ImmunoTools *special* Award 2015

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Mesenchymal stromal cells aging and its potential influence in the hematopoietic stem cells self-renewal, multipotency and differentiation.

Certainly, aging is one of the best identified features of the human biology, and is also the least understood. This is largely attributed to the fact that aging is gradual and fundamentally complex, due to all modifications in the physiological and phenotypic aspects occurred during the age advancing.

One of the most striking features of aging is the decreased ability to maintain homeostasis and tissue repair. Consistent with those findings, many of the pathophysiological conditions affecting aging, such as anemia, dysplasia, osteoporosis and sarcopenia, suggest an imbalance between cell losses and the ability to self-renew or differentiation.

The decline in homeostatic maintenance and regenerative potential of tissues during aging has been associated with changes in stem cells.

Increasing evidences point to the stem cells as major accountables for the aging pathophysiology in several tissues. Thus, studies in mammals comprise a careful evaluation of mechanisms connected to stem cells.

The increasing age is accompanied by many pathophysiological changes in the hematopoietic system wherein the etiology suggests loss of homeostatic control and a possible involvement of stem and progenitor cells. The clinically relevant changes are related to adaptive immune system diminished competence, the increase of myeloid diseases including leukemia and the onset of anemia in the elderly.

The hematopoietic stem cells ability to give rise to progenitor cells substantially decreases during their transition from the fetal liver to the umbilical cord blood and then to the adult bone marrow, suggesting a progressive decline in activity of the stem cells during their aging.

Stem cells of several tissues reside very near to specialized support cells that are able to extrinsically regulate self-renewal and differentiation. For example, in Drosophila, the germ stem cell is regulated, at least in part, by the niche. The decline of the bone morphogenetic proteins signaling pathway in the Drosophila ovary or a ligand called "unpaired" in the testis, affects the germ stem cell. In both cases, the reduction of adhesion mediated by cadherin of germ stem cell to the niche, and among cells, correlates with the declining in numbers and function of those cells.

Our hypothesis is that in the adult bone marrow niche, the mesenchymal stromal cells aging affects, at least in part, the process of self-renewal, pluripotency and differentiation of hematopoietic stem cells.

To prove our hypothesis, we will culture hematopoietic stem cells and co-culture them with mesenchymal stromal cells from different ages. So, it is important to maintain the hematopoietic stem cells alive in the cultures. For that reason it will be necessary to add to theses cultures human recombinant growth factors and cytokines such as GM-CSF, IL-4, IL-6, Flt3L and stem cell factor. We also intend to measure the homing capacity of hematopoietic stem cells, thus we will need to set a migration system using the human chemokine CXCL12.

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includes 21 reagents

human ELISA-set for 96 wells, rh IL-6, IL-8, rh IL-10 (each 3 reagents)

recombinant human cytokines: rh Flt3L /CD135, rh GM-CSF, rh IL-2, rh IL-4, rh IL-6, rh SCF, rh SDF-1α / CXCL12a, rh SDF-1β /CXCL12b, rh CCL2, rh CCL19, rh CCL20 and rh CCL21 DETAILS more AWARDS