New West Nile and Japanese encephalitis vaccines produced

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University of Texas Medical Branch at Galveston researchers have developed new vaccines to protect against West Nile and Japanese encephalitis viruses. The investigators created the vaccines using an innovative technique that they believe could also enable the development of new vaccines against other diseases, such as yellow fever and dengue fever, which are caused by similar viruses.

The scientists showed that the vaccines successfully protected laboratory mice and hamsters against the viruses, which can cause fatal brain inflammation in humans. They reported their findings in back-to-back papers published in the current issue of the journal *Vaccine*.

"These vaccines were created using a system that we think is applicable to producing vaccines that can protect against a wide range of diseases caused by the flaviviruses, an important family of viruses that afflict populations throughout the world," said UTMB pathology professor Peter Mason, senior author of the Vaccine papers. "Flaviviruses cause tremendous human suffering, but we still only have vaccines for a few of them."

Currently approved flavivirus vaccines are either "live-attenuated virus" vaccines, which contain weakened but still genetically intact versions of the target virus, or "inactivated-virus" vaccines, which contain viruses that have been chemically neutralized. In each case, the viral material stimulates the immune system to block the progress of any future infection by the virus in question.

The new vaccines — based on a concept devised by Mason and UTMB microbiology and immunology associate professor Ilya Frolov — are known as "single-cycle" or "pseudoinfectious" vaccines, and contain flaviviruses that have been genetically modified so that each virus can only infect a single cell. Unable to spread from cell to cell and create disease, these crippled viruses nonetheless continue to copy themselves within the cells they infect, thus producing the viral proteins needed to induce immune protection.

"With these vaccines, we mimic a viral infection and get amplification of the antigens that are important for stimulating an immune response without amplification of the virus," Mason said.

To make the West Nile vaccine, the researchers deleted the piece of the West Nile virus genome that codes for a "capsid" (or "C") protein, a part of the virus particle that encloses the genetic material of the virus and is essential to its ability to move between cells. They then introduced this truncated RNA into cells specially designed to produce high concentrations of the C protein. The result: large numbers of virus particles that had capsids but lacked the ability to pass the C gene on to their progeny.

"A vaccine virus particle grown in the C-protein expressing cells can only infect one cell in a vaccinated individual," Mason said. "Once it gets into that cell, in order to make a new particle, it needs the C protein—and cells in the vaccinated host do not have the gene to make the C protein. But it can still make all the immunogenic proteins that the virus normally makes, and it can still generate strong immunity."

The Japanese encephalitis vaccine was built from the West Nile vaccine, using the C-less West Nile genome but replacing the genes for two key immunogenic proteins with their Japanese encephalitis virus counterparts, a process called "chimerization." The success of such

genetic mixing and matching, Mason noted, could open the door for the creation of a wide variety of "chimerized" single-cycle flavivirus vaccines for other diseases.

Source: University of Texas