

ROTATION GUIDE

Cell and Developmental Biology

2009-2010

H. Scott Baldwin, M.D.

Div Chief of Pediatric Cardiology
Professor of Pediatrics
and Cell and Developmental Biology

Lab: 9435 MRB IV Tel #: 2-2703
Office: 9435A MRB IV Tel #: 2-2703
scott.baldwin@vanderbilt.edu

Research Interest: Delineating the molecular basis of vascular development in the mammalian embryo as an approach to understanding the etiology of congenital heart diseases.

Rotation Projects: Dr. Baldwin's research efforts are based on the hypothesis that the developing vasculature provides important patterning information that directs subsequent cardiac and pulmonary morphogenetic events. Current efforts are focused on defining the "upstream" and "downstream" mechanisms by which NFATc regulates semilunar valve formation and strategies include chimeric analysis by ES cell blastocyst complementation, microarray screening, as well as quantitative anatomical and physiological assessment. In addition, the laboratory has determined that endocardial cells differentiate as a unique population of endothelial cells in ES cell cultures and are currently defining the parameters for optimal endocardial differentiation in ES cell systems as well as defining strategies for endocardial differentiation of iPS cells. Finally, the laboratory is developing strategies for endothelial specific gene mutations using the Cre-Lox system and defining inducible endothelial specific promoters to allow temporal and spatial gene manipulation throughout the vascular system with a focus on the role of the RTK, Tie1, in multiple facets of vascular ontogeny.



R. Daniel Beauchamp, M.D.

Professor, Surgery,
Cell and Developmental Biology
and Cancer Biology
Member, Vanderbilt Ingram Cancer Center

Lab: D-2300 MCN Tel #: 3-8401
Office: D-4316 MCN Tel #: 3-2363
daniel.beauchamp@vanderbilt.edu

Research Interest: Regulation of metastatic processes in colon cancer

Rotation Projects: My laboratory investigates the mechanisms behind the metastatic behavior of cancer cell with particular emphasis on the developmental process of Epithelial to Mesenchymal Transition (EMT). Rotation projects are designed to engage students to the fundamentals of hypothesis driven research using cellular and molecular tools in the study of EMT. Ongoing research projects in the laboratory include the use of the molecular features of mouse models to predict recurrence in colon cancer patients, the functional importance of BMP family and Wnt signaling pathway interactions in colon cancer and metastasis, and the study of specific genes regulating planar cell polarity in colon cancer development and metastasis. A diverse group of physician-scientists and basic research scientists, the members of my

laboratory are highly engaged and interactive, participating in regular data presentation group meetings, journal clubs, writing workshops and travel to scientific conferences.



Stephen (Steve) Brandt, M.D.

Professor, Medicine,
Cell and Developmental Biology,
and Cancer Biology

Lab: 540-542 PRB

Tel #: 6-1808

Office: 540B PRB

Tel #: 6-1809

stephen.brandt@vanderbilt.edu

Research Interests: Regulation of gene expression in normal and leukemic blood cells

Rotation Projects: Our laboratory is interested in the function of transcription factors, particularly those of the basic helix-loop-helix (bHLH) family, in normal and leukemic hematopoiesis. Rotation projects will employ a combination of molecular biology, protein biochemistry, and mammalian cell culture techniques. Current interests include the actions of the bHLH transcription factor TAL1 (or SCL) in mouse monocyte/macrophage differentiation and the functions in transcriptional regulation and differentiation of two recently discovered components of TAL1-containing complexes, the single-stranded DNA-binding proteins SSBP2 and SSBP3. Students potentially interested in rotations are encouraged to phone or e-mail for more details.



Vivien A. Casagrande, Ph.D.

Professor, Cell and Developmental Biology,
Psychology,
Ophthalmology & Visual Sciences

Lab: T-2304 MCN

Tel #: 2-2694

Office: T-2302 MCN

Tel #: 3-4538

vivien.casagrande@vanderbilt.edu

Research Interest: Our laboratory is interested in the functional significance and structural correlates of proposed parallel visual information channels in primates.

<http://www.psy.vanderbilt.edu/faculty/Casagrande/Casagrandelab/index.htm>

Rotation Projects: Students who rotate in this laboratory will be trained in a variety of techniques used to examine the function and structure of the visual system using anesthetized and awake behaving primates. Specific projects for this year include: 1) Comparison of the morphologies of axons from two main inputs to a higher visual cortical area to determine if signature profiles of a driver axon can be established. This project uses a variety of tools including surgery, electrophysiology, optical imaging, immunocytochemistry and confocal microscopy to compare the morphologies of specific types of axon in relationship to physiology. 2) Determine under what conditions auditory input influences visual responses in the visual thalamus of awake, behaving monkeys. This project uses electrophysiological recording to examine firing of individual cells while the monkey performs different tasks while auditory and visual stimuli are presented. 3) Examine the responses of pulvinar neurons to complex visual stimuli in anesthetized primates to determine if these responses are similar to responses seen in cortical target neurons. This project uses electrophysiological tools and analysis. 4) Determine the role of feedback from higher cortical visual areas to lower visual areas by pharmacologically manipulating the feedback pathway and examining for changes in response properties in a lower visual cortical area. This project uses as combination of optical imaging,

recording and pharmacological manipulations. 5) Explore the role of synchrony as a mechanism for coding visual features using multielectrode recording. This project using a hundred electrode array to record from multiple single visual cortical cells simultaneously in an anesthetized primate. All of these rotation projects involve collaborative interactions with other laboratories especially the laboratories of Dr. Jeffrey Schall (Psychology), Dr. A.B. Bonds (Electrical Engineering and Computer Science) and Dr. Mark Wallace (Department of Hearing and Speech Sciences).



Jin Chen, M.D., Ph.D.

Associate Professor, Medicine,
Cell and Developmental Biology,
and Cancer Biology

Lab: A-4323 MCN

Tel #: 3-3820

Office: A-4323MCN

Tel #: 3-3819

jin.chen@mcm.vanderbilt.edu

Research Interests: Eph receptor tyrosine kinase, blood vessel formation, cancer metastasis
http://medschool.mc.vanderbilt.edu/facultydata/php_files/part_dept/show_part.php?id3=747

Rotation Projects: Our goal is to understand the molecular mechanisms that regulate angiogenesis in an effort to identify new targets for therapeutic intervention in cancer and cardiovascular diseases. Rotation projects are aimed at providing an introduction to molecular and cell biology while contributing to our goal of understanding the role of Eph RTK in angiogenesis and tumor metastasis. Projects are expected to evolve from open discussion. Examples of rotation project includes, but not limited to, generation of Eph receptor mutants, siRNA knock down of signaling molecules in the Eph receptor pathway, imaging of tumor-induced endothelial cell migration, and analysis of tumor sections from transgenic/knock out mice.



Chin Chiang, Ph.D.

