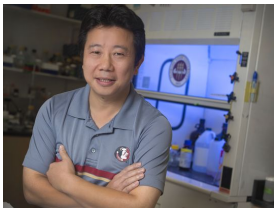
FSU, Johns Hopkins researchers make major discovery about Zika virus

Byron Dobson, Democrat senior writer *1:04 p.m. EST March 4, 2016*

Breakthrough report published Friday in Cell Stem Cell journal



(Photo: FSU Photography Services)

Sitting in his third-floor office inside the King Life Sciences Building at Florida State University, Professor Hengli Tang points to a picture on his computer screen showing a display of white, green and red dots.

The white dots show untouched lab-generated stem cells. The green dots show Zika-infected cells. The red dots show dying cells.

The FSU biology professor says the dots on the screen represent what he and scientists from Johns Hopkins and Emory universities believe is a breakthrough in determining if the Zika virus specifically targets developing brain cells, leading to the link between the virus and microcephaly. That condition causes babies to be born with unusually small heads and stunted brain development.

“It’s significant because we’re literally the first people in the world to know this, to know that this virus can infect these very important cells and interfere with their function,” Tang said. “Research is rewarding in general, but when you have something this timely and this clinically relevant, it’s extra satisfying because we’ll be helping people in the long run.”

Their findings, which eventually could lead to identifying pharmaceuticals that effectively treat the virus at the onset, will be published today in Cell Stem Cell. Tang is the lead author. His co-authors are Guo-li Ming and Hongjun Song, both neuroscientists at Johns Hopkins University School of Medicine, and Peng Jin, a geneticist at Emory University Hospital.

Graduate student Sarah Ogden has been working on Zika virus research with FSU Professor Hengli Tang *(Photo: FSU Photography Services)*

The Cambridge, Massachusetts-based monthly (http://www.cell.com/cell-stem-cell/home (http://www.cell.com/cell-stem-cell/home)) is a regularly-cited journal that publishes research around the world related to stem cell science.

“We answered some specific questions about the cell type the virus can infect and also the potential effect the virus has on these cells,” Tang said. “This enables drug screening in these important cells. By targeting the very cells that are important for brain development, the Zika virus can directly affect brain development.

“This is a very short study. The follow-up is a long-term study to determine the long-term effect on brain development. Our study was designed to answer the most important question.”

Tang said the research did not identify how the virus gets transmitted to the brain.

“There are many cells in the brain,” he said. “We found the virus affects the neural stem cells and then this slows down their growth.”

Florida leads country in cases

The study comes at a time when Florida is the leading state with reports of people infected with the Zika virus. As of Thursday, three new cases were reported in Miami-Dade County, bringing the state total to 47, with 22 of them in Miami-Dade. No cases have been reported in Leon or surrounding counties, but the Department of Health is not naming which counties four pregnant women testing positive for the virus live.

On Feb. 3, State Surgeon General and Department of Health Secretary Dr. John Armstrong, at the request of Gov. Rick Scott, declared a public health emergency for the 11 Florida counties where cases have been confirmed.

Health officials are particularly concerned about pregnant women. Brazil and other South American countries hard hit by Zika have also seen a dramatic increase in microcephaly. The World Health Organization has declared an international public health emergency.

“It was a little known virus prior to the World Health Organization public health emergency,” Tang said. He said the Zika virus first was identified in 1947, but the current health concern has escalated given the increase in cases of microcephaly.

Professor of Biological Science Hengli Tang confers with graduate student Sarah Ogden about the next steps in their Zika research in his lab at FSU. *(Photo: FSU Photography Services)*

Tang said the virus is very similar to the Dengue virus, which is included in his research funded by the National Institutes of Health. Both viruses are transmitted through mosquito bites, he said, and have been found in similar tropical areas like South America and the Caribbean.

“Because we were studying a similar virus and the World Health Organization declared a public health emergency, we started studying it (Zika), just last month,” he said.

A team assembled

Tang said he reached out to Johns Hopkins University’s School of Medicine colleagues who have expertise in brain development. Emory University School of Medicine researchers were brought on board because of their previous research collaborations with Johns Hopkins.

“The collaboration between us, who study the Zika virus and those two labs was the right combination to study any potential effect of Zika on brain development,” said Tang who attended graduate with the two Johns Hopkins University neuroscientists. “We didn’t waste any time. We worked quickly.”

FSU already had the virus stored in its lab, Tang said. A research team from Johns Hopkins visited last month, bringing with them neural stem cells. They were infected with the virus by Tang. His team then sent the infected cells to Emory, where they were evaluated.

