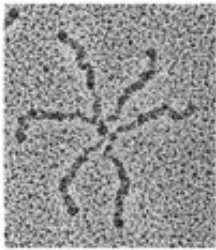


Breast milk protein may be key to protecting babies from HIV infection

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This is an electron microscope image of TNC. Credit: Harold Erickson

A substance in breast milk that neutralizes HIV and may protect babies from acquiring HIV from their infected mothers has been identified for the first time by researchers at Duke Medicine.

The [protein](#), called Tenascin-C or TNC, had previously been recognized as playing a role in wound healing, but had not been known to have antimicrobial properties. The discovery could lead to potential new HIV-prevention strategies.

Reporting in the journal *Proceedings of the National Academy of Sciences* during the week of Oct. 21, 2013, the researchers describe how the TNC protein in breast milk binds to and neutralizes the HIV virus, potentially protecting exposed [infants](#) who might otherwise become infected from repeated exposures to the virus.

"Even though we have antiretroviral drugs that can work to prevent mother-to-child transmission, not every pregnant woman is being tested for HIV, and less than 60 percent are receiving the prevention drugs, particularly in countries with few resources," said senior author Sallie Permar, M.D., Ph.D., assistant professor of pediatrics, immunology and molecular genetics and microbiology at Duke. "So there is still a need for alternative strategies to prevent mother-to-child transmission, which is why this work is important."

Worldwide in 2011, an estimated 330,000 children acquired HIV from their mothers during pregnancy or birth, or through breastfeeding according to UNICEF. As international health organizations have set a goal of eliminating mother-to-child infections, researchers have worked to develop safe and affordable alternatives to antiretroviral therapy that can be used to block HIV transmission to infants.

Permar and colleagues focused on breast milk, which has long been recognized as having some protective quality that inhibits mother-to-child transmission despite multiple daily exposures over months and even years of nursing. Earlier studies had identified some antiviral properties in breast milk, but the majority of the HIV-neutralizing activity of breast milk remained unexplained. More recent studies pointed to a large protein that had yet to be identified.

In their study, the Duke team screened mature milk samples from uninfected women for neutralizing activity against a panel of HIV strains, confirming that all of the detectable HIV-neutralization activity was contained in the high molecular weight portion. Using a multi-step protein separation process, the researchers narrowed the detectable HIV-neutralization activity to a single protein, and identified it as TNC.

"TNC is a component of the extracellular matrix that is integral to how tissues hold themselves together," Permar said, noting that co-author

Harold Erickson, Ph.D., professor of cell biology at Duke, was among the first to identify and describe TNC in the 1980s. "This is a protein involved during [wound healing](#), playing a role in tissue repair. It is also known to be important in fetal development, but its reason for being a component of breast milk or its antiviral properties had never been described."

Further analysis described how TNC works against HIV by blocking virus entry. The protein is uniquely effective in capturing virus particles and neutralizes the [virus](#), specifically binding to the HIV envelope. These properties provide widespread protection against infection.

"It's likely that TNC is acting in concert with other anti-HIV factors in breast milk, and further research should explore this," Permar said. "But given TNC's broad-spectrum HIV-1-binding and neutralizing activity, it could be developed as an HIV-prevention therapy, given orally to infants prior to breastfeeding, similar to the way oral rehydration salts are routinely administered to infants in developing regions."

Permar said TNC would also appear to be inherently safe, since it is a naturally occurring component of breast milk, and it may avoid the problem of HIV resistance to antiretroviral regimens that complicate maternal/infant applications.

"The discovery of the HIV inhibiting effect of this common protein in breast milk provides a potential explanation for why nursing infants born to HIV-infected mothers do not become infected more often than they do," said Barton F. Haynes, M.D., director of the Duke Human Vaccine Institute. "It also provides support for inducing inhibitory factors in [breast milk](#) that might be even more protective, such as antibodies, that would completely protect babies from HIV infection in this setting."

More information: Recognition of synthetic glycopeptides by HIV-1

broadly neutralizing antibodies and their unmutated ancestors,
www.pnas.org/cgi/doi/10.1073/pnas.1317855110

Provided by Duke University Medical Center

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