Lab vaccine shields mice against Zika virus

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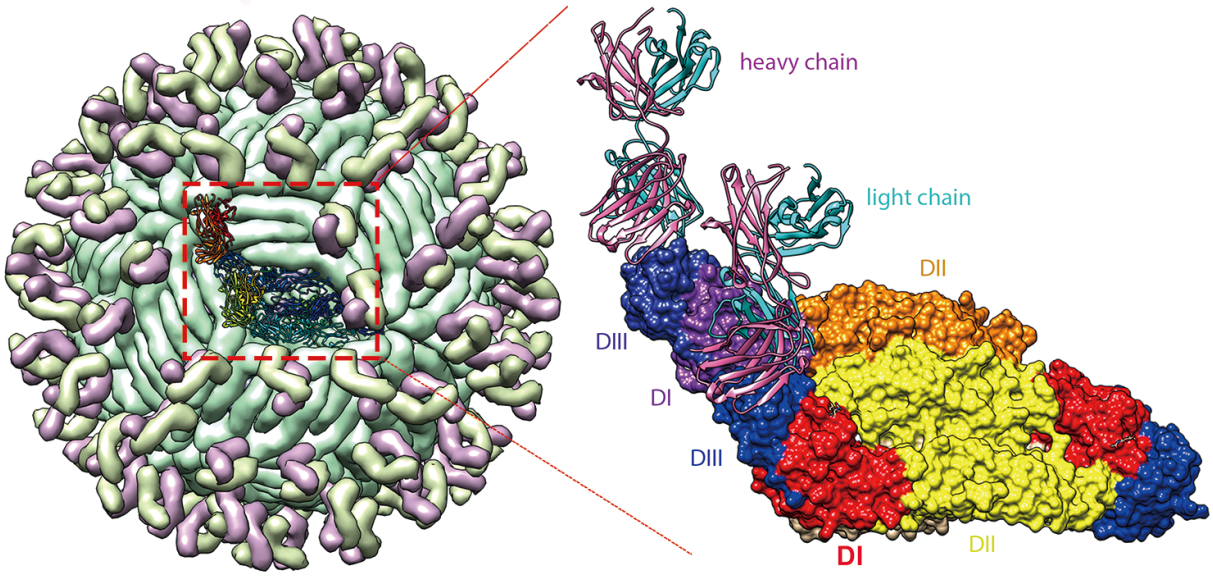

Overall view of antibody Z23 bound to the Zika virus particle. Credit: Gao et al., *Science Translational Medicine* (2016)

Antibodies drawn from a patient infected with Zika could form the basis of a vaccine against the notorious virus, a new animal study suggests.

Antibodies are protective proteins produced by the immune system. In laboratory studies, two antibodies drawn from the blood of a Zika-infected patient shielded mice from Zika virus infection, according to a team of Chinese researchers.

Further, these antibodies appear to avoid one of the problems researchers have come up against in trying to develop a Zika vaccine, the study authors noted.

Zika belongs to the flavivirus family, a group of mosquito-borne viruses that also includes dengue, yellow fever and West Nile virus.

Flaviviruses tend to cross-react, meaning that prior infection with any of them can increase a person's risk of contracting a nastier version of another flavivirus, explained Dr. Daniel Caplivski. He's an associate professor of infectious diseases at the Icahn School of Medicine at Mount Sinai in New York City.

"Antibodies are usually neutralizing, meaning they prevent the virus from replicating further," Caplivski said. "In the case of flaviviruses, sometimes those antibodies—instead of neutralizing the virus—allow it to enter cells with more efficiency."

That's one hurdle vaccine researchers must face, "to make sure they're not going to develop an antibody that's potentially going to increase infectivity," he noted.

The antibodies identified by the Chinese researchers—known as Z23 and Z3L1—appear to focus specifically on Zika virus strains. In lab studies, the antibodies did not cross-react with any of four strains of dengue.

Dr. Amesh Adalja is a senior associate with the University of Pittsburgh's UPMC Center for Health Security. He said, "Because of Zika's similarity to dengue and the possibility of paradoxically enhancing infection, it will be important that countermeasures developed against Zika are highly targeted to produce the most effective vaccines and therapies."

Adalja explained that "in this new study, highly Zika-specific neutralizing antibodies—targeted to specific components of the viral structure—were isolated from a Chinese patient that did not exhibit cross-reaction to dengue and were able to protect mice from infection."

Zika can cause devastating birth defects in babies exposed to the virus in the womb. One of these birth defects, microcephaly, can cause babies to be born with a smaller than normal head and an underdeveloped brain. Zika infections can also cause neurological complications, such as Guillain-Barre syndrome, in adults.

More than 80,000 people in 69 countries have been infected by the virus during an ongoing outbreak that originated in Brazil in 2015, the study authors said in background notes.

"These findings could form the basis for better vaccine design as well as for antibody-based therapies," Adalja said.

The two antibodies appear to block infection by interfering with Zika's ability to enter cells and begin replicating, study author Qihui Wang, of the Institute of Microbiology at the Chinese Academy of Sciences in Beijing, and colleagues reported.

To test potential effectiveness, the researchers exposed groups of three to five mice to Zika, and injected them with the antibodies a day later.

Mice treated with Z23 or Z3L1 were completely protected against Zika infection, the investigators found. Four out of five mice were protected by another antibody called Z20.

The Chinese researchers said their findings add to the current arsenal of antibodies in development for much-needed antiviral therapies and vaccines.

However, the study authors added that further analysis is needed to better understand how Z23 and Z3L1 specifically offer protection. And studies in animals often fail to produce similar results in humans.

Caplivski said it will be some time before a vaccine based on these results can be available to humans.

"One of the issues with vaccine research is they tend to have a very long period to build enough data to prove they're safe and to make it into vaccine trials for humans in an area where they can be effective," he said.

"The time it takes to discover an antibody and develop it in a mouse model and get it into the field is such a long process, that places hit by Zika tend to have a tail-off, as people get immune to it naturally," Caplivski explained.

The new study was published online Dec. 14 in the journal *Science Translational Medicine*.

More information: "Molecular determinants of human neutralizing antibodies isolated from a patient infected with Zika virus," *Science Translational Medicine*, stm.sciencemag.org/lookup/doi/ … scitranslmed.aai8336

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