

# Immune Cells in Breast Milk Reduce Mother to Child HIV Spread

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G Brennan

HIV can be transmitted either horizontally, from one person to another, or vertically, from mother to child. Mother-to-child transmission of HIV-1 is responsible for more than 400,000 infected infants annually, and most of these new infections occur in resource-poor areas. Infants are exposed to HIV from their mothers in utero, during birth, or post-partum, particularly via breast milk. Interestingly, even in the absence of antiretroviral therapy, only about one-third of infants who are HIV negative at birth will contract HIV-1 through breastfeeding, in spite of continuous exposure to the virus, suggesting that the mother's immune response may inhibit transmission of HIV.

There are two arms of the adaptive immune response, antibodies which bind and prevent virus from infecting cells, and cell-mediated responses, which detect and kill cells that have already been infected. Breast milk, particularly in the early post-partum period, is rich in both antibody and cell-mediated immune effectors. Previous studies have shown that most infected women have HIV-specific effector memory T-cells in their breast milk; however, it is unclear if these cells can prevent mother-to-child transmission.

To address this question, Dr. Barbra Richardson (Vaccine and Infectious Disease Division) and Dr. Julie Overbaugh (Human Biology Division), along with their collaborators in the Seattle/Kenya project, evaluated the correlation between HIV-specific IFN- $\gamma$  responses, a measure of cell-mediated immunity, and early post-partum transmission in a cohort of women from Nairobi, Kenya. The study, led by Barbara Lohman-Payne, who is based in Nairobi, and Grace John-Stewart at University of Washington, examined HIV Gag-specific IFN- $\gamma$  responses to four different peptide pools in paired peripheral blood (n=248) and breast milk (n=183) samples and compared them to transmission status (n=148). They found that 69% of women had detectable IFN- $\gamma$  responses from cells in breast milk and these responses were positively correlated with breast milk viral load (a higher IFN- $\gamma$  response correlated with higher viral load). In earlier studies, the team showed that breast milk viral load positively correlates with the development of an IFN- $\gamma$  response in exposed infants. In this study, there was no correlation between the maternal IFN- $\gamma$  response and detection of an IFN- $\gamma$  response in uninfected infants. However, detection of cytokines in breast milk associated with the cellular immune response (MIP-1 $\alpha$ , MIP-1 $\beta$ , RANTES, and SDF-1) positively correlated with the strength of the maternal IFN- $\gamma$  response (p<0.05 for each). Taken together, these data suggest that

protection is occurring in the breast milk rather than being transferred from the mother to the infant. In multivariate analyses, detection of any breast milk IFN- $\gamma$  response to any of the four peptide pools was associated with a 71% decrease in transmission (OR=0.29, 95%CI=0.092-0.91). Interestingly, the odds of mother-to-child transmission decreased by 35% for each additional peptide pool that elicited an IFN- $\gamma$  response (OR=0.65, 95%CI=0.44-0.97).

This study demonstrates that high levels of HIV-specific immune cells in breast milk positively correlate with the prevention of mother-to-child transmission, and that the broader this response is, the better the protection. However, IFN- $\gamma$  is produced by several different types of immune cells, including T-lymphocytes and NK cells, so the cell types responsible for this effect are still unknown. Future studies should determine which cells are responsible for the protective effect. More broadly, this study underlines the importance of Gag as an HIV vaccine target, because a vaccine that elicits breast milk Gag-specific responses might decrease the 400,000 mother-to-child transmission events that occur every year.

[Lohman-Payne B, Slyker JA, Moore S, Maleche-Obimbo E, Wamalwa DC, Richardson BA, Rowland-Jones S, Mbori-Ngacha D, Farquhar C, Overbaugh J, John-Stewart G.](#) 2012. Breast milk cellular HIV-specific IFN- $\gamma$  responses are associated with protection from peripartum HIV transmission. *AIDS*. 2012 Oct 23;26(16): 2007-16.



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Illustration of horizontal transmission between individuals (top) and vertical transmission between a parent and child (bottom). Mother to child transmission may occur in utero, during delivery, or during breastfeeding.