Experimental vaccine protects monkeys against chikungunya

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Imagine a mosquito-borne virus that has already infected millions of people in recent outbreaks in South and Southeast Asia, the islands of the Indian Ocean, Africa and northern Italy. Although seldom fatal, it causes highly painful arthritis-like symptoms that can linger for months or even years. It's capable of adapting to spread through a mosquito species common in much of North America. And no vaccine or treatment exists to protect humans from its effects.

The scenario may sound like something dreamed up as a training exercise by public health authorities, but the virus is all too real. Called chikungunya, from an East African tribal word describing the contorted postures of its pain-wracked victims, the pathogen has been the focus of intense scientific interest ever since a 2006 outbreak on the island of La Reunion in the Indian Ocean infected about 266,000 people, killing 260 of them.

Now, researchers at the National Institute of Allergy and Infectious Diseases, the University of Texas Medical Branch at Galveston, Purdue University and Bioqual Inc. have developed an experimental vaccine for chikungunya virus and successfully tested it in monkeys. Described in a paper appearing in the March issue of Nature Medicine, the vaccine is composed of noninfectious "virus-like particles." Although coated with the same proteins that enable chikungunya to pass through cell membranes, the vaccine particles lack the proteins that chikungunya uses to replicate inside cells. They look like chikungunya to the immune systems of rhesus macaques, however, which respond to exposure by

generating antibodies that defend the monkeys from infection by the real virus.

"This vaccine did an excellent job of protecting the macaques from chikungunya," said UTMB professor Stephen Higgs, one of the paper's authors. "That it worked so well in a primate model is good news — these macaques are quite similar to humans in their response to chikungunya, and we badly need to develop an effective human vaccine for this virus."

To create the virus-like particles used in the experimental vaccine, the researchers used genetic engineering techniques to produce the structural proteins that produce the spiky, roughly spherical exterior possessed by chikungunya viruses before they have entered a cell. The proteins then assembled themselves into harmless balls that resembled particles of Sindbis virus — a relative of chikungunya and a fellow member of the alphavirus genus, which also includes a number of insect-borne viruses capable of causing dangerous encephalitis in humans.

Serum drawn from rhesus macaques injected with the virus-like particles contained substantial levels of antibodies that inactivated chikungunya virus. Two groups of macaques were then inoculated, either with virus-like particles or with a sham solution containing no vaccine. When the researchers challenged the monkeys by injection with chikungunya 15 weeks later, they found that the vaccine had completely protected the animals from the virus.

Dr.Gary Nabel, director of the NIAID's Vaccine Research Center and corresponding author on the Nature Medicine paper, said that the vaccine's effectiveness against chikungunya had led his group to plan follow-up investigations into whether the same approach would work against other alphaviruses, such as Western and Eastern equine encephalitis viruses (both responsible for periodic outbreaks in the

United States), and Africa's o'nyong-nyong virus.

Provided by University of Texas Medical Branch at Galveston