MedicalXpress

Preliminary Zika vaccines prevent neurological disorders in newborn mice

October 3 2016

Two vaccines against Zika virus developed at the University of Pittsburgh School of Medicine have successfully conveyed immunity from female mice to pups conceived weeks after the mother's vaccination.

When challenged with Zika virus within a week of their birth, both vaccines protected the pups against neurological damage better than pups with no maternal-conferred immunity. The results are published online today and scheduled for the November issue of *EBioMedicine*, a journal supported by Cell Press and *The Lancet*.

"We've not only developed a promising vaccine candidate to move toward larger preclinical and, eventually, human clinical trials, but also a delivery format that would be inexpensive to produce and distribute to hundreds of thousands of people," said senior author Andrea Gambotto, M.D., associate professor of surgery in Pitt's School of Medicine.

Zika is a virus spread primarily through the bite of an infected mosquito of the Aedes species. When pregnant women are infected, the virus can pass to their fetus, which can damage the developing baby and cause severe neurological birth defects, including microcephaly, or an abnormally small head.

One of the two vaccines uses a "microneedle array" to deliver the vaccine just below the surface of the skin through tiny crystals that dissolve after being affixed to the skin by a Band-Aid-like patch. The

technology was co-invented by Louis D. Falo, M.D., Ph.D., chair of Pitt's Department of Dermatology and co-author of the study.

The other vaccine uses the traditional needle delivery format and adenovirus, a type of common cold virus, to present Zika antigens to the immune system to induce immunity.

Both vaccines used proteins on the "envelope," or outer shell, of the virus as the antigen to prime the immune system so it can quickly recognize and fight off the actual virus. This approach has worked in the past to develop West Nile, yellow fever and dengue vaccines.

Three groups of female mice, with five mice per group, were immunized with either one of the two vaccines or a saline solution with no vaccine for the control group. Two weeks after the initial vaccination, the mice received a booster of the same vaccine they originally received.

Blood tests were performed at vaccination and every two weeks afterward. The mice showed immunity against Zika two weeks after immunization with the adenovirus Zika vaccine and six weeks after immunization with the microneedle array Zika vaccine.

Five weeks after initial immunization, the female mice were mated with unvaccinated males. Because mice do not develop microcephaly, giving the mothers Zika while pregnant would be unlikely to affect the pups. So the researchers waited until one week after the pups were born and then exposed them to Zika. All of the pups from the mothers immunized with adenovirus Zika vaccine and half of the pups from the mothers who received the microneedle array vaccine survived infection. Only 12.5 percent of the pups from mothers in the unimmunized control group survived.

Furthermore, all of the control group pups showed signs of neurological

damage, including loss of balance, muscle weakness and hind-limb paralysis. Five out of six of the microneedle array group pups also exhibited neurological issues, though they weren't as severe as the control group's symptoms. None of the adenovirus vaccine pups showed significant neurological problems.

Although the adenovirus Zika vaccine definitely performed better in this study, Dr. Gambotto said it was used as a proof-of-principle vaccine in mice to quickly develop and test if the envelope protein antigen would work in a mouse model. It wouldn't work well in humans because the vast majority of us have already had adenovirus colds so our immune systems would simply neutralize the vaccine and not develop proper Zika antibodies.

"We decided to move forward with the microneedle array Zika vaccine and have since developed a promising, second-generation vaccine," said Dr. Gambotto. "We are hopeful, now that Congress has approved the $1.1 billion bill to provide funding for Zika prevention and research, that we'll be able to do larger-scale studies to evaluate and develop this vaccine for possible human clinical trials in the future."

Provided by University of Pittsburgh Schools of the Health Sciences