College of Engineering
School of Chemical, Materials and Biomedical Engineering
UNIVERSITY OF GEORGIA

Multiple graduate student openings in new research lab focused on advancing cell manufacturing for regenerative medicine

Functional heterogeneity is a significant barrier to the clinical translation of many cellular therapies, including mesenchymal stromal cells (MSCs). Though MSCs have shown promise in treatment of immune diseases, the mechanisms of action and critical quality attributes (CQAs, predictors of function) in different therapeutic settings are largely unknown. **The overall goal of the Marklein Lab is to develop innovative approaches incorporating high-throughput, therapeutically relevant single cell profiling to assess cellular heterogeneity and accelerate translation of MSC therapies.** To accomplish this goal, the Marklein Lab has multiple openings for graduate students to work on the following projects:

1. Harness high-throughput morphological screening technologies to optimize MSC manufacturing. Significant heterogeneity exists among research labs in terms of manufacturing processes, which arise from differences in donor, tissue source, culture media, cryopreservation techniques, and culture vessels. As the CQAs for MSCs are largely unknown, it is difficult to assess the effects of these manufacturing changes on MSC function in a rapid, high throughput manner. This project will combine high content imaging with screening libraries of microenvironmental cues to create 'morphological landscapes' that reveal manufacturing conditions that enhance MSC function, limit functional heterogeneity, and ensure safety.

2. Development of robust approaches to identify functional MSC subpopulations using dynamic morphological profiling. The morphological response of MSCs to functionally-relevant stimuli (e.g., IFNγ) can be indicative of their ability to suppress T cell activation, which is believed to play a role in treatment of immune diseases. To better understand the relationship between morphology and function, a more comprehensive assessment of single cell MSC responses must be performed. This project will consist of developing machine learning approaches to characterize the dynamic morphological response of MSCs to inflammatory cytokines and to identify distinct dynamic subpopulations. Using morphology as a 'backbone panel,' this project will determine dynamic surface marker expression for enrichment of subpopulations and potential enhancement in immunosuppressive function. This project will also assess the clonality of MSC subpopulations and relate the dynamic morphological response of different MSC clones to their surface phenotype and functional properties.

3. Determination of MSC immunosuppression mechanism of action through comprehensive single cell profiling and secretome analysis. Although quantitative methods of assessing MSC immunosuppressive capacity exist, these assays typically monitor a few (and in many cases singular) functional outcomes such as $CD8^+$ or $CD4^+$ T cell proliferation. However, these functional assays typically involve co-culture of MSCs (or MSC-derived products) with a heterogeneous population of PBMCs, which contain not only T cell subsets, but additional immune cells (neutrophils, B cells, macrophages, dendritic cells, etc.) that can also participate in the observed effect. This project will explore the effects of MSCs on different immune cell populations using mass cytometry, which enables high dimensional surface phenotyping of immune cell populations. Additionally, this project will characterize both MSC surface markers and secreted factors to enable determination of their MoA, as well as identify novel CQAs that could serve as surrogate potency markers.

The Marklein Lab is a member of the Regenerative Biosciences Center (rbc.uga.edu) and the NSF Center for Cell Manufacturing Technologies (cellmanufacturingusa.org). Future lab members will be exposed to an exciting, collaborative environment as they will be able to make immediate and lasting contributions to the field of regenerative medicine through their research pursuits and academic outreach. A wealth of resources is available at the University of Georgia including flow cytometry core, microscopy core, bioinformatics, robotic handlers, world class animal facilities, and support for commercialization and translation of research discoveries. The ideal candidate for each project will have a degree in Biomedical Engineering, though individuals with degrees in Biological Sciences or other related fields are encouraged to apply. Preference will be given to candidates with experience in three or more of the following areas: cell culture, image analysis, automated microscopy, flow cytometry, statistics, programming, and large dataset analysis.

Interested individuals can apply to the graduate school here -> http://www.engineering.uga.edu/graduate-programs/admissions (Deadline: 12/15).

Please contact Dr. Ross Marklein (ross.marklein@uga.edu) with any questions related to the postings.