Associate Professor
Cell and Developmental Biology

Lab: 4114 MRB III

Tel #: 3-4916

Office: 4110 MRB III

Tel #: 3-4922

chin.chiang@vanderbilt.edu

Research Interest: Sonic hedgehog signaling in development and disease

Rotation Projects: Sonic hedgehog (Shh) is a secreted signaling molecule that specifies cell fates by instructing cells to either proliferate or differentiate in a context-dependent manner. Therefore, it is not surprising that dysregulation of the Shh signal, either at the level of Shh secretion, movement or reception, has been linked to various birth defects and cancers. Over the past several years, we have generated a number of mouse mutants serving as paradigms for human diseases. Additionally, we have also generated several transgenic mouse lines that enable us to generate tissue-specific deletion of Shh pathway activity. Rotation projects will include the utilization of these tools to understand the cellular and molecular mechanisms of Shh signaling in brain development and cancer.



Robert J. Coffey, M.D.

Professor, Medicine,
Cell and Developmental Biology

Lab: 10415 MRB IV Tel #: 3-6230

Office: 10415 MRB IV Tel #: 3-6228
robert.coffey@vanderbilt.edu

Research Interest: The Coffey lab seeks a comprehensive understanding of the role of EGF receptor (EGFR) and its ligands in normal epithelial cell growth as well as how these functions are altered in cancer. Additional areas of interest include identification and characterization of colonic stem cells. A wide range of biochemical and molecular approaches are applied to a number of model systems.

https://medschool.mc.vanderbilt.edu/facultydata/php_files/show_faculty.php?id3=749

Rotation Projects: The EGFR has critical functions in regulating developmental processes as well as normal cell function in the adult. EGFR function is often misregulated in cancer, and this misregulation can help to drive carcinogenesis. Our lab is interested in the normal and aberrant functions of EGFR through studying the ligands that bind and activate it. We focus on the trafficking and processing of four of these ligands TGF- β amphiregulin, HB-EGF and epiregulin. TGF- β amphiregulin and HB-EGF each have unique characteristics that lead to different downstream signaling events. We are interested in understanding the diverse molecular consequences of these various ligands in regulating growth and differentiation of polarized epithelial cells. We are also interested in other pathways, such as the Wnt pathway, that intersect with EGFR signaling, addressing their roles in cancer using cell culture models, mouse models and in human cancers directly. Potential rotation projects include: 1) Validating proteomic data that has identified a novel class of basolaterally targeted exocytic vesicles that contain TGF- β as a cargo and Naked2, a putative negative regulator of Wnt signaling, as a coat; 2) Analyzing a tumor suppressor role for Naked2 using recently generated conditional knockout and transgenic mice; 3) Characterize a novel stem cell marker in the GI tract and determine its role in colon cancer, using a battery of newly generated inducible Cre driver mice; 4) Characterize a novel mode of EGFR ligand signaling via exosomes; 5) Characterize a novel non-coding RNA expressed in the colonic crypt that when overexpressed in normal colonic epithelial cells results in highly invasive tumors.

**Mark P. deCaestecker, M.D., Ph.D.**

Assistant Professor of Medicine,
Cell and Developmental Biology
and Cancer Biology

Lab: C-3111 MCN Tel #: 2-3081

Office: C-3126 MCN Tel #: 3-2844
mark.de.caestecker@vanderbilt.edu

Research interests: Kidney development, stem cells, Wilms' tumor, intrauterine growth retardation, BMP signaling and pulmonary hypertension

Rotation Projects: Three rotation projects are available to study: a) Post translational modifications regulating the sub-cellular localization of Cited1. Studies will use embryonic mice, protein purification and mass spectrometry (supervised by a graduate student, Mark Jones); b) IGF pathway components in fetal tissues from mice with intrauterine growth retardation. Involves analysis IGF signaling pathways in embryonic tissues and cells from mice with intrauterine growth retardation (supervised by a post-doctoral fellow, Tatiana Novitskaya); and c) Protein trafficking defects associated with Bmp receptor mutations in pulmonary endothelial cells from patients with an inherited form of pulmonary hypertension. These studies involve

biochemical analysis of endogenous mutant receptor localization and ER processing in cultured endothelial cells (supervised by another graduate student from my lab, Jon Lowery).



Kevin C. Ess, M.D., Ph.D.

Assistant Professor, Pediatric Neurology
Cell and Developmental Biology

Lab: 6158 MRB III Tel #: 6-4181
Office: 6158C MRB III Tel #: 6-4113
josh.gamse@vanderbilt.edu

Research Interest: Our research focuses on the neurobiology of progenitor cells, specifically the mechanisms by which neural progenitors make cell fate decisions during development. We have used the human genetic disease tuberous sclerosis complex (TSC) as a model system to investigate neural progenitor cell differentiation. TSC is due to inactivation of the *TSC1* or *TSC2* genes and afflicts approximately 1:6,000 people. Multiple organs are affected in TSC though brain abnormalities generally cause the greatest suffering with many patients having seizure disorders (epilepsy), autism, developmental delay, psychiatric, and behavioral problems. These neurologic features are thought to be due to brain malformations called tubers that prominently feature abnormally differentiated neurons and glial cells.

While multiple alterations have been discovered, dysregulation of mTOR kinase signaling pathway appears to be a central abnormality. This insight is being exploited to generate new therapeutics for TSC and related disorders.

Rotation Projects: Students rotating in my laboratory perform experiments using molecular and developmental biology techniques to investigate abnormalities of neural progenitor cells. To this end we utilize transgenic mouse models of TSC as well as induced pluripotent cells (iPS) derived from patients with TSC. These complementary approaches allow us to dissect mechanisms of abnormal development and study perturbations at the cellular as well as organismal level.



Joshua T. Gamse, Ph.D.

Assistant Professor, Biological Sciences
Cell and Developmental Biology

Lab: 4274 MRB III Tel #: 6-5575
Office: 4270D MRB III Tel #: 6-5574
josh.gamse@vanderbilt.edu

Research Interests: Left-right asymmetry in the brain: the role of cell specification, migration, neurogenesis, innervation, and growth factor signaling in creating a lateralized brain.

Rotation Projects: We are using genetic, biochemical, and embryological techniques in zebrafish to unravel the formation of a lateralized brain. In particular, we study the formation of the epithalamus, a simple brain region consisting of the pineal organ, the left-sided parapineal organ, and the left and right habenular nuclei. Ablation experiments indicate that the parapineal organ acts as an organizer of asymmetry in the habenular nuclei. Rotation projects could include analysis of candidate signaling pathways, characterization of mutation phenotypes, lineage labeling, time lapse imaging of morphogenesis, or testing potential protein interactions during the development of asymmetry in the epithalamus.



James R. Goldenring, M.D., Ph.D.

Professor, Surgery,
Cell and Developmental Biology

Lab: 10435 MRB IV Tel #: 2-8453

Office: 10435G MRBIV Tel #: 6-3726
jim.goldenring@vanderbilt.edu

Research Interest: Our laboratory studies intracellular mechanisms underlying the regulation of vesicle trafficking and signal transduction in normal and neoplastic epithelial cells.

