Replication advantage and host factor-independent phenotypes attributable to a common naturally occurring capsid mutation (I97L) in human hepatitis B virus

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摘要

Abstract

Mutations of human hepatitis B virus (HBV) occur frequently within the capsid (core) protein in natural infections. The most frequent mutation of the core protein in HBV from Southeast Asia occurs at amino acid 97, changing an isoleucine (I) to a leucine (L). In our systematic study of virus-host interactions, we have examined the replication efficiency of a site-directed mutant, I97L, and its parental wild-type HBV in several different hepatoma cell lines. Interestingly, we found that this capsid variant replicated in human Huh7 hepatoma cells approximately 4.8-fold better than its parental wild-type HBV. A similar phenomenon was observed in another hepatoma cell line, J3. In addition, the level of encapsidated RNA pregenome in mutant I97L was about 5.7-fold higher than that of the wild-type HBV in Huh7 cells. Unlike Huh7 cells, no significant difference in viral DNA replication between the same I97L mutant and its parental wild-type HBV was observed in HepG2, a human hepatoblastoma cell line. This finding of a profound replication advantage for mutant I97L in Huh7 and J3 cells but not in HepG2 cells may have important implications for the emergence of this mutant in chronic HBV carriers. We speculate here that the mutation confers a host factor-independent growth advantage for the survival of HBV variants in gradually dedifferentiating hepatocytes and thus helps prolong viral persistence