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Scientists Learn in Greater Detail How HIV Kills Immune Cells

Depicted in broad brush strokes, the HIV virus does its damage by killing vital immune cells, called CD4+ T cells. Now for the first time scientists have sketched out in much finer detail how this process occurs, step by step. To do so, Jacques Corbeil and his colleagues at the University of California at San Diego collaborated with researchers from the Veterans Affairs (VA) San Diego Healthcare System and the company Affymetrix. Using the latest in microarray gene chip technology and bioinformatics, they monitored nearly 7,000 genes at eight points in time over 72 hours. The results—which appear in the July issue of *Genome Research*—reveal how HIV not only suppresses the activities of genes essential for immune cell maintenance and repair but also prompts programmed cell death, or apoptosis.

The researchers tested some 10 million CD4+ T cells at different time intervals after HIV infection using microarray gene chips to learn which genes were active when. They then analyzed these patterns of gene expression with UCSD-developed software called 2HAPI (High-density Array Pattern Interpreter, version 2), available at www.array.ucsd.edu. "With this technology, our ability to study HIV has moved from observing clinical manifestations of HIV to studying the molecular machinery of the cell as the virus changes and affects the cell's living process," explains Daniel Masys, Director of Biomedical Informatics at the UCSD School of Medicine and co-inventor of the HAPI software.

Within 30 minutes of infection, HIV had shut down more than 500 genes in the tested immune cells. It ultimately activated another 200-some genes, among them those associated with cellular defense and self-destruction. And within three days, infected cells had only half of the 1,400 active genes found in healthy cells. "Now that we have the ability to see the specific genes that are modulated by HIV, we're probing further to find the promoter regions of these genes where activation begins or is suppressed," Corbeil says. "We want to determine how they are expressed, as well as the length of time the genes are turned on or off." Such information could lead to new approaches for preventing or treating HIV infection.