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The metastability of multipotent hematopoietic cells is attenuated by bone marrow niche cells

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Abstract

We and others have reported phenotypic and functional heterogeneity within the populations of embryonic stem cells and adult neural, intestinal and hematopoietic stem cells (HSCs), as well as the existence of inter-convertible cell subsets among HSCs which alternate between several metastable states. It is likely that currently unknown extrinsic mechanisms emanating from HSC niches in the bone marrow (BM) regulate HSC heterogeneity and metastability. We utilized the multipotent hematopoietic cell (MHC) line EML, a well-established *in vitro* surrogate for HSCs and multipotent progenitors, to show that EML cells consist of several heterogeneous cell subsets with distinct expression of HSC markers, cell cycle profile and propensity to differentiate. Our studies have further shown that EML cells oscillate between several inter-convertible cell states with distinct phenotypic and functional features which are homeostatically maintained and tightly regulated by currently unknown cell intrinsic mechanisms. The perpetual maintenance of EML cells in the absence of niche cells could be augmenting their metastability. Thus, we investigate how BM niche cells affect the metastability of EML cells in a co-culture system. Our current results show that mesenchymal and osteoblastic cells attenuate the metastability of EML cells, shifting the process towards increased production and maintenance of more quiescent cell subsets. Importantly, the cells that effect EML cell metastability do so reversibly. These data suggest that BM niche cells are an important factor in the regulation of MHC. This data also infers that characterization of MHCs should be viewed in the context of their surroundings, or lack thereof.

Biography

Wendy Weston completed her Ph.D. from the University of Miami, Miller School of Medicine in Molecular, Cell and Developmental Biology investigating the heterogeneity, metastability, and effect of BM niche cells on HSCs. She received her M.S. in Biological Sciences, minor in Chemistry, from Cal Poly, Pomona studying somatic gene therapy for muscle atrophy and characterization of B-MHC promoter activity following spinal cord transection. At Loma Linda VA, she worked on bone formation and acceleration of fracture healing in the rat. She has recently begun work on effects of radiation on BM stem cells and the efficacy of potential therapeutic interventions.