Manipulating Genetic Switch Suppresses HIV Reservoir

This finding from early laboratory research may aid in the quest for cure therapies.

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Researchers have found that eliminating or silencing a genetic component of immune cells key to HIV reproduction prevents viral rebound from the reservoir after discontinuation of treatment for the virus.

Standard antiretroviral (ARV) treatment does not eradicate HIV from the body because the virus remains hidden in latently infected, or inactive, cells. Because such cells are not replicating and churning out new copies of HIV, the virus they harbor remains under the radar of ARVs, which work only on HIV in active cells. These inactive cells are the major component of what is known as the viral reservoir.

Cure therapies seek to shrink or, ideally, eliminate the reservoir to prevent the reactivation of latently infected cells, which may repopulate the body with new virus if ARVs are discontinued.

Publishing their findings in the journal mBio, a research team led by Tariq Rana, PhD, a professor of pediatrics and genetics at the University of California, San Diego School of Medicine, conducted the first genome-wide expression analysis of long noncoding RNA (lncRNA) in HIV-infected macrophages.

Macrophages are immune cells that drive inflammation in tissues, stimulate other immune cells and clear foreign debris from the body.

LncRNAs typically do not give rise to new proteins as other RNAs do; instead, they play a role in determining whether certain genes are expressed in a cell.

The study authors found that a particular lncRNA called HIV-1 Enhanced LncRNA (HEAL) is seen at higher levels among people with HIV. They believe that HEAL emerged relatively recently in human evolution and that it regulates the replication of HIV in immune cells, including macrophages, microglia (which function like macrophages in the central nervous system) and T cells.

“This is one of the key switches that the HIV field has been searching for three decades to find,”

Rana said in a press release.

In laboratory experiments, the researchers found that either silencing HEAL or snipping it out with the CRISPR-Cas9 gene-editing mechanism prevented viral rebound from latently infected cells after ARVs were discontinued.

The investigators aim to conduct additional experiments in animals and hope to ultimately do so in people with HIV.

“Further studies are needed to explain the mechanism that leads to HEAL expression after an individual is infected by HIV,” Rana said, “but this finding could be exploited as a therapeutic target.”

To read a press release about the study, click here.

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