The Association of Haptoglobin Genotype with the Development of Liver Disease and a Strategy for Personalized Treatment of NASH

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Background Haptoglobin is a binding protein that scavenges free hemoglobin and is highly expressed in the liver. The human haptoglobin gene (HP) is polymorphic, consisting of two alleles, HP1 and HP2. Recent studies have found that haptoglobin variants are strongly associated with cholesterol levels, as haptoglobin is capable of binding apolipoprotein E and regulating HDL function\(^3\)-\(^4\). Together, these functions allow haptoglobin to play a significant role in the transport of cholesterol from tissues to the liver. Goal Study the association of haptoglobin genotypes with the development of nonalcoholic steatohepatitis (NASH) using 2000 NASH CRN patient DNA samples. Methods Allelic differences were determined using TaqMan genotyping PCR and were analyzed on an ABI7300 real-time PCR machine. Following allele identification, the association between genotype and phenotype was determined, with focus on NASH scores and other relevant measurements. Results The distribution of haptoglobin genotype frequencies were 46% HP1/HP2, 39% HP2/HP2, and 15% HP1/HP1, with no gender differences. The results suggest that HP2/HP2 is associated with specific liver disease states such as an NAFLD score of 6, fibrosis in zone 2 of the liver and periportal area, and a steatosis grade of 34-66%. The most abundant genotype observed was heterozygous for several ethnic groups, as expected. However, patients of Asian ancestry demonstrated homozygous HP2 as the majority genotype. Conclusion HP genotype plays an important role in liver disease development. Genotyping distribution differences in ethnic groups may inform personalized treatment strategies, such as recommending Vitamin E for patients homozygous for HP2\(^2\).

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