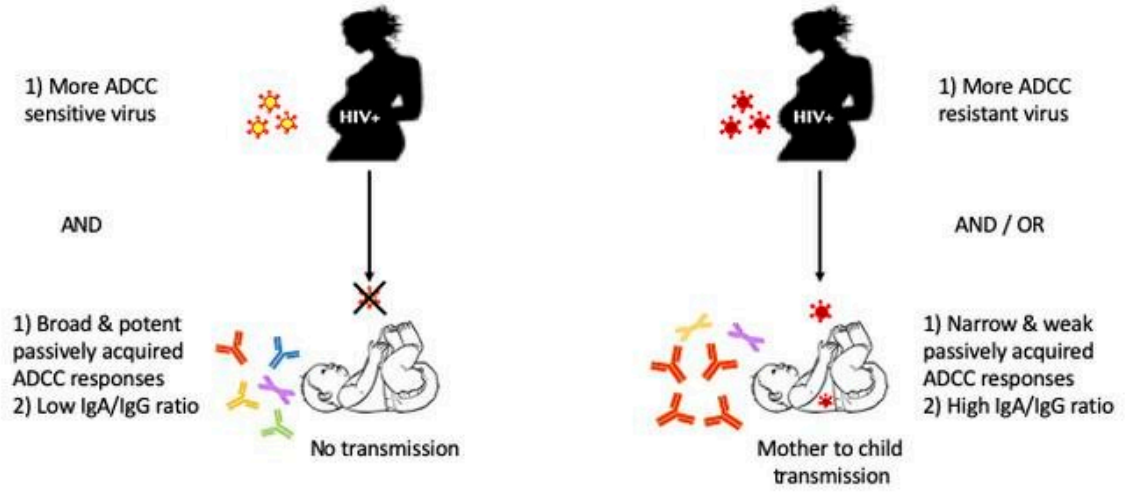
Antibody dependent cellular cytotoxicity may help prevent HIV transmission from mother to child during breastfeeding

April 20 2022



Credit: Allison S. Thomas et al, *JCI Insight* (2022), DOI: 10.1172/jci.insight.159435

According to new research from Boston Medical Center, the antibody function known as antibody dependent cellular cytotoxicity (ADCC) and the ADCC sensitivity of HIV strains may influence the transmission of

HIV from mother to child during breastfeeding. These data imply that enhancing ADCC, through a vaccine, for example, may not be sufficient to prevent transmission because chronically infected individuals can harbor ADCC-resistant strains. Published in JCI Insight, the findings provide novel insights about immunologic characteristics that a vaccine may need to elicit to help block HIV transmission.

Researchers evaluated ADCC and neutralizing antibody (nAb) properties in pre-transmission plasma from HIV-1 exposed infants and from the corresponding transmitting and non-transmitting mothers' breast milk and plasma from samples from a well-defined mother to child HIV transmission cohort. All the mothers were HIV infected, while their babies were born uninfected. Although all babies were breastfed for up to a year of life, some got HIV, while others did not.

This study shows that infants with a combination of higher pre-transmission ADCC and exposure to more ADCC susceptible strains are less likely to acquire HIV-1. This implies that efforts to eliminate transmission will need to both improve ADCC responses in at-risk individuals and account for the ADCC susceptibility of the strains circulating in the infected individuals most likely to transmit the virus.

"With about 150,000 transmissions yearly, transmission of HIV from mother to child remains a significant global problem, and vaccines are needed urgently," said Manish Sagar, an infectious diseases physician at Boston Medical Center, associate professor of medicine and microbiology at Boston University School of Medicine, and corresponding author on this study. "This study and its findings are highly relevant for developing possible new strategies to help prevent the further spread of HIV."

Improving outcomes in the infants that become infected is important, especially due to limited access to antiretroviral therapy. Without

antiretroviral treatment, the risk of transmission during the breastfeeding period is between 10 and 20 percent depending on duration of breastfeeding, which may suggest natural immune mechanisms that protect against HIV acquisition.

The results of this study provide new insights for HIV-1 vaccine efforts—in particular that at a minimum, a possible vaccine may need to elicit antibodies that can mediate ADCC. While traditional vaccine efforts have focused on eliciting neutralizing antibodies, previous studies from Dr. Sagar's group, along with other investigations, have found that high levels of neutralizing antibodies do not protect against HIV acquisition and that ADCC may help prevent acquisition, even in the absence of neutralizing responses. At this time, it remains unclear if ADCC can be elicited using current vaccine technologies, and it would still be insufficient in preventing HIV transmission, as strategies will need to account for the ADCC sensitivity of the circulating strains in individuals likely to transmit HIV-1.

More information: Allison S. Thomas et al, Antibody-dependent cellular cytotoxicity (ADCC) responses along with ADCC susceptibility influence HIV-1 mother to child transmission, *JCI Insight* (2022). DOI: 10.1172/jci.insight.159435

Provided by Boston Medical Center