BHE-039

Novel Sensors for Cell Differentiation: Detection of Signaling Network Targets Induced by Multiple Morphogens

Phil Campbell
Associate Research Professor, Institute for Complex Engineered Systems, Carnegie Mellon University, Pittsburgh, PA

Julie Jadlowiec
Molecular Biosensor and Imaging Center, Carnegie Mellon University, Pittsburgh, PA

Industry Participants
SpectraGenetics, Pittsburgh, PA

Abstract

In order to better understand the process of tissue formation and thus, better equip ourselves to engineer replacement tissues, new technologies to measure, quantify and predict cell responses to multiple stimuli are required. This proposal describes the rationale and strategy to develop an enabling technology to quantify differentiative cell responses to *multiple stimuli*. Real-time of quantification of downstream signaling targets will be our metric to detect cell differentiative response to multiple stimuli. *In vivo*, cells respond to multiple stimuli simultaneously from their environment and interpret the signals into changes in cell activity, fate and lineage specificity. Cells secrete a specific extracellular matrix (ECM) consisting of scaffolding ECM proteins, hormones (morphogens), interstitial fluid and glycosaminoglycans to form unique tissue-specific microenvironments. The composition of these niches drives tissue development and cell functions through activation and integration of intracellular signaling pathways such as the Smad pathway. Bone morphogenetic proteins (BMPs) are strong inducers of Smad signaling. We hypothesize that cell fate decisions tailored to multiple stimuli can be detected via downstream targets of the BMP/Smad pathway such as Osterix (Osx), Smad6 and Id1-4. Our approach is to create patterned substrates of multiple stimuli. Our model system will be the osteogenic lineage; however Smad signaling is relevant to many other non-osseous tissues. We will combine our established ink-jet printing technology to create multiple morphogen patterns with an emerging technology to visualize cell differentiation in real time. We will develop real-time visualization of patterned cell differentiation using central dogma (CD)-tagging of key Smad targets. Successful completion of the proposed study will enable detection and quantification of cell response on engineered 2D and 3D biomimetic ECMs for applications in the regenerative medicine, tissue engineering, drug delivery and developmental biology fields. Our corporate partner, SpectraGenetics will benefit through the application of new pathways and cell lineages as additional proof-of-concept for their emerging CD-tagging technology. The proposed technology could lead to new commercial applications for monitoring cell response or build upon existing technologies with corporate partners.