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Genetic alterations in the gene encoding the major hepatitis B surface antigen: DNA and immunological analysis of recurrent HBsAg derived from monoclonal antibody-treated liver transplant patients. Gerald McMahon*, Paul H. Ehrlich, Zeinab A. Moustafa, Linda A. McCarthy, Diane Dottavio, Mark D. Tolpin, Paul I. Nadler, and Lars Ostberg. Sandoz Research Institute, East Hanover, New Jersey, 07936, USA

A gene region encoding a segment of the major surface protein, hepatitis B surface antigen (HBsAg), of hepatitis B virus (HBV) was analyzed from serum samples following orthotopic liver transplantation of three HBV chronic carrier patients treated with a human anti-HBV monoclonal antibody (SDZ OST 577). Each of these three patients became HBsAg-negative after transplantation and therapy with the human anti-HBV monoclonal antibody but returned to HBsAg positivity (first detected 143, 251, and 252 days after the transplantation). Polymerase chain reaction (PCR) DNA amplification was performed on DNA from serum samples showing low levels of recurrent HBsAg and reduced antigen reactivity with SDZ OST 577 antibody. PCR DNA included a 230 bp highly conserved, major S gene region that was cloned into M13 bacteriophage; analysis of this DNA segment provided a consensus of DNA sequences for the serum samples exhibiting altered reactivity with the therapeutic monoclonal. Analysis of independent DNA clones from serum samples of patients exhibiting low but detectable recurrent serum levels of post-therapy HBsAg revealed the presence of S protein variant sequences when compared to PCR DNA derived from the original infected liver or pre-therapy serum HBsAg. Genetic variation was predominant in a highly conserved peptide domain which has previously been implicated in antibody binding and neutralizing antibody epitopes. Administration of serum containing one of these variant viruses to a single hepatitis B-naive chimpanzee resulted in subclinical hepatitis. Anti-HBsAg and anti-HBcAg immune responses were observed 49 and 70 days after virus administration, respectively. HBV DNA was recovered on liver biopsy between 6 and 8 weeks after inoculation although the animal remained persistently seronegative for HBsAg. DNA sequence analysis of both primate and patient liver HBV confirmed the presence of the DNA encoding the S protein variant and associated this DNA with liver infection.

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Ribavirin Therapy For Chinese Patients With Chronic Hepatitis C

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Eleven Chinese patients with chronic hepatitis C virus infection were treated with a 1,200 mg daily dose of ribavirin per oral for 4 weeks. The pretreatment serum alanine aminotransferase (ALT) levels were normal in 6 patients, and abnormal (>90 IU/L) in 5 patients. In the normal serum ALT group, no change of ALT was noted during the ribavirin therapy; while in the abnormal serum ALT group, their mean serum ALT levels decreased from 203 IU/L at baseline to 119 IU/L after four weeks of treatment, but rose to 199 IU/L at 5 months after discontinuation of therapy. No change in titers of anti-HCV was observed in all patients during and after treated with ribavirin. The main side effect of the ribavirin therapy was anemia which resolved within two months after discontinuation of therapy.