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## Defensins ward off HIV in two ways

The body attempts to protect itself from HIV infection via the innate immune system. Defensins are proteins found in cells, which have been shown to have anti-HIV activity. However, the mechanism by which the defensins control HIV infection has not been known. Appearing online on February 17 in advance of publication in the March 1 print edition of the *Journal of Clinical Investigation*, Theresa Chang and colleagues from Mount Sinai School of Medicine analyze how alpha-defensin-1, in particular, inhibits HIV infection in CD4+ T cells. CD4 + T cells are white blood cells that have molecules called CD4 on their exterior. They help orchestrate the body's response to viruses and therefore play important roles in the immune system.

The researchers show that alpha-defensin-1 fights HIV in two different ways. Without serum (the watery portion of blood that remains when blood cells are removed) and under conditions where viral burden is low, alpha-defensin-1 directly inactivates HIV virus. When serum is present, alpha-defensin-1 acts on vulnerable cells to block HIV infection at the stage when the virus is taken up by the cell and begins replicating itself and integrating into the host. The authors also show that the way alpha-defensin-1 blocks HIV infection in cells is by inhibiting a CD4+ cell-signaling molecule called PKC.

The finding that alpha-defensin-1 acts on both the virus and the cell offers insights into the function of alpha-defensin-1 in innate immunity against HIV. In addition, this study provides a basis to develop defensin-like drugs for prevention of HIV and for therapeutic use in patients who are already infected.

TITLE: Alpha-defensin-1 has a dual role in anti-HIV-1 innate immunity: effects on the virion and the cell

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