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New study on hepatitis C virus entry factor: Researchers identify disruption of iron uptake receptor

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Hepatitis C virus (HCV) infects more than 170 million people worldwide. Approximately 80 percent of infections lead to chronic illness including fibrosis, cirrhosis, cancer and also hepatic iron overload. A new study completed by researchers at Loyola University Chicago Stritch School of Medicine reveals that HCV not only alters expression of the iron-uptake receptor known as transferrin receptor 1 (TfR1) but that TfR1 also mediates HCV entry.

"We have not yet discovered a cure for Hepatitis C, however discovering the relationship between HCV and TfR1 sheds more light on the complex, multistep process required for the virus to get into liver cells," said senior author Susan L. Uprichard, PhD, virologist and Director of Hepatology Research, Loyola. "This new knowledge reveals important insight into how the virus interacts with and changes our liver cells for its own benefit. As such, it may facilitate the development of entry inhibitors or treatments for HCV-associated iron overload."

The research findings could also potentially be used in the clinical setting for the care of patients not only for those with chronic liver disease but also for post liver transplant where it might help prevent infection of a new liver or at least slow disease progression. Uprichard says her HCV research lays important groundwork. "This research is like finding one of the four corners of a puzzle," she said. "It creates a key building block toward finding a medical solution to Hepatitis C."

The new study is part of a project initially directed at understanding how HCV may disrupt cellular iron homeostasis. "TfR1 plays a role in HCV infection at the level of glycoprotein-mediated entry, acts after CD81 and is possibly involved in HCV particle internalization," said Danyelle Martin, the first author of the study who performed this research as part of her Ph.D work at University of Illinois at Chicago (UIC) and is now manager of the newly established Clinical Research Office Biobank at Loyola University Medical Center. "More studies will need to be done to determine if and how the interaction between TfR1 and HCV leads to the hepatic iron overload seen in HCV infected patients."

Results of the HCV study are published in the *Proceedings of the National Academy of Sciences* (*PNAS*) the week of June 10, 2013.

"The Hepatitis C Virus is fascinating and complex; we are still learning about the biology of the virus including the liver cell factors the virus needs to replicate and how these interactions cause the specific liver dysfunction observed in patients," said Uprichard, who also began the research while at UIC.

More information: Identification of transferrin receptor 1 as a hepatitis C virus entry factor, www.pnas.org/cgi/doi/10.1073/pnas.1301764110

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