Mechanobiology in Epithelial 3D Tissue Constructs

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LECTURES

GRK 2415

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Extracellular matrix mechanobiology

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Online on Zoom:
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Abstract: It is well appreciated that extracellular cues stemming from the matrix dictate a multitude of cellular functions, from motility to stem cell differentiation. Yet, the extracellular environment is inherently complex and thus hinders our full understanding of specific matrix-based contributions to cellular behavior. Our work focuses specifically on the context of age-related matrix remodeling and engineering materials capable of recapitulating matrix properties in vitro at both the micro and nano length scales. This talk will highlight some of our material approaches to control cell-matrix interactions in the context of cardiac aging and mechanobiology. In the first, we describe methods for developing tunable stiffness gradient polyacrylamide (PA) hydrogels using a two-step polymerization method. These platforms are capable of spanning the diverse physiological and pathological mechanical landscapes present in the heart for gaining a more thorough understanding of mechanosensitive processes on cardiac function. Our second material strategy is able to maintain matrix composition and organization independent of matrix stiffness through hydrogel-stabilized decellularized cardiac tissue slices of young and aged mouse hearts. Subsequent culture of cardiac fibroblasts (young and aged) show that the matrix ‘age’ can outweigh matrix mechanics in driving fibroblast activation. In our third approach, we mimic ligand presentation at the nanoscale using Block Copolymer Micelle Nanolithography (BCMN), in which highly ordered gold nanoparticle arrays are deposited onto surfaces with defined interparticle spacing. These particles are subsequently functionalized with peptides and we find that cardiac cell adhesion and mechanomarker expression are enhanced at 35 vs. 50 nm interparticle spacing. Our strategies ultimately aim to interrogate the cell-matrix interface using highly defined biomaterial systems at different length scales that can inform future matrix-based treatment strategies.

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Bio: Jennifer Young was trained as a bioengineer at the University of California, San Diego (Ph.D.). During her Ph.D. with Prof. Adam Engler, she studied the role of mechanics in cardiac development, and created a hydrogel system capable of mimicking dynamic tissue properties in vitro. Inspired by the role of extracellular matrix (ECM) in dictating cell behavior and fate, she joined the Cellular Biophysics group of Prof. Joachim Spatz at the Max Planck Institute for Medical Research (Heidelberg, Germany) to study the contribution of nanoscale ECM cues to cellular function. There, she discovered that variations in nanoscale ligand presentation alone affect chemoresistance in breast cancer cells, which has great implications in cancer treatment strategies. Last year, she joined the Mechanobiology Institute and Biomedical Engineering Department at the National University of Singapore where her work focuses on identifying and mimicking micro-to-nanoscale matrix properties and unraveling their contributions to cellular behavior in a diverse set of biological environments.