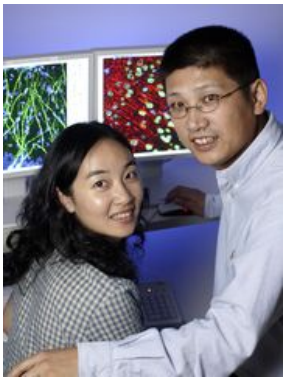
“We applied or infected those cells with the virus and determined the effects of the virus on the cells,” Tang said.

Tang said the FSU team consisted of himself, graduate assistants and a staff scientists from FSU’s College of Medicine. The graduate students put in 20-hour days, worked weekends. Lead researchers regularly held phone conferences at night with their counterparts at Johns Hopkins and Emory.

Researchers found the virus targets a cell type called human embryonic cortical neural progenitors in as little as three days after being exposed to the virus. They also discovered that these infected cells replicate the Zika virus, posing potential treatment problems, and that the virus is directly interfering with cell growth and function. Some of the cells died after being infected.

This could be a critical finding, said Guo-Li Ming, the Johns Hopkins neuroscientist.

“Potentially, this could explain why there is a link to microcephaly, but there is a lot more work needed to show the direct causal effect,” she said. “The



Johns Hopkins University School of Medicine neuroscientists Guo-li , left, and Hongjun Song, sent a team equipped with neural stem cells that were treated by the Zika virus leading to their breakthrough discovery with FSU biology professor Hengli Tang. *(Photo: FSU Photography Services)*

significance is we provide the first biological evidence that Zika can infect neural stem cells very efficiently. We can speculate that it will spread in the brain."

The goal was to find if there is any link, said Tang.

"Our data is consistent and it supports that hypothesis, but it is not definitive proof," Tang said, agreeing that more research must be conducted. "We are adding critical information to build the case but the case is still being built.

Looking ahead

Tang said the next steps include:

♦Screening for drugs that will block the virus or that can be used for treatment.

♦Further study of the research model to determine the long-term effect of the virus on the neural stem cells (what is it doing and how is it doing it) and brain development and how to stop it.

Tang said FSU and Johns Hopkins next week are bringing in an expert in High Throughput Screening, or compound screening, from the National Institutes of Health.

High Throughput Screening means you can screen millions of compounds all at once or very quickly, he said. The compounds that appear to work can become candidates for anti-Zika drugs.

"We hope this will open up more research," Tang said. "We will continue to contribute to our own research and if this screening works as expected, we might have a candidate for developing therapeutics.

"That is the ultimate goal for this type of research. This information will be of interest not just to scientists but to government agencies and clinicians, for sure, and the general public."

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What is Zika:

Zika fever is a mild febrile illness caused by a mosquito-borne virus similar to those that cause dengue and West Nile virus infection. It has been identified in several countries in Central and South America, Mexico, and the Caribbean since 2015. Outbreaks have previously been reported in Africa, Southeast Asia, and the Pacific Islands. Local transmission has been reported in Puerto Rico, but not elsewhere in the United States. Cases of Zika fever have been reported in travelers returning to the United States.

-Source: Florida Department of Health

Zika information:

Only about 1 in 5 people infected with Zika virus are symptomatic

Zika fever is a mild illness. Severe disease requiring hospitalization is uncommon.

Signs and symptoms of Zika fever may include: acute onset of low-grade fever, rash, joint pain, conjunctivitis (reddening of eye), body aches, headache, eye pain, and vomiting.

Treatment is symptomatic since there is no specific treatment against the virus. Illness typically resolves within a week.

Tips for travelers

Travelers to a tropical or sub-tropical area (Africa, Asia, Caribbean, Mexico, Central and South America), can protect themselves from Zika and other mosquito-borne diseases by following these prevention suggestions:

· Use insect repellant with any of the following active ingredients

- DEET (up to 30%)
- Picaridin
- Oil of lemon eucalyptus
- Para-menthane diol
- IR3535
- Always follow product label instructions and make sure repellent is age-appropriate.
- It is safe for pregnant or nursing women to use EPA-approved repellents if applied according to package label instructions.
- Apply repellent on bare skin or clothing, not under clothing.
- Cover skin with long-sleeved shirts and long pants
- Apply a permethrin repellent directly to clothing or purchase pre-treated clothing. Follow the manufacturer's directions and do not apply directly to the skin.
- Keep mosquitoes out of hotel rooms
- Choose a hotel or lodging with air conditioning or screens on windows and doors.
- Sleep under a mosquito bed net when outside or in a room that is not screened.

Source: Florida Department of Health

Keep updated

Each day at 2 p.m., the Florida Department of Health issues a daily update. For information, visit http://www.floridahealth.gov/ (http://www.floridahealth.gov/)

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