

Participating Mentors

Sanford Program for Undergraduate Research

Applicants: List 3 mentors in the indicated spaces on your application. Please note that if there is a high demand for one specific mentor, you may be placed with one of your alternate choices or another mentor who fits your research interests.

Michelle Baack, M.D.

Sanford Children's Health Research Center

The effects of diabetes and obesity during pregnancy extend beyond those of the mother, increasing the risk of potentially devastating consequences in the developing fetus that include birth defects, neonatal disease and an increased risk of obesity, diabetes and cardiovascular disease even into adulthood. Our lab investigates the role of altered circulating fuels that cross the placenta and cause lifelong changes in the structure and function of the body in offspring of diabetic mothers. Most preventative measures focus on glucose control, but we have found that altered lipids may play a role in this abnormal developmental programming. Utilizing rodent models of diabetes and obesity during pregnancy, we explore other potential nutritional and therapeutic interventions to decrease the growing risk of complications in seen in this population of infants.

Subhash C. Chauhan, Ph.D.

Sanford Cancer Biology Research Center

The primary research interest of Dr. Chauhan's lab is to identify and characterize the diagnostic and therapeutic targets for gynecological malignancies. Main focus of our research group is to elucidate the regulatory mechanisms of cell-cell adhesion and anti-adhesion molecules that cause cancers. This research is aimed for the identification and characterization of biomarkers that aberrantly express or localize in cancer cells of reproductive tract in order to develop newer tools for early disease diagnosis. We are utilizing genomics and proteomics approach for identification of novel early diagnostic markers. Recently we have identified a novel trans-membrane mucin MUC13 which is highly over-expressed ovarian and pancreatic cancer cells. This may be potential biomarker for early cancer diagnosis as well as a good target for antibody guided targeted cancer therapy. The other research interest of Dr. Chauhan's lab is to develop novel radioimmunotherapy (RIT) and radioimmunodiagnostic (RID) modalities for the treatment and diagnosis of gynecological malignancies. This research project is aimed to develop novel genetically engineered antibody molecules with reduced immunogenicity, desirable size and altered pharmacokinetics for the RID/RIT applications. We are also developing a novel nanotechnology based gene therapy for ovarian cancer.

Jetty L. Duffy-Matzner, Ph.D.

Chair, Augustana College Chemistry Department

This work would involve the production of novel biologically active molecules, in particular we would center on compounds designed to have anti-microbial and anti-fungal properties. This organic synthetic research would center on the production of heterocycles from 1,3 –dipolar cycloadditions with nitrile oxides or nitrosilones as intermediates via intramolecular cycloadditions. The anti-fungal project would involve the synthesis of a novel class of compounds with hoped for increased biological activity. The chemosensor work would once again include the production of heterocycles

as comonomers for the development the next generation of fluorescent polymeric organic/inorganic hybrid chemosensor materials based on a molecular wire approach. These new materials will be developed to be highly specific and selective for metal contaminants in aqueous solutions such as ground water or biological systems. By combining recent advances in polymer synthesis and coordination chemistry, a new approach to selective metallopolymer chemosensors that uses photoinduced electron transfer and energy transfer to create a “turn-on” and “turn-off” fluorescent sensor response. We will be specifically working on turn-off chemosensors that are sensitive for iron and mercury ions. In time we would plan to further this research from in-solution to solid-state detectors of these toxic and environmentally important metal ions. These research projects would be an excellent opportunity for many students interested in both the chemistry and biology behind biomedical research.

Kristi Eglund, Ph.D.

Sanford Cancer Biology Research Center

Early and personalized diagnosis for breast cancer patients is crucial for optimizing treatments leading to long-term survival. It has been previously shown that cancer proteins can elicit an immune response in patients. These autoantibodies recognize tumor-associated antigens (TAA), autologous cellular proteins that are mutated, modified or aberrantly expressed in tumor cells. Because anti-TAA antibodies reflect and amplify the cellular changes associated with tumorigenesis, detection of anti-TAA antibodies in the sera of breast cancer patients may provide a non-invasive mechanism for the early detection of breast cancer. We took a molecular approach to identify potential tumor antigens that elicit an antibody response in breast cancer patients by generating a cDNA library (MAPcL), enriched with genes encoding membrane and secreted proteins, which are more likely to induce an antibody response in patients compared to intracellular proteins. Our laboratory has established an expression strategy to generate MAPcL Fc-fusion proteins that retain their native conformation and are efficiently recognized by patients’ antibodies. The long-term goal of my laboratory is to develop a blood test for breast cancer based on detecting a patient’s antibodies generated against cancer proteins. In addition, we have selected previously uncharacterized MAPcL genes that encode proteins overexpressed in breast cancers but have restricted expression in the normal essential organs, and we are characterizing the role of these MAPcL proteins in breast tumorigenesis.

