DEVELOPMENTAL MECHANISMS AND MOLECULAR GENETICS OF THE VASCULATURE

GOALS

1. Describe the evolution of vascular structures and patterning among different organisms.
2. Understand the embryonic origin of endothelial cells, and the process of blood vessel formation.
3. Define the "critical moments" during the development of embryonic vasculature in vertebrates
4. Review the genetic and signaling pathways that regulate blood vessel formation.

READING

Required reading:

1. Coultas L, Chawengsaksophak K, Rossant J. Endothelial Cells and VEGF in Vascular Development. *Nature* 2006; 438: 937-945.

Suggested reading:

1. Hellstrom M, Phng L-K, Hofmann JJ, Wallgard E, Coultas L, Lindblorn P, Alva J, Nilsson A-K, Karlsson L, Gaiano N, Yoon K, Rossant J, Iruela-Arispe ML, Kalen M, Gerhardt H, Betsholtz C. *Nature* 2007 [Epub ahead of print]
2. Kamei M, Saunders B, Bayless KJ, Dye L, Davis GE, Weinstein BM. Endothelial Tubes Assemble from Intracellular Vacuoles *in vivo*. *Nature* 2006; 442: 453-456.
3. Zhong TP, Childs S, Leu JP, Fishman MC. Gridlock Signaling Pathway Fashions the First Embryonic Artery. *Nature* 2001; 414: 216-220.
4. Mukoutyama YS, Shin D, Britsch S, Taniguchi M, Anderson DJ. Sensory Nerves Determine the Pattern of Arterial Differentiation and Blood Vessel Branching in the Skin. *Cell* 2002; 109: 693-705.

SUMMARY

This lecture is about the developmental origin of endothelial cells and how blood vessels develop. Our fundamental understanding of this critical process is based on decades of detailed study by anatomists. Thus, spatial and temporal analyses of the evolution of vascular structures have provided us with a series of snapshots of how blood vessels form, growth, differentiate, and remodel. More recently, we have begun to dissect the genetic pathways and cellular interactions that lead to the formation of vascular structures and the specialization of vascular beads. In spite of these recent advances, basic questions

remain to be fully answered: where do endothelial cell precursors arise; when do they begin to differentiate; how do they influence organ development; how do they activate genetic programs that specify endothelial identity (i.e., arterial vs. venous); how do defects in those programs manifest as vascular abnormalities?

QUESTIONS

1. Do all endothelial cells of a vertebrate have the same precursors? What are the implications for the development of vascular disease?
2. Is vascular patterning random, or follows specific developmental rules?
3. It is now clear that pre-specified genetic programs control blood vessel development. Is there a role for epigenetics? If so, how do you think that environmental cues influence blood vessel formation and differentiation?