CHEMICAL ENGINEERING
UNIVERSITY of WASHINGTON

SEMINAR

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Tissue Engineering Strategies to Investigate Angiocrine Signals in Disease and Regeneration

1-2 pm PST Monday July 5th, 2021
Zoom link is provided via email, or
contact dyss@uw.edu

Bio

Mai Ngo is currently a Kilachand Postdoctoral Fellow affiliated with the Biological Design Center at Boston University. Under the mentorship of Professor Christopher Chen, her current research focuses on developing new strategies to vascularize biomaterials for regenerative medicine or cardiovascular disease treatments. Prior to arriving at Boston University, Mai earned her Ph.D from the Department of Chemical and Biomolecular Engineering at the University of Illinois Urbana-Champaign. As a member of Professor Brendan Harley's lab, she used tissue engineering strategies to create vascularized disease models of brain cancer. During graduate school, Mai was an Illinois Distinguished Fellow and a National Science Foundation Graduate Research Fellow. Mai additionally earned her B.S in Chemical Engineering from Virginia Tech. Outside of research, Mai is passionate about STEM outreach and has participated in initiatives to present science activities to K-12 students.

Abstract

Blood vessels are an essential component of mammalian tissues because they play a critical role in supplying nutrients and oxygen to the surrounding tissue. Blood vessels also influence tissue homeostasis, repair, and dysfunction via signaling cues that originate from the cells that comprise blood vessels, namely endothelial and perivascular stromal cells. For example, vascular-derived cues, also known as angiocrine cues, influence the balance between liver repair and scarring, direct stem cell renewal versus differentiation, and heighten the aggressiveness of various cancer cells. Identifying the precise mechanisms by which angiocrine cues influence tissue repair or dysfunction will lead to a new class of therapeutic strategies to facilitate tissue regeneration or mitigate disease progression. However, progress in investigating angiocrine signaling is currently hindered by the lack of physiologically-relevant *in vitro* models that can recapitulate the architecture, cell-cell interactions, and cell phenotypes of interest in vascularized tissue microenvironments. To overcome this limitation, we employ tissue engineering strategies to generate vascularized biomaterial platforms for probing the effects of angiocrine cues on the behavior of tissue-specific or diseased cells. By encapsulating endothelial and perivascular stromal cells in methacrylamide-functionalized gelatin (GelMA) hydrogels, we can generate three-dimensional vascular networks that recapitulate the morphology and functional markers of vasculature *in vivo*.

My talk will highlight two stories that utilize our vascularized GelMA platform to investigate the role of angiocrine cues in disease and regeneration. First, we develop a vascularized model for glioblastoma (GBM) (**Fig 1A**), which is the most common primary malignant brain tumor. GBM tumor cells are known to associate closely with vasculature, but the effects of angiocrine signals on tumor cell behavior are largely unknown. We demonstrate the ability to generate brain-mimetic microvascular networks that recapitulate markers of blood-brain barrier function. Tumor cells cultured within our model exhibit close association with the surrounding vasculature, heightened invasion, and maintenance of stem cell markers, which are established phenotypes of GBM cells *in vivo*. We subsequently use our model to determine the effects of angiocrine cues on tumor cell proliferation and therapeutic response, and we identify secreted and transcriptomic mediators of invasion and drug resistance that arise from tumor-vascular interactions. Secondly, I will describe the use of microfluidic mixing devices to create biomaterial microenvironments that contain spatial gradients in vascular density. We control the extent of vascular network formation across a biomaterial by fabricating gradients in cell, matrix, or biomolecule density. We apply these gradient vascularized biomaterials as combinatorial platforms to explore the effect of vascular density on hematopoietic stem cell (HSC) behavior (**Fig 1B**). HSCs are commonly used for bone marrow transplantations, but challenges remain in expanding adequate numbers of viable and functional HSCs for successful engraftment within the patient. We find that HSCs cultured in regions of increasing vascular density have the capacity to produce large numbers of differentiated hematopoietic cells while maintaining a subpopulation of quiescent, undifferentiated stem cells. Taken together, this work demonstrates how engineered vascularized microenvironments can be used to identify the roles and mechanisms of angiocrine signaling in tissue function and degeneration, thereby providing new targets for pro- regenerative or anticancer therapies.

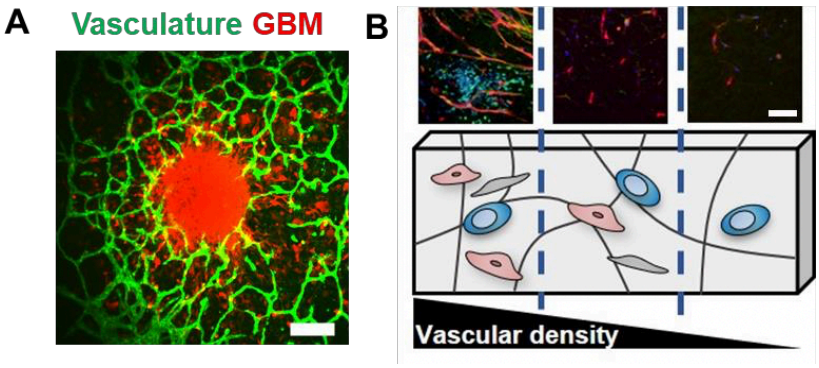

Figure 1. A) Tumor-vascular co- cultures in GelMA hydrogels for investigating the role of angiocrine cues in glioblastoma progression. Scale bar = 0.2 mm **B)** Hydrogels containing gradients in vascular density serve as combinatorial platforms to explore the dose- dependent role of angiocrine cues in directing hematopoietic stem cell fate. Scale bar = 0.1 mm