# SNP Research in Liver Disease

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Hepatitis B virus (HBV) infection is a global public health problem with more than 350 million chronic carriers worldwide. The reasons for the variation in the natural history of HBV infection are unknown, but are probably related to host immune factors. Cytokines such as tumor necrosis factor-$\alpha$ (TNF-$\alpha$), interferon-$\gamma$ (IFN-$\gamma$), and interleukin-10 (IL-10) play significant roles in inflammatory and immune defense. The most common type of genetic variation in human is the single nucleotide polymorphism (SNP), a stable substitution of a single base, which is found in more than 1% of the population. SNPs in the promoter region of various cytokine genes have been shown to be responsible for phenotypic variations. Recently, we showed that there is no association between mannose binding lectin gene SNP and natural course of HBV infection. To clarify whether the inheritance of cytokine gene SNPs could serve as a candidate for determining clinical outcomes of the disease caused by chronic HBV infection, we assessed SNPs in IL-10 promoter (-1082, -819, -592), TNF-$\alpha$ promoter (-308, -238), INF-$\gamma$ (+874), IFN-$\gamma$ receptor-1 (-56 and +95), IFN-$\gamma$ receptor-2 (Q64R), interferon regulatory factor (IRF) (-410, -388), IL-1 beta (-511, -31), IL-1B receptor antagonist (IL-1BRN)(S130S, 3'UTR) genes in Korean patients with HBV infection (n=412, HBV persistence group), and in HBsAg negative controls who had eliminated HBV (n=204, HBV clearance group). SNPs were detected by single base primer extension assay (SNP IT$^{TM}$). As a result, TNF-$\alpha$ GG haplotype homozygotes were more frequent in HBV persistence group than clearance group (82.8% vs. 75.5%). The carriers of IL-10 592 A allele had a high risk of HBV persistence after HBV infection compared to C/C genotype carriers (The age and sex adjusted ORs; 0.40, 95% CI 0.22-0.73; p=0.003). Polymorphisms in INF-$\gamma$, IFN-$\gamma$ receptor-1 and 2, IRF, IL-1B and IL-1BRN were not related to HBV clearance or disease progression. But cytokine expression may also be disease stage-specific, determination of the exact functional consequences of these polymorphisms must await more detailed and careful *in vitro* as well as *in vivo* studies.