SIGNIFICANT DIFFERENCES IN VIRAL KINETICS IN BASAL CORE PROMOTER AND PRECORE VARIANTS OF HEPATITIS B

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Background: Chronic hepatitis B infection (CHB) is associated with significant long-term morbidity and mortality. The hepatitis B virus (HBV) variants including the basal core promoter (BCP) and precore (PC) variants influence the natural history of patients with CHB. BCP and PC variants reduce and abolish HBeAg production, respectively, and are associated with increased risk of fibrosis progression and hepatocellular carcinoma. However, the underlying pathogenesis for those differences is unknown.

Aims: To characterize the viral kinetics and immunopathogenesis of BCP / PC variants using a mouse model of CHB.

Methods: An overlength HBV plasmid of 1.2 mer on an adeno-associated viral vector was mutated using site-directed mutagenesis to introduce BCP and PC mutations. Plasmids were hydrodynamically injected in the tail vein of C57/BL6 mice. Interferon-alpha receptor knockout (IFNaR-KO) mice were used to investigate the role of Type 1 interferon. Viral DNA was extracted from serum and measured with qPCR and serology was performed.

Results: Significant differences in virological profile were seen with the BCP and PC mutants compared to WT. There was a rapid drop in viral load in the mutants in the early stage of disease, suggesting a stronger innate immune response. The experiment was repeated in IFNaR-KO mice and the difference was abolished. In later stages, there is a significant recrudescence in viraemia indicating a weaker adaptive immune response in mutants.

Conclusions: There are significant differences in the viral kinetics of BCP and PC mutants compared to WT HBV . An early drop in VL may be due to a vigorous Type 1 interferon response.