A genome-wide association study confirms PNPLA3 and identifies TM6SF2 and MBOAT7 as risk loci for alcohol-related cirrhosis

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Alcohol misuse is the leading cause of cirrhosis and the second most common indication for liver transplantation in the Western world. We performed a genome-wide association study for alcohol-related cirrhosis in individuals of European descent (712 cases and 1,426 controls) with subsequent validation in two independent European cohorts (1,148 cases and 922 controls). We identified variants in the MBOAT7 (P = 1.03 x 10(-9)) and TM6SF2 (P = 7.89 x 10(-10)) genes as new risk loci and confirmed rs738409 in PNPLA3 as an important risk locus for alcohol-related cirrhosis (P = 1.54 x 10(-48)) at a genome-wide level of significance. These three loci have a role in lipid processing, suggesting that lipid turnover is important in the pathogenesis of alcohol-related cirrhosis.
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