# Protein discovered that prevents HIV from spreading

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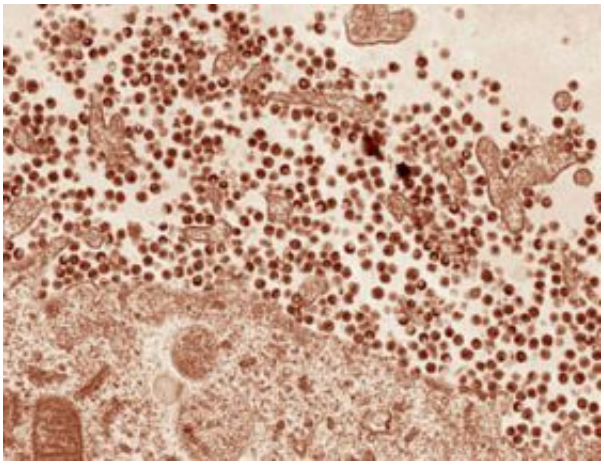

Sticky situation. HIV-1 particles (dark circles) lacking Vpu are unable to extricate themselves from the surface of their host cell. Instead, tetherin keeps them locked to the surface of the cell's outer membrane, or causes them to be sucked back in and digested by the cell's endosomes. Credit: Rockefeller University

In a study that could open up the field of virology to an entirely new suite of possibilities and that paves the way for future drug research, scientists at Rockefeller University and the Aaron Diamond AIDS Research Center have pinned down a molecule on the surface of human cells that helps keep particles of mutant strains of HIV from spreading.

Rather than floating off to infect more cells, the protein contains the

virus particles by keeping them attached to the parent cell's outer membrane, as if stuck there with glue.

Two years ago, Paul Bieniasz — head of the Laboratory of Retrovirology and ADARC scientist — discovered that normal HIV-1 particles are able to extricate themselves from the sticky membrane surface using a protein called Vpu. Bieniasz has been searching for the source of the glue itself ever since. Now, in an advanced online publication in Nature, he and his colleagues report that they found it: a protein they dubbed "tetherin" for its ability to keep viruses tied to a cell.

"All we knew when we started this two and a half years ago was that a virus lacking Vpu was released less efficiently from cells." Bieniasz says. "And we had some electron micrographs that showed virus particles stuck there on the surface and clustered inside cells." Once they started looking carefully at the reasons behind this, they found an antiviral mechanism keeping the HIV-1 mutant particles tethered to the cell. And it wasn't just HIV — the glue appeared to interfere with the spread of other membrane-encapsulated (or "enveloped") viruses, too.

To track down the cause of stickiness — and the likely reason HIV evolved Vpu — Bieniasz and his team looked at gene activity across all known human genes, making comparisons between cells that require Vpu for HIV-1 release and those that don't. Ultimately, they narrowed it down to one very likely candidate. And the candidate, the tetherin protein, passed all the tests the researchers threw at it: When Vpu was not present but tetherin was, large numbers of virus particles piled up on the cell surface. When tetherin was missing, however, even the Vpu-deficient viruses were able to escape.

"We've discovered a new way that cells defend themselves against viruses," Bieniasz says. "I think this will open up a new area of study in virology: how this protein antagonizes other viruses, and how viruses

learn to get around it." Going forward, his lab will focus on how broad tetherin's antiviral activity is, and whether variations of it exist that might confer additional immunity or sensitivity to HIV and other viruses. And, he notes, if drug researchers are able to interfere with the interaction between tetherin and Vpu, their newly discovered protein might even provide a potential therapeutic target.

Source: Rockefeller University