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Researchers find clue to how Hepatitis C virus harms liver

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Researchers at the University of Southern California (USC) have discovered a trigger by which the Hepatitis C virus enters liver cells — shedding light on how this serious and potentially deadly virus can begin to damage the liver.

The findings, reported in the Dec. 7, 2012 issue of the Journal of Biological Chemistry, may give scientists a target for future development of treatments for the virus.

In the early stages of a Hepatitis C Virus (HCV) infection, the researchers found, the virus binds to receptors on the liver cells' surface and activates PI3K and AKT, two proteins that control cell growth and metabolism, and which allow HCV to enter liver cells.

"When these two protein factors are activated, they trigger a cascade of reactions, altering the physiology of infected cells," said corresponding author and lead researcher James Ou, professor of molecular microbiology and immunology at the Keck School of Medicine of USC. "Later, by continuing to disturb this pathway, the virus may sensitize the liver cells to eventually become cancerous."

The findings were reported in a paper titled "Transient Activation of the PI3K-AKT Pathway by Hepatitis C Virus to Enhance Viral Entry." First author was Zhe Liu, a postdoctoral research associate in Ou's lab. Serving as co-investigators were Keck faculty members Keigo Machida, assistant professor of molecular microbiology and immunology, and

Michael M.C. Lai, distinguished emeritus professor of microbiology and immunology, and neurology.

There are four-million carriers of HCV in the U.S. Often, people don't know that they have the virus until they already have some liver damage, which can take many years to develop. In time, the virus can lead to serious and deadly liver conditions: cirrhosis, a chronic, degenerative condition; cancer; and organ failure.

Some 20 percent of HCV patients will develop severe liver cirrhosis and may require liver transplantation, Ou noted. About five percent develop liver cancer after 20 to 30 years.

Ou has been studying HCV for 20 years and Hepatitis B virus for 30 years. The most recent study reflects his long-term interest in understanding the interactions between these two viruses and their host cells, and how they cause liver cancer.

"The next step, which we've just begun, is to understand how the activation of the PI3K-AKT pathway allows the [HCV] virus to enter the cell," Ou said. "This research has led to the identification of a novel target for the development of new anti-HCV drugs. Compounds that disrupt the PI3K-AKT pathway are expected to prevent the virus from entering liver cells, causing the virus to disappear."

More information: www.jbc.org/content/287/50/41922.abstract

Provided by University of Southern California