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Correlation of Antiretroviral Agents Activity Against HIV-1 and SIV: Implications for Studies in Non-Human Primate Models. R. F. Schinazi[1*], B. F. H. Eriksson[1], C. K. Chu[2], C. L. Hill[1], B. H. Arnold[1], D. L. Cannon[1], H. McClure[3], D. Anderson[3], and P. Fultz[3]. Veterans Admin. Med. Ctr./Emory University, Atlanta, Ga[1]; Univ. of Georgia, Athens, Ga [2]; and Yerkes Primate Center/Emory University, Atlanta, Ga[3].

In preparation for studies in rhesus monkeys infected with Simian Immunodeficiency Virus (strain SIV_{SMM}), the antiviral potency of nucleoside analogues and heteropoly acids (HPA-23, HS-20 and HS-21) with known anti-human immunodeficiency virus type 1 (HIV-1) activity was determined in *human* peripheral blood mononuclear (PBM) cells. The median effective concentration (EC_{50}, μM) for the compounds were (SIV/HIV): 3'-azido-3'-deoxythymidine (AZT) = 0.0021/0.0020; 3'-azido-2',3'-dideoxyuridine (CS-87) = 0.28/0.20; 2',3'-dideoxycytidine (d2C) = 0.0075/0.011; 3'-deoxythymidine (d2T = 0.12/0.17; 2',3'-dideoxycytidin-2'-ene (d4C) = 0.064/0.005; 3'-deoxythymidin-2'-ene (d4T) = 0.035/0.009; HPA-23 = 0.12/0.32; HS-20 = 0.52/1.0; and HS-21 = 2.34/3.17. When treatment was delayed for 3-4 days, similar inhibition profiles were obtained for both SIV and HIV for the nucleoside analogs, but not for the heteropoly acids. Since it is important to test the sensitivity of the virus to the antiviral drug in *homologous* cells prior to evaluation of the drug in infected animals, we will also report on studies in SIV-infected rhesus monkey PBM cells. These cells were found to induce high levels of thymidine and AZT phosphorylating activity. The value of evaluating antiviral drugs in SIV-infected rhesus monkeys as a model for HIV-1 infections in humans will be discussed. *(Supported by USPHS grant 44094, RR-00165, and the Veterans Administration)*

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Murine Retrovirus Models in AIDS Drug Development. J.T. Rankin, M.A. Ussery, M. Kende, M.A. Chirigos, and P.G. Canonico. United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Maryland 21701-5011. U.S.A.

Promising antiviral compounds which had been previously identified in a human immunodeficiency virus (HIV) tissue culture (ATH8) screen were evaluated in both Rauscher murine leukemia and Laterjet-Duplan-derived, BM-5-infected mouse models. The splenomegaly normally observed with Rauscher-infected BALB/c mice had been reported to be a reliable measure of viremia. We measured reductions in splenomegaly in the Rauscher model as our initial screen of candidate compounds for antiviral activity. Other Rauscher model parameters examined were total IgM and IgG levels by antibody capture ELISA, reverse transcriptase activity, and XC syncytial assays of serum samples. In the BM-5 model, we measured total IgG and IgM levels, reverse transcriptase activity, and time to death. In the Rauscher model, daily injection of each antiviral drug from day -1 to +10 reduced splenomegaly as follows: azidothymidine (100 mg/Kg) 91%, ribavirin (100 mg/Kg) 82%, 1-beta-D-ribofuranosyl-1,2,4-triazole-3-carboxamidine hydrochloride (355.5 mg/Kg) 70%, and 4-acetyl-4-phenyl piperidine (31 mg/Kg) 11%. A single injection of 31 mg/Kg of MVE-4, an immunomodulator, on day -1 resulted in a 17% reduction in splenomegaly. These results demonstrate the significant potential of murine retrovirus models when used initially to screen candidate antiviral agents which may ultimately be found to be effective against HIV.