Turning On Old Genes to Prevent HIV

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Researchers may be better poised to develop a cream or gel that might help prevent transmission of HIV, thanks to the results of a study published April 28 in *PloS Biology*. The cream would work by reawakening an inactive virus-fighting human gene.

The immune system cells of all animals, including humans, are able to make proteins called defensins. Defensins fight bacteria and viruses by binding to surface receptors on the microorganisms and then creating a pore, or hole, to allow germ-destroying chemicals into the infectious particles. Monkeys have a type of defensin called retrocyclin that effectively damages the monkey version of HIV, called simian immunodeficiency virus (SIV), before it can infect a cell. Humans also have a gene capable of making retrocyclin, but somewhere during the course of our evolution we developed a second gene—called a "codon stop" or "nonsense" gene—that terminates the activity of the retrocyclin gene.

A team of researchers, headed by Nitya Venkataraman, PhD, and Alexander Cole, PhD, from the University of Central Florida (UCF) in Orlando, set out to determine whether human retrocyclin is active against HIV and, if so, whether codon stop can be suppressed therapeutically.

The group first succeeded in disrupting the codon stop gene in select immune cells, allowing them to produce human retrocyclin. They then tested the human retrocyclin against HIV and found that it effectively blocked the virus from infecting new cells.

Next, Venkataraman and Cole explored whether it would be possible to disrupt the codon stop gene on a larger scale. They trained their eyes on aminoglycosides, a family of antibiotics known to shut down genetic protein production. Not only did the antibiotics block the codon stop gene, thus enabling cells to make retrocyclin, but the cells also made enough retrocyclin to suppress HIV.

In a UCF news release, Cole says he hopes that it might be possible to turn the antibiotics into a microbicide capable of blocking HIV infection. "Much more work would be needed to demonstrate the safety and effectiveness of this approach. We would certainly have to have human trials," he says, "but these findings represent a promising step in that direction."

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