Human mode of responding to HIV vaccine is conserved from monkeys

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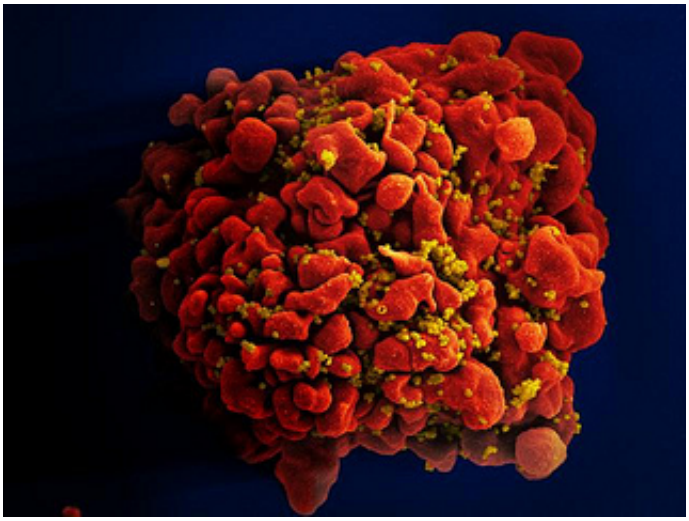

Scanning electron micrograph of an HIV-infected H9 T cell. Credit: NIAID

The antibody response from an HIV vaccine trial in Thailand was made possible by a genetic trait carried over in humans from an ancient ancestry with monkeys and apes, according to a study led by Duke Medicine researchers.

In a study published in the journal *Immunity*, the researchers report that an investigational vaccine that elicited an immune response in an estimated 31 percent of participants was able to do so because of a particular antibody gene motif that is shared with rhesus macaques and other primates.

When activated by the vaccine, the antibody gene makes it easy for the immune system to recognize and attack the HIV virus at a specific location on the outer coat of the virus.

The finding helps further the understanding of how the vaccine candidate, tested in Thailand in a trial known as RV144, triggered an immune response that provided modest protection. The RV144 study is the only vaccine trial to show any efficacy, so it provides data for scientists to mine. Duke researchers have played a key role in an international collaboration that has discovered many important clues into why RV144 worked and what it will take to develop a more efficacious HIV vaccine.

In their analysis, the researchers tracked the immune response in rhesus macaques that were immunized with a vaccine regimen similar to that used in the RV144 human trial in Thailand. The researchers found that the monkeys' immune response was similar to what was seen in humans, and was actually the dominant response.

"It turns out that this antibody response that can recognize this part of the HIV envelope is encoded in the genes present throughout primate development," said lead author Kevin Wiehe, Ph.D. "We found it in almost every primate species we studied - macaques, gorillas, bonobos and lemurs.

"When we found it in that many primate species, we then traced it back to when the common ancestor of humans and lemurs diverged - 87 million years ago. HIV has not been around that long, but other monkey retroviruses likely have, so this is an ancient antibody recognition motif that has been retained through evolution that is also used to recognize HIV."

Wiehe and colleagues said the ancient genetic trait enables primates to

produce antibodies easily to retrovirus proteins, and presents an opportunity to seek ways of boosting this ability or building upon it to create an effective vaccine.

The drawback, however, is that this specific response might compete with broadly neutralizing antibodies that can defuse the virus regardless of how it mutates.

"The place on the envelope to which antibodies were made in the RV144 trial is also a site of rare broadly neutralizing antibody binding," said senior author Barton F. Haynes, director of the Duke Human Vaccine Institute. "What we have found is that the mode of making the non-broadly neutralizing antibodies is so dominant, that it is conserved throughout primate development over millions of years.

"Thus, our primate immune systems have been trained over many years to respond in this manner," Haynes said. "To make broadly neutralizing antibodies, we need to bypass this remarkably highly conserved mode of antibody response to train our immune systems to respond in a new manner. That is where our current studies are focused."

Wiehe said eliciting broadly neutralizing antibodies remains one key goal of HIV vaccine development, because the HIV virus mutates so rapidly.

"We need antibodies that can recognize multiple strains of the virus," he said.

Provided by Duke University