

Dissecting the genetic risk of hepatocellular carcinoma in alcoholic cirrhotics by genome-wide scanning: a case-control-study

Summary

State of Research: Hepatocellular carcinoma (HCC) shows a rising incidence worldwide, and the largest burden of disease in Western countries derives from patients with alcoholic liver disease (ALD) and cirrhosis (ALC), the latter being the premier premalignant factor for HCC. Approximately 10% of ALC develop HCC as a complication within 5 years of follow-up. To date, carriage of the *PNPLA3* rs738409 G allele is the only robustly confirmed genetic risk locus, which however explains only a fraction of the host genetic risk in ALC.

Objectives: The present research endeavour aims at addressing two major aims to: 1. Identify genetic variants which reveal a significant association with HCC in patients with ALC by means of a genome-wide case control study; 2. To validate the putative genetic variants associated with the risk to develop HCC with genome-wide significance in an independent cohort of cases and controls.

Samples and Methods: We aim to perform the first GWAS comparing ALC with HCC (cases) vs ALC without HCC (controls) in European Caucasians with a subsequent validation in an independent European cohort by means of a genome-wide case control study using the HumanOmniExpress DNA BeadChip technology by Illumina, and TaqMan- and Sequenom-based replication genotyping of top hits.

Expected value: The proposed study has the potential to identify yet unknown genetic risk factors that determine the risk of ALC to develop HCC. Identification of such genetic risk factors would greatly improve the understanding of how alcohol promotes primary liver cancer, to develop strategies of its prevention, and hopefully, the development of novel treatments.