Stem Cells Interact with their Microenvironment

Retention and engraftment

Mobilization

Homing

Differentiation

Vascular niche

Osteoblastic niche

Trafficking of Stem / Progenitor Cells

HSC

Bone marrow

BM sinusoid

TOXICANT

BONE
BONE

HSC

Differentiated Lineage Cells

Multipotent Progenitors

Multipotent Progenitors

In Vitro Cultures + Cytokines & Growth Factors

Do the In Vitro Systems used for Stem Cell Differentiation Accurately Recapitulate that Existing in the Niche?
Differentiated Lineage Cells

Multipotent Progenitors

In Vitro Cultures + Cytokines & Growth Factors

HSC

Multipotent Progenitors

TOXICANT

Osteoblastic Niche

[O2]
PROLIFERATION AND DIFFERENTIATION OF STEM CELLS: IN VIVO NICHE vs. IN VITRO CULTURE

• Metabolism (and Kinetics) of Toxicant by Niche / Stem / Progenitor Cells

• Different Regimens of Cytokines/Growth Factors (and $O_2$) Present at Different Phases of Differentiation - Are the Cues for Differentiation the Same? How Does this Affect Methylation Patterns (Epigenetic Effects)?

• Effects of Toxicant on Stem Cells vs Progenitor Cells vs. Niche Cells

• Interactions of Stem / Progenitor Cells with Niche May be Affected by Toxicant

• Phenotypic vs Functional Endpoints
STEM CELL MODELS FOR ENVIRONMENTAL HEALTH: Suggestions For Research Avenues

• **Models of Stem Cell Differentiation That Accurately Recapitulate Niche-mediated Pathways / Programming Processes.** Taking into account stages of differentiation (e.g. different levels of progenitor cells, and pathways leading to fully differentiated states)

• **Better Understand Cues within Niche that Mediate Differentiation** (i.e. mechanistic understanding of niche-mediated programming)

• **Development of Functional Endpoints of Toxicity that Complement Phenotypic Endpoints** (How do exposed stem cells interact with niche? Also, do exposures affect niche directly and stem cells indirectly?)

• **Assessment of how Epigenetic Changes are Affected by Niche vs. In Vitro systems** (and as altered by toxicant exposure)