Challenge #1 Sponsored by BCRegMed Initiative

Proposer: Dr. Stephanie Willerth – Director of the Centre for Biomedical Research and Associate Professor of Biomedical Engineering at the University of Victoria

Title: Development of an effective sieving method for the size sorting of drug releasing microspheres for stem cell-based tissue engineering applications

Background: Microspheres are small particles on the order of microns. These microspheres can serve as a novel tool for drug delivery when bioactive compounds are encapsulated inside. Materials used to fabricate such delivery systems are mostly biocompatible and biodegradable polymers These drug releasing microspheres can produce homogeneous, sustained release of drugs on their own and when incorporated into 3D cell aggregates. Such polymer-based system slowly releases the encapsulated drug through a combination of diffusion and degradation and the fabrication conditions determine the concentration of drugs released. When incorporated into cell aggregates, these microspheres serve as way to expose cells to consistent quantities of morphogens without needing to add drugs into the culture media on a regular basis. Adding the soluble drug in the media can lead to differences in the concentration of drug in the inner layers of the cell aggregates. On the other hand. the presence of the microspheres within many layers of the cell aggregates overcome these challenges by providing similar concentrations of drugs within all the layers of the aggregate.

The size of the microspheres is an important factor for both controlling the rate of drug delivery and when incorporating such microspheres into cellular aggregates. Particles that are too large can block cell-cell interactions necessary to maintain viability, proliferation, and differentiation into specific cell types. Additionally, large microspheres can cause the formation of excessively large cell aggregates to be formed with too large a diameter, which in turn limits the diffusion of nutrient and oxygen diffusion into the centres of the aggregates – resulting in necrotic centers. Typically, desired microsphere size is <10µm to provide a linear release profile over time. Our microsphere fabrication process is volatile, producing particles with great variation in size. The particles need to be filtered to separate those below the size threshold from the larger unusable ones. The Willerth Lab currently uses a reversible strainer with a 37µm pore size and a diameter of ~1cm. We typically filter ~320mg of microspheres in one batch. The filter is rapidly blocked by large particles and constantly needs to be cleared, making the whole process takes upwards of an hour or two depending on the overall quality of the produced microspheres. The strainer must also be loaded and cleared manually meaning no other work can be completed during that period. The blocked filter also captures smaller particles that get cleared with the larger ones leading to loss in yield.

Challenge: The challenge here is to find a more efficient and effective method of size separating drug releasing microspheres. Such a solution would greatly benefit the lab by reducing time spent filtering as well as raising yield.

In-kind support: Dr. Willerth (willerth@uvic.ca) will serve as a mentor along with Dr. Akbari (makbari@uvic.ca) and Laura De la Vega (laura.dlvr@gmail.com) on this project and donate microspheres as an in-kind contribution. She will also support each team with up to $300 worth of supplies to develop their filtration mechanisms and will provide microspheres for sorting to test devices.