Metobolomics uncovers key indicators of nonalcoholic fatty liver disease

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A recent metobolomics study by researchers from Virginia Commonwealth University Medical Center in Richmond found that impaired peroxisomal oxidation of polyunsaturated fatty acids (PUFA) is associated with the progression of nonalcoholic fatty liver (NAFL) to nonalcoholic steatohepatitis (NASH). The study also found significantly higher plasma monounsaturated fatty acids in the blood of patients with NAFL and NASH. Full findings appear in the December issue of *Hepatology*.

Nonalcoholic fatty liver disease (NAFLD) affects a third of the U.S. adult population, with many cases found in obese individuals. NAFLD ranges from NAFL, a benign condition where fat accumulates in the liver of people who drink little or no alcohol, to a more serious state known as NASH where inflammation or scarring of the liver occurs and which can progress to liver failure.

Study participants included 50 in a lean normal control, 25 subjects with NAFL and 50 patients with NASH. Researchers classified the NAFL group by a diagnosis of fatty liver with the presence of accumulated liver fat of at least grade 1 severity according to the NASH Clinical Research Network criteria. The NASH group included those with at least a grade 1 severity in accumulated liver fat, inflammation and cytologic ballooning of at least grade 1 severity in each. The nonalcoholic nature of the disease was established by clinical assessment that the alcohol consumption was less than 20 gm/day for women and 30 gm/day for men. Lean normal controls were identified by a body mass index

between 18-25 kg/m2, absence of symptoms or signs of disease, normal liver enzymes and hepatic sonogram.

The research team, headed by Arun Sanyal, M.B.B.S., M.D., used mass spectrometry (a technique that determines the basic composition of a sample) to analyze blood lipids and metabolites of the NAFL and NASH subjects comparing them with the control group. Data revealed that the development of NAFL is accompanied by increased lipogenesis, Δ 9 desaturase and LOX activity. "Our study provides the most comprehensive picture of lipid metabolism in NAFLD to date," said Dr. Sanyal.

Results indicate that when the condition of the liver progresses to NASH the lipogenic activity levels off or declines modestly while the LOX activity increases. Simultaneously, there is impaired peroxisomal PUFA metabolism and increase in levels of products of non-enzymatic oxidation of arachidonic acid. "Further study of the role specific metabolic pathways play in the establishment and progression of NASH are needed," concluded Dr. Sanyal. "Our findings serve as a basis for future research of NAFLD."

More information: "The Plasma Lipidomic Signature of Nonalcoholic Steatohepatitis," Puneet Puri1, Michelle M. Wiest, Onpan Cheung, Faridoddin Mirshahi, Carol Sargeant, Hae-Ki Min, Melissa J. Contos, Richard K.Sterling, Michael Fuchs, Huiping Zhou, Steven M. Watkins, and Arun J. Sanyal. Hepatology; Published Online: November 24, 2009 (DOI: 10.1002/hep.23229); Print Issue Date: Dec 2009. www3.interscience.wiley.com/jo … l/122542493/abstract

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