Bio-Instructive Nanofibers Regulate Cell Morphology and miR Expression Patterns

Merve Buluk¹, Jess Frith, Ph.D.², Justin L. Brown, Ph.D.¹

¹Department of Biomedical Engineering, The Pennsylvania State University, University Park, PA, ²Department of Materials Science and Engineering, Monash University, Melbourne, Australia

Many of the biopolymers present in the extracellular matrix (ECM) organize into a heterogeneous array of fibers. These fibers present an array of potential extracellular geometries to a cell. Ranging from highly organized parallel fibers to 3D gels of randomly oriented fibers. Whereas most evaluations examine matrix stiffness, it is important to recognize that the diameter of ECM fibers varies from 10’s of nanometers to nearly 1µm, which enables a dramatic shift in the cellular microenvironment. We have demonstrated unique activation of MAPK and GTPase signaling in response to synthetic fibers presenting altered diameters and alignments. (1-3) Furthermore, we have connected these signaling changes to long term cell fate events, such as, differentiation. This abstract examines the role of micro RNAs (miRs) as possible intermediates in mechanosensing fibers presenting either a parallel or orthogonal arrangement. Results obtained demonstrate significantly different cellular and nuclear morphologies on parallel and orthogonal nanofibers, notably nuclei on orthogonal fibers present a ‘bean-like’ shape. Additionally, results obtained demonstrate synergy between nanofiber diameters of 800nm and orthogonal arrangement in significantly increasing the expression of miR 21, 100 and 143. All 3 have previously demonstrated a role in promoting osteogenic differentiation. (4) Efforts are currently underway to identify if miR expression patterns are the effectors in the altered MAPK activation we have identified in response to orthogonal fibers presenting 800nm diameters. Additionally, efforts are evaluating whether the miR expression is a function of the altered nuclear morphologies on parallel and orthogonal fibers.