Wu, Yimin **929**, 930, **1155**
 Wu, Yun 1438, **229**
 Wuertz, Stefan 1032
 Wurapa, Eyako 444, 592, 920, 917
 The WWARN ACT Africa Baseline Study Group 651
 The WWARN Community 214
 The WWARN In Vitro Pilot Project Group 647
 The WWARN Smart Surveillance Study Group 854

X

Xaymounvong, Khounkham 1083
 Xia, Ai 1111
 Xiang, Xiaoxiao 598
 Xiao, Lihua 883
 Xiao, Tengfei 1004
 Xiao, Wenming 992
 Xie, Stanley C. **1263**, **1263**
 Xu, Guang **1164**, 716

Xu, Hanfu 979
 Xu, Jiannong **1361**, 874, 980
 Xu, Jing 942
 Xu, Sui 366
 Xu, Weiping 1286
 Xuya, Marvin 554

Y

Yactayo, Sergio D. 1470
 Yadao, Federico 835
 Yadava, Anjali 973
 Yadavalli, Raghavendra **362**
 Yagoure, Bilkissou 1348
 Yaguo-Ide, Lucy E. 802
 Yakob, Laith 565
 Yakubu, Habib 685
 Yamada, Keiichi 793
 Yamasaki, Tsutomu 1315, 222
 Yaméogo, Bienvenue K. 928
 Yaméogo, Koudraogo B. 1330
 Yan, Guiyun 1119, 1361, 336, 366, 530, 670
 Yan, Jasper S. 528
 Yanagi, Tetsuo 656
 Yang, Amy 218
 Yang, Henglin 825
 Yang, Ivana V. 1250
 Yang, Jing 1503
 Yano, Kazuhiko 793
 Yanow, Stephanie 1158, 1158, 196, 449
 Yao, Franck A. 1330
 Yasaña, Antonio 835
 Yasnot, Maria F. **1127**, 1180
 Yassi, Annalee 626
 Yatich, Nelly 151
 Yattara, Mohamed 323
 Yava, Ricardo 1305
 Yawson, Alexander E. 1343
 Ye, Maurice **369**
 Ye, Yazoume 859, 863, 1333, **1334**, 500
 Ye, Yixin H. **876**, 57
 Yeboah-Antwi, Kojo 1078, 653
 Yeboah-Manu, Dorothy 1173, **87**
 Yeka, Adoke 195, 204, 557
 Yellow Fever Expert Committee 1470
 Yen, Tsai-Ying **1060**
 Yeo, Tsin W. 1098, 1251, 334, 635, 995
 Yeo, Tun K. 8
 Yerbanga, Rakiswendé S. **1330**
 Yerbanga, Serge R. 386, 928
 Yeshanehe, Wendemagegn Embiale **239**
 Yeshiwondim, Asnakew 1311
 Yevstigneyeva, Violetta 102
 Yinges, Shiret 792
 Yip, Fuyuen 1374
 Yizengaw, Mekides 762

Yoder, Jonathan 527, **883**
 Yokobe, Lindsay 263
 Yokouchi, Yuki 1316
 Yoksan, Sutee 593
 Yongkang, He 1239
 Yongolo, Sidney 1415
 Yoon, In-Kyu 1061, 117, 120, 126, 441, 443
 Yoon, In-Kyn 614
 Yoon, Steven S. 204
 Yori, Pablo P. 356, 709
 Yoti, Zabulon 910
 Young, Ginger R. 514
 Yount, Boyd 1399
 Yu, Elaine A. 405
 Yu, Sun N. **285**
 Yu, Wanqin 1361, 874, 980
 Yu, Xue-jie 1390
 Yuan, Wang 492
 Yukich, Joshua O. **1253**, **1295**, 1425, 1426
 Yun, Seung-Gyu 350
 Yung, Chee-Fu **111**
 Yunta, Cristina 1459
 Yunus, Muhammad Hafiznur 234
 Yunus, Md. 704
 Yusibov, Vidadi 1155

Z

Zaidi, Anita 1066, 1079, 1368, 1406
 Zaidi, Samana 1368
 Zaki, Sherif 133
 Zakutansky, Sara E. 1152
 Zaloumis, Sophie 1263, 1263
 Zaman, K. 937
 Zaman, Umber 1368
 Zambrano, Julio 130
 Zambrano, Laura D. **712**
 Zamora Perea, Elvira 1464
 Zampieri, Ricardo A. 791
 Zamudio, Rodrigo 287, 752, 753
 Zandotti, Christine 1191
 Zangger, Haroun 1501
 Zapata, Sonia 1471
 Zarife, Maria A. S. 1204
 Zarlring, Stasya **666**
 Zeba, Augustin N. **144**
 Zedar, Rebecca 599
 Zegers de Beyl, Celine 1138, **1325**, **1335**, 202, 499
 Zegeye, Mulugeta M. **762**
 Zehrbach, A. M. **890**
 Zeituni, Amir E. 42
 Zeldenryk, Lynne **1414**, 252
 Zeleke, Hunegnaw M. **137**
 Zeller, Herve 1215
 Zelman, Brittany 1327
 Zelnor, Jonathan 205
 Zenaishvili, O. 297
 Zenaishvili, Z. 418

Zeng, Qiang 180
 Zerpa, Rito **1378**
 Zghenti, Eka **744**
 Zhan, Bin 1486
 Zhang, Genwei 1119, 698
 Zhang, Jia 293
 Zhang, Jian **389**
 Zhang, Lixin **960**
 Zhang, Peng 1004
 Zhang, Veronica **359**
 Zhang, Yong-Kang **648**, 811
 Zhang, Zaixing 961
 Zhang, Zhongsheng 23, 27
 Zhao, Junlong 492
 Zhao, Qinying **814**
 Zhao, Wenyi 46
 Zheng, Hong 24, 5
 Zheng, Zengwang 903, **904**
 Zhong, Daibin 366
 Zhong, Kathleen 1011
 Zhong, Lina 285
 Zhou, Guofa 336, 366
 Zhou, Huayun 1278, 366
 Zhou, Jinlin **91**
 Zhou, Luwen 224
 Zhou, Shuisen 825
 Zhou, Yanqin 492
 Zhou, Zhaoxia 285
 Zhou, Zhiyong **1252**, 1268
 Zhu, Guoding **366**
 Zhu, Xiaohua 300
 Zielinski-Gutierrez, Emily 568, 1064
 Ziem, Juventus 490
 Zikursh, Melinda J. 1254
 Zilnik, Gabriel 572
 Zilversmit, Martine 992
 Zimicki, Susan 1082, 1083, 81
 Zimmerman, Peter 1319, 1319, 259, 7, 1254, 1455, 574, 996
 Zinöcker, Severin **1441**
 Zinszer, Kate **860**
 Zoerhoff, Kathryn L. 1236
 Zompi, Simona 122, 1403
 Zongo, Issaka 322
 Zorrilla, Pilar 384
 Zou, Xiaoyan **1313**, 1439
 Zoungrana, Amadou **329**
 Zouré, Honorat G. M. 1238
 Zoya, John 1132, 455
 Zubaidah, Siti 1365
 Zulu, Zulisile 836
 Zunt, Joseph 1227, 1386
 Zyambo, Khozya D. 541
 Zyongwwe, Nancy M. 541