Researchers pinpoint peptide that blocks hepatitis C virus entry

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(Medical Xpress) -- Researchers at the University of Pittsburgh's Graduate School of Public Health (GSPH) have identified a specific peptide that may block the entry of the hepatitis C virus (HCV) into the liver, representing a potential target for new drug development.

The results are available online now and will be published in the August 2012 print edition of *Hepatology*, the official journal of the American Association for the Study of Liver Disease.

"Viral entry is a multi-step process, involving a number of host factors; therefore, these findings represent a promising target for new antiviral drugs," said Tianyi Wang, Ph.D., associate professor, Department of Infectious Diseases and Microbiology, GSPH, and the study's lead author.

Previous research indicates that human apolipoprotein E (apoE), which occurs naturally in the body, forms complexes with HCV, the scientists said. They constructed peptides, dubbed hEP, containing the portions of apoE to which other proteins and lipids typically bind.

In lab tests, they found that hEP blocked the virus from binding to liver cells, preventing infection. That suggests apoE is involved with HCV's initial entry into the cells, Dr. Wang said. It's possible that hEP thwarts infection because it competes with HCV for a cell surface receptor.

In addition, researchers determined that the ability of hEP to block the

virus appears to be dependent on the peptide's length and sequence. Shorter versions could not stop infection, possibly because the shape of the proteins—and thus their binding ability—was altered.

"Our findings highlight the potential of developing peptides that mimic hEP as new hepatitis C viral inhibitors," said Dr. Wang.

Worldwide, more than 170 million people are infected with the hepatitis C virus, which often is asymptomatic and can cause severe liver disease and liver cancer. There is no cure for HCV and no vaccine. Existing treatments are effective in only 40 percent to 80 percent of patients and can cause severe side effects.

Despite the recent U.S. Food and Drug Administration approval of two new antiviral drugs designed to treat chronic HCV infection, patients may rapidly develop resistance. Much like current HIV therapies, successful treatment of HCV may involve multiple inhibitors of different targets, researchers said.

"New antiviral drugs are urgently needed to treat HCV infection independently, or in combination with current therapies," said Dr. Wang.

Collaborators on the studies include Shufeng Liu, Ph.D., and Kevin D. McCormick, M.S., Department of Infectious Diseases and Microbiology, GSPH, University of Pittsburgh; Wentao Zhao, Ph.D., and Daping Fan, Ph.D., Department of Cell Biology and Anatomy, School of Medicine, University of South Carolina; and Ting Zhao, Department of Pathology, University of Pittsburgh School of Medicine.

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