Focal Adhesion Mechanotransduction: Cellular Response to Nanoscale Mechanical Factors

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Mammalian cells react to factors such as force, adhesivity, matrix stiffness, and geometrical structure that altogether form the physical aspects of the cellular "microenvironment". Mechanical factors are known *in vitro* to regulate cellular functions such as proliferation, contractility, migration, and differentiation and can ultimately influence the health of our tissue. The mechanism for how cells sense and respond to these factors has been elusive due to shortcomings in the techniques that operate at the length scale of cells. In my presentation, I will discuss the micro- and nanofabrication approaches we are using to advance the understanding of how mechanical factors influence cellular function. It is our working hypothesis that cells are able to detect microenvironmental cues primarily through focal adhesions. These "spot-weld" protein structures use integrin receptors to adhere the cell to the extracellular matrix of the tissue. Signaling pathways associated with focal adhesions can affect cell function and several can be activated specifically when force is applied. Understanding focal adhesion mechanotransduction has been difficult because of their nanoscale structure and obstruction to mechanical probing. By using bio-functionalized polydimethylsiloxane (PDMS) micro- and nano-pillars that cells attached to, we are able to measure cellular traction forces through optical measurement of the pillars' tip displacements, which are generated at focal adhesions by cells to migrate or gauge their microenvironmental properties. We have also integrated cobalt magnetic nanowires into the pillars. By applying a uniform magnetic field ($B < 0.3$ T), we induce magnetic torque on the nanowires that is transmitted to a cell's focal adhesion site as an external force (1-45 nN). This approach allows us to monitor the cellular mechanical and biochemical response to force with improved accuracy and spatial-temporal resolution. I will also report on the microfluidic approaches and computational modeling that we have developed to better understand focal adhesion mechanotransduction. With these new tools and models, we seek to understand how mechanical factors in the microenvironment can causes maladaptive changes that can eventually lead to diseases such as atherosclerosis and hypertension.