A substitution in the pre-S1 promoter region is associated with the viral regulation of hepatitis B virus.

Mutations of Hepatitis B virus (HBV) influence the clinical course of HBV infection. As large (L) protein plays a crucial role for viral entry, we hypothesized that mutations in the pre-S1 promoter region might affect the expression of L protein and change the biological characters of virus. Patients infected with HBV were enrolled. HBV DNA sequences were analyzed by TA cloning method. Pre-S1 promoter activity was analyzed using HepG2 cells. In total, 35 patients were enrolled and 13 patients had a single base substitution in the pre-S1 promoter region; the most frequent substitution was a G-to-A substitution at the 2765th base (G2765A) in the Sp1 region. The HBV viral load showed a negative correlation with the substitution ratio of the Sp1 region or G2765A. HepG2 cells transfected with the G2765A substitution vector showed reduced luciferase activity of the pre-S1 promoter, as well as reduced expression of pre-S1 mRNA and L protein. Furthermore, the G2765A substitution reduced the L protein expression level of vector-produced virus particles. G2765A substitution in the pre-S1 promoter reduced the expression of L protein and resulted in the less severe disease in chronic HBV infection.