

Higher Levels of HIV Target Cells May Increase Superinfection Risk

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HIV-1 infects CD4+ helper T lymphocytes, and the loss of these cells over time leads to immunodeficiency. Disease progression to AIDS is accelerated by inflammation and immune activation, presumably because activated CD4+ lymphocytes support higher levels of viral replication. However, there are conflicting data as to whether or not these same factors also increase the likelihood of acquiring HIV-1 infection. In a recent study published in the *Journal of Virology*, Drs. Catherine A. Blish and Julie Overbaugh (Division of Human Biology) along with an international team of collaborators demonstrate that the total number of target cells may be a more significant contributor to the overall risk of HIV-1 acquisition than immune activation status.

To define correlates of HIV-1 acquisition, Blish and colleagues examined the rate of superinfection in an established cohort of HIV-1 infected women. This study design allowed the investigators to approach this question in a prospective manner and match individuals with similar risk behaviors for analysis. Over the course of the study, the team evaluated 10 patients that were superinfected and 29 non-superinfected control patients. Once superinfection was documented, blood cells collected at the clinic visit preceding superinfection were analyzed by flow cytometry to characterize, as closely as possible, the immune activation status of the patient prior to HIV-1 infection. The team found that increased frequencies of CD4+ CCR5+ T lymphocytes, the primary target cell for HIV-1, were associated with an increased risk of superinfection. In fact, a patient's risk of superinfection increased 1.69-fold for every 1% increase in the frequency of these cells among total lymphocytes (95% confidence interval = 1.02-3.36, $p = 0.04$). However, they did not find any association between markers of immune activation, such as Ki-67+, and an altered risk of superinfection.

HIV-1 acquisition is influenced by a variety of factors, including multiple circulating viral strains and differences in individual immune responses. "By examining women who acquired an infection with a second, distinct HIV strain, we were able to show that the overall level of inflammation is not a major factor driving HIV-1 transmission," said Dr. Catherine A. Blish. "However, HIV affects a particular type of cell, and individuals with more of those cells seem to have higher risk of infection." Moving forward, additional studies will confirm these results in other at-risk patient cohorts.

[Blish CA, Dogan OC, Jaoko W, McClelland RS, Mandaliya K, Odem-Davis K, Richardson BA, Overbaugh J.](#) 2014. Association between Cellular Immune Activation, Target Cell Frequency, and Risk of Human Immunodeficiency Virus Type 1 Superinfection. *J Virol.* 5894-9.



Image courtesy Dr. Julie Overbaugh

The Ganjoni sex worker clinic in Mombasa, Kenya.