SIV shrugs off antibodies in vaccinated monkeys

August 11 2015

New research on monkeys vaccinated against HIV's relative SIV calls into question an idea that has driven AIDS vaccine work for years. The assumption: a protective vaccine only needs to stimulate moderate levels of antibodies that neutralize the virus.

However, scientists at Yerkes National Primate Research Center and the Emory Vaccine Center have found that when SIV manages to infect vaccinated monkeys that have potent neutralizing antibodies in their blood, the virus appears to shrug the antibodies off. No stealthy escape by mutation was necessary.

The results were published in *Proceedings of the National Academy of Sciences*, Early Edition on Monday, August 10.

While published studies have shown that experimental vaccines can protect a majority of monkeys from repeated challenge with SIV, the Yerkes and Vaccine Center team's findings are sobering and puzzling, says senior author Cynthia Derdeyn, PhD, professor of pathology and laboratory medicine at Emory University School of Medicine and Yerkes National Primate Research Center.

In an infected individual, HIV (or SIV) is always mutating; Derdeyn's ongoing research shows how HIV changes in newly infected humans in order to escape pressure from the immune system.

"We were surprised because we expected the virus that breaks through to be resistant to the vaccine-induced antibodies," she says. "We need to know more about whether antibodies are present and protective on the mucosal surfaces where transmission occurs, and whether active vaccination might be increasing susceptibility to infection."

Derdeyn's work is an extension of several vaccine studies Rama Amara, PhD, and his colleagues conducted at Yerkes in which rhesus macaques were immunized and then repeatedly challenged with SIV with a schedule that is consistent from study to study. After 12 challenges, 100 percent of control animals became infected, but with the most effective vaccination regimens, nearly 70 percent remained uninfected.

"There is a protective effect, but it's incomplete," Derdeyn says. "So we want to know what's happening in those animals where the virus gets through the barrier."

Researchers obtained samples of the viral strain that established infection in 14 vaccinated-yet-infected monkeys. The infections recapitulated the "genetic bottleneck" effect seen in human HIV transmission, where a single viral variant establishes infection. In 13 of 14 cases, antibodies from the monkeys' blood could neutralize the

particular viral variant that established infection.

According to the authors, possible explanations could be:

- neutralizing antibodies are present in the blood, but not in sufficient levels in mucosal secretions
- immunization may increase the number of target T cells for the virus in mucosal tissues and a balance between protective antibody response and target cell frequency ultimately determines protection
- in vitro antibody tests don't reflect how in vivo transmission occurs

Derdeyn's team is continuing with an investigation of how SIV's infectivity differs depending on whether viral challenge occurs rectally or vaginally. The first author of the paper is lead research specialist Samantha Burton in the Derdeyn lab.

More information: Breakthrough of SIV strain smE660 challenge in SIV strain mac239-vaccinated rhesus macaques despite potent autologous neutralizing antibody responses, Samantha L. Burton, *Proceedings of the National Academy of Sciences*, DOI: 10.1073/pnas.1509731112

Provided by Emory University

provided for information purposes only.