

GB Virus C/Hepatitis G Virus Does Not Induce Expression of p44 Antigen in Chimpanzee Hepatocytes

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The cytoplasmic antigen, p44, was originally discovered in hepatocytes of chimpanzees experimentally infected with the parenterally transmitted form of non-A, non-B hepatitis virus (NANBHV) (1). Expression of the antigen, found in parallel with unique ultrastructural alterations (2), appeared to be a host-response to infection with NANBHV or hepatitis delta virus, but not to infection with hepatitis A virus, hepatitis B virus, or enterically transmitted NANBHV. Until hepatitis C virus (HCV) was molecularly cloned in 1989, showing that most parenterally transmitted NANBHV infections, p44 was useful as a reliable marker for the NANBHV (now HCV) infection. The gene encoding p44 was subsequently isolated and shown to be a member of the family of interferon- α/β inducible genes (3). It is now speculated that p44 is possibly one of the mediators involved in the antiviral action of interferon.

Recently, GB virus C (also called as hepatitis G virus) (GBV-C/HGV), which is closely related to but distinct from HCV, was discovered. Although they share little sequence homology, HCV and GBV-C/HGV have a quite similar genetic organization, with the exception that the latter almost lacks sequences encoding a core protein. We were interested to know if GBV-C/HGV induces p44, as both viruses presumably replicate via double-stranded RNA replicative intermediate, an interferon inducer.

When we retrospectively examined samples from the NANBHV transmission studies conducted in the 1980s, we

found chimpanzees whose sera were positive for GBV-C/HGV RNA by RT-PCR. Utilizing the liver biopsy specimens collected from these chimpanzees, we investigated appearance of the p44 antigen and the related tubular structures in hepatocytes.

The inoculum used for the transmission study was obtained from an implicated donor. A 61-year-old woman received thrombocytes from her son, a healthy individual negative for hepatitis B surface antigen (HBsAg) and antibody to hepatitis B surface antigen (anti-HBs), in the course of a splenectomy in 1981. She developed acute NANB hepatitis; her level of serum transaminase (ALT) rose 10 days after transfusion and peaked at 15 days. Serum was again collected from the donor 3 months after donation, and 1 ml of 10^{-2} , 10^{-4} , and 10^{-6} dilution was inoculated into chimpanzee #1310, #429, and #125, respectively. All of the chimpanzees developed hepatitis as evidenced by the elevated level of serum ALT; the peak was at week 2 for #1310, at week 12 for #429, and at week 5 for #125.

Serum samples and liver biopsy specimens collected at intervals from chimpanzees #429 and #125 were available for the present assays. For both chimpanzees, all of the serum samples were negative for HCV RNA as measured by RT-PCR, as well as anti-C100 HCV antibody as measured by ELISA, throughout the observation period of 35 weeks. GBV-C/HGV RNA, as detected by RT-PCR with primers detecting the 5' non-coding region of the viral genome, became transiently positive at 1-2 weeks and then continuously positive at 10-35 weeks in chimpanzee #429 (Fig. 1A). In chimpanzee #125, GBV-C/HGV RNA was detected at 3-8 weeks, then reappeared

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