Protein Signature May Predict Who Responds to Hepatitis C Treatment

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(PhysOrg.com) -- A tell-tale set of newly-identified proteins may be able to predict who will most likely respond to standard therapy for hepatitis C infection, say researchers in the Duke Clinical Research Institute (DCRI). It is a development that could help patients facing one of the most taxing therapeutic regimens in medicine.

The research was presented today at the annual meeting of the American Association for the Study of Liver Disease.

The findings are also the first to emerge from a $35 million grant to Duke from real estate developer David Murdock, who created the North Carolina Research Campus in Kannapolis, N.C., to support genomic studies that help match treatments to patients' unique genetic profiles.

"Those of us who treat patients with hepatitis C (HCV) know that treatment can be very difficult, in terms of side effects, and most patients need to be in therapy for almost a year," says Dr. John McHutchison, the senior author of the study and associate director of the Duke Clinical Research Institute. "When treatment demands this much commitment, it would be nice if we had something to help us - and our patients - decide in advance who is most likely to benefit, and who should try other options."

Hepatitis C is the most common blood-borne viral infection in the United States and it is one of the main causes of chronic liver disease. Some people with HCV can lead long lives with few symptoms, but for

others, HCV leads to end-stage liver disease, cancer and death. It is estimated that at least four million people in the U.S. and 170 million people world-wide are infected with HCV.

Standard treatment for the disease includes weekly injections of interferon and the oral antiviral agent, ribavirin. While the regimen can be curative - roughly 40 percent of patients with the most common subtype of HCV in the U.S., called genotype 1, will respond to it - it's not clear who is likely to respond and who is not. The result is that thousands of people spend long months on treatment without any significant long-term benefit.

Sifting through an extensive DCRI biorepository of blood and tissue samples from three thousand patients with HCV, investigators selected serum samples from 30 patients. Ten were from patients with genotype I who responded to therapy and were cured; ten samples were from patients with genotype I who did not respond to therapy and the rest were from patients with genotypes 2 or 3 who had also responded to therapy and were cured.

Researchers broke down the proteins in the serum into peptides and then used liquid chromatography/mass spectrometry to sort the peptides according to molecular weight and charge. Using factor modeling in conjunction with software designed to analyze proteomic data (Rosetta Elucidator) Duke scientists Will Thompson, Joe Lucas and Art Moseley discovered three factors representingclusters of proteins or peptides that can predict in nine cases of out ten who will respond to therapy and who will not.

"This is just a first step," says Moseley, who is director of the proteomics laboratory in the Duke Institute for Genome Science & Policy. "We still have to figure out which protein pathways these clusters are associated with. That, in turn, may yield information that could lead

to new treatment options or more informed treatment decisions using current therapies."

"We have needed something like this for a long, long, time," says Keyur Patel, M.D., the lead author of the study and a member of the DCRI. "We are now validating our initial findings in a second set of 30 serum samples from the same biorepository. We are hoping to use these protein signatures in a clinical trial within a year or so."

Additional authors on the study include Laura Dubois, Diane Uzarski, Hans Tillman, Robert Califf and Jeanette McCarthy, all from Duke.

The North Carolina Research Campus, located in Kannapolis, North Carolina, is a private-public venture designed to foster collaborative research in biotechnology, agriculture and nutrition that will improve the health of people world-wide.

Provided by Duke University