

We are addressing this subject in several ways, and I will present data demonstrating progress toward this end. Using transgenic techniques and high-resolution time-lapse imaging, we are studying the membrane and cytoskeletal dynamics that occur during FBMN migration, and how they are altered following genetic knockdown of *pk1b*. In addition, we are using genetic techniques to analyze the interaction between *pk1b* and other PCP components.

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CHARACTERIZATION AND MOLECULAR REGULATION OF HEMOGENIC ENDOTHELIUM WITHIN THE AORTA-GONAD-MESONEPHROS (AGM) REGION IN THE MIDGESTATION MURINE EMBRYO

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Blood and blood vessels develop in parallel in mammalian embryos. During definitive hematopoiesis, hematopoietic stem/progenitor cells are derived from the endothelium. We aim to characterize hemogenic endothelial cells that give rise to hematopoietic stem/progenitor cells and elucidate the molecular regulation of their specification and differentiated function. Previous work in our lab defined a population of Hoechst dye-effluxing (SP), Flk+/cKit+/CD45- hemogenic endothelial cells residing in the developing yolk sac. The goal of this research is to determine whether such cells reside within the aorta-gonad-mesonephros (AGM) region, the first intra-embryonic site of definitive hematopoiesis, and function as hemogenic endothelial cells capable of giving rise to all blood lineages. Toward this goal, we have isolated cells by endothelial and hematopoietic cell surface marker expression and SP phenotype from the AGM region at various stages of development, and have tested their hematopoietic potential *in vitro*. We are using both immunohistochemical techniques, as well as *in vivo* imaging, to track these cells throughout development and demonstrate their differentiation from cells residing within the endothelium to blood cells within systemic circulation. We have also been optimizing an explant culture system for use in time-lapse imaging of Flk1::H2B-EYFP transgenic mice. This system allows us to monitor endothelial cell behavior in the AGM during the initiation of intraembryonic definitive hematopoiesis. A greater understanding of the interdependent regulation of blood and blood vessel formation will aid in the development of therapeutic strategies to treat human vascular and hematopoietic diseases.

09-106

MODULATORS OF BLOOD PRESSURE: DISCOVERING NOVEL PROTEINS IN THE WNK4 KINASE SIGNALING CASCADE

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Hypertension (or high blood pressure) is a complex disorder affecting one billion people worldwide and is a major risk factor for mortality through myocardial infarction, stroke, end-stage renal disease and congestive heart failure. Despite being a major public health challenge, its pathogenesis remains largely unknown and its treatment suboptimal. Human genetic studies have identified missense mutations in serine/threonine kinase WNK4 that cause Pseudohypoaldosteronism type II (PHAII), a rare hereditary disease featuring hypertension and elevated blood potassium levels, due to increased NaCl reabsorption and impaired renal K⁺ secretion, respectively (Wilson, et al., Science 2001). WNK4 localizes to tight junctions in the distal nephron in the kidney and regulates proteins involved in sodium chloride reabsorption, potassium secretion, and paracellular chloride flux. PHAII-causing mutant WNK4 disrupts these processes causing the PHAII phenotypes (Lalioi, et al., Nature Genetics, 2006). The upstream regulators of WNK4 are poorly understood and what proteins modulate WNK4 and ultimately its final effectors are unknown. To gain insight into WNK4 regulation we developed Madin-Darby canine kidney cell lines, expressing inducible WNK4 genes, as model systems for WNK4 function in kidney. We then used two dimensional difference gel electrophoresis (DIGE) to dissect WNK4 specific changes in the proteome of our cell lines. We observed specific physiological effects of WNK4^{WT} and WNK4^{PHAII} on the paracellular ion transport properties of our cell lines. In addition, DIGE analysis revealed novel proteins that might be components of a WNK4 regulatory network. These results demonstrate that we can observe WNK4 dependent physiologic and proteomic changes in our model systems. Our aim is to uncover novel proteins that may work together with WNK4 to modulate blood pressure.

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HOSPITAL-BASED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS SCREENING AND PREVENTION TECHNIQUES PROVIDE NUMEROUS BENEFITS TO THE COMMUNITY AT LARGE

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In the emergency preparedness community, great attention is given to improving the recognition, prevention, and response to incidents. With a continuous awareness of potential disasters along with the availability of a well-developed emergency response plan, many local incidents may be adequately contained and prevented from developing into larger disasters. While disasters come in all shapes and sizes from earthquakes generated by the slipping of massive tectonic plates to microscopic organisms causing pandemic diseases, for hospital emergency coordinators, one of the most concerning potential disasters involves a tiny organism called methicillin-resistant *Staphylococcus aureus*. Methicillin-