Stem Cellular Assembly of Vascular Tissue

Introduction

This research involves the development of a vascular-like cellular assembly system for high-throughput pharmacological and toxicological testing in human systems. We have previously developed a vascular co-culture model for studying disease states, such as intimal hyperplasia and flowing vascular interventions[1]. The complex interactions of two different cell types, endothelial and smooth muscle cells, have been elucidated. Various growth factors and the extracellular matrix play pivotal roles.

Our laboratory has also developed expertise in the culture of embryonic stem cells, and stem cells have the potential to be used not only in the treatment of vascular disease, but also as testbeds for developing pharmacological agents and assessing the human toxicity of chemical, biological, and physical insults to human tissue.

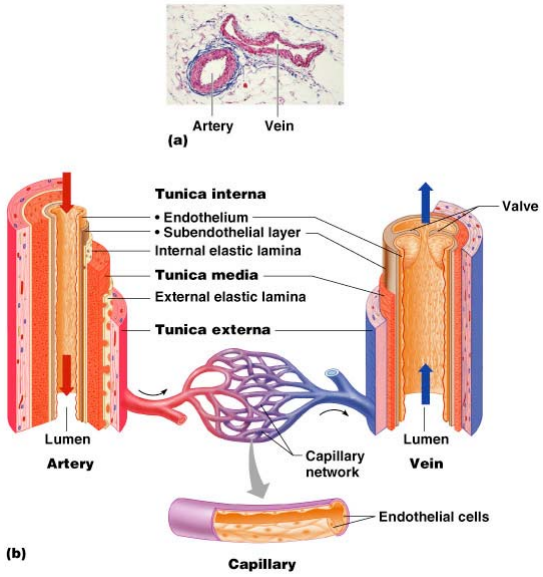

Figure 1. Model of the Human Vascular System

Results

Our hypotheses and testing of various growth factors is summarized in the figure below.

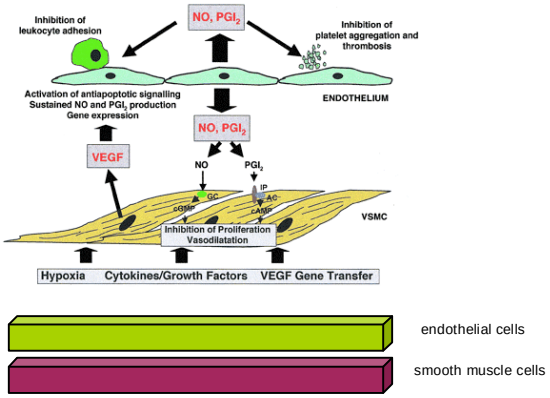

Figure 2. Co-culture model of the vascular system.

Both VEGF and b-FGF have been shown to play critical regulatory roles in the maintenance of functional vascular tissue. These results have helped guide us in developing an in-vitro stem-cell-based system that mimics progenitor vascular tissue.

Stem Cell Based Model

Stem cells have shown the ability to develop into highly functional differentiated tissue both in-vivo and in-vitro. Since stem cells have the ability to differentiate or "become" a multitude of differentiated cells types, they are ideal candidates for use in pharmacological profiling, testing, and efficacy studies. The ability to create and express different cell types will help in minimizing side-effects of pharmacological compounds, as well as explore in-vitro compound efficacies to a variety of specific tissue types.

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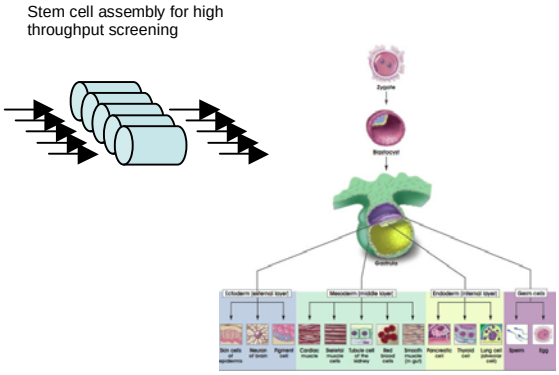
Our model is depicted below.



We are currently developing a co-culture model using both differentiated cells and stem cells in a progenitor vascular model in order to demonstrate the feasibility of this approach.

References

1. S. Mocherla and M. H. Peters, Inhibitory Effects of Growth Factors on Proliferation of Porcine Smooth Muscle Cells in the Direct Co-Culture System, Circulation, under review. This study is based on the PhD dissertation by S. Mocherla, December 2007.

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