

# Molecular Study of Interactions between Hematopoietic Stem Cells and Stromal Cells

Biao Luo, Choong Meng-Ling, Amenda Heard, Zhe Li, Kateri Moore, Chris Kaiser, Ihor R. Lemischka, Miranda Yap, Harvey F. Lodish

*Abstract*—Multipotent hematopoietic stem cells (HSCs) are progenitors of all types of hematopoietic cells, and the efficient isolation and propagation of HSCs will significantly enhance our ability to manage many human disorders with bone marrow transplantation, stem cell transplantation and gene therapy. We employed "Signal Sequence Trap (SST)" method with yeast invertase to clone proteins on the surface of or secreted by stromal cells that enhance or inhibit the propagation of HSC's in culture. AFT024, a mouse fetal liver stromal cell line that maintains stem cell activity in long-term culture, was subjected to SST analysis. We identified more than 60 signal sequences or transmembrane domain containing genes expressed by AFT024 cells. We compared their expression levels between AFT024 cells and BFC012 cells, a mouse fetal liver stromal cell line that was developed in the same way as for AFT024 cells but could not support HSC in long-term culture. Pleiotrophin, T16, Sca-1, deltalike and cytokine receptor like-1 (CLF-1) are expressed significantly higher in AFT024 cells than in BFC012 cells. We recently employed Affymatrix genechip technology to study the interaction of HSCs and their microenvironment. In genechip experiments, Sca-1, deltalike, pleiotrophin and CLF-1 are among the most differentially expressed genes between AFT024 and BFC012 cells, while T16 was not represented on the chip. In addition, osteopontin, pigment epithelium-derived factor, proliferins, activin subunit, CXC chemokines GRO1 and LIX are more abundant in AFT024 cells than in BFC012 cells. Genechip technology was also applied to bone marrow stromal cell lines, including MS5, S17 and OP9 cells. Two murine multipotent hematopoietic cell lines, FDCP.mix and EML cells, were also analyzed. Data from these experiments are presented.