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Nucleoside Anti-HIV Efficacy in the Xenotransplanted Nude Mouse Model. B.M. WELSH, S.W. BELZER, and N.T. WETHERALL. ViroMed Laboratories, Inc., Minneapolis, MN, USA.

Currently there is no validated small animal model of HIV infection, and putative antiretroviral compounds are being tested in HIV-infected humans. The advantages of performing *in vivo* efficacy testing prior to clinical trials are numerous, not the least of which are the financial and time savings. Since HIV is a uniquely human virus, novel means are required to introduce this virus into rodent hosts. One such means is through the xenotransplantation of human HIV permissive cells into sublethally irradiated athymic mice. We previously demonstrated that the CEM cell line infected with the IIIB strain of HIV-1 can reproducibly demonstrate high levels of p24 antigenemia using this novel approach. Recent studies have shown that antigenemia can be detected consistently in mice transplanted with CEM cells infected at a very low input MOI (0.001), and that this antigenemia can be prevented with administration of AZT, ddC or 3TC. All drugs were administered dissolved in drinking water: 2 groups received AZT (0.4 or 2.0 mg/mouse/day), 2 groups ddC (1.6 or 3.2 mg/mouse/day), and one group received 3TC (4.0 mg/mouse/day). Plasma p24 was found in the untreated HIV-infected control group but was undetectable in the group treated with 3TC or the groups treated with the higher doses of AZT or ddC. The same trend was apparent for the presence of HIV-expressing antigens (by immunofluorescent detection methods, IFA) on cells taken from the CEM tumors of AZT- and ddC-treated mice. No proviral DNA was detected by PCR in the tumors from mice treated with the higher dose of AZT, and thus it can be concluded that HIV replication in these animals was effectively arrested. An *in vitro* study was also recently completed to address the possibility of HIV-X-MuLV pseudotype formation during virus passage in the mouse. Virus was recovered from tumor cells of untreated HIV-xenotransplanted mice, and *in vitro* infections were attempted in a panel of 9 cell lines of human and rodent origin. Cultures were maintained for 30 days, and tested weekly for expression of HIV cell surface antigens by IFA. Results were confirmed by testing supernatants for p24 levels and RT activity. The results indicate that the host range of the mouse passaged virus was not expanded beyond the CD4+ human cell lines infected by the original (laboratory stock) virus. This model is continuing to be developed as a useful tool with which to test potential anti-HIV agents in a relatively inexpensive animal model.