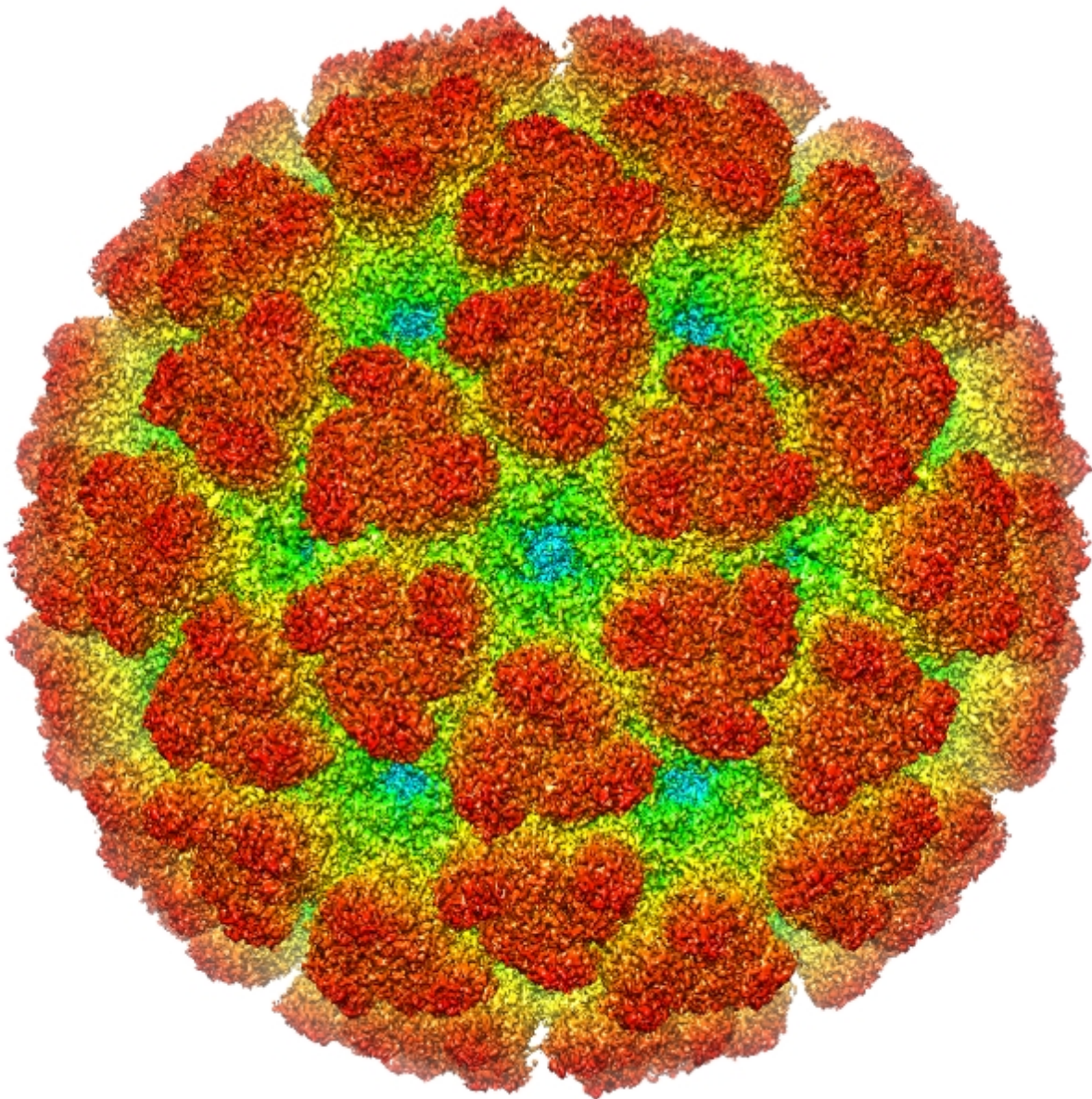


Researchers develop antibodies to fight chikungunya virus

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Cryoelectron microscopy reconstruction of Chikungunya virus. From EMDB entry 5577. Credit: Wikipedia

In late 2013 the Caribbean had its first case of the mosquito-borne chikungunya virus. Today there have been almost 1.2 million cases in 44 countries or territories, including 177 cases in 31 U.S. States.

Vanderbilt University Medical Center's James Crowe, M.D., Ann Scott Carell Professor and director of the Vanderbilt Vaccine Center, and his team are reporting the first large panel of antibody treatments against this disease in the current issue of *Cell Host and Microbe*.