Rotation Projects: are available for graduate students in any of the three major research areas covered in the laboratory: 1) AKAP350A regulation of Golgi apparatus and RNA trafficking, 2) Rab proteins and vesicle trafficking and 3) mechanisms regulating the induction of pre-cancerous gastric metaplasia. For the first, AKAP350A regulation, projects are available analyzing the role of AKAP350A in coordinating a complex with caprin and CCAR1, which regulates movement of RNAs within cells. Studies are available to analyze the molecular mechanisms for protein and RNA assembly as well as the functional role of the complex in RNA movement. Projects are also available analyzing the association of AKAP350A with the Golgi apparatus, including split-ubiquitin and proteomic approaches to identifying Golgi proteins anchoring AKAP350A to the cis-Golgi. In the case of Rab proteins and trafficking, projects are available on available investigating the roles Interacting proteins for Rab11a and Rab25 in the regulation of dynamic trafficking through early and recycling endosomes. In addition, projects are available analyzing the role of Rab25 in the regulation of transformation in intestinal epithelial cells. Finally, in terms of gastric metaplasia, projects are available examining the role of soluble factors up-regulated during the induction of metaplasia as autocrine factors for sustaining metaplasia and progression to cancer.



Kathleen L. Gould, Ph.D.

Investigator, HHMI
Professor, Cell and Developmental Biology

Lab: B-2309 MCN Tel #: 3-9500

Office: B-2309A MCN Tel #: 3-9502
kathy.gould@vanderbilt.edu

Research Interest: Regulation of cell division

Rotation Projects: My laboratory is interested in understanding the mechanism and regulation of cytokinesis, and how cytokinesis is normally entrained to the nuclear division cycle to prevent aneuploidy. Rotation projects are designed to introduce students to genetic, cytologic and/or molecular genetic analyses while asking a biological question of fundamental significance in cell division research. As examples, a student might learn how to follow a protein's intracellular distribution through the cell cycle using confocal microscopy, undertake a classical genetic suppressor screen to identify novel components in cell cycle signaling pathways, prepare and analyze complex protein samples by mass spectrometry, and/or evaluate the functional significance of post-translational modification on signaling molecules.



Todd R. Graham, Ph.D.
Professor
Biological Sciences,
Cell and Developmental Biology

Lab: SC 2433 **Tel #:** 2-3439
Office: SC 2433 **Tel #:** 3-1835
tr.graham@vanderbilt.edu

Research Interest: Protein transport and membrane biogenesis

Rotation Projects: We are interested in defining molecular mechanisms for how proteins and lipids are sorted and transported within the secretory and endocytic pathways. The Golgi complex is a major protein sorting station and this organelle produces a number of different transport vesicles that deliver proteins to either the plasma membrane, the endosomal/lysosomal system, or back to the endoplasmic reticulum. Using genetic approaches in the yeast model system *Saccharomyces cerevisiae*, we have discovered that a large family of type 4 P-type ATPases (P4-ATPases) plays an essential role in budding a variety of transport vesicles from Golgi and endosomal membranes. Most P-type ATPases pump ions or heavy metals across a membrane against their electrochemical gradients; however, the P4-ATPases appear to be flippases that pump specific phospholipid molecules from the luminal leaflet (or extracellular leaflet) of the membrane to the cytosolic leaflet. In addition to facilitating vesicle budding, the flippase activity of P4-ATPases is thought to establish the asymmetric concentration of phosphatidylserine and phosphatidylethanolamine to the cytosolic leaflet, a fundamental feature of the eukaryotic cell plasma membrane. In mammalian cells, regulated exposure of phosphatidylserine on the cell surface is an important “eat-me” signal in cells undergoing programmed cell death (apoptosis) and potently stimulates clotting reactions in platelets and red blood cells. Moreover, P4-ATPases are linked to liver disease, obesity, type 2 diabetes and male fertility. Recently, we have uncovered a surprising connection between P4-ATPase function, membrane phospholipid asymmetry and the intracellular, nonvesicular transport of cholesterol. It appears that a P4-ATPase helps establish a plasma membrane structure that “locks” cholesterol in place. Thus, P4-ATPases have a central function in defining the protein and lipid composition of specific membranes and are thereby critical for membrane biogenesis. Current projects in the lab include 1) defining the biochemical mechanism for phospholipid flip by a P4-ATPase, 2) characterizing positive and negative regulators of flippase activity in Golgi membranes, 3) determining how flippase activity couples to vesicle budding machinery, and 4) further characterizing the relationship of P4-ATPase function to intracellular sterol transport.



Guoqiang Gu, Ph.D.
Assistant Professor
Cell and Developmental Biology

Lab: 4128 MRB III **Tel #:** 6-3632
Office: 4130A MRBIII **Tel #:** 6-3634
guoqiang.gu@vanderbilt.edu

Research Interest: How endocrine islet cells are made during embryogenesis and how they are maintained after birth

Rotation Projects: We use mouse and chicken embryos as models to study what factors are required for endocrine islet differentiation and maintenance. We identify factors that are sufficient to induce endocrine differentiation in model organisms and then determine whether they induce islet production from embryonic stem cells. Typical rotation projects in the lab include: 1) determine the expression patterns of candidate genes in pancreatic tissues, determine the effect of expressing these candidate genes in chicken embryos; 2) characterize

Gu continued

the pancreatic phenotypes in several mouse mutants; 3) create gene knockout and knockin constructs.



Steven. K. Hanks, Ph.D.

Professor
Cell and Developmental Biology

Lab: U-4200 MCN **Tel #:** 3-8501
Office: U-4206 MCN **Tel #:** 3-8502
steve.hanks@vanderbilt.edu

Research Interests: Role of integrin-mediated tyrosine kinase signaling in the control of cell behavior.

Rotation Projects: Cell adhesion to the ECM, mediated by integrin receptors, is essential for many cellular processes including proliferation, survival, and motility. We discovered an integrin-associated tyrosine kinase called “FAK” (focal adhesion kinase) that becomes activated following cell/ECM adhesion, and showed that signaling by FAK is an important event leading to changes in actin cytoskeleton organization and cell motility. We also identified a protein called “CAS” (Crk-associated substrate) as a major tyrosine kinase substrate associated with FAK and Src that plays a key signaling role in cell motility and invasion. Our research interests focus on developing a better mechanistic understanding of how FAK-, Src-, and CAS-associated signaling events are able to affect these cell behaviors. Rotation projects could involve any of a number of experimental approaches (*e.g.* molecular/genomic, biochemical/proteomic, live cell imaging) that are currently being pursued to achieve this goal.



Antonis Hatzopoulos, Ph.D.

Associate Professor
Medicine, Cell and Developmental Biology

Lab: 319 PRB **Tel #:** 6-5614
Office: P425C MRBIV **Tel #:** 6-5529
antonis.hatzopoulos@vanderbilt.edu

Research Interest: Molecular and cellular mechanisms of embryonic heart development and cardiac regeneration after ischemic injury.

