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*[1 2].

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