Vaginal Langerhans Cells Mediate HIV Infection

November 14, 2011

J Graham

In the design of HIV vaccines or preventative treatments, much research has examined the series of events that occur between the exposure at a mucosal site and the systemic spread of infection. While CD4+ T-cells have been identified as the major target for infection, it is unclear how HIV reaches these cells and how different elements of the mucosa may either enhance or inhibit infection. One cell type thought to play a role in spreading and enhancing HIV infection are Langerhans cells (LC), a type of dendritic cell located in the vaginal or foreskin epithelium. Previously, Vaccine and Infectious Disease Division (VIDD) faculty member Dr. Florian Hladik had shown that a type of human vaginal LCs efficiently and rapidly endocytose HIV-1 virions, but until now no proof has existed that these cells can pass on the infection to CD4+ T-cells. This study by the Hladik research group, by lead authors Lamar Ballweber and Barry Robinson, is the first to clarify the role that mucosal LCs play in systemic HIV infection.

The group used an *ex vivo* infection model of vaginal epithelial sheets from 11 donors, which were then inoculated with HIV-1 and cultured. Multiple rounds of cell sorting were completed to select for and increase the number of discrete LCs. DNA was then isolated, and a specific type of PCR assay was performed which will only amplify viral DNA if it has been integrated into the host cell genome, as in infection. No viral integration was detected in any of the LC samples, indicating that the cells do not support a productive infection.

Next, the group tested whether these LCs could pass along the virus to T-cells, despite not being productively infected. The LCs were co-cultured with peripheral blood-derived lymphoblasts, and co-cultures were maintained for 28 days. By the end of the assay, all cultures had turned positive by Gag p24 release assay. This indicates that the LCs can pass along the virions to CD4 T-cells, which can then become productively infected. Examination by confocal microscopy showed that a specific subset of vaginal LCs lacks langerin expression, and this may aid HIV-1 in bypassing a langerin-mediated degradation pathway

In summary, the Hladik group has shown that LCs mediate HIV infection by migrating from the epithelium to transmit virus to CD4+ T-cells. Productive infection of LCs is not necessary for them to transmit the virus, and in fact may aid HIV in avoiding antiviral innate immune responses. In addition,

the LCs containing HIV move away from the mucosa where topical antiviral drugs are used, so this potential mechanism of viral evasion must be considered in clinical use of the microbicide products.

Ballweber L, Robinson B, Kreger A, Fialkow M, Lentz G, McElrath MJ, Hladik, F. 2011. Vaginal Langerhans cells non-productively transporting HIV-1 mediate infection of T cells. *Journal of Virology*. doi: 10.1128/JVI.05615-11

Dr. Florian Hladik