MedicalXpress

Scientists identify mechanism T-cells use to block HIV

May 17 2010

Scientists at Duke University Medical School and Mount Sinai School of Medicine have found a new role for a host protein that provides further insight into how CD8+ T cells work to control HIV and other infections. Study authors say the finding may yield new strategies for prevention or treatment.

The discovery, published in the Proceedings of the National Academy of Sciences, centers around the anti-HIV function of a tiny protein called prothymosin-alpha. Previous studies from the group have shown that the protein can block HIV viral replication once HIV invades a cell, but until now, no one has understood exactly how that happened.

"But now we have a much clearer understanding of how this protein works," said Mary Klotman, MD, chair of the department of medicine at Duke and the senior author of the paper.

The discovery of the antiviral activity of this protein is another piece of the long-standing quest to define the natural substances made by specific immune cells, in this case CD8+ T cells, that have potent anti-HIV activity.

Klotman, along with Arevik Mosoian, PhD, and Avelino Teixeira, PhD, colleagues at Mount Sinai, conducted a series of laboratory tests and studies in mice and in human cells, and discovered that prothymosin-alpha binds to an important cell receptor called TLR4, and stimulates these cells to produce interferon. Interferons are part of the body's innate

immune system and are powerful, naturally-occurring proteins that can kill many types of pathogens, including bacteria, cancer cells and viruses, like HCV and HIV.

"We found this fascinating," said Klotman. "Usually, it takes an invading virus to trigger interferon production. But here we have a case where the body's own defense system - a host protein - is inducing it."

"This is a perfect example of two arms of the immune system working together. A protein produced by CD8+ cells of the adaptive immune system is exerting potent viral-suppressive activity through a mechanism thought to be reserved for cells of the innate immune system," said Mosoian.

Klotman, Mosoian and Teixeira performed their experiments in macrophages, special immune cells that are one of the first lines of defense against viruses and infectious microbes, and also among the key targets HIV invades. "Macrophages are also important because we think they also function as a safe haven for HIV; protective spaces where HIV can hide and bide its time. It's good to know we've identified a pathway that we might be able to exploit to sabotage this function," said Klotman.

Mosoian says that figuring out how prothymosin-alpha stimulates production of interferon could reveal novel pathways for protection and treatment of viral infections. "But much more work needs to be done. The structure of the protein invites interaction with other proteins that could potentially affect its current function."

Provided by Duke University Medical Center