University of Rochester

BME PhD Defense Seminar

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Supervised by
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"Recapitulating Acute Myeloid Leukemia–Induced Bone Marrow Dysfunction in a Microenvironment-on-a-Chip Platform"

Seminar Abstract: Acute myeloid leukemia (AML) is the most common and aggressive type of leukemia in adults that result in a 5-year survival rate of less than 30%. About 70% of patients >60 years old succumb to the disease after 1-year of diagnosis. AML cells hijack the bone marrow microenvironment (BMME) to create a favorable niche for expansion and protection from chemotherapy. This interaction dysregulates the function of hematopoietic stem and progenitor cell (HSPC) and niche cells including osteoblasts, bone marrow stem/stromal cells (BMSCs), and endothelial cells. Thus, recent research has focused on the BMME to develop therapies that will be more effective and better tolerated than traditional chemotherapy. However, in vitro models of the AML-BMME to study microenvironmental interactions are severely lacking.

Our goal is to develop a clinically relevant 3D model of the healthy (BMME-chip) and leukemic microenvironment (AML BMME-chip) that can recapitulate the phenotypes of AML. We developed a multicompartment BMME-chip using Emulate Chip-S1™ containing an apical channel with a mineralized osteoblastic layer and a fibrin-gel encapsulating whole bone marrow cells (WBMCs) and BMSCs, and a basal channel with a flow-induced endothelium layer mimicking blood vessels using murine cells. In BMME chip model, HSPC frequency was maintained at 0.29 ± 0.13% of total cells comparable to native BM at 0.15 ± 0.04% and cells were able to successfully engraft in a murine BM transplant model, giving rise to ~60% of total peripheral blood mononuclear cells (PMBCs) with myeloid and lymphoid cells at similar frequencies compared to murine transplant controls. To generate the AML-BMME-chip, murine leukemic cells were incorporated into the apical, bone marrow compartment of the BMME-chip. We observed dysregulation of the osteoblast compartment, HSPC populations, and mature hematopoietic cell numbers. These findings suggest that the chip provides a supportive microenvironment for HSPC survival and replicates leukemic cell and BMME interaction during leukemia. We showed significant reduction of erythroid cell numbers in the effluent of AML-BMME-chip, a recapitulation of anemia in patients and mice. Findings from murine cells experiment help optimize the development of human cell-based BMME-chip for future mechanistic and drug discovery experiments.

Wednesday, June 17, 2026 | 9:30am EST | Upper Auditorium (3-7619, Med Center)
Zoom: https://rochester.zoom.us/j/91314854930

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