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[9] Cytokine Combinations on The Potential of *Ex Vivo* Expansion of Murine Hematopoietic Stem Cells

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The limited number of hematopoietic stem cell (HSC) in human bone marrow and cord blood has led to experimental approaches using cytokines for *ex vivo* expansion of HSC. Here, we studied the expansion of murine hematopoietic stem cells with different cytokine combinations and characterized the hematopoietic gene expression profile of expanded cells, aiming to facilitate the development of optimal HSC culture condition. Murine HSC with immunophenotype Lineage-Sca-1+c-Kit+ (LSK) were cultured in five different cytokine combinations: SCF/TPO/Flt3-L, SCF/ TPO/Flt3-L/VEGF, SCF/TPO/Flt3-L/IL-3, SCF/IL-3/IL-6 and SCF/TPO/Flt3-L/IL-3/IL-6/VEGF. The effects of cytokines were compared in terms of total cell number expansion, proportion of HSC enrichment, and expression pattern of hematopoietic genes that are associated with HSC activity (*Bmi-1*, *Runx1*, *Tal-1* and *Lmo2*) or multi-lineage commitment (*Gata1*, *Gata3*, *Pu.1* and *Pax5*), after short-term (7 days) or prolonged (14 days) *ex vivo* culturing. We demonstrated that all five cytokine combinations promoted expansion of murine HSCs, among which SCF/TPO/Flt3-L/IL-3 and SCF/IL-3/IL-6 showed a dramatic effect on HSC enrichment. We further examined the expression of hematopoietic genes and found that cytokine combination SCF/IL-3/IL-6 was the most effective in induction of HSC-associated genes up to 14 days of *ex vivo* culture. A moderate induction of lineage commitment genes suggests a sub-population of expanded cells is in myeloid or lymphoid progenitor status. Taken together, our findings suggest that SCF/IL-3/IL-6 is the optimal cytokine combination among the five being tested in HSC expansion. Molecular characterization supports that the expanded HSCs maintains stem or progenitor cell properties.