Transmitted by the bite of infected mosquitoes, it's one of the largest outbreaks of any virus in the world. And you don't even necessarily have to travel out of the country to get it. The virus is not spread from person to person but spreads with a domino effect from an infected mosquito to a person and from that person to a previously uninfected mosquito, and on to the next person.

Crowe and his team are developing antibodies to fight [chikungunya](#). The virus is transmitted by two types of Aedes mosquitoes, both now found in the southeastern U.S.

Chikungunya virus causes a flu-like illness with headaches and fever and then disabling joint pain that can last for years. Up until now, there has been no effective treatment for the virus infection, and there is no licensed vaccine to prevent it.

The development process in Crowe's laboratory works like this: With a few ounces of blood from a previously infected person, researchers find chikungunya antibody-secreting cells, and then those cells are processed

to retrieve their DNA and antibody genes.

The team started about two years ago acquiring blood from people who had chikungunya as children and has isolated 3 dozen chikungunya antibodies so far. "Amazingly even decades after an infection, people still have cells in their blood making antibodies for chikungunya," Crowe said.

In what Crowe calls a "needle in the haystack" technology, developed at Vanderbilt, his team is able to pull the B-cells (which secrete antibodies) from the blood, and using molecular biology, make antibody drugs. About 1-2 ounces of blood is taken from each individual who has been infected. The white and [red blood cells](#) are separated and only the white are retained. Once the cells start making antibodies, the cells are pulled out, and the genes are pulled from those.

They are testing in model systems, but the goal is to test one or more of the antibodies in human beings in about a year. When current laboratory studies identify the very best drugs among the several dozen available, Vanderbilt will hand their gene findings over to a drug company for mass manufacturing of the treatments.

"It's frustrating, because the outbreak is ongoing now," Crowe said. "I wish we had the drug ready to test in humans now, but you need to be careful and prepare these materials correctly. It takes a long time to manufacture and test and prove that materials are safe for humans."

Crowe said using antibodies for treatment, and the body's natural immune defense, may be more effective than trying to develop a synthetic drug, which typically has a high rate of failure. "It's not only a more natural way to make the drugs, it's a more powerful way, because human beings make the most amazing antibodies," he said. "Why didn't we always do this? Because it's not always easy to find the people, and

the techniques didn't exist in years past."

The [chikungunya virus](#) was first identified in Africa 50 years ago, and has been mostly in Asia and occasionally southern Europe until it hit the Caribbean this year. It was only a matter of time before it came to the U.S.

"There are about 1 million people who travel to the Caribbean and back in the U.S. each year," Crowe said. "If you go to Haiti on a mission trip, there's a very high chance you'll be infected with chikungunya if you are in an infected area. There are at least 30 organizations in Nashville that do development or mission work in Haiti, so while mosquitoes may only travel 50-100 feet their entire lives, there are a high number of people going back and forth between the U.S and the Caribbean. We talk to groups who have a dozen people down there, and 10 come back infected."

Crowe believes an outbreak could occur in the South.

"We have mosquitoes over three-fourths of the country, so potentially, and definitely in the South, we could have just as brisk of an outbreak as they do in the Caribbean," Crowe said.

"Public health experts argue we may not, because we love our air conditioning and we stay inside. But it's a numbers game - are there enough people outside getting bitten at the same time? Once it starts it burns like wildfire. It's very transmissible, very infectious."

Crowe said that joint pain from chikungunya can be "disabling, like chronic arthritis." The name 'chikungunya' derives from a word in the Kimakonde language, meaning "to become contorted" and describes the stooped appearance of sufferers with joint pain.

Once the drug is developed and tested in humans, Crowe said it would be given to infected people early in the infection, prior to the debilitating [joint pain](#).

"This would be similar to what you do with flu drugs right now - you develop a fever for a day, you take the test, and take the drug a day or two after," he said.

A vaccine that induces long-term protection could be more convenient and cost-effective in the long run than giving shots of the antibody to try to prevent infection, he said.

"You'd have to have an injection of antibody every month if you lived in one of these endemic areas," Crowe said. "But coming up with a vaccine that induces long-term protection will take longer to develop. We would definitely prefer a vaccine, but vaccine licensure historically has taken about 25 years."

Crowe's lab is also working on [antibodies](#) to Ebola and Marburg viruses.

Provided by Vanderbilt University Medical Center

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