

Intelligent design: Engineered protein fragment blocks the AIDS virus from entering cells

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In what could be a potential breakthrough in the battle against AIDS and a major development in the rational design of new drugs, scientists have engineered a new protein that prevents the virus from entering cells. This protein is based on a naturally occurring protein in the body that protects cells from viruses, except the man-made version does not cause inflammation and other side effects at the dosages needed to inhibit AIDS. This discovery was published in the April 2011 issue of *The FASEB Journal*.

"This is science fiction made reality. These researchers took a protein apart and removed the portion that causes harm, then stabilized and modified the section that has a therapeutic effect," said Gerald Weissmann, M.D., Editor-in-Chief of *The [FASEB Journal](#)*. "Not only is this good news for people with AIDS, it's good news for all of us as this research paves the way for similar work for many, many other illnesses."

The protein fragment is based on a naturally occurring protein called RANTES, which is part of the body's immune system. RANTES naturally defends the body against HIV/AIDS, but cannot be used as a drug or [drug candidate](#) because it has several other biological effects which could cause harmful [inflammation](#). After examining the precise molecular structure of the RANTES protein, the researchers discovered that only a small fragment of the RANTES protein is actually responsible for blocking HIV entry into cells. From there, they dissected

the desired section of the RANTES protein and worked to stabilize it without compromising its protective effects. After several sequential steps of molecular refinement and some virtual modeling, the researchers created a peptide with very high potency against HIV, with possible benefits for treating [inflammatory diseases](#) such as arthritis and lupus, as well as the prevention of transplant rejection.

"We're finally able to design smart anti-HIV drugs aimed at the right target. That's because scientists have spent decades figuring out the molecular details of how the virus enters cells, and the exact chemical structures involved," Weissmann added. "As the Renaissance sculptors wrought art from crude marble, today's molecular engineers today use intelligent design to create life-saving chemical masterpieces."

More information: Paolo Lusso, Luca Vangelista, Raffaello Cimbro, Massimiliano Secchi, Francesca Sironi, Renato Longhi, Marina Faiella, Ornella Maglio, and Vincenzo Pavone. Molecular engineering of RANTES peptide mimetics with potent anti-HIV-1 activity. *FASEB J.* April 2011 25:1230-1243; [doi:10.1096/fj.10-167627](https://doi.org/10.1096/fj.10-167627)

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