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Phosphonylmethoxyethyl Adenine (PMEA) Therapy of FeLV-FAIDS Infection in Cats. E.A. Hoover*, J.P. Ebner*, N.S. Zeidner*, and J.I. Mullins**, *Department of Pathology, Colorado State University, Fort Collins, Colorado, 80523, USA, **Department of Microbiology and Immunology, Stanford University, Stanford, California 94305, USA.

Cats infected with molecularly cloned FeLV-FAIDS isolate of feline leukemia virus develop persistent infection and immunodeficiency syndrome which is prefigured by persistent antigenemia, viremia, decline in circulating CD4+ T lymphocytes, and impaired T-dependent immune response. We have evaluated the capacity of early therapy with 9 phosphonylmethoxyethyladenine (PMEA) to abort the progression of FeLV-FAIDS infection and enhances the development of protective immunity. PMEA inhibited the replication of FeLV-FAIDS at concentrations of 0.5 µg/ml or greater in feline fibroblasts and T lymphocytes *in vitro*. *In vivo*, PMEA administered to FeLV-FAIDS-infected cats during the early post-exposure period prevented the development of persistent antigenemia and the subsequent induction of FeLV-FAIDS disease. In contrast to placebo treated controls, cats successfully treated experienced regressive viral infection marked by the development of neutralizing antibody and were resistant to subsequent challenge with virulent virus. Prolonged (4 to 7 week) treatment with maximal tolerated therapeutic doses of PMEA resulted in progressive decline in erythroid and leukocyte counts, and in some animals in diarrhea, however, hemopoietic toxicity was manageable and reversible with decreased dosage. Studies conducted in the FeLV-FAIDS model, therefore, indicate PMEA to be a potent antiretroviral agent with therapeutic and toxicologic indices which compare favorably with AZT.

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Woodchuck Hepatitis Virus: A Model for the Development of Antiviral Therapies Against HBV. BE Korba[1], PJ Cote[1], BC Tennant[2] and JL Gerin[1]. [1]Georgetown University., Division of Molecular Virology and Immunology, Rockville, MD, USA and [2]College of Veterinary Medicine, Cornell University, Ithaca, NY, USA.

The Woodchuck hepatitis virus [WHV] and its natural host, the Eastern Woodchuck (*M. monax*) constitute the relevant animal model system for the study of hepatitis B virus [HBV]-induced infection and disease in man, including chronic hepatitis and hepatocellular carcinoma. Based upon predictable responses to experimental WHV infection, we investigated the effects of antiviral compounds and immune modifiers on the outcomes and underlying mechanisms of hepadnaviral infections. Relative efficacy and safety were based upon (i) the analysis of serologic markers of WHV infection (WHV DNA, WHsAg, anti-WHs antibodies) and liver disease (ALT, SDH, GGT), (ii) the state of WHV DNA replication, RNA transcription and virus-induced disease in liver tissues, and (iii) clinical status of the animals (body weights, hematology, blood chemistry). Woodchucks were treated at various times (1 to 18 months) following the onset of serologic patterns indicative of chronic WHV infection. Concurrent control groups consisted of WHV carrier animals treated only with drug delivery vehicles. Depending upon the specific agent employed, both short (7-10 days) and long term (4-12 weeks) treatment protocols were utilized. Nucleoside analogs generally induced marked (up to 10,000-fold), but transient, depressions in the levels of circulating WHV virions which returned to pretreatment levels after the cessation of drug administration. Treatment with one nucleoside analog, 2'-fluoro-5-ethyl-1-β-D arabinofuranosyluracil (FEAU), reduced serum WHV DNA to undetectable levels and abolished both WHV DNA replication and WHV RNA production in the liver, but was unacceptably toxic. Prolonged treatment with an immune modifier, thymosin α_1, reduced serum WHV DNA levels to undetectable levels and significantly depressed WHV DNA replication in the liver.