Retrovirology

Oral presentation

HIV-1 infection and CD4 T cell depletion in humanized Rag2-/-γc-/- mice

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Previously well established mouse-human xenograft systems, namely, the SCID-hu and hu-PBL-SCID mouse models have been instrumental for several advances in HIV research. However, as these models lacked the capacity for generating primary immune responses, viral pathogenic effects on the human cells could only be evaluated in the context of the absence of an active immune response. Intra-hepatic injection of human CD34 hematopoietic stem cells into immunodeficient Rag2 common gamma chain knock out (Rag2-/-γc-/-) mice results in multilineage human hematopoiesis with de novo production of T cells, B cells, monocytes and dendritic cells, and the generation of a functional immune system. Therefore this in vivo model shows great potential to study HIV infection and evaluation of therapeutic approaches. As a first step towards developing this model, humanized Rag mice (Rag-Hu mice) were infected intraperitonially with either X4 tropic or R5 tropic HIV-1. Prolonged viremia (up to 12 weeks so far) could be demonstrated in the infected mice. CD4 T cell depletion together with lymphadenopathy was also seen in viremic mice. Further characterizations are currently underway. Several new experimental approaches are now possible in these humanized mice that include vaccine testing, viral latency and evaluation of novel therapeutics.