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Hepatitis C Virus Infection in SCID Mice Using Xenografted Human Livers. Schinazi, R.F.,[1]* Hough, L.M.,[1] Yao, X.,[1] Lloyd, R.L., jr.,[1] Fallon, M.,[1] Sommadossi, J.-P.,[2] Fried, M.W.,[1] and Mead, J.R.[1] Emory University School of Medicine/VA Medical Center,[1] Decatur, Georgia, and University of Alabama, Birmingham, Alabama, USA.[2]

Hepatitis C virus (HCV) infections causes chronic liver disease for which there is no effective vaccine or therapy other than interferon. The development of a SCID mouse model system could accelerate the discovery of novel antiviral agents. In this study, explants of HCV-infected human liver segments were implanted subcutaneously into the backs of 6-8 wk old SCID mice (CB-17 *scid/scid*). Histopathological examination after implantation revealed that the human hepatic architecture at 2-3 weeks was destroyed, but the liver bile ductules could survive in the host, and even proliferate in SCID mice for at least 15 weeks. Mouse livers from the engrafted animals presented a morphology consistent with mild hepatitis on the paraffin-embedded specimens taken by 1-15 wk after implantation; *in situ* hybridization results are pending. Normal saline preserved human livers engrafted into mice were not as successful as Wisconsin's preserved livers. PCR products from tissues obtained from the excised implanted human liver indicated very sharp and intense bands corresponding to the predicted molecular weight for the amplification product, especially from mice sacrificed at 2-3 weeks. Subsequent PCR on purified clones yielded amplicons of the correct size and sequence for HCV. These results unambiguously demonstrated that the PCR products were indeed of HCV origins even at 10 weeks after engraftment. This work provides the foundation for an HCV animal model system appropriate for extended immunological and antiviral studies.

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EFFECT OF CIDOFOVIR ON THE TUMOR GROWTH OF SiHa (HUMAN CERVICAL CARCINOMA) CELLS IN NUDE MICE

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The activity of cidofovir [HPMPC, (*S*)-1-(3-hydroxy-2-phosphonylmethoxypropyl)cytosine] against papilloma virus was first described in rabbits and was confirmed in several patients suffering from severe recurrent laryngeal papillomatosis and anogenital human papilloma virus (HPV) infections. We have now examined the effects of HPMPC on the growth of the human cervical epithelial tumor cell line SiHa (containing HPV-16) in nude mice. Athymic mice (BALB/c, nu/nu) between the age of 6-8 weeks were injected subcutaneously (s.c.) with 5 to 10 x 10^6 cells. Once tumors were established (approximately after 20 to 30 days), the mice were divided into several groups (4 to 5 mice per group) and injected with HPMPC, AraC or PBS at the tumor site. The animals were treated 5x/week, once per day, during 4 weeks with 10 µl of PBS or different doses of HPMPC or AraC. At various times after the beginning of the treatment the tumor size for each animal was measured and the percentage of tumor growth was calculated. Groups treated with HPMPC at a dose of 5 or 10 mg/ml showed a dramatic reduction in the percentage of tumor growth as compared to the placebo group and AraC group. When animals were treated at different doses of HPMPC (10, 5 and 1 mg/ml) 1x, 3x or 5x per week during 1 month, a clear dose-dependent response was noted. If HPMPC was administered s.c. at a dose of 50 mg/kg either 3x/week or 5x/week or at a dose of 100 mg/kg 3x/week during 1 month, no decrease in the size of the tumors was observed. Thus, our results demonstrate that intratumoral injections of HPMPC are effective in reducing tumor growth induced by SiHa cells in nude mice.