Rotation Projects: Our laboratory focuses on the role of selected BMP and wnt antagonists in heart development using zebrafish as a model vertebrate system. We further explore the potential of these proteins to promote differentiation of mouse embryonic and adult stem cells to cardiovascular lineages *in vitro* and following ischemic injury *in vivo*. Our goal is to discover new ways to improve cardiac tissue repair and regeneration in human patients after myocardial infarction. Rotation projects include studies on: the regulation of stem cell differentiation to endothelial cells and cardiomyocytes; the role of BMP antagonists in heart development in zebrafish; and, immunohistological approaches to monitor cardiac tissue recovery after ischemic injury in the mouse



Stacey S. Huppert, Ph.D.
Assistant Professor
Cell and Developmental Biology
Vanderbilt Center for Stem Cell Biology

Office: 9415E MRB IV **Tel #:** 3-4024
Lab: 9415 MRB IV **Tel #:** 6-7391
stacey.huppert@vanderbilt.edu
<http://www.vcscb.org/labs/huppert>

Research Interest: Coordination of progenitor/stem cell lineage restriction during liver organogenesis, regeneration, and disease

Rotation Projects: The goal of our lab is to explore how intercellular signaling pathways are integrated during developmental and disease programs of the liver. These studies will provide novel insights into the molecular mechanisms guiding normal processes that determine liver biliary and vascular architecture and how these processes may be involved in chronic liver diseases and pathologies. We are initially examining the role of the Notch signaling pathway in coordinating cell fate decisions during liver development and regeneration.

1. Determine the cell lineages that require Notch signaling to support liver progenitor/stem cell proliferation and morphogenesis during liver development and/or following adult liver injury.

A. Disrupt Notch signaling in the endoderm to determine whether Notch directly acts in the liver progenitor/stem cells.

B. Disrupt Notch signaling in endothelia to determine if Notch signaling indirectly influences the liver progenitor/stem cells.

2. Determine the relationship between patterning of the intrahepatic bile duct system and the vascular systems of the liver during development and regeneration. The technique of resin casting and three-dimensional analysis by microCT will be employed to quantitate direct and indirect structural changes in the liver vasculature upon alterations in Notch signaling within the endothelial and endodermal populations.

3. Identify the cell lineages that activate Notch1 during adult liver regeneration. A novel Notch signal-regulated lineage-tracing tool will be used to permanently mark a subset of cells and their derivatives that have undergone Notch1 activation in the liver following surgical and chemical liver injury. Identification of the cells that activate Notch after injury provides insight into regenerative mechanisms. For example, Notch could be functioning in an indirect mode by providing the proper niche environment to support proliferation and remodeling of the liver architecture. Alternatively, Notch signaling is often utilized during stem cell asymmetric division, a process where a stem cell produces one stem cell daughter and the other a committed progenitor. This direct role for Notch can influence proliferation and differentiation of progenitor/stem cells in a permissive manner inhibiting the proliferating cells from differentiating and therefore keeping them immature until it is time for the cell to become committed into a certain lineage.

4. Determine if chronic loss or activation of Notch signaling affects Hepatocellular Carcinoma (HCC) progression. A tumor induction protocol in genetically modified mouse models will be used to assess tumor progression in the background of deficient or constitutively active Notch signaling.



Irina Kaverina, Ph.D.
Assistant Professor
Cell and Developmental Biology

Lab: 3160 MRB III **Tel #:** 6-5568
Office: 3160A MRB III **Tel #:** 6-5567
irina.kaverina@vanderbilt.edu

Research Interest: How microtubules organize cellular architecture

Rotation Projects: Microtubules (MTs) serve as highways for organelle and molecular transport within a cell. They drive delivery of signals and organelles thereby defining cell shape and polarity. MT network can perform multiple actions due to functional diversity of MT sub-populations. We study mechanisms defining specific MT properties as well as pathways that they regulate.

Sample rotation projects:

1. **MT dynamics:** Interphase MTs are traditionally thought to nucleate at the centrosome. We have recently discovered a novel MT array, which originates at the Golgi membrane and is important for the Golgi organization. MT nucleation at the Golgi is regulated by a microtubule-associated protein CLASP. The aim of this rotation project is role of CLASP phosphorylation in MT formation. Techniques: siRNA knockdown, point-mutation analysis, immuno-fluorescence microscopy, confocal live cell imaging.
2. **Trafficking:** Our preliminary data suggest that Golgi-derived MTs are involved in proper regulation of endosomes. This rotation project will determine which part of endosomal trafficking depends of Golgi-derived MT array. Techniques: siRNA knockdown, immuno-fluorescence microscopy, confocal live cell imaging, photoactivation microscopy.
3. **Actin and contractility:** Our preliminary data reveal that actin organization in vascular smooth muscle cells, which is critical for vascular tonus and blood pressure regulation, depends on MTs. This rotation project will test whether and how MTs regulate actin cross-linking proteins. Techniques: siRNA knockdown, immuno-fluorescence microscopy, TIRF (Total Internal Reflection Fluorescence) live cell imaging, contractility measurement techniques (flexible substrates).
4. **Cell migration:** MTs are necessary for directional cell migration on 2D substrates. In organisms, cells often migrate in 1D fashion along collagen fibers. This rotation project will address role of distinct MT sub-populations in 1D migration on patterned substrates. Techniques: 1D substrate generation by 2-photon laser, live cell imaging, siRNA knockdown.



Anne Kenworthy, Ph.D.
Assistant Professor
Molecular Physiology and Biophysics,
Cell and Developmental Biology

Lab: 718 LH **Tel #:** 2-6617
Office: 718A LH **Tel #:** 2-6615
anne.kenworthy@vanderbilt.edu

Research Interests: Structure and function of membrane microdomains and regulation of intracellular targeting and trafficking of Ras.

Rotation Projects: Our research interests focus on cell membranes and membrane trafficking processes, including the structure and function of membrane microdomains and how lipid modifications of proteins mediate their intracellular targeting and trafficking. Research approaches in our laboratory rely heavily on live cell imaging approaches and biophysical measurements of protein and lipid dynamics using techniques such as confocal fluorescence recovery after photobleaching (FRAP). Examples of possible rotation projects include testing the ability of the glycolipid-binding toxin cholera toxin B-subunit to generate membrane domains

required for its internalization; evaluating how the membrane-curvature inducing protein caveolin-1 contributes to the assembly of caveolae and the function of the Golgi complex; and determining how cholesterol depletion, a classical method for studying the structure and function of lipid rafts, alters the structure of the plasma membrane and is sensed by the cell.



