OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Clinical & Cellular Immunology
October 15-17, 2013 Hampton Inn Tropicana, Las Vegas, NV, USA

Bone marrow Lin$^-$/Sca-1$^+$/C-Kit$^+$ and Lin-/Sca-1$^-$/C-Kit$^+$ cells induce stable mixed chimerism and permanent skin graft acceptance in a mouse model

Baskiewicz-Halasa M[1], Hałasa M[1], Dziedziejko V[2], Pius E[1] and Machaliński B[1]
[1]Department of General Pathology, Pomeranian Medical University, Poland
[2]Department of Biochemistry et Medical Chemistry, Pomeranian Medical University, Poland

Mixed chimerism is a potential induction method for alloantigen-specific tolerance. Although the phenomenon has been broadly studied over recent years, some important aspects remain to be elucidated. The aim of our study was to identify the optimal mouse stem/progenitor cell population for mixed chimerism induction purposes.

To induce stable mixed chimerism, B6.SJL-*PtprcaPep3b* (CD45.1; H-2^s; I-E-) mice were exposed to 3-Gy total body irradiation (Day -1) as well as the CD40L (Day 0, and 4) and CD8 (Day -2) blocking antibodies. The animals were transplanted with 10x10^6 Balb/c (CD45.2; H-2^d; I-E$^+$) unfractionated bone marrow cells (Day 0). Since mouse stem/progenitor cells are found among lin- population and they possess Sca-1 and c-kit antigens, mice were given 2x10^5 of lin$^-$/Sca-1$^+$/c-kit$^-$, lin$^-$/Sca-1$^+$/c-kit$^+$ or lin$^-$/Sca-1$^-$/c-kit$^+$ bone marrow-derived cells. Mixed chimerism was measured in peripheral blood leukocytes several times during the 26-week experiment. In addition, the chimerism rate and the kinetics of the percentage of CD4, CD8 and NK1.1 cells in the peripheral blood were assessed. The tolerance to Balb/c mouse antigens induced by the stem/progenitor cells was tested by analyzing the proportions of the Vβ5 and Vβ11 TCR-expressing lymphocytes as well as by assessing skin graft (Day 0) acceptance.

The lin$^-$/Sca-1$^+$/c-kit$^+$ and lin$^-$/Sca-1$^-$/c-kit$^+$ cells, but not the lin$^-$/Sca-1$^+$/c-kit$^-$ cells, induced a high degree of stable (26 weeks) multilineage mixed chimerism. In the chimeric mice, we observed an elimination of donor-reactive lymphocytes as well as permanent skin graft acceptance. We found a correlation between the initial chimerism rate, especially in the mononuclear cell populations, and graft survival.

Based on our study, we can recommend well-selected cell populations expressing c-kit receptor that possibly facilitate the induction of mixed chimerism and immune tolerance. Therefore, our findings contribute to a better understanding of mixed chimerism and may promote its use in clinical practice.

poziomka@pum.edu.pl