

Innate Immunity as a Pivotal Player in Mobilization of Hematopoietic Stem Cells from Bone Marrow into Peripheral Blood

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Abstract

In steady state conditions low number of HSPCs always circulates in peripheral blood (PB) and lymph and undergoes a circadian rhythm in their PB circulation, with the peak occurring early in the morning and the nadir at night. The number of circulating HSPCs increases in PB in response to (1) systemic or local inflammation, (2) strenuous exercise, (3) hypoxia and (4) tissue/organ injuries. Moreover, in clinical settings, administration of some agents may induce forced egress of HSPCs into PB and increase their number in PB up to 100 fold in a process known as pharmacological mobilization. Such drugs include cytokine granulocyte colony stimulating factor (G-CSF) and the small molecular CXCR4 antagonist AMD3100; known as Plerixafor. Pharmacological mobilization is exploited as a means to obtain HSPCs for hematopoietic transplantations. Our previous research demonstrated that mobilization of HSPCs is a part of innate immunity response. This evolutionary ancient process is orchestrated by granulocytes and monocytes that trigger activation of complement cascade and collateral also coagulation cascade. Initiation of complement cascade activation and subsequently activation of coagulation cascade occurs in mannan binding-lectin (MBL) complement activation pathway dependent-manner. Mannan binding lectin activates subsequently MBL-associated serine proteases (MASP-1 and MASP-2) that cleave third complement component C3 and prothrombin. Cleavage of C3 leads to formation of classical C5 convertase and cleavage of prothrombin generates thrombin that possesses C5-like convertase activity. Finally, both C5 convertases cleave fifth complement cascade protein C5 and activate distal part of complement cascade that is crucial for egress of HSPCs from BM niches into PB. Mobilization of HSPCs as we recently learned is negatively regulated by heme-oxygenase-1 (HO-1) and inducible nitric oxide synthetase (iNOS). Therefore, inhibition of these enzymes by small molecular inhibitors may enhance mobilization process, which is an important clinical implication for patients that are poor mobilizers.

Biography:

Mariusz Z Ratajczak is a Professor of Medicine, the Henry M and Stella M Hoenig Endowed Chair in Cancer Biology and the Director of the Developmental Biology Research Program at the University of Louisville's, James Graham Brown Cancer Center, USA. He is an internationally known specialist in the field of adult stem cell biology. He is also known for his work on novel mechanisms of mobilization and homing of stem cells, biological role of extracellular microvesicles

and molecular mechanisms of cancer metastasis. Among his prestigious awards are the 2014 Karl Landsteiner Life Achievement Award from the German Society of Transfusion Medicine and Immunohematotherapy and the 2008 Cancer Researcher of the Year award. He has published numerous books and more than 450 peer-reviewed publications and is a frequent speaker at conferences worldwide. He is a Visiting Professor at Kansai University in Osaka, Japan and Fudan University in China.