Researchers uncover direct evidence on how HIV invades healthy cells

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Using sophisticated detection methods, researchers at the Saint Louis University Institute for Molecular Virology (IMV) have demonstrated the molecular mechanism by which the HIV virus infects, or integrates, healthy cells. The discovery could lead to new drug treatments for HIV.

Although scientists theorized that two ends of the virus' DNA must come together inside a healthy cell in order to infect it, until now, investigators have not been able to illuminate the process.

"Many biological and structural aspects of HIV integration are undefined," said Sibes Bera, Ph.D. "Therefore, any insight into the molecular mechanism of this process is significant in developing integrase inhibitors."

Integrase, which was discovered by SLU researchers in 1978, is one of three HIV proteins crucial to the infection's survival. The first protein, reverse transcriptase, converts the ribonucleic acid (RNA) in HIV into deoxyribonucleic acid (DNA).

Integrase then inserts the HIV DNA into the immune cell's DNA, making it a permanent part of the cell. The third protein, protease, processes viral proteins and is essential to make infectious virus.

Drugs such as AZT and drug combinations (cocktails) exist to inhibit reverse transcriptase and protease. As of yet, there are no drugs to counter integrase.

By using a biophysical methodology known as Fluorescence Resonance Energy Transfer, Bera and his colleagues showed that the integrase holds the two ends of the viral DNA together prior to integration. Once inside the cell, the two viral DNA ends are fused by the integrase to the cell's chromosome. The integrated viral DNA allows virus replication. If the two ends of the viral DNA do not come together, infection does not take place. Millions of HIV tainted cells can be launched from a single infected cell.

"We will use this technique in our ongoing studies of the effects of drugs in the process of assembly and disassembly of the viral DNA integrase complexes," Bera said.

Source: Saint Louis University