Alcoholics beware -- genetic variation linked to liver cirrhosis in Caucasians

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A new study by German researchers found that a variation in the PNPLA3 (adiponutrin) gene was associated with cirrhosis of the liver and elevated transaminase (liver enzyme) levels in alcoholic Caucasians. The risk of cirrhosis in alcoholics in the genetic high risk group might be as high as 25% to 50%. Full findings are published in the January 2011 issue of *Hepatology*, a journal of the American Association for the Study of Liver Diseases.

Alcoholic liver disease (ALD)—ranging from alcoholic fatty liver to alcohol induced liver fibrosis and cirrhosis—accounts for more than 50% all chronic liver disease in industrialized countries and was responsible for over 25,000 deaths in the U.S. alone in 2005. Studies have shown that while all heavy drinkers display signs of hepatitis steatosis (fatty liver), only 10% to 35% of alcoholics develop hepatic inflammation, with up to 20% progressing to cirrhosis. Further medical evidence suggests a link between PNPLA3 gene variation and liver fat content; specifically the single nucleotide polymorphism (SNP) rs738409 was reported previously to be associated with advanced alcoholic liver disease in alcohol-dependent individuals of European and Native American descent.

The German research team led by Jochen Hampe, MD, from Christian-Albrechts-Universität Kiel determined the genotype and allele frequencies of PNPLA3 rs738409 in 1043 alcoholics with or without alcoholic liver injury and in 376 at-risk drinkers from a population-based cohort. Cirrhosis and steatosis was determined by liver biopsy and

standard diagnostic testing. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were established using routine clinical chemistry testing.

Participants were categorized as alcoholic liver cirrhosis (ALC); alcoholics with liver steatosis on ultrasound and elevation of ALT as alcoholic liver damage (ALD); alcoholic liver steatosis and normal liver enzyme levels as alcoholic fatty liver (AFL); and alcoholics with normal appearance of the liver on ultrasound and normal liver enzyme levels as alcoholic controls.

Researchers discovered that SNP rs738409 was strongly over-represented in patients with ALC and ALD compared to alcoholics without liver damage. Additionally, the frequency of allele PNPLA3 rs738409 in AFL participants was lower than in alcoholics without steatosis and normal liver enzymes. "Our findings show PNPLA3 rs738409 carriers represent a subpopulation of high risk individuals susceptible to progression from clinically silent alcoholic liver disease to obvious cirrhosis," Dr. Hampe concluded. "Carriers of this risk allele should be targeted for future pharmaceutical treatments and non-pharmacological interventions."

More information: "Genetic Variation in the PNPLA3 Gene is Associated with Alcoholic Liver Injury in Caucasians." Felix Stickel, Stephan Buch, Katharina Lau, Henriette Meyer zu Schwabedissen, Thomas Berg, Monika Ridinger, Marcella Rietschel, Clemens Schafmayer, Felix Braun, Holger Hinrichsen, Rainer Günther, Alexander Arlt, Marcus Seeger, Sebastian Müller, Helmut Karl Seitz, Michael Soyka, Markus Lerch, Frank Lammert, Christoph Sarrazin, Ralf Kubitz, Dieter Häussinger, Claus Hellerbrand, Dieter Bröring, Stefan Schreiber, Falk Kiefer, Rainer Spanagel, Karl Mann, Christian Datz, Michael Krawczak, Norbert Wodarz, Henry Völzke, Jochen Hampe. *Hepatology*; Published Online: December 7, 2010 (DOI: 10.1002/hep.24017); Print

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