

Gene variant heightens risk of severe liver disease in cystic fibrosis

September 8 2009

Researchers at the University of North Carolina at Chapel Hill have discovered a genetic risk factor for severe liver disease in people with cystic fibrosis. Those who carry a particular variant of the SERPINA1 gene (also known as alpha-1-antitrypsin or alpha-1-antiprotease) are five times more likely to develop cirrhosis and other liver complications than patients who carry the normal version of the gene.

The study, which appears in the Sept. 9 issue of the *Journal of the American Medical Association (JAMA)*, could lead to earlier detection and diagnosis of <u>cystic fibrosis</u> liver disease and better treatment options for the patients affected by the disease. In addition, it could pave the way for similar studies in more common forms of liver disease.

"I predict that as we uncover more risk factors of liver disease in cystic fibrosis we may also find that they play a role in how rapidly people with a more common malady, such as viral hepatitis, develop liver complications (or "fibrosis")," said senior study author Michael R. Knowles, M.D., professor of pulmonary and critical care medicine at UNC.

Cystic fibrosis is the most common fatal genetic illness among Caucasians. In the disease, defects in the <u>CFTR gene</u> cause the lungs, intestines and pancreas to become clogged with mucus, resulting in breathing problems and other difficulties. Though every patient with cystic fibrosis carries mutations in both copies of their CFTR gene (one inherited from the mother and one from the father), symptoms can vary



widely from patient to patient. For instance, about five percent of cystic fibrosis patients develop liver disease so severe it requires a <u>liver</u> <u>transplant</u>.

For the last decade, researchers have been investigating what other genetic factors might modify the effects of the disease-causing mutations in the CFTR gene, further altering the biological conditions under which the disease unfolds to either make it milder or more severe. Several genes have emerged as potential "genetic modifiers," and studies to replicate some of those findings have recently been accomplished.

In this study, the UNC researchers collaborated with an international team of scientists to compile the largest number of samples ever from cystic fibrosis patients with severe liver disease. The study was initially conducted in 124 cystic fibrosis patients with severe liver disease and 843 cystic fibrosis patients without liver disease. The team evaluated nine sequence variants in five genes that previous studies had suggested might be associated with liver disease.

They found that more cystic fibrosis patients with liver disease had a particular version of the SERPINA1 gene -- called the Z allele - than patients without liver disease, indicating that the gene variant plays a role in the development of this ailment. The researchers confirmed their results in a separate set of cystic fibrosis patients, 136 with liver disease and 1088 without.

According to lead study author Jaclyn R. Bartlett, Ph.D., discovering such risk factors will enable clinicians to identify cystic fibrosis patients who may be predisposed to develop <u>liver disease</u>. "We also hope that further research will show how the presence of this particular gene affects the liver on a molecular level in cystic fibrosis patients," said Bartlett, a research associate scientist at UNC.



Aided by their international collaborators, the researchers are now searching for genetic modifiers associated with other complications of cystic fibrosis, including lung disease, intestinal obstruction and diabetes.

Source: University of North Carolina School of Medicine (news : web)

Citation: Gene variant heightens risk of severe liver disease in cystic fibrosis (2009, September 8) retrieved 9 May 2024 from <u>https://medicalxpress.com/news/2009-09-gene-variant-heightens-severe-liver.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.