HIV

Infection, superinfection and (lack of) protection

Superinfection with HIV-1 occurs when an individual who is already infected with one strain of HIV-1 acquires a second strain from a different partner. Because a re-infection event suggests that the immune response generated against the original infection is not sufficient to protect against later exposures, there are obvious implications for HIV-1 vaccine design. However, despite the potential importance of superinfection in HIV disease and vaccine development, there is uncertainty regarding its incidence and timing. Now, an in-depth, population-level assessment of HIV-1 superinfection, published in *PLoS Pathogens*, confirms that natural HIV-1 infection does not always elicit a protective immune response, and that this lack of protection is largely independent of the timing of re-exposure and the relatedness of the virus strains.

Prior to this study, approximately twenty cases of HIV-1 superinfection had been reported in the literature, which suggested that natural infection does not always generate a protective immune response. However, if researchers are to accurately assess the impact of superinfection on the success of an HIV-1 vaccine, questions need to be answered about the frequency of superinfection and whether this process is restricted to the times in infection when an HIV-1-specific immune response has not yet developed.

To address these issues, Piantadosi and colleagues screened a cohort of high-risk Kenyan women for HIV-1 superinfection by comparing 2 partial gene sequences (*gag* and *envelope*) over a 5-year period, beginning at the time of primary infection. Analysing more than one region of the HIV-1 genomes allowed the authors to detect cases in which the initial and superinfecting viruses had recombined, a frequent event during HIV-1 replication. By analysing the proviral sequences from 36 women infected with HIV-1, seven cases of superinfection were detected, including 3 cases in which both viruses belonged to the same HIV-1 subtype; this finding indicates that closely related viruses do not confer protection. The authors also showed that in 5 of the 7 cases, infection with the second virus occurred over 1 year after the initial infection, and, in some cases, 5 years after initial infection. In other words, superinfection occurred after the host immune response to the first HIV-1 strain should have had time to develop and mature.

> “…this lack of protection is largely independent of the timing of re-exposure and the relatedness of the virus strains.”

This study clearly demonstrates that HIV-positive individuals are at continued risk of acquiring a second HIV infection. Indeed, if the lack of protection against re-infection is shared by at least a proportion of all HIV-infected individuals, the potential value of an HIV-1 vaccine that attempts to mimic the immune response to natural infection is called into question. Follow-up studies to compare the immune responses of those individuals that become superinfected with those that do not, and deciphering the contribution of these responses to immune protection, will be the focus of future research.

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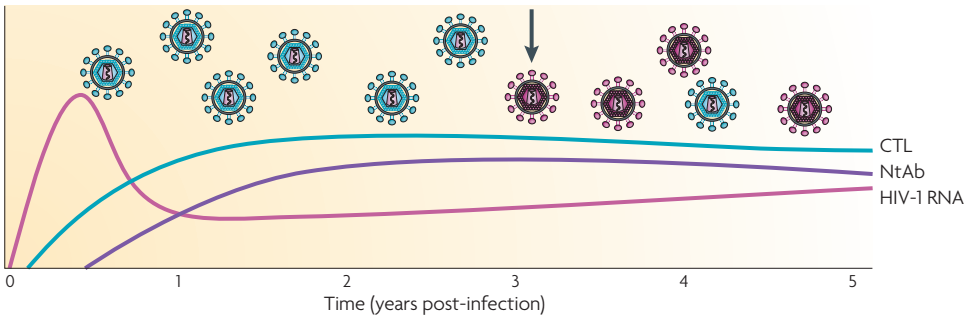

Superinfection with an HIV-1 virus from a second partner (pink) can occur several years after an initial HIV-1 infection (green). At this time (see arrow), cytotoxic T-cell responses (CTL) and neutralizing antibody responses (NTAb) to the first infection have had time to develop. Figure redrawn, with permission, from one kindly provided by Julie Overbaugh, Fred Hutchinson Cancer Research Center, Washington, USA.

ORIGINAL RESEARCH PAPER Piantadosi, A. *et al.* Chronic HIV-1 infection frequently fails to protect against superinfection. *PLoS Pathog.* **3**, e177 (2007)