Paper of the December Issue of Stem Cell Reviews and Reports Presents a Comprehensive Review of the Current Knowledge on Complexity of Hematopoietic Stem Cell Aging

Mariusz Z. Ratajczak¹

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This month our Editorial Team has selected for special attention of our readership the review of Dr. Hal Broxmeyer and his collaborators at the Indiana University School of Medicine entitled “*Fate of Hematopoiesis During Aging. What do we really know, and what are its implications*”.

Aging is an inevitable consequence of life and accelerates after achieving reproductive age, leading with time to the malfunction of tissues and organs that have completed the reproductive period of life, which finally results over time in biological death. The hematopoietic system is not an exception to this rule and the aging process has negative effects on hematopoietic stem/progenitor cells (HSPCs). Several mechanisms are currently proposed that accelerate this process and not all of them are well understood. It is accepted that, the aging process impairs the regenerative potential of HSPCs and skews their differentiation towards the myeloid lineage. The age-associated pathophysiological changes of the hematopoietic system include the onset of anemia and diminished adaptive immune competence, and may lead to development of myelodysplasia and leukemia, all of which can be explained by the loss of normal homeostatic controls in the hematopoietic tissues. Therefore, it is so important to study and to elucidate the mechanism that lead to these pathologies.

Overall it is a remarkable review written by Dr. Broxmeyer and his collaborators at the Indiana University School of Medicine who are top experts in experimental hematology. In this comprehensive review, authors approach this problem from different angles reviewing on one hand the literature relevant to this topic and on the other presenting their own insight to mechanism that govern aging process. What is very important is that this excellent review addresses also a danger

of potential artifacts related to the collection and processing procedures of HSPCs in the experimental setting of aging, that may not always be fully representative to situations that occur in vivo in bone marrow microenvironment. One of the important factors discussed by authors is to avoid exposure of collected HSPCs to ambient air conditions, as even their short exposure to ambient 21% O₂ level may change biology of these cells that in steady state conditions reside in bone marrow at around 3% O₂. As pointed out in this review, collection of cells in ambient air subjects them to a phenomenon of Extra Physiological Oxygen Shock Stress (EPHOSS) that results in a rapid loss of their stemness due to their differentiation into progenitor cells.

Moreover, Dr. Broxmeyer et al. discuss in this paper effects of chronic inflammation, changes in hematopoietic microenvironment, age related clonal hematopoiesis, involvement of microbiome, sirtuins, mitochondria and reactive oxygen species on aging of HSPCs. There are also discussed age related problems relevant to processing, mobilization, transplantation homing and engraftment of these cells. Authors also ask based on their very recent work if COVID19 will have similar negative effect on stem cell compartment in young and old individuals. Finally, Dr. Broxmeyer points out to some still under-investigated areas such as for example a role of molecular chaperons and heat shock proteins on aging of HSPCs and discusses some potential approaches that may prevent aging and allow increasing robustness of HSPCs.

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✉ Mariusz Z. Ratajczak
mariusz.ratajczak@louisville.edu

¹ University of Louisville, Louisville, KY, USA