Ela W. Knapik, M.D.
Associate Professor, Medicine,
Cell and Developmental Biology

Lab: 1165 LH **Tel #:** 2-7559
Office: 1165B LH **Tel #:** 2-7569
ela.knapik@vanderbilt.edu

Research interest: neural crest specification and differentiation

Rotation projects: The neural crest is an embryonic cell population that contributes to the development of a diverse set of adult structures. It is perhaps the defining feature of the vertebrate embryo, as its evolution permitted the morphological and functional development of many structures that distinguish vertebrates from the lower chordates. Disruption in normal neural crest development leads to numerous craniofacial, heart and gut birth defects, while deregulation of its growth and differentiation results in pediatric malignancies like melanoma and neuroblastoma. Our laboratory is interested in understanding the molecular and cellular mechanisms that orchestrate neural crest induction, specification and differentiation. We approach these questions with many strategies, including using forward genetics and gain- and loss-of-function studies. Furthermore, we have many collaborative projects with other investigators at Vanderbilt and elsewhere. Our rotation projects are intended to introduce students to genetic, molecular and developmental analyses of the zebrafish, an excellent model for studying neural crest development. Projects might involve characterization of the zebrafish neural crest mutant phenotypes, mutation identification with positional cloning approaches, and analysis of gene function by gain-of-function and loss-of-function approaches. Neural crest development has also led us to study the development of the pharyngeal arches in zebrafish. We have several investigations concerning the cell biology of chondrocytes during the early development of the arches. This has given our lab a unique *in vivo* model for conducting genetic and molecular analyses of protein trafficking in secretory cells – a model that has broad clinical relevance, since the etiology of many human diseases lies within the secretory pathway.



Patricia A. Labosky, Ph.D.
Associate Professor
Center for Stem Cell Biology
Cell and Developmental Biology

Lab: 9415 MRB IV **Tel #:** 2-4378
Office: 9415D MRBIV **Tel #:** 2-2540
trish.labosky@vanderbilt.edu

Research Interest: Our lab is interested in the molecular regulation of progenitor cells in the mammalian embryo with a focus on embryonic stem cells (ES cells) and neural crest stem cells.

Rotation Projects: Our previous work demonstrated that Foxd3, a member of the Forkhead family of proteins, is required for the maintenance of embryonic ectoderm and therefore establishment of embryonic stem cells (ES cells). When Foxd3 is removed from ES cells they lose their ability to self-renew and undergo precocious differentiation while they maintain

expression of other stem cell factors. This puts Foxd3 in a unique position potentially downstream of tumor promoting stem cell genes but upstream of multipotency. There are conflicting reports in the literature about precisely how this protein functions as a transcription factor, and we wish to understand the gene regulatory networks controlling stem cell behavior. Therefore, we are taking a targeted approach to determining this at a mechanistic level using Foxd3 as a tool to unravel these networks. Foxd3 is also expressed later in the embryo in the multipotent neural crest (NC), and a tissue specific deletion of Foxd3 using the Cre-LoxP system to selectively mutate the gene in NC showed a catastrophic loss of those cells affecting bones of the skull, the enteric and peripheral nervous systems and the outflow tract of the heart. Future experiments will focus on analysis of this mutant and are designed to understand the gene regulatory networks controlling this multipotent cell type. Rotation projects are available for any of these projects in the laboratory.



Ethan Lee, M.D., Ph.D.
Assistant Professor
Cell and Developmental Biology

Lab: U-4200 MRB III **Tel #:** 2-1412
Office: U-4225 MRBIII **Tel #:** 2-1307
ethan.lee@vanderbilt.edu

Research Interests: Wnt signaling in development and human disease

Rotation Projects: The Wnt pathway is an ancient signaling system present in all metazoans from planaria to humans. Our lab primarily uses *Xenopus laevis* embryos, biochemical extracts, and cultured mammalian cells to study the basic mechanism of Wnt signal transduction, the role of Wnt signaling in normal vertebrate development, and the misregulation of Wnt signaling in human diseases. Towards these aims, we use combinations of embryology, cell biology, biochemistry, and chemical biology. Possible rotation projects include 1) *in vitro* and *vivo* validation of monoclonal antibodies against the Wnt pathway for potential use as therapeutic agents in cancer and heart disease, 2) testing the role of heterotrimeric G proteins in Wnt signaling, and 3) exploring the use of small molecules in perturbing Wnt signal transduction.



Mark A. Magnuson, M.D.
Earl W. Sutherland, Jr. Professor
Center for Stem Cell Biology

Lab: 9465 MRB-IV **Tel #:** 3-0037
Office: 9465 MRB-IV **Tel #:** 2-7006
mark.magnuson@vanderbilt.edu

Research interest: Stem and progenitor cell biology

Rotation projects: Research in the Magnuson Laboratory is focused on the genetic manipulation and directed differentiation of human and mouse embryonic stem (ES) cells towards pancreatic cell fates. Rotation projects are chosen after discussing a student's potential interests and prior experiences but are likely to involve one of two different types of projects. The first involves using genetically altered mouse or human ES cells that express fluorescent proteins under control of either the Sox17, nephroc, pdx1 or ptf1a genes. This will require learning to culture and differentiate mouse ES cells with agents that induce their differentiation first into definitive endoderm and then into pancreatic progenitor-like cells. Using fluorescence microscopy, real time PCR and FACS it is straightforward to analyze the effects of various stimuli. The second type of project would be to generate a DNA construct that would

serve as an exchange vector for inserting new reporter genes into cassette acceptor alleles (e.g. docking sites) that we have been previously generated in both mouse and human ES cells. In this case the student would learn how to design a fusion gene construct and assemble it using BAC recombineering methods. If time allows, the student will then be taught how to perform recombinase-mediated cassette exchange into mouse ES cells.



Anna L. Means, Ph.D.
Assistant Professor of Surgery,
Cell and Developmental Biology

Lab: 10445 MRB IV **Tel #:** 3-0932
Office: 10445 MRB IV **Tel #:** 3-0922
anna.means@vanderbilt.edu

Research Interest: The Means lab studies the ways in which growth factor signaling regulates development and disease of the pancreas. In particular, we focus on the epidermal growth factor receptor (EGFR) which we have found regulates outgrowth and differentiation in the embryonic pancreas, and glucose-stimulated insulin secretion and cancer initiation in the adult pancreas.

Rotation Projects: Project 1: Determine whether the activated Kras oncogene is sufficient to induce pancreatic ducts to develop cancerous lesions. Pancreatic cancer has been hypothesized to originate in a particular cell type, the pancreatic duct, but we have been unable to test this hypothesis until recently. We now have genetically engineered mice that will allow us to express a mutated version of the Kras oncogene in pancreatic ducts.

Project 2: Determine the role of the epidermal growth factor receptor (EGFR) in pancreatic development. We have analyzed the pancreas in mice that have complete loss of the *Egfr* gene and found a variety of defects in pancreatic development. We now have the genetic tools to delete the *Egfr* gene just in specific cell types to determine which cells require this growth factor.

