of cardiac NC cells onto various substrates in vitro and determined if any of the observed effects might be due to altered intracellular calcium signaling. We found Hcys enhanced cardiac NC cell attachment in a dose- and substrate-dependent manner within the 30-min period allotted for the reattachment of the NC cells. Ionomycin (increases cytoplasmic levels of calcium) mimicked Hcys' effect on NC cell attachment while BAPTA-AM (a chelator of cytoplasmic calcium) or U-73122 (a phospholipase C inhibitor), blocked Hcys' effect. Neither lanthanum chloride (a general plasma membrane calcium channel blocker) nor MK801+ (an NMDA receptor blocker expressed by NC) had any effect on NC cell attachment. These results showed Hcys rapidly alters NC attachment properties by triggering an increase in intracellular calcium possibly by increasing phospholipase C activity and generating inositol triphosphate through an unknown mechanism. Hence, the teratogenic effect ascribed to Hcys may be due, in part, to perturbation of normal intracellular calcium signaling during cardiac NC cell morphogenesis.

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Program/Abstract # 433
Morphogenesis of blood vessels during mouse vasculogenesis

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The formation of embryonic blood vessels and their morphogenesis into a highly stereotyped vascular network requires precise control of endothelial cell (EC) migration, proliferation, growth and patterning. Similar to neurons, ECs exhibit growth cone-like lamellipodia that grow and extend along molecularly defined tracks, integrating both attractive and repulsive cues present in the microenvironment. Recent studies provide evidence that molecules controlling neuronal guidance and pathfinding, also play an analogous role in EC migration and organization. Here, we have identified and characterized multiple 'neuronal' molecular guidance cues that drive endothelial vessel formation during mouse vasculogenesis. Our data reveals that a striking coordination of both positive and negative cues is required to build a blood vessel at a precise location. In addition, we identify the mouse notochord as a critical source of multiple redundant negative cues, which together shape the paired dorsal aortae. We then show that anastomosis of the aortae is driven by a combination of morphogenetic movements of the embryo, as well as repression of midline repulsive cues. Finally, we investigate mouse mutants that lack the notochord, and show that absence of proper midline cues results in dramatic failure of vascular patterning. A novel *in vitro* whole embryo culture system is used to functionally assay each individual repulsive molecule. Molecular identification of the cues that attract or repel EC is critical for our understanding of cardiovascular development and will provide the foundation for the development of clinical pro- and anti-angiogenic therapies.

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Program/Abstract # 434
Notch can regulate VEGF-related signaling in embryonic vascular differentiation

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The signaling cascades that direct the morphological differentiation of the vascular system during early embryogenesis are not well defined. Both Notch and VEGF signaling are known to play a role in the formation of the vasculature in the mouse. To further understand the role of Notch signaling during endothelial differentiation, we are using a binary transgenic mouse model that expresses an activated NOTCH1 intracellular domain in the embryonic vasculature. Several defects are seen in these transgenic embryos, which do not survive after E10.5. Most notably, the vasculature of the yolk sac displays differentiation defects, with few matured vessels. Microarray analysis of RNA isolated from the yolk sac of transgenic embryos indicated aberrant expression in a variety of genes. In particular, two VEGF family members, placental growth factor (PGF) and VEGF-C, are increased significantly. This data suggests a potential vascular differentiation pathway regulated by Notch signaling. Based on these findings, a transgenic model will be generated which expresses high levels PGF in the endothelia using the binary transgenic system. Morphological and genetic analysis of the resulting embryos will allow us to determine the relevance of the overexpression of PGF in the observed NOTCH1 overexpression phenotypes. Completion of this work will provide information on cell signals and gene expression processes directing endothelial differentiation.

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Program/Abstract # 435
Control of angiogenesis and lymphangiogenesis by ephrin-B2

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The efficient transport of gases, liquids, nutrients, macromolecules and cells between distant organs is indispensable for vertebrate organisms. Blood vessels and the lymphatic