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Optimization of cord blood stem/progenitor cells expansion: Human adipose-tissue derived stromal cells in combination with hypoxia effectively support *ex vivo* multiplication of hematopoietic precursors

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Cord blood hematopoietic stem/progenitor cells (cbHSPCs) attract considerable interest as an alternative to bone marrow HSPCs. Low number of HSPCs in one sample limit its broad application. Thus far, the development of *ex vivo* cbHSPC amplification is a primary goal of cell technologies. Imitation of hematopoietic niche *ex vivo* may significantly improve cbHSPC expansion. In this work, HSPCs were selected from unfractioned cbMNCs through adhesion to adipose mesenchymal stromal cells (ASCs) under standard (20%) and tissue-related (5%) O_2. ASCs efficiently maintained viability and supported further HSPC expansion at both O_2 levels. A new floating generation of HSPCs grew up and was enriched with $CD34^+$ cells up to 100 (20% O_2) and 200 (5% O_2) times, included cobble-stone area forming cells and colony-forming cells (CFCs). The number of CFCs was 1.6 times higher than at 20% O_2 due to increase in multipotent precursors-BFU-E, CFU-GEMM and CFU-GM. These changes were at least partly ensured by increased of MCP-1 and IL-8 at 5% O_2. After HSPC/aMSC interaction, up-regulation of cell adhesion molecule genes (*ICAM-1, VCAM-1, CDH1*) and down-regulation of matrix remodeling genes (*COLs, MMPs, TIMPs, ADAMs, HAS1*) were demonstrated by RT-PCR. This indicates on activation of ASC stromal function at 5% O_2. Thus, the combination of cbMNCs and ASCs enables selection of HSPCs, whose further expansion without exogenous cytokines provides the $CD34^+$ cells enrichment. These data are important for elucidation of hematopoiesis mechanisms and as a tool for *ex vivo* HSPC expansion for the needs of regenerative medicine.

Biography

Ludmila B Buravkova (MD, Ph.D.) is a member of Russian Academy of Sciences, Head of Cell Physiology Lab, IBMP and Professor of Moscow State University. She is an expert in stem cell and gravitational physiology, cell signaling, a tutor of 19 Ph.D. students, has over 100 publications,12 patents, serves as Editorial Board Member of *Human Physiology, Cell Technologies in Biology and Medicine*, Advisory Boards in Russian Ministry of Science and Russian Found for Basic Research, PI of projects in cell physiology, received awards from Russian Government for Outstanding Scientific Results (2004) and from Pleiades Publishing for best publications in Life Sciences (2014).

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