Differentiating Human Pluripotent Stem Cells to Cardiovascular Lineages

Pluripotent stem cells (PSCs), including embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) hold tremendous promise in tissue engineering and regenerative medicine applications because of their unique combination of two properties, pluripotency and an extremely high proliferative capacity. Theoretically, almost unlimited supplies of cells and tissues could be generated from a single clonal source if we can regulate PSC growth and differentiation. Hurdles facing utilization of PSCs in regenerative medicine include a lack of effective systems that permit robust, large scale culture and expansion of undifferentiated cells and a lack of reliable methods to differentiate PSCs to desired developmental lineages.

Several critical factors regulate whether a PSC chooses to self-renew or differentiate. Soluble signals bind receptors and stimulate chemical pathways that lead to global changes in gene transcription and cell differentiation state. Likewise, immobilized extracellular matrix cues synergize with soluble signals to control cell signaling and differentiation. Cell-cell communication is also an important consideration in PSC culture; at low cell densities cell growth rates diminish while at high cell densities spontaneous differentiation occurs. Finally, mechanical signals have recently been shown to affect self-renewal and differentiation. I will discuss examples that illustrate how each of these microenvironmental stimuli can be incorporated in culture systems to expand or differentiate PSCs along desired lineages. We have developed materials that confine PSC colonies to specific sizes and shapes to assess how colony morphology and intercellular communication affect stem cell self-renewal and differentiation toward cardiomyocytes by regulating signaling pathways involved in development. We have used microenvironments to identify canonical Wnt signaling as a key regulator of cardiomyocyte differentiation and designed a protocol that produces high purity cardiomyocytes in a defined, growth factor free system via appropriate temporal presentation of small molecule modulators of Wnt signaling. Finally, I will present data illustrating differentiation of pluripotent stem cells to classes of functional vascular endothelial cells, including blood-brain barrier microendothelial cells. These cells are currently being used to construct in vitro models of the blood-brain barrier to predict drug passage to the brain.

Analytical Seminar

Thursday
Jan. 24
12:15 pm
1315 Chemistry

Professor Sean Palecek

UW Madison Engineering Dept.