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HIV pays a price for invisibility

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Mutations that help HIV hide from the immune system undermine the virus's ability to replicate, show an international team of researchers in the April 13 issue of the *Journal of Experimental Medicine*. The study was published online on March 23.

When HIV infects a cell, a complex of human immune proteins called HLA (short for human leukocyte antigen) alert killer T cells by displaying bits of the virus on the surface of the cell. The T cells recognize these HIV fragments and mobilize an attack.

Individuals who have certain types of HLA proteins control infection better than others. In people with HLA-B*5703, for example, the virus multiplies less than in people with some other HLA variants—likely because killer T cells in these individuals are quick to attack infected cells. But HIV is tricky. To get around HLA-B*5703, the virus mutates three amino acids that T cells need to recognize the infected cells, causing the killers to pass by the infected cell unnoticed. Thus by mutating, the virus becomes invisible to the immune system.

In the new report, Hayley Crawford at the University of Oxford and colleagues show that the virus pays a price for its invisibility. The triple mutant replicated 20 times slower than normal in cell culture.

The researchers went on to study Zambian couples in which one HLA-B*5703-expressing person infected with triple-mutant virus passed the infection to a partner who either did or didn't have the same HLA variant. When transmitted to a person without HLAB*5703, the virus

changed its mutated amino acids back to their original sequence, most likely because the benefit of avoiding killer T cells no longer outweighed the cost of reduced replication. However, when transmitted to another HLA-B*5703-expressing person, the triple-mutated virus came out on top despite its reduced replication. In these individuals, the avoidance of killer T cells allowed the infection to rapidly proceed to clinical illness. This study suggests that vaccines should be designed to produce a T cell response against a number of different viral peptides - something that experimental human vaccines so far have yet to achieve.

Source: Rockefeller University (news : web)