

Impact of leptin receptor gene variants on risk of non-alcoholic fatty liver disease and its interaction with adiponutrin gene.

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Abstract

BACKGROUND AND AIM:

Genetic polymorphism has been implicated as a factor for the occurrence of non-alcoholic fatty liver disease (NAFLD). This study attempted to assess whether polymorphisms in the leptin receptor (LEPR) gene and its combined effect with patatin-like phospholipase domain-containing protein 3 (PNPLA3/adiponutrin) are associated with risk of NAFLD.

METHODS:

A total of 144 biopsy-proven NAFLD and 198 controls were genotyped using the Sequenom MassARRAY platform.

RESULTS:

We observed a significant association between the LEPR rs1137100 and rs1137101 with susceptibility to NAFLD (odds ratio [OR] 1.64, 95% confidence interval [CI] 1.18-2.28, $P = 0.003$; and OR 1.61, 95% CI 1.11-2.34, $P = 0.013$, respectively) and to non-alcoholic steatohepatitis (OR 1.49, 95% CI 1.05-2.12, $P = 0.026$; and OR 1.57, 95% CI 1.05-2.35, $P = 0.029$, respectively). The LEPR rs1137100 is also associated with simple steatosis (OR 2.27, 95% CI 1.27-4.08, $P = 0.006$). Analysis of gene-gene interaction revealed a strong interaction between the LEPR and PNPLA3 genes (empirical $P = 0.001$). The joint effect of LEPR and PNPLA3 greatly exacerbated the risk of NAFLD (OR 3.73, 95% CI 1.84-7.55, $P < 0.0001$). The G allele of rs1137100 is associated with lower fibrosis score (OR 0.47, 95% CI 0.28-0.78, $P = 0.001$).

CONCLUSIONS:

We report an association between variants of LEPR rs1137100 and rs1137101 with risk of NAFLD. This study suggests that rs1137100, specifically the G allele, is associated with a less severe form of liver disease in patients with NAFLD. The interaction between LEPR and PNPLA3 genes showed increased risk of NAFLD compared to either gene alone.

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