

# New insights into how certain slow progressers control HIV infection

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People with a rare genetic trait who are infected with HIV progress more slowly to AIDS than others. But even within this group, there are wide variations in time to progression. A new study illustrates in detail how the immune system fights the virus in those subjects who progress more slowly. The research, which could prove useful to efforts to develop a vaccine against HIV, is published in the September *Journal of Virology*.

Absent [antiretroviral therapy](#), most of those infected with HIV progress to AIDS within a decade. But 5-15 percent remain symptom free for years even without therapy. A portion of these people maintain high CD4+T immune cell counts, along with low levels of virus for several years. Many of these people possess the afore-mentioned rare [genetic trait](#), the awkwardly-named HLA-B\*5701 allele (an allele is one possible version of a gene), and their time of progression can range from around six years to well beyond ten years.

The researchers, led by Melissa M. Norstrom and Annika K. Karlsson of the Karolinska Institute, Stockholm, Sweden, and Marco Salemi of the University of Florida, Gainesville, studied evolution of HIV, and immune responses in six untreated HIV-infected patients carrying the protective genetic trait, following them from soon after infection, for seven years. In particular, they studied a set of molecules that are produced by [immune cells](#) called CD8+T cells, which are involved in combating [viral infections](#).

"We found that subjects with lower risk of progressing to AIDS were

characterized by a higher proportion of CD8+T cells that produced several of these molecules simultaneously," says Norstrom. They also found that in these patients, the virus evolved much more slowly. Further, viral mutations, which normally occur somewhat haphazardly during [HIV infection](#), appeared to happen in a specific order, which the researchers postulate resulted from selective constraints exerted by the immune system.

"Understanding the mechanisms associated with slower progression to AIDS may ultimately provide new insights on how to cure HIV, or even how to develop a protective vaccine," says Salemi.

The research had a serendipitous origin, when Norstrom and Salemi met at a workshop on viral evolution, says Salemi. "The exciting discussions during that scientific meeting led to establishment of a successful multidisciplinary collaboration, which included experts in immunology and viral evolution, as well as with Dr. [Frederick M.] Hecht at the University of California, San Francisco, who provided samples from patients carrying this unique genetic trait."

**More information:** M.M. Norstrom, M. Buggert, J. Tauriainen, W. Hartogensis, M.C. Prospero, M.A. Wallet, F.M. Hecht, M. Salemi, and A.C. Karlsson, 2012. Combination of immune and viral factors distinguishes low-risk versus high-risk HIV-1 disease progression in HLA-B\*5701 Subjects. *J. Virol.* 86:9802-9816.

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