Gene variant ID could lead to better fatty liver disease diagnosis

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More patients could be diagnosed earlier with non-alcoholic fatty liver disease (NAFLD) after a cohort study presented at the International Liver CongressTM 2013 identified variants within four genes significantly associated with the histological features of the disease.

NAFLD is caused by a fatty liver; when fat is deposited in the liver not due to the use of alcohol. The spectrum of the disease is broad, ranging from simple fat deposition without inflammation (steatosis), to liver inflammation (steatohepatitis), eventually accompanied by a variable degree of fibrosis. In case of severe fibrosis progession, cirrhosis may develop. NAFLD is currently regarded as a major cause of cirrhosis of the liver of unknown cause.

As NAFLD patients are typically asymptomatic, even in the presence of more severe liver lesions, patient diagnostic techniques to identify at-risk individuals would be very helpful to improve the management of the disease.

Previous genome-wide association studies (GWAS) have provided important insights into modifier genes which influence the pathology of steatosis. Using data drawn from a large GWAS of 1125, European and North American Caucasian patients with NAFLD, this study applied a candidate-gene approach to re-examine the broader validity of these associations.

Variants within four genes significantly associated with the histological

features of NAFLD were identified including steatosis (PNPLA3 rs738409, GCKR rs780094, PPP1R3B rs11777327, TRIB1 rs2385114); steatohepatitis (PNPLA3, GCKR, TRIB1); and fibrosis (PNPLA3, GCKR, TRIB1).

This study has further established the overwhelming significance of the chromosome 22 PNPLA3 locus to all aspects of NAFLD and has, for the first time, demonstrated that some genetic variations previously associated with steatosis or mild biochemical abnormalities may in fact have broader pathological significance influencing inflammatory disease and progression to fibrosis in NAFLD. A screening of these genes could be used in future genetic diagnostics to identify patient prone to development of NAFLD, if these results will be confirmed in prospective studies.

More information: Anstee Q et al., A candidate-gene approach to validation of genetic modifier associations using a large cohort with histologically characterized non-alcoholic fatty liver. Abstract presented at the International Liver Congress 2013

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