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RAPID CD4 T CELL DEPLETION IN HUMAN-PBL-SCID MICE BY NON-CYTOMATIC MACROPHAGE-TROPHIC ISOLATES OF HIV. D. E. Mosier, R. J. Galizia, P. D. Machac, B. E. Torbett, and J. A. Levy. The Scripps Research Institute, La Jolla, CA 92037 and UCSF, San Francisco, CA 94143.

Distinct isolates of human immunodeficiency virus (HIV) differ in their tropism, rate of replication, pathogenicity, and the ability to induce syncytial formation in vitro. We have compared a panel of molecularly cloned HIV-1 or HIV-2 isolates which differ in these biologic properties for their ability to deplete CD4 T cells in vitro by using them to infect SCID mice (i.e., mice transplanted with human peripheral blood lymphocytes, hPBL-SCID mice). The macrophage-trophic strains HIV-1sg12g and HIV-2sg12, which are non-cytotoxic in vitro, induced the most rapid and extensive CD4 T cell depletion in the hu-PBL-SCID model, whereas the HIV-1 clone 1143s, which is highly cytotoxic for T cells in vitro, caused the slowest and least extensive CD4 T cell depletion in vitro. The rate of CD4 T cell depletion in hu-PBL-SCID mice was not correlated with viral burden, as HIV-1sg12g showed higher replication capacity than other strains in vivo as well as in vitro. The HIV sequences in the env gene that are associated with macrophage-tropic virus thus correlate with enhanced capacity for CD4 T cell depletion in the hu-PBL-SCID model, but not with cytopathic effects in tissue culture. The rate of CD4 depletion is more dependent on the particular viral strain than the extent of viral replication, implying a role for pathogenic sequencese in the env gene and gp120.