

# Hepatitis C virus may need enzyme's help to cause liver disease

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A key enzyme may explain how hepatitis C infection causes fatty liver – a buildup of excess fat in the liver, which can lead to life-threatening diseases such as cirrhosis and liver cancer, report University of Pittsburgh Graduate School of Public Health and School of Medicine researchers.

The study, published in the July 9 online issue of *Hepatology*, shows that an enzyme known to play a major role in lipid production, fatty acid synthase (FAS), was highly elevated in human liver cells exposed to the hepatitis C virus. While preliminary, the research suggests that testing for elevated levels of FAS could help determine which patients with hepatitis C virus may go on to develop more serious, long-lasting health consequences brought on by fatty liver.

Nearly 200 million people worldwide are infected by hepatitis C, including 4 million Americans. Seventy percent of people with hepatitis C develop chronic liver disease, and the infection is the leading reason for liver transplantation in the United States.

Unlike hepatitis A and B, there is no vaccine to prevent hepatitis C infection. Since hepatitis C typically has no symptoms, many people do not know they have the infection until they develop signs of liver failure or fatty liver, sometimes decades after infection. The virus replicates and mutates quickly, helping it to evade discovery and attack by the immune system and allowing it to slowly wreak damage on the liver.

"Our study has provided new insight into how hepatitis C causes fatty liver. This has important implications for future studies and efforts to understand how the virus causes an increase in fatty acid levels that can lead to serious liver conditions," said Tianyi Wang, Ph.D., assistant professor, Department of Infectious Diseases and Microbiology, University of Pittsburgh Graduate School of Public Health, and the study's lead author.

To identify possible proteins in the hepatitis C virus linked to an increase in fatty acids, Dr. Wang worked with Thomas Conrads, Ph.D., co-director of clinical proteomics at the University of Pittsburgh Cancer Institute, and colleagues on a mass spectrometry-based proteomics approach in which they measured protein expression from liver cell cultures exposed to the hepatitis C virus. The approach sorted proteins based on their weight and electrical charge, looking for divergent patterns linked to the virus. Of the 175 proteins they identified, only FAS was highly elevated in cell cultures. Furthermore, when they blocked the expression of FAS, they noted a three to four times decrease in the level of the virus, indicating that FAS is directly linked to the virus's expression.

"Viruses are very complex, so it is challenging to determine what proteins may be at play in their survival and growth," said Dr. Wang. "The proteomic approach we used revealed many proteins linked to hepatitis C that may be worthy of further study, but FAS appears to be the protein most strongly associated with the production of fatty acids that can cause liver disease."

"Our next step in this research is to see how high the level of FAS is in tissue samples from hepatitis C patients and determine whether elevated FAS levels directly result in overproduction of fat in livers. If we learn that FAS is highly present in tissue, testing for it may be a way to predict those at risk for liver disease."

Source: University of Pittsburgh

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