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New Receptor for AIDS Virus Found

Researchers have found a receptor for human immunodeficiency virus (HIV) that appears to play a key role in the transmission of the virus between individuals.

In the June 20, 1996, issue of *Nature*, a team headed by Dan R. Littman, a Hughes investigator at New York University Medical Center, reports that this receptor helps the most common form of HIV to infect humans. A second paper by John P. Moore of the Aaron Diamond AIDS Research Center (ADARC), reporting similar results, appears in the same issue of *Nature*.

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— Dan R. Littman

For more than a decade, scientists have known that HIV must bind with CD4—a molecule on the surface of immune cells—for infection to occur. Yet some immune cells that bear CD4 avoid infection. Scientists surmised that these cells must carry a second receptor that is also needed for HIV infection to occur.

Now, Littman's team, in collaboration with Nathaniel Landau of ADARC, has apparently found that receptor: CC-chemokine receptor 5, or CKR-5. The CKR-5 receptor stippled the surface of T cells and macrophages, which are cells of the immune system. Littman's team showed that CKR-5 and CD4 proteins work together to fuse cells with the HIV virus, allowing the virus to release its genetic material.

"This offers a potentially new target for blocking the viral life cycle at the earliest point before it enters cells," said Littman. "This could then give the immune system an edge in clearing the virus from the body."

To find CKR-5, Littman's team analyzed HIV samples taken from patients. These samples included a "macrophage-tropic" form of HIV—the most common form of HIV found in patients with AIDS. ("Macrophage-tropic"

means that the virus infects macrophages and T cells.) Earlier work had shown that drugs called chemokines could block the replication cycle of macrophage-tropic HIV.

With that information in hand, Littman's team examined why chemokines block macrophage-tropic HIV replication. To their surprise, they netted the chemokine receptor, CKR-5. They showed that CKR-5 must be present at the cell surface for infection to occur.

The discovery could lead to new drugs that block CKR-5, stopping HIV in its tracks. Further studies may also turn up other important secondary receptors, Littman notes. Meanwhile, animal models using CKR-5 should help researchers better understand how HIV leads to AIDS.