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Inhibitory effect of antisense oligodeoxynucleotides complementary to HBV on HepG2.2.15 cell line

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Abstract

AIM: To explore the therapeutic potential of antisense oligodeoxynucleotides on hepatocellular carcinoma (HCC).

METHODS: Four antisense phosphorothioated oligodeoxynucleotides (asON), complementary to different sites of HBV, were synthesized and assayed for their anti-HBV activity in HepG2.2.15 cells with ELISA. The most effective asON was chosen for the following study: FACSCAN, TRAP and immuno-staining were used respectively for checking apoptosis, telomerase activity and expression of oncogene $p21^{ras}$ and $p62^{C\text{-}myc}$ in HepG2.2.15 cells after treated by asON.

RESULTS: The oligomer directed against the initiator of pre-S2 was the most effective one with an inhibitory rate of 66% on HBsAg and 91% on HBeAg ($p < 0.02$). Two inhibitory peaks (bimodal) appeared. Telomerase activity as well as the expression of $p21^{ras}$ and $p62^{C\text{-}myc}$ decreased drastically 3 d after as ON-HbpreS-2 treatment. Meanwhile, apoptosis appeared in the experiments.

CONCLUSION: The inhibitory effects of as-preS2 on the HBV gene expression and the reversion of some malignant behaviour in HepG2.2.15 cells were the significant, effective therapy against HBV infection and hepatocellular carcinoma.

Key words: Liver neoplasms; Hepatitis B virus; Oligonucleotides, antisense; Transfection; Apoptosis; Flow cytometry; Gene expression; Gene therapy

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