Human CD34+ Hematopoietic Stem Cell (HSC) Repopulated Mouse Model

An important humanized mouse model used in the field of HIV/AIDS research is the the SRC (SCID Repopulating Cell) model. The SRC mouse model is established through injection of human HSCs into newborn or young adult SCID mice. It exhibits average engraftment efficiency above 25% (assessed as peripheral blood CD45 percentage) and supports the multiple-lineage development of injected HSCs and the elaboration of an innate human immune system. However, the limitation of the SRC model is that the T-cell response is mouse H2-restricted instead of human HLA-restricted. The use of immunodeficient IL2rγnull mice that totally lack natural killer (NK) cells permitted the generation of human T cells in the Hu-SRC-SCID model, but this generation is highly dependent on the age of the recipient at the time of HSC engraftment. Newborn NSG mice engrafted with HSCs, up to 3–4-weeks of age, support the development of human T cells. The SRC mouse model is considered a facile and reliable model for preclinical HIV/AIDS small animal studies, exemplified by the consistent engraftment of a human immune system and successful hematopoietic development. This hu-NSG mouse model exhibits high levels of bone marrow homing, susceptibility to HIV infection, and recapitulation of HIV infection and pathogenesis. Additionally, the hu-NSG mouse model responds appropriately to combinatorial antiretroviral therapy (cART) and recapitulates plasma viral rebound upon cART withdrawal, confirming the establishment of an HIV latency reservoir. This HIV latency reservoir is further substantiated by the production of replication-competent HIV viruses ex vivo induced by human resting CD4+ T-cells isolated from infected and cART-treated hu-NSG mice.

References:

Gorantla S, Sneller H, Walters L, Sharp JG, Pirruccello SJ, West JT, Wood C, Dewhurst S, Gendelman HE, Poluektova L. Human immunodeficiency virus type 1 pathobiology studied in humanized Babl/c-Rag2-/- gammac-/- mice. J Virol. 2007 Mar;81(6):2700-12. Epub 2006 Dec 20.

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.

Xia X, Li H, Satheesan S, Zhou J, Ross JJ. Humanized NOD/SCID/IL2rgnull (hu-NSG) mouse model for HIV replication and latency studies. J Vis Exp. 2019 Jan 7;(143). doi: 10.3791/58255.