Department of Chemical and Biological Engineering
UNIVERSITY OF WISCONSIN–MADISON

2020 Fall CBE Seminar Series

presents:

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Strategies for the Delivery of Therapeutics Across the BBB

The delivery of therapeutics to the central nervous system (CNS) is a complicated issue; the blood-brain barrier performs a critical role of maintaining brain homeostasis, but performs its job so well that it prevents the passage of >98% of therapeutics into the brain. This is further complicated by the difficulty of finding model systems that are able to recapitulate the tightly controlled transport characteristic of the BBB. Here I will attempt to address both of those points. Many current models of the BBB are composed of primary or immortalized endothelial cells cultured on transwells, often in the presence of additional cell types found in the brain. These models recapitulate certain aspects of the BBB, but are often lacking certain key characteristics. Brain microvascular endothelial-like cells (BMECs) derived from iPSCs have been shown to recapitulate many of the key characteristics of the BBB, making them a good possible alternative for *in vitro* models. Using these iPSC-derived BMECs in a 3D microvessel model we are able to more completely model the human BBB. This model has many potential applications from personalized disease modeling to mechanistic studies of potential therapeutics.

Many promising candidate therapeutics on the bench fail in clinical or pre-clinical trials, as the preclinical model systems do not accurately model transport of the therapeutic in to the brain. Many are not able to penetrate the brain at therapeutically relevant concentrations, without substantial off target effects halting their progression through clinical trials. Novel means of targeting the BBB to improve delivery efficiency of the candidate therapeutic and decrease off target effects are critical. It is clear that novel means of approaching delivery across the BBB are needed. Using variable lymphocyte receptors (VLRs) as a means of targeting and facilitating transport into the brain we hope to be able to overcome many of the issues faced by standard antibody-based therapeutics.

Tuesday, Sept. 29, 2020

Lecture at 4:00 p.m.

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