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An actively cycling hematopoietic stem cell population is selectively lost with conventional purification strategies

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Current dogma holds that hematopoietic stem cells (HSCs) are predominantly in a quiescent state. HSC dormancy has been established by studies focusing solely on highly purified populations of HSCs and such research of highly purified dormant HSCs have formed the basis for virtually all marrow stem cell research to date. In contrast, we have been exploring the cell cycle status of the population of HSCs in un-separated whole bone marrow (WBM). By using two distinct techniques, we have shown that there is a large population of actively cycling long-term multi-lineage engraftable cells in marrow and that these cycling stem cells are selectively lost during conventional marrow stem cell preparative techniques. If HSCs are cycling, they cannot be purified to "homogeneity" as they will be continually changing phenotype as they transit cell cycle. We propose that such phenotypic fluctuations will render the cycling HSCs impossible to purify using current antibody-mediated purifications strategies as these strategies rely on stable surface epitope expression. Based on our findings of an actively cycling population of marrow cells capable of long-term multi-lineage engraftment, we recommend that future studies must consider the total hematopoietic stem cell pool on a population level in order to provide a more comprehensive study of HSC biology.

Biography

Goldberg L R is currently an Assistant Professor at Brown University, Providence RI, in the Division of Hematology/Oncology with interests in stem cell biology and the translational implications of the proposed work with regard to stem cell transplantation. She obtained her MD and PhD in Molecular Genetics and Biochemistry from the Medical Scientist Training Program at the University of Pittsburgh, completed her residency in Internal Medicine at the University of Pittsburgh and her Hematology/Oncology Fellowship at the Warren Alpert Medical School of Brown University. Her current work is focused on the cycling nature of hematopoietic stem cells.

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