143

Effect of Castanospermine on Virus Titers in Rauscher MuLV Infected NIH Swiss Mice. L. Allen, L. Westbrook, B. Toyer, and M. Hollingshead. Southern Research Institute, Birmingham, AL 35255 USA.

Castanospermine (CS), an α-glucosidase I inhibitor, has been shown to inhibit HIV in vitro replication. Further, Ruprecht et al (1989) demonstrated a marked reduction in Rauscher murine leukemia virus (R MuLV) induced splenomegaly. We have evaluated the effect of CS (300, 200 and 134 mg/kg/day) on R MuLV virus titers. AZT (150 mg/kg/day) served as a positive control. Control mice were treated with drug diluent (saline). Treatments (10 mice/grp) were administered bid by oral gavage starting 4 hours post-virus challenge and continuing through Day 19. Drug toxicity was evaluated in uninfected mice (5/grp). R MuLV (2×10^4 pfu) was administered intravenously. All mice were maintained on a diet free of complex carbohydrates (AIN-76). Serum samples and spleens (weighed to nearest 10 mg) were collected on Day 20. R MuLV in spleen homogenates (10%) and serum samples was quantitated by the UV-XC plaque assay. No appreciable differences in spleen titers in CS treated mice [200mg/kg (9.5×10^5 pfu/g); 134mg/kg (9.8×10^5 pfu/g)] versus saline controls (1.1×10^6 pfu/g) were observed. Similarly, there were minimal differences in serum titers between the CS treated and the saline controls. In contrast, CS [200 mg/kg (0.17 g); 134 mg/kg (0.71 g)] produced a marked inhibition of splenomegaly compared to the saline controls (1.49 g). CS also produced a significant reduction ($p = 0.002$) in spleen weights of uninfected mice at the 200 mg/kg dose level. Splenomegaly and virus titers were significantly reduced in AZT-treated, infected mice. Although CS treatment significantly reduced splenomegaly, it did not reduce serum or spleen titers. Therefore, castanospermine treatment of retrovirus infections (i.e. AIDS patients) must be critically appraised since the benefits (questionable virus inhibition) may not outweigh the risks (potential weight loss and diarrhea) resulting from drug-induced aiterations in host carbohydrate metabolism. This work was supported by NCI Contract No. N01-CM-87274.

144

Failure of a Chronic Retrovirus-induced Immunodeficiency Syndrome to Respond to Interleukin-2 (IL-2) Alone or in Combination with Azidothymidine (AZT). J.A. Bilello, C. MacAuley, M. Bell, S.G. Shapiro, T. Fredrickson*, R.A. Yetter, and J.L. Eiseman. Univ. of Maryland Cancer Center and VAMC, Baltimore, MD 21218. *Dept. of Pathobiology Univ. of Connecticut Storrs, CT 06269 U.S.A.

LP-BM5 MuLV infection of C57BL/6 mice leads to the rapid development of a profound immunodeficiency syndrome called MAIDS because of its similarity to AIDS. We evaluated the efficacy of IL-2 alone and in combination with AZT early in an established LP-BM5 infection. IL-2 was administered by either an intraperitoneal alternate day schedule (25000 U per mouse per day) or by constant infusion. Three doses of IL-2 (100, 500, and 2500 Units IL-2 per hour) were delivered using ALZET™ 2002 miniosmotic pumps implanted subcutaneously. AZT was administered ad libitum at 1 mg/ml in the drinking water beginning at either 3 or 6 weeks post-infection. Disease progression was accelerated in mice receiving IL-2 alone. Therapy with IL-2 in combination with AZT at either 3 or 6 weeks p.i. with LP-BM5 MuLV did not slow the course of MAIDS. No significant alterations in natural killer (NK) cell activity or allogeneic CTL response were observed in the treatment groups. Serum immunoglobulin (IgM) levels were elevated 2 to 3-fold above uninfected controls in all treatment groups. Administration of IL-2 alone or in combination with AZT did not enhance the immune response and appeared to exacerbate retrovirus-induced immunodeficiency disease. (Supported by NIAID Contract NO1-AI-72666)