3'Azidothymidine (AZT) Prevents the Dissemination of Retrovirus in LP-BM5 MuLV-infected C57BL/6 Mice. J.A. Bilello, C. MacAuley, S. Forman, J.L. Eiseman and R.A. Yetter. Research Service, VA Medical Center, and University of Maryland Cancer Center, Baltimore, MD U.S.A.

The biology of retroviruses suggests that inhibitors of viral reverse transcription (RT) can prevent viral replication and associated disease in vivo. LP-BM5 MuLV induces a lymphoproliferative immunosuppressive syndrome in C57BL/6 mice which has a number of similarities to human AIDS. This study has examined whether there is an appropriate dose level of the RT inhibitor AZT which prevents or delays the dissemination of LP-BM5 MuLV in young adult male mice. AZT was administered to six week old C57BL/6 in the drinking water at concentrations of 0.1, 0.5, and 1.0 mg/ml beginning three days prior to challenge with LP-BM5 MuLV. Therapy was continued for a period of 6 weeks. Analysis of ecotropic virus indicated that 5 of 5 infected mice not receiving AZT had an average titer of 4.8 $\log_{10}$ PFU per 10^7 spleen cells. In contrast only 1 of 5 mice treated with 1 mg/ml AZT and 2 of 5 treated with 0.5 mg/ml were virus positive. All of the mice treated with 0.1 mg/ml AZT were virus positive at 6 weeks post infection. The average titer of virus, however, was markedly lower in the AZT treated groups. These results suggest that a dose of 1 mg/ml AZT or higher can prevent the dissemination of retrovirus while lower doses can be effective in reducing the virus load in LP-BM5 MuLV infected mice.

Treatment of Feline Leukemia Virus Induced Immunodeficiency Syndrome with Sustained Release Implantation of 2,3 Dideoxycytidine. N.S. Zeidner*, E.A. Hoover*, J. Strobel, J. Kalin**, D. Hill**. *Department of Pathology, Colorado State University, Ft. Collins, Co.,**Southern Research Institute, Birmingham, Al.**

2,3 dideoxycytidine (DDC) was blended with a 50:50 copolymer consisting of DL-Lactide glycolide and hydroxypropyl cellulose which was melt spun into fibers and encapsulated within a sheath of polyethylene glycol for subcutaneous implantation in vivo. Pharmacokinetic studies, conducted in cats receiving an average dose of 167 mg DDC, indicated: (1) an average peak plasma concentration of 14.2 µg/ml acheived at 6-7 hours post implantation and (2) an extension of plasma DDC half life from 1.5 (subcutaneous injection) to 20 hours (sustained release implantation). Sustained plasma concentrations of 1.5 to 10 µg/ml were maintained over a 72 hour period, equivalent to DDC levels previously shown to have anti FeLV-FAIDS activity in vitro. Implantation devices were replenished every 72 hours and elevated plasma levels were sustained for four weeks without sepsis, signs of clinical toxicity, or significant alterations in the hemogram. Initial studies using sustained release DDC implantation devices in vivo did not prevent the development of persistent viremia in cats infected with FeLV-FAIDS. Current clinical trials in the Feline Aids model involve the use of sustained release DDC implants combined with alpha interferon for the prevention of persistent viremia.