Josef Bodor, J Cancer Sci Ther 2014, 7:10
http://dx.doi.org/10.4172/1948-5956.C1.059

OMICS International
conferenceseries.com

8th Euro Global Summit on

Cancer Therapy

November 03-05, 2015 Valencia, Spain

Josef Bodor

Institute of Hematology and Blood Transfusion, Czech Republic

Hematopoietic stem cell-based therapy for HIV disease: Prostaglandinmodulated transplantation

At present, the general consensus is that 'true' self-renewing human hematopoietic stem cells (HSCs) are found within the CD34+ population and that engraftment of a suitably conditioned host with a sufficient number of such cells will result in long-term multilineage hematopoiesis. Umbilical Cord Blood (UCB) cells are a valuable source of HSCs for use in allogeneic transplantation. Key advantages are easy availability and less stringent requirements for HLA matching. However, UCB cells contain an inherently limited HSC count associated with delayed time of engraftment, high graft failure rates and early mortality. PGE2 derivative (16, 16 dimethylprostaglandin E2; dmPGE2) was recently identified to be a critical regulator of HSC homeostasis (1). Recent data have shown that brief ex vivo modulation with dmPGE2 could improve patient outcomes by increasing the 'effective dose' of HSCs with preferential long-term engraftment of the dmPGE2 treated HSCs in allogeneic transplantation. Moreover, it was demonstrated that conventional CD4+ T cells (Tcons) could be developed *in vitro* into CD4+CD25+Foxp3+ inducible regulatory T cells (iTregs) with an equivalent suppressive potential as naturally occuring regulatory T cells (nTregs) by continuous polyclonal activation with anti-CD3/CD28 mAbs (2). During the differentiation process, the iTregs express cyclooxygenase 2 (COX-2) and produce PGE2. Interestingly, neither resting nor activated nTregs express COX-2. The PGE2 production from iTregs can be fully suppressed by the COX inhibitor indomethacin. These data indicate that PGE2 plays an important role in differentiation of HSCs thus releasing stringency required for HLAmatching donors with potential recipients as well as with potential role in dominant suppressive effects of iTregs expressing COX-2 with acquired ability to produce copious amounts of PGE2 responsible for delivery of suppressive function through elevated levels of cAMP (3). Prostaglandin E2 (PGE2)-mediated mechanisms, which have potential to downregulate CCR5 expression in umbilical cord blood (UCB) cells heterozygous for CCR5Δ32 mutation (CCR5wt/Δ32), could reduce or eliminate surface expression of CCR5 (CCR5 null cells) and thus facilitate allogeneic transplantation, UCB cell-engraftment, and preferential cord chimerism in parallel with CCR5 downregulation. Key advantages of this process are higher frequency of heterozygous CCR5wt/Δ32 donors, less stringent requirements for HLA matching, and better engraftment of the cells resistant to HIV. To eliminate the need for indefinite treatment, our ultimate goal is to create a functional HIVresistant immune system through the use of modified HSCs with emphasis on post-transplant amelioration of GvHD enabled via potentiation of regulatory T cell (Treg) cell-mediated suppression.

Biography

Josef Bodor received his Ph.D. (1990) with honors from Institute of Molecular Genetics in Prague, Czech Republic. As of 2013, he is a Senior Investigator working at the Institute of Experimental Medicine in Prague, Czech Republic. Dr. Bodor is a senior scientist with faculty experience from Ivy League Institutions in US hosting on sabbatical leaves around the world (Harvard University Boston, MA, Columbia University; New York, NY, Kyoto University, Kyoto, Japan, Würzburg University, Würzburg, Germany, and Johannes Gutenberg University in Mainz, Germany). Dr. Bodor as an Associate Member of Transregio 52 published series of original reports summarized in authoritative reviews. Currently, Dr. Bodor is faculty member at the Institute of Hematology and Blood Transfusion in Prague, Czech Republic.

bodor@unimainz.de