Retrovirology

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Development of a Human Bone Marrow Progenitor Cell Line to Examine HIV-1 Susceptibility and LTR Activity

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from 2005 International Meeting of The Institute of Human Virology
Baltimore, USA, 29 August – 2 September 2005

Published: 8 December 2005

Retrovirology 2005, **2**(Suppl 1):P8 doi:10.1186/1742-4690-2-S1-P8

Previous studies have suggested that the bone marrow compartment may play an integral role in the genesis of HIV-1 dementia (HIVD). Interestingly, CD34+/CD38- pluripotent stem cells within the bone marrow are refractile to HIV-1 infection. The CD34+/CD38+ TF-1 cell line has been selected as a model to study HIV-1 infection during the differentiation process of hematopoietic progenitor cells. A number of cytokines such as GM-CSF, M-CSF, IL-1β, TNF-α, and IL-4 were used to induce differentiation and activation of TF-1 cells and their surface marker expression was monitored by flow cytometry. Interestingly, IL-1β treatment, alone or in combination with TNF-α, lead to up-regulation of CXCR4 and CCR5 surface presentation, and preservation of CD4 expression possibly providing an optimal cellular phenotype for HIV-1 infection of this cell population. The surface marker expression after this treatment also correlated with a more differentiated phenotype. To begin exploring the potential of these cells to support productive HIV-1 replication, a series of stably transfected cell lines were developed. To this end, macrophage-, T cell- and dual-tropic long terminal repeats (LTRs) were coupled to the gene encoding green fluorescent protein. These cell lines were utilized to explore the functional properties of specific cis-acting regulatory elements in LTR function within the bone marrow precursor cell population.