Human Peripheral Blood Lymphocyte (huPBL) Reconstituted Mouse Model

One humanized mouse model used in the field of HIV/AIDS research is the human peripheral blood lymphocyte (huPBL) reconstituted immune deficient mouse model. Engraftment of huPBLs is optimal in mice without their own lymphocytes, such as strains with a common cytokine receptor chain knockout including Balb/c-Rag2$^{-/-}\gamma_c^{-/-}$ and NOG/NSG, since they are not able to reject human cells. The human leukocytes in the PBL encompass all cellular elements required for a functional immune system. During the first three weeks following intraperitoneal injection of huPBLs, most injected cell types can be detected within the peritoneal cavity, but the numbers steadily decline. After one week to 10 days, depending on mouse strain, human leukocytes appear in other organs, all bearing T-cell or B-cell markers; no human macrophages or other accessory cells are detectable. T cells constitute the majority of these cells (96-100%); B cells occur in low numbers, are oligoclonal, and frequently are not detectable by flow cytometry. Under the experimental conditions huPBLs in the mouse environment become highly activated. Their phenotype changes from naïve CD45RA+ cells to activated CD45 R0+ effector cells with different patterns of HIV-1 co-receptor expression. Thus, the selection of the HIV-1 strain and timing of virus administration depends on the ultimate goal of the study. However, the human cells can proliferate in the mouse environment and invariably lead to a lethal xenogeneic graft-vs-host disease (xeno-GVHD), with the onset of GVHD correlating directly with levels of human cell engraftment. Ultimately xeno-GVHD is fatal for the immune deficient mice with longevity depending on mouse strain, number of transplanted human cells, compatibility of mouse and human major and minor MHC antigens and sex. Survival after human cell transplantation can be anywhere from 4-5 weeks for a mild reaction to 2-3 weeks for a severe reaction.

References:

Tary-Lehmann M, Saxon A, Lehmann PV. The human immune system in hu-PBL-SCID mice. Immunol Today. 1995 Nov;16(11):529-33.

Gorantla S, Poluektova L, Gendelman HE. Rodent models for HIV-associated neurocognitive disorders. Trends Neurosci. 2012 Mar;35(3):197-208. doi: 10.1016/j.tins.2011.12.006. Epub 2012 Feb 1.