HIV exploits competition among T-cells

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A new HIV study shows how competition among the human immune system's T cells allows the virus to escape destruction and eventually develop into full-blown AIDS. The study, which employs a computer model of simultaneous virus and immune system evolution, also suggests a new strategy for vaccinating against the virus – a strategy that the computer simulations suggest may prevent the final onset of AIDS.

The research, which is slated for publication in *Physical Review Letters*, is available online at arxiv.org/abs/q-bio.PE/0610018 .

"Competition among T cells exerts a small influence for most diseases, but it's fatal for HIV," said study co-author Michael Deem, Rice University's John W. Cox Professor in Biochemical and Genetic Engineering and professor of physics and astronomy.

The new computer model, created by Deem and Guanyu Wang, now an assistant professor of physics at George Washington University, is the first to accurately reproduce all three stages of HIV infection. The first is marked by an initial spike in virus production that's immediately followed by dramatic drop as the immune system recognizes the threat, mounts a defense and destroys most of the invading viruses. The second phase is a long period of clinical latency that can last up to 10 years. In this phase, a small amount of virus mutates fast enough to escape initial detection and continues to mutate over time. The third phase, AIDS, occurs when the virus has changed so much that the body's T cells are no longer effective at keeping it in check.

Deem and Wang's computer model accurately describes all three phases of HIV infection by incorporating a key component: competition among T cells. The model includes two forms of competition. The first form leads to a phenomenon known as deceptive imprinting, or original antigenic sin. Original antigenic sin is the tendency for memory immune cells produced in response to a first viral infection to suppress the creation of new immune cells in response to a second infection by a related strain. The second type of competition, immunodominance, occurs when several viral strains simultaneously infect one person. In this case, T cells compete to recognize the different strains. The winners – the T cells that the body produces in mass quantities to fight the disease – are the ones with the best overall record against the most recogniztable strains. Among the losers, however, there may be T cells that better control the other less recognizable, but still deadly, strains.

"Once the immune system chooses a winning set of T cells, it has a natural tendency to go with those cells when it's confronted by new strains of the same disease in the future," Deem said. "For HIV, which mutates rapidly, this is an Achilles' heel. We found a direct correlation between the level of competition among T cells and the rate at which the virus escaped."

Deem said one strategy to combat this effect would be to vaccinate against the strains of HIV that will inevitably evolve in the body in a manner that was designed to reduce immunodominance. One such strategy – polytopic vaccination – involves giving vaccines against different strains of the same disease simultaneously in different parts of the body. The approach capitalizes on the fact that different lymph nodes – the sites where T cells compete to be chosen as the winners against a particular disease – act as collection points for different parts of the body. Moreover, because it takes 4-5 days for T cells produced in a lymph node to begin to leave it, the possibility exists to set up simultaneous, independent competition against each of the multiple

strains that will evolve by injecting each strain simultaneously so that they drain to different lymph nodes. In this case, no single T cell is chosen as a winner. Instead, a separate winner for each strain is picked in each affected lymph node before immunodominance can come into play.

"In our simulations, this strategy appears effective at all but eliminating competition among T cells," Deem said. "As a result, HIV remained in a state of permanent latency and was never able to escape the immune system's grasp to develop into AIDS."

Source: Rice University