UW-Madison School of Medicine and Public Health: Researchers find way to disrupt HIV replication in human cells

Posted on Monday, Mar 20, 2017

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MADISON, Wis. – Researchers at the University of Wisconsin School of Medicine and Public Health have discovered a new potential means to stop production of HIV-1, the most widespread type of HIV in human cells.

Jordan Becker, a graduate student, and lead author of the paper describing their research, and Nathan Sherer, assistant professor of oncology at the UW School of Medicine and Public Health, showed that disrupting the movement of viral messenger ribonucleic acid molecules (mRNAs), which are responsible for producing HIV-1 proteins in the cell, can prevent the HIV-1 from creating new particles.

Their work, recently published in the Journal of Virology, showed that HIV-1 mRNAs and proteins in human cells don't follow a straight path – like an assembly line – to virus-particle assembly sites at the cell's plasma membrane.

Instead, when the RNA is released from the nucleus it spreads out like a liquid and binds to both cellular and viral proteins in the cytoplasm, the fluid-like material that fills up most of a living cell.

“HIV kind of takes over the cell, and things are happening all over the place. Viral RNAs and proteins interact in the cytoplasm and diffuse everywhere really rapidly,” said Sherer, who is also a member of the UW Carbone Cancer Center.

But, for HIV-1 to form a new virus particle, the assembly of the particle must happen at a specific place within a cell, he said.

After the HIV RNA and a protein called Gag bind, they move together to the lipid bilayer that surrounds the cell, known as the plasma membrane. There, new particles are formed and released from the cell.

These new HIV-1 virus particles can then infect another cell and spread infection.

Through their research – done in conjunction with the UW McArdle Laboratory for Cancer Research and the UW Institute for Molecular Virology – Becker and Sherer devised a way to disrupt HIV-1 RNA movements in the cytoplasm by physically tethering the RNAs to structures in the cell other than the plasma membrane.

“It completely abolished virus-particle production,” Sherer said.

Directly disrupting where the RNA collects to make new particles could be a new anti-viral strategy, according to the paper.

“That’s a next step,” Becker said.

If the strategy were to become reality, those diagnosed with HIV-1 would not be able to make the infectious virus particles, called virions, that transmit the disease through their blood or other bodily fluids, he said.

It is difficult to know if the strategy alone would kill the virus, but by combining this new idea with existing drugs, it could be possible to enhance the effectiveness of those drugs. That’s because it would keep the virus from adapting to the drugs since fewer new virus particles would be created, Becker said.

“There’s a general need for more and better drugs as time goes on because the virus is changing to form drug resistance, and the ones that we have are still not able to cure HIV-1,” Sherer said.

The potential of this discovery could have significant implications for HIV research and treatment, according to Sherer.

“The study is really the tip of an iceberg in terms of understanding when, where, and how HIV RNAs move inside cells. Some of the RNAs have really unique features and play multiple important roles during infection,” he said. “Thus, selectively targeting their movements should be both feasible and potentially a really great way to kill HIV.”

The discovery of the RNA’s location in the cell, and the ability to disrupt virion production could have broader implications beyond HIV-1, Sherer said.

“We are thinking more broadly that perturbing viral RNA distribution inside the cell could work for many if not all viruses from HIV to flu to Ebola, thus an exciting new direction,” he said.