

HIV exploits a human cytokine in semen to promote its own transmission

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A new report suggests that the concentration of one human cytokine, interleukin 7 (IL-7), in the semen of HIV-1-infected men may be a key determinant of the efficiency of HIV-1 transmission to an uninfected female partner. In their study published February 7 in the Open Access journal *PLOS Pathogens*, a research group from the Eunice Kennedy-Shriver National Institute of Child Health and Human Development (NICHD) led by Leonid Margolis report that the increased IL-7 concentration in semen facilitates HIV transmission to cervical tissue ex vivo.

<u>Semen</u> is a complex biological fluid containing not only spermatozoa but also cytokines, a group of extracellular proteins that modulate immune responses. As a result of <u>HIV infection</u>, the concentrations of various cytokines in semen is profoundly modified, in particular the concentration of interleukin 7 (IL-7) is greatly increased. Despite this evidence of strikingly elevated IL-7 levels in <u>seminal plasma</u>, there was limited knowledge about any effects this cytokine might have on HIV-1 sexual transmission.

To investigate the question about the effects of this increased IL-17 on HIV-1 sexual transmission, Andrea Introini and colleagues from the Margolis lab developed a system of explants of cervico-vaginal tissue that can be maintained outside of the body in culture for up to two weeks while preserving the cytoarchitecture of the tissue. In this system, HIV transmission can be simulated and studied under controlled laboratory conditions. When researchers added IL-7 in concentrations comparable



to that found in the semen of HIV-1 infected men, HIV was transmitted more efficiently and replicated to a higher level than without IL-7. Normally, HIV-1-infected cells quickly die as the result of apoptosis, a programmed death triggered by HIV infection. IL-7 inhibits apoptosis of infected cells, allowing them to produce more virus and thus increasing the chances of the incoming virus to disseminate through the tissue. Also, IL-7 stimulates T cell proliferation, thereby also providing to HIV even more potential targets to infect.

The authors speculate that IL-7, together with other cytokines, may determine sexual transmission rates of HIV-1 and that changes in the seminal cytokine load may explain differences in HIV transmission from different individuals. However, whether the effect of IL-7 that has been demonstrated ex vivo occurs also for sexual partners in vivo, is a subject for future research. If this increase does occur in vivo, then it should be investigated whether HIV-1 infected individuals that have been treated systemically with IL-7 in order to increase their T cell counts may have also resulted in the unintended increase of their seminal IL-7 levels. Finally, this study suggests that seminal cytokines may become new targets for HIV-preventive strategies.

More information: Introini A, Vanpouille C, Lisco A, Grivel J-C, Margolis L (2013) Interleukin-7 Facilitates HIV-1 Transmission to Cervico-Vaginal Tissue ex vivo. PLoS Pathog 9(2): e1003148. doi:10.1371/journal.ppat.1003148

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