Functional Characterization of Embryonic Stem Cell-Derived Endothelial Cells

Drew E. Glaser¹, Robert M. Gower², Nicholas E. Lauer¹, Kayan Tam², Alicia A. Blancas³, Albert J. Shih⁴, Scott I. Simon², and Kara E. McCloskey¹,³,⁴

¹Graduate Program in Biological Engineering and Small-scale Technologies
University of California, Merced; ²Department of Biomedical Engineering
University of California, Davis ³Graduate Program in Quantitative and Systems Biology
⁴School of Engineering, University of California, Merced
Tel: 209-228-7885 E-mail: kmccloskey@ucmerced.edu

Endothelial cells (EC) have been derived in vitro from embryonic stem cells (ESC), but require additional functional characterization before these cells should be used for cell therapies. We explore several physiologically relevant functions of ESC-derived EC (ESC-EC) including nitric oxide (NO) production, regulation of permeability, activation in response to inflammatory stimuli, migration and growth new blood vessels, extracellular matrix deposition, and take up low density lipoproteins. We also examined the ESC-EC ability to up-regulate NO in response to anti-inflammatory shear stress and down-regulate NO in response to pro-inflammatory TNF-alpha activation. All assays were compared with in vitro-derived mouse aortic endothelial cells (MAEC). The ESC-EC exhibit most aspects of functional endothelium, but interesting differences remain. The ESC-EC produced less NO on a per cell basis, but the same amount of NO if quantified based on the area of endothelial tissue. They also exhibit increased angiogenic sprouting and are more resistant to inflammatory signals. We further characterized the sub-phenotype of our ESC-EC and found that the ESC-EC were more consistent with a venous EC, but did contain some arterial cells as well. This data supports the hypothesis that the developmental default pathway is the venous EC, and that refinement of methods for differentiation towards arterial EC might be required for some applications.