Antiviral effect of hepatitis B virus S/C gene loci antisense locked nucleic acid on transgenic mice in vivo


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ABSTRACT. We investigated the effects of hepatitis B virus (HBV) S/C double gene loci antisense locked nucleic acid on replication and expression of HBV in hepatitis transgenic mice. HBV mice (N = 30) were randomly divided into five groups of six mice: 5% glucose solution control, empty liposome control, single-target S, single-target C, and dual-target SC groups. An antisense locked nucleic acid fragment was injected into the mice. Serum HBsAg, serum HBV DNA, HBV C-mRNA expression in liver tissue, HbsAg and HbcAg expression in hepatocytes, serum albumin, alanine transaminase (ALT), urea nitrogen, and creatinine were detected. Liver and kidney sections were examined for the effects of antisense locked nucleic acid. The expression of HBsAg was markedly inhibited; the inhibition rates of the S, C, and SC target groups were 36.63, 31.50, and 54.87%, respectively; the replication of HBV DNA was also inhibited: 23.97, 21.13, and 35.83%, respectively. After injection at 1, 3, and 5 days, the corresponding rates for HBsAg inhibition were 14.40, 25.61, and 31.33%, and for HBV DNA inhibition they were 11.04, 19.24, and 24.13%. Compared with the control group, the differences in serum albumin, ALT, urea nitrogen,
and creatinine in each group were not statistically significant, and the number of HbsAg- and HBcAg-positive cells in the mouse liver was significantly reduced. The liver and kidney tissues were normal. The gene therapy had significant inhibitory effects on the replication and expression of HBV in transgenic mice, and double-gene targeting was better than single-gene targeting.

**Key words:** Liposome; Locked nucleic acid; Gene therapy; HBV; Hepatitis B virus; Transgenic mice