Human Liver Mouse Model

Small xenograft animal models with human hepatocytes and a human immune system can recapitulate the human biology of the HIV liver disease pathogenesis. A protocol has been described to establish a dual humanized mouse model through human hepatocytes and CD34+ hematopoietic stem/progenitor cells (HSPCs) transplantation to study liver immunopathology as observed in HIV-infected patients. To achieve dual reconstitution, male TK-NOG (NOD.Cg-Prkdcscid Il2rgtm1Sug Tg(Alb-TK)7-2/ShiJic) mice are intraperitoneally injected with ganciclovir (GCV) doses to eliminate mouse transgenic liver cells, and with treosulfan for nonmyeloablative conditioning, both of which facilitate human hepatocyte (HEP) engraftment and human immune system (HIS) development. Human albumin (ALB) levels are evaluated for liver engraftment, and the presence of human immune cells in blood as detected by flow cytometry confirms the establishment of a human immune system. This model resembles multiple components of liver damage from HIV-1 infection. Its establishment can provide an essential tool for studies of hepatitis virus co-infection and for the evaluation of antiviral and antiretroviral drugs.

Reference:

Dagur RS, Wang W, Makarov E, Sun Y, Poluektova LY. Establishment of the dual humanized TK-NOG mouse model for HIV-associated liver pathogenesis. J Vis Exp. 2019 Sep 11;(151). doi: 10.3791/58645.