Retrovirology

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Oral presentation

Disseminated and sustained HIV-infection in CD34+ cord blood cell transplanted Rag2-/-gc-/- mice

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Background

We evaluated a novel mouse model that is based on the transplantation of human cord blood CD34+cells into immunodeficient Rag2-/-gc-/- newborn mice for studying HIV.

Results

Reconstituted mice (CD45+ cell engraftment: 29 ± 18%) were permissive to HIV with up to 2 × 10^6 copies/ml 2–6 weeks after infection. Thereafter, viremia stabilized at lower levels for up to 4 months. A marked CD4+ cell depletion occurred in all mice infected with X4- strains simultaneously with the initial rise of plasma HIV RNA while this was not the case in R5-infected mice. Spleens and lymph nodes of mice infected with either R5- or X4-strains contained p24+ cells. In thymi, however, p24+ cells were detected rather exclusively following infection with X4- strain, consistent with the expression of CXCR4 but not CCR5 on human CD4+ thymocytes. Similarly as in humans, HIV-infected macrophages were only occasionally found.

Conclusion

Rag2-/-gc-/- mice transplanted with human CD34+ cells develop long-term, high-titer, and lymphoid organ disseminated infection irrespective of co-receptor selectivity of HIV strain, closely resembling HIV infection in man. In particular, by using HIV strains with distinct co-receptor selectivity, we clearly illustrate the higher cytopathic potential of X4- strains as compared to R5- strains. This straightforward to generate and cost-effective in vivo model should be valuable to study virus-induced pathology, and to rapidly evaluate new approaches aiming to prevent or treat HIV infection.