A new 3p25 locus is associated with liver fibrosis progression in human immunodeficiency virus/hepatitis C virus-coinfected patients

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There is growing evidence that human genetic variants contribute to liver fibrosis in subjects with hepatitis C virus (HCV) monoinfection, but this aspect has been little investigated in patients coinfected with HCV and human immunodeficiency virus (HIV). We performed the first genome-wide association study of liver fibrosis progression in patients coinfected with HCV and HIV, using the well-characterized French National Agency for Research on AIDS and Viral Hepatitis CO13 HEPAVIH cohort. Liver fibrosis was assessed by elastography (FibroScan), providing a quantitative fibrosis score. After quality control, a genome-wide association study was conducted on 289 Caucasian patients, for a total of 8,426,597 genotyped (Illumina Omni2.5 BeadChip) or reliably imputed single-nucleotide polymorphisms. Single-nucleotide polymorphisms with P values <10-6 were investigated in two independent replication cohorts of European patients infected with HCV alone. Two signals of genome-wide significance (P <5 Œ 10-8) were obtained. The first, on chromosome 3p25 and corresponding to rs61183828 (P = 3.8 Œ 10-9), was replicated in the two independent cohorts of patients with HCV monoinfection. The cluster of single-nucleotide polymorphisms in linkage disequilibrium with rs61183828 was located close to two genes involved in mechanisms affecting both cell signaling and cell structure (CAV3) or HCV replication (RAD18). The second signal, obtained with rs11790131 (P = 9.3 Œ 10-9) on chromosome region 9p22, was not replicated.; This genome-wide association study identified a new locus associated with liver fibrosis severity in patients with HIV/HCV coinfection, on chromosome 3p25, a finding that was replicated in patients with HCV monoinfection; these results provide new relevant hypotheses for the pathogenesis of liver fibrosis in patients with HIV/HCV coinfection that may help define new targets for drug development or new prognostic tests, to improve patient care. (Hepatology 2016;64:1462-1472).
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