Trying to halt hepatitis C's molecular hijacking

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Researchers at the University of Colorado School of Medicine have figured out intimate details of how the hepatitis C virus takes over an invaded cell, a breakthrough that could point to way for new treatments for the virus.

Hep C hijacks the machinery by which a cell makes proteins and uses it instead to create proteins for the virus. Over the last two decades, researchers have figured out that Hep C uses an RNA molecule to do this. Now they're trying to fill in the details.

One key detail is reported in a paper published online Dec. 23 in Nature Structural and Molecular Biology. It's written by Jeffrey Kieft, PhD, an associate professor at the CU medical school's Department of Biochemistry and Molecular Genetics and an Early Career Scientist of the Howard Hughes Medical Institute, and his former graduate student, Megan Filbin, PhD, a graduate of the Program in Molecular Biology.

Working with researchers from the lab of Tamir Gonen at the Janelia Farm Research Campus of the Howard Hughes Medical Institute, Kieft used ultra high-power electron microscopes to take images of individual RNA molecules from Hep C as they interacted with the cell's machinery. The researchers combined those images with a variety of other experiments and these clues led them to identify a new way that the virus' RNAs takes over the cell's machinery.

Specifically, the researchers focused on how a ribosome, the cell's

protein-making factory, can be manipulated by the Hep C RNA to affect a part of the protein process called translocation. And they saw something else – that even very small changes in the interactions important for that hijacking process can be blocked.

"This points the way to developing drugs to fight hepatitis C in ways that current therapies do not," Kieft says.

Provided by University of Colorado Denver

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