Project 3: Determine the underlying mechanism whereby adult pancreatic cells can be induced to give rise to new insulin-producing cells. A number of researchers have hypothesized that new insulin cells can arise from other cell types such as ducts or acinar cells that change their identity, or transdifferentiate, into insulin cells. We will test this hypothesis by using genetic lineage tracing to determine which cell(s) gives rise to insulin cells in culture.



David M. Miller, Ph.D.
Professor
Cell and Developmental Biology

Lab: 3120 MRB III **Tel #:** 3-3448
Office: 3120A MRB III **Tel #:** 3-3447
david.miller@vanderbilt.edu

Research Interest: Motor neuron differentiation and function.
http://www.vanderbilt.edu/exploration_dev/news/news_worm.htm

Rotation Projects: Animal movement depends on motor neurons, specialized cells that link the nervous system to muscles. We utilize the nematode, *C. elegans*, an organism with a simple, well-defined nervous system and powerful genetics, to identify key molecules regulating motor neuron differentiation and function. We have shown that the UNC-4 homeodomain transcription factor governs the pattern of synaptic inputs to a specific class of motor neurons in the *C. elegans* nerve cord. A major focus of this lab is to identify other genes in this pathway

and to reveal their mechanism of action. To accomplish this goal we have developed powerful new microarray based methods for obtaining gene expression profiles of specific *C. elegans* cells. In addition to using these approaches to identify UNC-4 target genes, we are employing these strategies to delineate the downstream players in other interesting developmental events that are also under transcriptional control. These include separated pathways that regulate synaptic remodeling and sensory neuron morphogenesis. Other applications include a project to correlate neuron-specific gene expression with the wiring diagram of the *C. elegans* nervous system and a “modENCODE” funded grant to identify all active genes in the *C. elegans* genome as a model for regulation of human gene expression. An additional project exploits the genetic facility of *C. elegans* to reveal key players in the mechanism of neuron-specific degeneration.



Melanie D. Ohi, Ph.D.

Assistant Professor
Cell and Developmental Biology

Lab: 4160 MRB III **Tel #:** 6-7780
Office: 4160A MRB III **Tel #:** 6-7780
melanie.ohi@vanderbilt.edu

Research Interests: Our laboratory is interested in understanding how large molecular machines involved in pre-mRNA processing and ubiquitination are structurally organized and how this organization translates into function within the cell. The lab uses single particle cryo-electron microscopy (EM), as well as a combination of biological and biochemical techniques to reach this goal.

Rotation Projects: Rotation projects will focus on providing students with an introduction to single particle EM and image analysis. Current projects focus on spliceosomal complexes and the APC/C, an E3 ligase critical during mitosis. Typically, rotation students will purify these complexes from the fission yeast *S. pombe* using TAP-tag technology. Complexes suitable for structural analysis will be analyzed using single particle EM.



Ryoma (Puck) Ohi, Ph.D.

Assistant Professor
Cell and Developmental Biology

Lab: 4154 MRB III **Tel #:** 6-7783
Office: 4150A MRB III **el #:** 6-7782
ryoma.ohi@vanderbilt.edu

Research Interests: Cell division, Microtubule Cytoskeleton, Kinesin-like proteins

Rotation Projects: Our group is broadly interested in how cells divide. During cell division, the microtubule cytoskeleton is organized into a transient structure called the mitotic spindle. This apparatus attaches replicated chromosomes *via* kinetochores and generates forces that power the equal division of chromosomes among two daughter cells. We apply a multidisciplinary approach to several model systems to examine the process of mitotic spindle assembly and how the interface between kinetochores and microtubules is regulated to promote error-free chromosome segregation. We use quantitative light microscopy to investigate protein behavior in the mitotic spindle, biochemistry to understand the function of key mitotic regulators, and small molecules to perturb spindle function. Currently, our lab is studying how several kinesin-like proteins impact spindle assembly and function. Rotation projects in the R. Ohi lab include: **1)** Determine if a fission yeast motor (Klp5/6) has a biochemical activity that is similar to

its human homologue (Kif18A); **2)** Determine how phosphorylation of a mitotic motor (Kif18A) affects its localization to kinetochores; **3)** Characterize the role of a motor protein (XCTK2) during spindle assembly using the *Xenopus* egg extract system; and **4)** Characterize the properties of spindle-bound motors in *Xenopus* extracts using a microtubule tracking assay.



John S. Penn, Ph.D.

Snyder Professor and Vice Chairman
Ophthalmology and Visual Sciences
Professor Cell and Developmental Biology, Pharmacology

Lab: 8109 MCE **Tel #:** 6-3400
Office: 8009 MCE **Tel #:** 6-1485
john.penn@vanderbilt.edu

Research Interest: Ocular angiogenesis.

Rotation Projects: Dr. Penn explores methods of treating and preventing ocular angiogenesis, the leading cause of blindness in developed countries. Angiogenesis is the unregulated growth of new blood vessels from existing blood vessels. Blood vessel proliferation in the eye often leads to retinal detachment and hence blindness. Angiogenesis is a critical pathologic component of such conditions as retinopathy of prematurity, diabetic retinopathy, macular degeneration, vein occlusion retinopathy, sickle cell retinopathy and other blinding conditions.

Using in vitro and in vivo models developed in his laboratory, Dr. Penn is characterizing the process of angiogenesis on the cellular and molecular levels. Through this activity his lab is identifying rational therapeutic targets. The Penn lab is at the leading edge of partnering with industry to develop novel antiangiogenic drugs for application to the eye. Rotating students will be exposed to a wide variety of techniques employing cells and tissues of the eye, with an emphasis on retinal and choroidal vasculature.



D. Brent Polk, M.D.,

Professor, Pediatrics,
Cell and Developmental Biology

Lab: 1035 MRB IV **Tel:** 2-4449
Office: 1025D MRB IV **Tel:** 3-9034/5669
d-brent.polk@vanderbilt.edu

Research Interest: Mechanisms regulating intestinal epithelial cell homeostasis.

Rotation Projects: Our laboratory is focused on the regulation of growth and development of the intestinal cell as it relates to ontogeny and disease. The long-term goal is to understand the cellular pathways controlling response to injury and repair that have significant overlap with both developmental and tumorigenic programs. Current areas of investigation include epidermal growth factor, tumor necrosis factor and *Helicobacter pylori*-initiated signaling mechanisms leading to proliferation, differentiation or migration of intestinal cells. We have identified novel intracellular signaling pathways that regulate these responses. Further, these findings have been extended to understanding the relationship between enteric bacterial flora and regulation of intestinal cell proliferation and apoptosis. These studies are performed using mouse and human intestinal cell lines and various mouse knockout lines.

Rotation projects include proteomic and DNA microarray analyses to determine targets of these pathways and the mutational analysis of target molecules regulating cellular response to injury

Polk continued

and repair. There are also number of ongoing projects in the laboratory with targeted experiments that will permit the rotation student to develop skills in protein biochemistry, signal transduction, cellular imaging and in vitro and in vivo models of cellular migration, proliferation, differentiation and apoptosis.



