

HIV Infection Provides Partial Protection from Superinfection

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Does an initial HIV infection provide any degree of protection from subsequent HIV infections? We may now have evidence that it does. A recent study by postdoctoral fellow Dr. Keshet Ronen in the laboratory of Dr. Julie Overbaugh in the Human Biology Division showed, for the first time, that the risk of acquiring a second HIV infection (superinfection) is lower than the risk of acquiring an initial HIV infection. In this longitudinal study published in *PLoS Pathogens*, next-generation sequencing of plasma samples from women in a high-risk cohort in Kenya revealed that the risk of acquiring a second infection is approximately one-half that of acquiring an initial infection.

Scientists from the Overbaugh Lab, in collaboration with Erick Matsen's group in Public Health Sciences and researchers at the UW and in Kenya, utilized previously reported data on HIV superinfection and appended new data to increase overall sample size. The researchers analyzed high-throughput sequencing of three HIV genes (*gag*, *pol* and *env*) from patient samples obtained over the course of several years. Cases of superinfection were identified upon the appearance of a different HIV clade that was phylogenetically distinct from the initial HIV infection at a later time point. Of the 146 women in the cohort at risk of superinfection, 21 cases of superinfection were detected. When the incidences of initial infection and superinfection were calculated, a statistically significant difference was found ($p=0.0019$). The larger size, greater statistical power and more advanced methods of the current study compared to previous studies allowed the researchers to observe significant differences between the incidences of initial and superinfection for the first time. The researchers controlled for behavioral and clinical differences that might affect infection risk when making the comparison. Additionally, when the timing of superinfection events was analyzed, Ronen *et al.* found that the reduced risk of superinfection did not appear until after six months had elapsed since the initial infection.

"These results suggest HIV infection provides some protection from subsequent infection, an effect which may be mediated by a protective immune response," explained Dr. Ronen. Researchers have long assumed that the immune response to HIV infection would likely provide some level of protection from subsequent infections. However, the mere existence of superinfection cases shows

that this supposed protection is not fully complete. Until this study, compiling sufficient data to provide significant evidence in support of or against the theory of a protective effect following initial infection has not been easy to come by.

The results of this study suggest that an adaptive immune response triggered by an initial HIV infection provides at least partial protection from secondary infection; the risk of superinfection is highest in the first six months after initial infection, before a potential adaptive immune response has had time to fully mature. However, in contradiction to this theory, a majority of the cases of superinfection involved distinct viruses of the same subtype. If protection from superinfection were the result of an adaptive immune response, one would expect the cases of superinfection to have been from less closely related viruses. Another potential explanation is that protection arises from the normal depletion of HIV-susceptible cells during immune system deterioration caused by the initial infection.

The positive news of this outcome is that these results will undoubtedly help us to better understand the immune response during HIV infection. Dr. Ronen is optimistic about the future of these studies. "Characterizing this immune response could inform vaccine design, so we are now exploring the response of singly infected and superinfected individuals to identify immune functions that correlate with superinfection susceptibility."

[Ronen K, McCoy CO, Matsen FA, Boyd DF, Emery S, Odem-Davis K, Jaoko W, Mandaliya K, McClelland RS, Richardson BA, Overbaugh J.](#) 2013. HIV-1 superinfection occurs less frequently than initial infection in a cohort of high-risk Kenyan women. *PLoS Pathogens*. 9: e1003593.

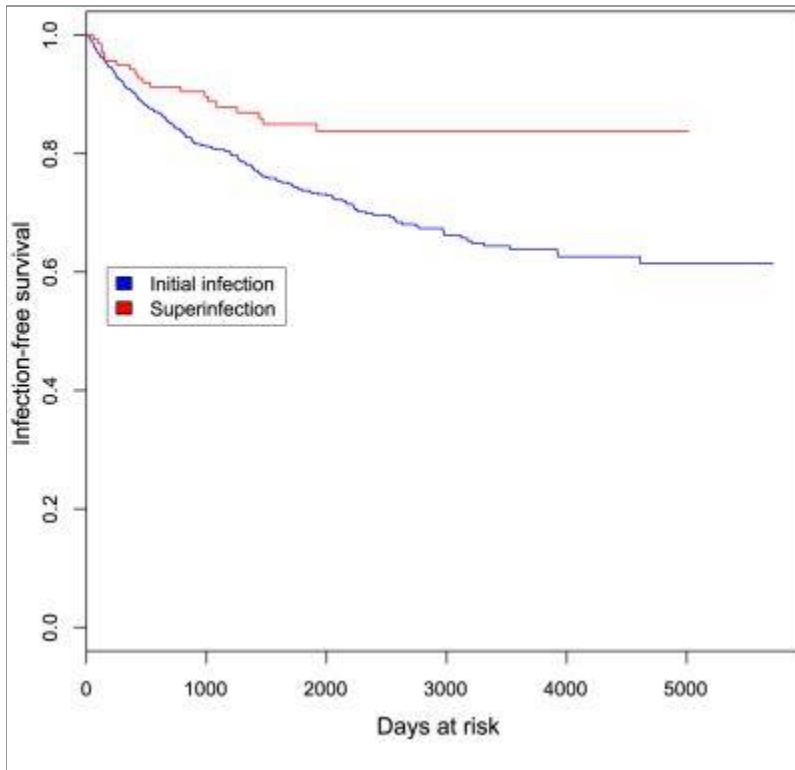


Image from the manuscript published in the open access journal *PLoS Pathogens*.

Kaplan-Meier curve showing initial and superinfection events over time at risk. The risk of superinfection following an initial infection is less than the risk of initial infection.