Antibody response linked to lower mother-to-child HIV transmission

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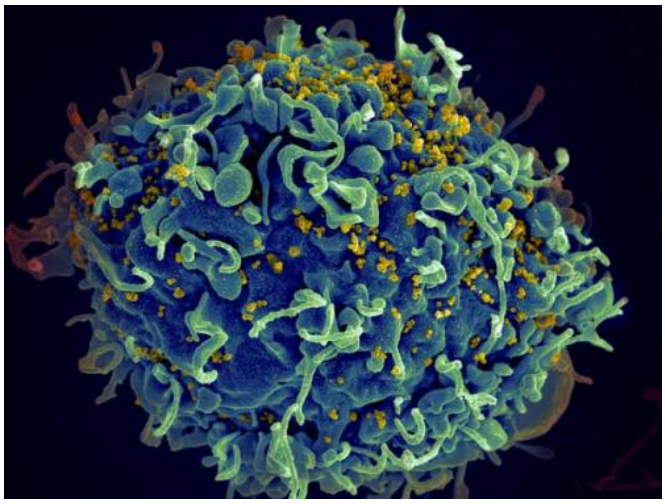

HIV, the AIDS virus (yellow), infecting a human immune cell. Credit: Seth Pincus, Elizabeth Fischer and Austin Athman, National Institute of Allergy and Infectious Diseases, National Institutes of Health.

How most babies are protected from acquiring HIV from their infected mothers has been a matter of scientific controversy. Now researchers at Duke Medicine provide new data identifying an antibody response that had long been discounted as inadequate to confer protection.

Mother-to-child transmissions account for about 250,000 HIV infections per year worldwide, despite greatly expanded access to antiretroviral drug regimens that can interrupt transmission into low-resource settings. Ongoing problems with access to the drugs, late initiation of the drug regimens during pregnancy, and acute maternal infection during pregnancy and breastfeeding all contribute to the ongoing infant transmission.

Even in the absence of antiretroviral drug regimens, however, the majority of newborns are naturally protected against HIV, despite chronic virus exposure. The Duke research team sought to define what is different in the babies who become infected compared to those who don't.

"We know that mothers pass antibodies to fetuses in-utero, but a true understanding of how maternal antibodies were contributing to protection had never been established," said Sallie Permar, M.D., Ph.D., associate professor of pediatrics at Duke and lead author of a study published online June 8, 2015, in the *Journal of Clinical Investigation*.

Permar and colleagues at the Duke Human Vaccine Institute and the Fred Hutchison Cancer Research Center analyzed data from a U.S. study in the 1990s that predated therapies such as AZT. The study included mothers and babies, yielding information about risk factors and transmissions in a pre-treatment environment.

By profiling the immune responses of mothers in this early study, the researchers were able to pinpoint the differences between those who transmitted the virus to their infants, and those who did not.

Among mothers whose babies were shielded from infection, they found a strong antibody response to a particular region on the HIV virus envelope (the HIV envelope third variable or V3 loop) that has been considered too variable and too inaccessible to be a relevant target for a neutralizing antibody.

"That was very surprising," Permar said, "because this type of weak neutralizing antibody response, which had previously been thought to be inconsequential for HIV transmission, could potentially be effective in preventing mother-to-child transmission. And there are current HIV vaccine candidates, such as recombinant HIV envelope protein immunization, in early-stage clinical testing that can elicit this type of response."

Permar said the team's study raises a compelling

question about why the V3 neutralizing antibody response seems to be enough to reduce mother-to-child transmission, yet is not protective in other modes of HIV transmission.

"The difference in mother-to-infant transmission might be that the infant is only being exposed to the mother's virus, and the infant is born with antibodies that are transferred from the mother," Permar said. "The presence of antibodies that were raised against the mother's virus prior to exposure to the same virus makes the infant transmission setting very different from that of other modes of HIV transmission. So how well the mother's antibody can neutralize her own virus could be the key to whether the baby is infected."

Permar said additional research at Duke will focus on testing newer experimental HIV vaccines to raise this potentially protective antibody response in mothers to neutralize her virus and thereby protect the baby.

"We hope this will be a major clue to making a vaccine to effectively prevent all mother-to-child HIV transmission, since these antibodies are the type that our current experimental HIV vaccines can boost," said M. Anthony Moody, M.D., a co-author and chief medical officer in the Duke Human Vaccine Institute. "For protecting unborn and newborn children, we may be closer to testing a vaccine that can induce this type of common HIV-specific antibody response for its ability to protect infants than previously thought."

Provided by Duke University Medical Center