Lawrence S. (Lance) Prince, MD, PhD

Assistant Professor, Pediatrics and
Cell and Developmental Biology

Lab: 9415 MRB IV

Office: 9425C MRB IV

Tel #: 2-2635

Tel #: 2-6220

lance.prince@vanderbilt.edu

Research Interest: Molecular Mechanisms of Fetal Lung Development

Rotation Projects: Our laboratory studies how inflammation can inhibit normal lung development in preterm infants, leading to a chronic lung disease known as bronchopulmonary dysplasia, or BPD. To better understand the molecular events that disrupt normal lung formation, we use different transgenic and knockout mouse strains, tissue explant systems, live cell microscopy, and cell culture models. Rotation student projects could involve testing how inflammatory signals regulate the transcription of key lung growth factors including FGF-10, studying cell-cell interactions during lung airway branching by confocal microscopy, or isolating fetal mouse lung macrophages and examining how their response to immune stimuli might change during development. We use many different experimental approaches to better understand the basic mechanisms of lung development and how lung morphogenesis might be altered in human disease



Michelle Southard-Smith, Ph.D.

Assistant Professor
Medicine and Cell & Developmental Biology

Lab: 1175 Light Hall

Office: 1165 Light Hall

Tel #: 6-2174

Tel #: 6-2172

michelle.southard-smith@vanderbilt.edu

Research Interest: We are investigating the developmental genetics of neural crest (NC) progenitors that contribute to several aspects of the autonomic nervous system. Our primary goal is to identify genes, gene interactions, and developmental mechanisms that control formation of enteric ganglia in the gut using mouse models of Hirschsprung disease. Secondly we are tracing lineages of NC in the gut and lower urinary tract to comprehensively define the contribution of NC to these organ systems and investigate mechanisms and temporal processes that control NC lineage diversification.

Rotation Projects: Genetic approaches using both candidate gene and genome wide strategies have identified several genes that modify the severity of congenital aganglionosis in the *Sox10^{Dom}* mouse model of Hirschsprung disease. We are currently investigating the mechanism of interaction between these modifiers and Sox10 using congenic lines of mice, quantitative analysis of gene expression in flow-sorted populations of enteric NC stem cells and comparative genome sequence analysis to identify variants responsible for these effects. Moreover, our studies indicate that altered lineage divergence may contribute to aspects of gut dysmotility in regions of the intestine that are innervated. Consequently, we are also investigating lineage segregation in mouse models of Hirschsprung disease.

In a second line of research we are using Sox10 transgenes in mice to study NC lineages that contribute to autonomic innervation of visceral organs. Modified bacterial artificial chromosomes (BACs) have been engineered to drive reporter molecules (lacZ, GFP, CRE) that allow visualization of NC progenitors during migration and are being actively deployed to trace NC lineages during normal and pathogenic development.

Rotating students may participate in the following projects:

- 1) Evaluate candidate modifier loci in fetal gut RNA samples for variation in expression between *Sox10^{Dom}* congenic lines and in F1 hybrid samples.
- 2) Define Sox10+ NC derivatives in developing organs (heart, gut, bladder) visualized by Sox10 transgenic expression.
- 3) Investigate effects of NC mutant alleles on the migration of NC in the developing gut and bladder by imaging of Sox10 transgene expression



Roland Stein, Ph.D.

Professor
Molecular Physiology & Biophysics,
Cell and Developmental Biology

Lab: 723 Light Hall **Tel #:** 2-7026
Office: 723 Light Hall **Tel #:** 2-7027
roland.stein@vanderbilt.edu

Research Interests: Our lab is interested in determining how transcription factors control islet beta cell development and function.

Rotation Projects: Listed below are several subject areas that are currently being actively worked on & represent rotation topics. The student or post-doc working in the topic area would supervise a rotating student.

- 1) Determining the role of MafA &/or MafB in islet beta cell development and function using knockout mice.
- 2) Identifying MafB and Isl1 regulated genes in beta cells by ChIP-Seq, a high-throughput sequencing method to localize sites of bound transcription factors in the genome.
- 3) Isolating and characterizing the transcription factors involved in controlling spatial and temporal *Pdx-1* and *MafA* expression.
- 4) Determining the role of MafB during islet beta cell expansion during pregnancy



William P. Tansey, Ph.D.

Professor
Cell and Developmental Biology

Lab: 4140 MRB III **Tel #:** 2-1993
Office: 4140A MRB III **Tel #:** 3-4261
william.p.tansey@vanderbilt.edu

Research Interest: Control of transcription by the Ubiquitin–Proteasome system in normal and cancer cells.

Rotation Projects: We are interested in how gene expression is regulated in normal and cancer cells. Our specific focus is centered on the control of transcription by components of the ubiquitin–proteasome system (UPS). Previous research in our laboratory has demonstrated that the UPS—which is typically thought of within the context of protein destruction—is directly and mechanistically involved in the control of gene activity. We are anxious to explore the underlying biochemical mechanisms at work, and to expose the biological significance of this connection.

Our current research efforts are divided into two areas. To understand how the transcription and ubiquitin–proteasome systems intersect, we perform biochemical and genetic analyses in the yeast *Saccharomyces cerevisiae*. To probe the significance of this intersection, we study ubiquitin-mediated regulation of the oncoprotein transcription factor Myc, using a combination of biochemical and genetic analyses in tissue culture and mouse model systems of cancer. I am happy to host rotation students for both sets of studies, depending on their interests.



Matthew J. Tyska, Ph.D.

Assistant Professor
Cell and Developmental Biology

Lab: 3154 MRB III Tel #: 6-5461
Office: 3154 MRB III Tel #: 6-5504
matthew.tyska@vanderbilt.edu

Research Interests: Investigating the mechanism and function of actin-based motor proteins in polarized cells

Rotation Projects: Motor proteins generate the mechanical forces that are essential for a vast array of critical cellular processes (e.g. trafficking of membranes, establishment and maintenance of cell morphology, cell division). Research in our laboratory is focused on elucidating the function of actin-based motor proteins, collectively referred to as “myosins.” Present in virtually all eukaryotic cells, these molecular machines transduce energy derived from ATP hydrolysis into force and motion directed along actin filaments. Humans express ~11 structurally distinct classes of myosins and mutations in these proteins result in disease states ranging from cardiomyopathies to sensory defects such as deafness. Our efforts are guided by two general questions: (1) what are the specific cellular tasks performed by a given myosin? (2) how are the biophysical properties (e.g. ATPase activity) of a given myosin “tuned” for efficient cellular function? To address question #1, our laboratory employs a combination of biochemical and cell biological approaches to characterize knock-out mice lacking specific myosin isoforms or cultured cells expressing mutant or truncated myosin variants. To answer question #2, we are implementing a biophysical approach based on “optical tweezers” -- a form of nanotechnology capable of measuring cellular and molecular level mechanical forces ($\sim 10^{-12}$ N). We plan to exploit this technology to study the mechanical activity of myosins *in vitro* and in living cells. Currently, we are investigating the function and mechanism of myosin-1a (Myo1a), a membrane binding motor that is highly expressed in polarized epithelial cells such as the enterocytes that line the GI tract. Our recent studies show that Myo1a plays critical roles in controlling cell membrane tension and in powering a novel secretory pathway in polarized epithelial cells. Potential rotation projects related to these studies include characterizing Myo1a and Myo1a/cargo complex dynamics in live cells, and characterizing the mechanical/motile properties of Myo1a *in vitro*.



