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Applications of biomaterials for mechanistic modeling of host-microbe interactions and perturbation of microbiomes

Abstract:

The mucosal epithelium represents a major class of tissue architecture with unique functions. It serves as a regulator of mass transport, defenses against pathogens, and is a source of mucosal extracellular matrix (ECM) where microbes reside and interact with human cells. This complex epithelium-microbe ecosystem along the oral-airway mucosal membrane supports commensal as well as opportunistic microbes, some of which have been implicated in acute and chronic human diseases. To date, few in vitro systems support controlled co-culture of living microbes with mammalian cells while being technically accessible to standard life science laboratories. This is in part due to the rapid rate of microbial growth which can easily upset the chemical balance of culture media, making it inhospitable to mammalian cells. Our group addresses this challenge by using aqueous two-phase system (ATPS) to create stable liquid scaffolds that can confine living microbial colonies directly in contact with mammalian cells. Using the well-studied ATPS formulation consisting of polyethylene glycol (PEG) and dextran (DEX), we have demonstrated that single species as well as polymicrobial DEX bioink can be printed to reproducibly create biofilms within 24 hours. We are currently creating applications specific to ATPS and hydrogel platforms to support long term co-culture, as well as mucoadhesive oral microbial delivery platform to restore eubiosis. By tuning the physical parameters via rational material design, we can recapitulate the interactions within the epithelium-microbe niche using this chemically connected yet physically separated co-culture model, and subsequently better understand disease progression and identify translatable therapeutic targets.

Research interest:

Biomaterials, microfabricated disease models, microbial-mammalian co-culture models, tissue engineering, regenerative medicine, microfabricated tumour models

Biography and lab info:

Dr. Brendan Leung is a biomedical engineer and received his undergraduate training in biochemistry and chemical engineering from the University of Ottawa. He began his research career as an undergraduate trainee, investigating the roles of XIAP in ovarian cancer chemoresistance in Dr. Benjamin Tsang's lab. He earned his Master's and Doctorate in biomedical engineering from the University of Toronto, supervised by Dr. Michael Sefton and focused on cardiac tissue regeneration. Later, Dr. Leung joined Dr. Shuichi Takayama's group at the University of Michigan to investigate polymeric liquid scaffolds for host-microbe co-culture systems. In 2016, Dr. Leung started his research group at Dalhousie University, and in 2022, he was promoted to associate professor with tenure and received the Dalhousie President's Research Excellence Award. His current research program focuses on the development of advanced tissue construct platforms and assay technologies to understand fundamental phenomenon that govern tissue homeostasis and maladaptation in human diseases. Specifically, he is interested in creating in vitro tools to understand the role of human associated microbes in chronic disease, including metabolic diseases, fibrosis, and cancer. His multidisciplinary research group at Dalhousie focuses on combining multiple tissue components, including epithelium, mesenchyme, immune cells, and microbial colonies in minimalistic fashions to recapitulate tissue level phenomenon, while maintaining the ability to gather meaningful measurements. The group is also invested in the creation and/or adaptation of cutting-edge methods to perturb these engineered tissue models to facilitate biomedical research.