GDCB Seminar

4:10 p.m. • Tuesday, Oct. 5, 2021 • Online Meeting (link below)

'Constructing the Hematopoietic Stem Cell Specification Niche'

Abstract: The vertebrate hematopoietic system is comprised of multiple cellular lineages that perform diverse essential organismal functions including oxygen distribution, immune surveillance, pathogen elimination, and tissue remodeling. Hematopoietic lineages are continually replenished from rare hematopoietic stem cells (HSCs). HSCs are the clinically relevant component of transplant therapies for leukemia, as well as a growing number of non-malignant conditions including sickle cell disease, congenital cytopenias, and autoimmune disease. Issues of donor compatibility for such therapies have raised interest in directed differentiation and expansion of HSCs from pluripotent precursors, a goal that necessitates a detailed understanding of the normal physiological mechanisms guiding HSC specification during embryonic development. Despite decades of research to define the precise inputs specifying HSCs from precursor cells, it remains impossible to generate HSCs with normal self-renewal and lineage potential without permanent genetic modification, indicating that key inputs remain to be defined. HSC specification is directed by the molecular, cellular, and physical microenvironment, which we have termed the "specification niche." The specification niche is different from the adult homeostasis niche (in mammals the bone marrow): while the function of the adult niche is to support decisions in quiescence/proliferation and lineage determination, the embryonic specification niche guides de novo specification, proliferation with maintenance of oligopotency, and mobilization to subsequent sites of expansion and maturation. HSCs are born in the trunk region of vertebrates from specialized cells termed hemogenic endothelium that are constituents of the primitive descending aorta or its cognate vessel in lower vertebrates. Our approach has been to define the cellular composition of the specification niche as a means to understand the molecular and physical factors that direct original specification of HSCs from hemogenic endothelium. We have identified the first known niche cells, derived from neural crest and a subcompartment of the embryonic somite known as the sclerotome. Our studies further define key downstream molecular mechanisms essential to niche formation including maturation of the extracellular matrix and specific signal transduction pathways essential for the earliest HSCs to be specified.

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Research Lab: https://www.stjude.org/research/labs/clements-lab.html

Host: Clyde Campbell, GDCB adjunct assistant professor

Join meeting:

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