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Gene variant increases fatty liver risk and fibrosis progression

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New research confirms that a variant on the patatin-like phospholipase-3 (PNPLA3) gene increases risk of steatosis and fibrosis progression in patients with chronic hepatitis C virus (HCV). The PNPLA3 single nucleotide polymorphism (SNP) rs 738409 may represent an important genetic predictor and potential therapeutic target in chronic HCV liver damage. Study details are published in the July issue of *Hepatology*, a peer-reviewed journal of the American Association for the Study of Liver Diseases.

According to a report by the World Health Organization (WHO) roughly 170,000 million individuals worldwide are infected with chronic HCV—a leading cause of liver disease and liver transplantation. Research shows that only 20% of HCV patients develop cirrhosis, but fibrosis progression remains highly unpredictable. A recent study identified a genetic variant in the PNPLA3 gene (rs738409 C>G) associated with fatty liver (steatosis) and was also found to influence fibrosis severity in non-alcoholic fatty liver disease.

The present study led by Christophe Moreno, MD, PhD, from Erasme Hospital and the Université Libre de Bruxelles in Belgium examined the impact of the rs738409 polymorphism and other variants in the PNPLA3 gene on liver damage and response to antiviral therapy in chronic HCV. Researchers recruited 527 Caucasian patients with chronic HCV from centers in Belgium (n=229), Germany (n=171), and France (n=137). More than half of the participants were male with a mean age ranging from 47 to 52 years.

"Our findings show that the PNPLA3 SNP rs738409 favors steatosis and fibrosis progression in chronic HCV," confirmed Dr. Moreno. After adjusting for age, gender, body mass index, alcohol consumption and diabetes, the team determined that carriers of two copies of the rs738409 mutant G allele (i.e. GG homozygotes) remained at higher risk for developing fatty liver, fibrosis, and fibrosis progression, with an odds ratio of 2.55, 3.13 and 2.64, respectively.

Further analysis determined that the SNP rs738409 was not associated with antiviral treatment failure and did not influence clinical or biological variables such as stage of fibrosis, alanine aminotransferase (ALT), viral load, or type 2 diabetes. "This SNP represents a valuable genetic predictor of liver damage," concluded Dr. Moreno. "Further studies are needed to confirm our results and evaluate the PNPLA3 gene variant as a potential therapeutic target in chronic HCV."

More information: "Impact of Patatin-like Phospholipase-3 (rs738409 C>G) Polymorphism on Fibrosis Progression and Steatosis in Chronic Hepatitis C." Eric Trépo, Pierre Pradat, Andrej Potthoff, Yukihide Momozawa, Eric Quertinmont, Thierry Gustot, Arnaud Lemmers, Pascale Berthillon, Leila Amininejad, Michèle Chevallier, Jerome Schlué, Hans Kreipe, Jacques Devière, Michael Manns, Christian Trépo, John Sninsky, Heiner Wedemeyer, Denis Franchimont and Christophe Moreno. Hepatology; Published Online: June 24, 2011 (DOI: 10.1002/hep.24350); Print Issue Date: July 2011.

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