Zika’s Balloon Popped by Peptide Needle

An engineered peptide demonstrates potential as a brain-penetrating antiviral against Zika and other membrane-enveloped viruses. (NTU Singapore)

A new antiviral drug candidate attacks the Zika virus where it may be most vulnerable—the lipid membrane, which envelops Zika’s RNA payload. The drug candidate is an engineered peptide that punctures the membrane, directly stopping the Zika virus particle by rupturing it, rather than interfering in Zika’s replication. Even better, the peptide, as demonstrated in mice on cross-reacting, the most improbable blood-brain barrier. Protecting against Zika in the brain is of critical importance, given Zika’s targeting of the brain and central nervous system.

The peptide was developed by scientists based at Nanyang Technological University (NTU), Singapore, in collaboration with colleagues at the Federal University of Acessns, Brazil, and Queen’s University, London. When these scientists injected the peptide to Zika-infected mice in the lab, they succeeded in reducing disease symptoms and the number of deaths.

Dissolved findings appeared October 22 in the journal Nature Medicine. In an article titled, “Therapeutic Treatment of Zika Virus Infection using a Brain-penetrating Antiviral Peptide,” the authors argue that the new “bubble-busting” approach could be useful against a range of membrane-enveloped viruses, not just Zika.

A new antiviral peptide can differentiate between Zika viral membranes and membraneless membranes because the virus particles are much smaller and more porous, while the membrane-less viruses are larger and more solid. (NTU Singapore)

“Therapeutic treatment protected against mortality and markedly reduced clinical symptoms, viral loads, and neuroinflammation, as well as an mitigated microgliosis, neurogenesis, and brain damage,” the authors’ newspaper. “In addition, controlling systemic infection, the peptide crossed the blood-brain barrier to reduce viral loads in the brain and protected against Zika virus-infected blood-brain barrier injury.”

The lab tests showed that when the peptide was administered, 10 out of 12 infected mice survived. In comparison, all the mice in the control group died within a week post-infection. In addition, therapeutic concentrations of the peptide were able to cross the blood-brain barrier, allowing it to inhibit viral replication in the brain.

“There are currently no vaccines for the Zika virus, while available medicines only alleviate symptoms such as fever and pain,” says Joao Alves, the senior author of the current study and an associate professor at NTU’s School of Environmental and Biological Engineering. “This newly created peptide hold great promise in becoming a future antiviral that can act directly on viral infections in the brain.”

The virus is transmitted by Aedes mosquitoes and infections during pregnancy are linked to both defects as microcephaly, a condition in which a baby is born with an abnormally small head and brain. The World Health Organization declared the Zika disease an international emergency in 2016, and it remains a large threat globally today.

In general, most antiviral drugs target the reactivation process of viruses. However, viruses often mutate quickly and additional drugs that target viral replication can become obsolete. Attacking the physical structure of viral enzymes is a new approach to developing new antiviral drugs. It offers promise for the peptides to be effective even if the Zika virus attempts to mutate.

“Therapeutic antiviral peptides should be able to lead to an epidemic in a short time, leaving communities unprotected,” Cho notes. “By targeting the lipid membrane of virus particles, scientists may devise more robust and effective ways to stop viruses.”

“The peptide differentiates between Zika viral membranes and membraneless membranes because viruses frequently are much smaller and more porous,” while the membrane-less viruses are larger and more solid. (NTU Singapore)

“By cross-linking a bubble, the peptide sticks to the viral membrane. Once they infect, the virus will be ruptured.”

The Zika virus belongs to the Flaviviridae family and is related to other mosquito-borne viruses such as dengue, chikungunya, and yellow fever. As all flaviviruses have virus particles that are 40 to 50 nanometers in diameter and are enveloped by a lipid membrane, the peptide engineered by the scientists from NTU has the potential to work against these viruses too.

Laboratory tests in this study confirm this potential and in future, researchers intend to study the effects of the peptide on disease caused by these other viruses in greater detail. The team will also extend the trials to larger animals, and subsequently plan to initiate human clinical trials, once relevant preclinical studies have been completed and regulatory approvals obtained.