Susan R. Wente, Ph.D.

Associate Vice Chancellor for Research
Senior Associate Dean for Biomedical Sciences
Professor and Chair
Cell and Developmental Biology

Lab: U-3209 MRB III Tel #: 6-3436
Office: U-3209 MRB III Tel #: 6-3443
susan.wente@vanderbilt.edu

Research interest: Regulation of nucleocytoplasmic transport and inositol signaling
<http://www.mc.vanderbilt.edu/vumcdept/cellbio/wentelab>

Rotation projects: Research projects in my laboratory are focused on using yeast and vertebrate model systems to understand the mechanism of nucleocytoplasmic communication. The selective, bidirectional exchange of proteins and RNA between the nucleus and cytoplasm is essential for proper cell function, and transport is precisely regulated during cell cycle and developmental switches. Our main strategy has been to attack at the site of entry and exit, nuclear pore complexes (NPCs). These large structures span the nuclear envelope and provide the only known portals for transport. We have also recently expanded our efforts to investigate a novel nuclear inositol polyphosphate kinase signaling pathway that regulates cell communication and NPC function. Through our multiple approaches, we hope to understand the complexities of nucleocytoplasmic transport from the cellular to the disease level. Cancer cells can alter gene expression by perturbing nucleocytoplasmic transport, and many viruses pirate the cellular transport machinery to allow viral gene expression. Thus, analyzing the NPC assembly and translocation mechanism will reveal steps for controlling transport pathways during cancer cell growth or viral pathogenesis. Our work in zebrafish has also shown that inositol polyphosphate signaling is required for proper organ placement, and there are established links between inositol signaling and disease states that include cancer of the brain, prostate, and skin and neurological disorders. We have also recently invested effort to reveal how an essential mRNA export factor discovered in our lab is linked to a human motor neuron degenerative disease. Typical rotation projects include utilizing a combination of genetic, biochemical, molecular and cell biological based strategies: (1) to reveal the mechanism of nuclear pore formation and NPC assembly, (2) to elucidate the role of NPC proteins in mediating the movement of cargo through the NPC, 3) to analyze how mRNA export is regulated as a key gene expression step, or 4) to pinpoint roles for inositol signaling and mRNA export molecules in vertebrate development and disease. Rotation students will be mentored to independently execute the selected project, to critique the appropriate primary literature background, and to participate in weekly laboratory and small groups meeting.

**Christopher V.E. Wright, D. Phil.**

Professor, Cell and Developmental Biology
Director, Vanderbilt University Program
in Developmental Biology

Lab: 3144 MRB III Tel #: 3-8258
Office: 3140A MRB III Tel #: 3-8256
chris.wright@vanderbilt.edu

Research Interest: Pancreas Differentiation; Organogenesis; Body Plan Specification Left-Right Asymmetry; Stem Cell Differentiation.

Rotation Projects: Rotation projects can be selected from all kinds of high-resolution analyses (molecular, cell biological, genetic, biochemical) of the function of transcription factors and signaling molecules in controlling organogenesis, cell type differentiation and maintenance, as well as embryonic body plan formation and tissue morphogenesis. One part of the lab is

focused on obtaining a complete understanding of the transcription factor and intercellular signaling networks that control pancreas organogenesis. We made pioneering discoveries on 2 genes, *Pdx1* and *Ptf1a* [both encode transcription factors], which are vital for the first steps of pancreas formation, and in later formation of the organ's mature cells, e.g., insulin-secreting beta cells. The rules of normal pancreas formation and cell differentiation that are determined from our *in vivo* studies will aid in efforts to differentiate embryonic or adult stem cells towards beta cells, for cell-based diabetes therapy. Other important lab projects center on determining how intercellular signals control the formation of different regions of the early vertebrate embryo: the overall organization of its basic body plan, and its conserved left-right anatomical asymmetry. We use gain- and loss-of-function methods, as well as molecular epistasis manipulations and sophisticated genome engineering strategies, in the mouse, frog, and zebrafish.



Roy Zent M.D., Ph.D.

Associate Professor, Medicine,
Cell and Developmental Biology
and Cancer Biology

Lab: C-3210 MCN

Office: C-3210 MCN

roy.zent@vanderbilt.edu

Tel #: 2-4631

Tel #: 2-4632

Research Interest: Role of cell-extracellular matrix interactions in epithelial cell polarity.

Rotation Projects: The laboratory works on the basic role of integrins in epithelial cell biology. We utilize the kidney as a model system and perform biochemical techniques as well as cell biology and whole organ culture to understand the basic mechanisms whereby integrin-ECM interactions modify epithelial cell function.

A typical rotation in the laboratory would involve performing cell and biochemical based assays to investigate cell-ECM interactions of epithelial cells. In addition the student might determine abnormalities in function of the transgenic and knockout animals we have made.



Sandra Zinkel, M.D., Ph.D.

Assistant Professor, Medicine,
Cell and Developmental Biology,
and Cancer Biology

Lab: 548 PRB

Office: 548 PRB

sandra.zinkel@vanderbilt.edu

Tel #: 6-1800

Tel #: 6-1801

Research Interest: Understanding the mechanism by which normal and malignant cells regulate programmed cell death or apoptosis. Our current studies focus on a member of the BCL-2 family of proteins, BID. Deletion of BID in mice prolongs the life of blood cells, resulting in a fatal disorder closely resembling the human disease chronic myelomonocytic leukemia. Studies of BID-deficient bone marrow cells have revealed that BID plays a role in control of apoptosis, carried out at the mitochondria, and plays an additional role in cell cycle checkpoint control following DNA damage, carried out in the nucleus. BID, with its position at the interface of the DNA damage response and apoptosis, is well situated to play a key role in directing the outcome of a cell following DNA damage. In addition, we are looking at the role of other BCL-2 family members in regulation of blood cell development, stem cell function, and leukemogenesis, using mouse models.

Rotation Projects: Use molecular and cellular techniques to study the interplay between the DNA damage and apoptotic roles of BID. Additional projects involve the use of mouse models of leukemia to study the role of other BCL-2 family members in leukemogenesis. **1.** What is the role of BCL-2 family members in leukemogenesis? Evaluate the gene pathways in tumor cells from mouse models of leukemia. **2.** What is the role of the BCL-2 family in directing blood cell development and maintaining stem cell function? Evaluate the ability of bone marrow from mice deficient in Bcl-2 family members to differentiate into all blood lineages.

