Protein that provides innate defense against HIV could lead to new treatments

May 25 2008

By identifying a protein that restricts the release of HIV-1 virus from human cells, scientists believe they may be closer to identifying new approaches to treatment. The research is published in the advance online edition of *Nature Medicine*.

Scientists have known that most human cells contain a factor that regulates the release of virus particles, but until now they have been uncertain about the factor's identity. Now a research team from Emory University School of Medicine, Vanderbilt University School of Medicine, and Mayo Medical School has identified CAML (calcium-modulating cyclophilin ligand) as the cellular protein that inhibits the release of HIV particles.

CAML works by inhibiting a very late step in the virus lifecycle, leading to the retention of HIV particles on the membrane of the cell. The virus has developed a means of counteracting CAML, through the action of the viral Vpu protein. When Vpu is absent, HIV particles don't detach from the plasma membrane and instead accumulate by a protein tether at the cell surface.

When the research team depleted CAML in human cells in the laboratory, they found that Vpu was no longer required for the efficient exit of HIV-1 particles from the cell. When they expressed CAML in cell types that normally allow particles to exit freely, the particles remained attached to the cell surface.

"This research is important because it identifies CAML as an innate defense mechanism against HIV," says senior author Paul Spearman, professor of pediatrics (infectious diseases) at Emory University School of Medicine. "We are continuing to work on the mechanism that Vpu uses to counteract CAML and on defining exactly how CAML leads to virus particle retention on the infected cell membrane. We hope this will lead us to new treatments."

Source: Emory University