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*Editor's Note: Please hyperlink to the study on the AJTMH site once the embargo lifts.*

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## **Comprehensive Genomic Study Provides Evidence that Dengue Has Become Endemic and Diverse in China**

*Study suggests dengue can persist year-round in China,  
increasing the risk of more frequent and severe outbreaks*

Oakbrook Terrace, Ill. (October 12, 2015)—The first-ever comprehensive genomic analysis of the virus that causes dengue fever suggests that it may survive year-round in southern China. The study, published in the *American Journal of Tropical Medicine and Hygiene*, provides evidence that China may be at increased risk for more frequent and severe dengue fever outbreaks similar to the 2014 outbreak in Guangdong Province that sickened more than 40,000 people.

“We now have compelling evidence that dengue can persist in China—in some cases up to six to eight years,” said Rubing Chen, an evolutionary virologist at the University of Texas Medical Branch, Galveston, and lead investigator of the study. “Further, we found a surprisingly complex and diverse mix of viral subtypes represented in China, a factor that can mean greater risk of epidemic dengue in the future.”

Researchers have disagreed about whether dengue persists in China between disease outbreaks. Several recent studies suggested that dengue remains an imported disease in China, but these studies used small datasets. This study provides one of the most extensive analyses to date, according to Chen, and could be a critical tool in adjusting dengue prevention and control efforts to protect millions of people in China.

Dengue fever, a viral disease first recognized during outbreaks in the 1950s, is spreading rapidly as the range of the mosquitoes *Aedes aegypti* and *Aedes albopictus* that transmit it expands throughout the world. Also known as “break bone fever” for the severe pain caused by infection, dengue now infects 50 million people annually, with 500,000 severe cases of dengue hemorrhagic fever and 22,000 deaths, according to the World Health Organization. There is currently no effective treatment for dengue fever and no preventive vaccine, although there are vaccines in development. The best current prevention is avoiding contact with the mosquitoes that transmit the disease through use of insect repellents and mosquito control programs.

In many areas of the world, dengue has now become endemic, meaning that the virus exists at low levels year-round, and infections occur annually during the rainy season when mosquito populations increase rapidly. Endemic regions are at increased risk of

epidemic outbreaks when new variants of the virus emerge and infect people who have never been exposed to that particular strain of the virus.

### **Complex genetic diversity found**

Dengue infections are similar to influenza in that an individual can become infected over and over by different strains of the virus. But what makes dengue particularly dangerous is that people who have had previous infections are more likely to have severe symptoms if they catch the disease multiple times.

Chen and her colleague Guan-Zhu Han, an evolutionary biologist based at Nanjing Normal University, Nanjing, China, evaluated all dengue virus sequences from China available in the public database GenBank—about 1,000-4,000 samples each for the four dengue serotypes (DENV 1-4), for almost 10,000 total. The team found 50 individual variants of DENV-1 in China, with 20 variants of DENV-2, and lower numbers of variants of DENV-3 and DENV-4. The researchers also identified multiple variants of both DENV-1 and DENV-2 during the 2014 Guangdong outbreak.

“Even within the same year, a person can catch dengue more than once if distantly related variants are circulating in the same region,” said Chen. “That’s why we become concerned about public health when many variants are found, as was the case in our study.”

### **Evidence of year-round risk**

This new study found that the same grouping of Guangdong DENV strains persisted yearly from 2006-2014. However, given the incomplete information on strains in other Southeast Asian countries such as Indonesia, Laos and Vietnam, it is possible that these strains were imported each year from the same location, according to Chen. But it is also possible that southern China is now part of an integrated pattern of dengue circulation that includes all of Southeast Asia and southern China, she said.

Regardless of the exact transmission pattern, the study authors say China is facing a substantial dengue threat, with potential invasion into broader areas of the country, as sporadic cases have been identified in several provinces in recent years. The combination of a hot, humid climate ideal for breeding mosquitoes and large population centers in southern China combine to make this area a particular concern for public health officials.

Because dengue is an emerging disease, its patterns of infection and potential to cause epidemics are still unclear. Chen said public health officials and scientists from throughout Southeast Asia must collaborate to fill in missing genetic data about various strains of the virus and to better track the strains’ movements across the region, both for prevention efforts and to identify potential vaccine candidates.

“This study illustrates how genomic science, especially relating the genomes of globally important infections like dengue virus to disease patterns, is rapidly moving into the realm of applied public health,” said Christopher V. Plowe, president of the American Society of Tropical Medicine and Hygiene. “It is also a nice example of how scientists from different countries—here in the United States and China—can join forces irrespective of the ups and downs of international politics. Tropical infectious diseases don’t respect borders, and our shared goal of improving global health makes it easy to work together.”

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