76

The Nude Mouse Transplanted with HIV Infected Cells as a Model for the Evaluation of Antivirals. N.T. WETHERALL, X.Q. LI, and M.A. USSERY. ViroMED Laboratories, Minnetonka, MN, and the U.S. FDA, Rockville, MD, U.S.A.

Small animal models of HIV disease provide supporting *in vivo* data for compounds with *in vitro* anti-HIV activity. Due to the unique genome of HIV, models which utilize full length replicating HIV are the most relevant and useful. We have used γ irradiated Nude mice transplanted with HIV infected CEM cells to investigate whether AZT can effectively inhibit HIV within this model system. Four groups of 8 mice were challenged with HIV_{IIIB} infected CEM cells; 2 at 0.1 MOI, 1 at 1.0 and 1 at 0.01 MOI. One group at 0.1 MOI was administered AZT, 2mg/mouse/day in drinking water beginning 24 hrs prior to HIV challenge and continued throughout; others received water. A group of 3 mice served as a cell control. All mice were monitored for 27 days, with CEM transplants biopsied at day 19. Upon sacrifice, the CEM tumor was aseptically removed and dissociated into a cell suspension. After 37°C incubation overnight, the cells were assayed for HIV by IFA and supernatants were quantitated for infectious virions by microtitration using MT-2 cell CPE as an endpoint. HIV was detected from untreated groups on day 19, and subsequently recovered in a viral dose related manner on day 27. Serum AZT at 1.5 μM effectively ablated viral infectivity and p24 ag production. Our results indicate that this model of HIV disease can be used to evaluate anti-HIV agents *in vivo*.

77

RABBIT AND MOUSE: RELIABLE ANIMAL MODELS FOR HIV-1 INFECTION AND FOR STUDIES OF ANTI-HIV-1 ACTIVITY OF CD4 SYNTHETIC OLIGOPEPTIDES AND AZT.

P.M.Cereda, G.Filice*, M.Debiaggi, E.Romero
*Institutes of Microbiology and Infectious Diseases - University of Pavia, Italy

Studies of activity of vaccines or drugs to HIV-1 infection require reliable experimental systems different from human lymphocyte cell cultures in order to obtain reproducible data and results similar and comparable with those observed in human infection. We present data concerning a reliable technique for rabbit and mouse HIV-1 infection representing a reproducible model for a persistent HIV-1 infection. Rabbits and mice intraperitoneally inoculated with HIV-1, after peritoneal macrophagic stimulation, showed a persistent HIV-1 production as revealed by ELISA for HIV-1 p24 and gp41 specific antigens using recombinant proteins or synthetic peptides, electron microscopy and reisolation of HIV-1 in H9 cell cultures. Treatment of rabbit with synthetic oligopeptides corresponding to residues 37-53 (A) and 37-55 (B) of the V1 domain of CD4 and with AZT showed interesting preliminary results particularly with CD4 A and B oligos when rabbits were treated before HIV-1 infection as determined by ELISA, ME, RT and reisolation assays. Other interesting data were also observed when A and B oligos were administered after HIV-1 infection. AZT showed other more complex results.