HIV’s Incredible Endgame

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Cult members stood up by an alien spaceship aren’t the only adherents of mass suicide. New research suggests that the strain of HIV—called syncytium-inducing (SI)—common in late-stage disease may prompt CD8 cells (key virus suppressors) to destroy themselves, a process known as apoptosis. This cellular suicide is a normal mechanism used by the body to eliminate damaged or cancerous cells. But researchers at the University of California at San Francisco and the Picower Institute for Medical Research at New York’s North Shore University Hospital report that when the SI virus binds to a surface protein called CXCR4—found on both CD8 cells and macrophages (microbe-scavenging cells)—the result is massive destruction of healthy CD8s. They believe that this might help explain why many PWAs experience a sudden, sharp slide toward illness after years of relative health.

The strategy the virus uses is notably different from the way it commandeers the CD4 cell. Instead of infiltrating and taking over its machinery, the virus’ binding to CXCR4 appears to be interpreted by the CD8 as a death signal. The mechanism that waves the white flag and triggers apoptosis is likely a cell-produced chemical called tumor necrosis factor-alpha (TNF-alpha). The researchers report that this mass apoptosis only occurs when macrophages are present, and that both they and the CD8 cells produce TNF-alpha. The result is a steep decline in CD8 cells, and therefore a decreased control of HIV. In turn, this results in greater vulnerability to opportunistic infections.

Although limited to test-tube studies so far, the researchers believe that this new understanding may lead to new avenues of therapy. Eric Verdin of UCSF says, “Right now, everyone’s focused on finding ways to block CCR5,” the molecule that allows cells to become infected by the non-syncytium-inducing, early-stage HIV. “Our research shows that it may be just as important to find ways to stop viruses that bind to CXCR4.”