

Mucosal immune regulation: Does it help thwart HIV?

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The impact of HIV on the mucosal compartment is now well recognized and contributes to driving immune activation, a characteristic of HIV pathogenesis. The mucosal immune system is greatly affected by HIV from the first days of the infection. A massive depletion of the mucosal CD4⁺ T cells, over production of chemokines and cytokines and dysregulation of the epithelial barrier are some of the mucosal hallmarks of HIV infection. Individuals who control HIV replication, such as elite controllers (EC), or who maintain normal CD4⁺ T cell counts, such as long-term non-progressors (LTNP), seem to maintain a balance within their mucosal environment that contributes to the delayed progression. At the female genital tract, which is the main route of entry of the virus in male to female heterosexual transmission, sexual activities have been associated with changes in mucosal immune activation that may influence the risk of HIV infection. However, not all exposures to HIV lead to infection and it seems that the immune mucosal milieu of the female genital tract is a critical determinant of HIV susceptibility. HIV Exposed Seronegatives (HESN) represents a group of individuals, such as female commercial sex workers, who are at high risk of infection but remain HIV uninfected. Repeated unprotected sex with many different partners makes them highly susceptible to HIV infection, yet it seems that they can prevent the establishment of HIV infection. What makes them “resistant” to HIV infection? In this review, we will focus on the regulation of the mucosal immune system during exposure and infection with HIV. What goes wrong in HIV infection and what goes right in HESN individuals? Lessons learned from HESN might help to have a better understanding of mucosal immune regulation and develop effective HIV preventive strategies.

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