Hepatitis B Virus e Antigen Variants

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Abstract:

More than 300 million people worldwide are chronically infected with hepatitis B virus (HBV). Considering the very short generation time for a virus, and the high error rate associated with the reverse transcription step of HBV replication, decades of HBV infection are probably equivalent to million years of human evolution. The most important selective force during the natural course of HBV infection appears to be the immune response. The development of anti-HBe antibody in hepatitis B patients usually correlates with reduction of HBV viremia. As a consequence, escape mutants of anti- HBe are selected. The core promoter mutants express less HBe antigen (HBeAg) through transcriptional down regulation, while precore mutants express truncated products. We recently identified additional mutations that modulate HBeAg translation initiation, proteolytic cleavage, and secondary structure maintenance through a disulfide bond. The core promoter mutants have been associated with the development of fulminant hepatitis during acute infection and liver cancer during chronic infection. Consistent with their enhanced pathogenicity, core promoter mutants were found to replicate at up to 10-fold higher levels in transfected human hepatoma cells than the wild-type virus. Moreover, some core promoter mutants are impaired in virion secretion due to missense mutations in the envelope gene. These virological properties may help explain enhanced pathogenicity of core promoter mutants in vivo.

Key Word:
Hepatitis B virus; HBeAg; naturally occurring mutations; immune escape; replication; secretion