Paul Eglund, Ph.D.

Augustana College Biology Department

www.augie.edu/dept/biology/Web/faculty/Eglund/Eglund.htm

Human dental plaque is a well-recognized example of a multi-species bacterial community. Dr Eglund’s research interest lies in the interaction between different bacterial species found in dental plaque and the study of communication between different species of bacteria in the plaque community. This communication includes cell-cell contact and metabolic interactions between organisms in the biofilm. Eglund’s current research focus include studies of communication that occurs between two members of the plaque community, *Veillonella atypica* and *Streptococcus gordonii*. When these organisms are growing together, *S. gordonii* induces expression of an alpha-amylase gene that is not expressed when *S. gordonii* is grown without *V. atypica*. Goals of the lab are to identify the mechanism of signaling that occurs between these species, identify the genes involved and determine the importance of amylase expression to development of the mixed-species community.

Zhiguang Guo

The Sanford Project

The goal of current research in Dr. Guo's laboratory is to evaluate and develop therapeutic approaches to treating type 1 diabetes by ameliorating autoimmunity and promoting beta cell regeneration. His current research interests are focused on: (1) understanding therapeutically relevant mechanisms of modulating the inflammatory response and stimulating beta cell regeneration in nonobese diabetic (NOD) mice, a mouse model of human type 1 diabetes; (2) targeting G protein-coupled receptor (GPR) 119 using small molecular agonists alone and in combination with dipeptidyl peptidase-4 (DPP-IV) inhibitors to stimulate beta cell regeneration; and (3) investigating human beta cell regeneration in vitro and in vivo.

Jennifer A. A. Gubbels, Ph.D.

Augustana College Biology Department

<http://www.augie.edu/dept/biology/Web/faculty/Gubbels/Gubbels.html>

The long-term goal of this research is to determine mechanisms of immune escape and metastasis in both ovarian cancer and endometriosis. Certain proteins expressed on the surface of ovarian cancer cells can alter the way that the immune system recognizes and eliminates these cells. The protein we are currently studying is called SUSD2, which is overexpressed by both ovarian and breast cancer tumors. Kristi Eglund's lab at Sanford has shown that this protein binds to Galectin-1, which has been known to cause apoptosis in T cells. In collaboration with Dr. Eglund, we have performed several different types of immunoassays to further characterize the immunomodulatory capabilities of this protein. In addition, we are also studying its potential role in metastasis of ovarian tumors. Another goal of this lab is to determine the subsets of immune cells that are present in the peritoneal fluid of endometriosis patients. Endometriosis can lead to ovarian cancer, therefore, the immune cell phenotype in these diseases may be similar.

Two recent papers written by Dr. Gubbels:

1. Gubbels JA, Gadbow B, Buhtoiarov IN, Horibata S, Kapur AK, Patel D, Hank JA, Gillies SD, Sondel PM, Patankar MS, Connor J. "Ab-IL2 fusion proteins mediate NK cell immune synapse formation by polarizing CD25 to the target cell-effector cell interface." *Cancer Immunol Immunother.* 2011 Jul 27
 2. Gubbels JA, Felder M, Horibata S, Belisle JA, Kapur A, Holden H, Petrie S, Migneault M, Rancourt C, Connor JP, Patankar MS. MUC16 provides immune protection by inhibiting synapse formation between NK and ovarian tumor cells. *Mol Cancer.* 2010 Jan 20;9:11.
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Carrie L. Hall, Ph.D.

Augustana College Biology Department

Maternally inherited commensal bacteria that obligatorily reside in gonadal tissue of arthropods can increase their prevalence in a population by manipulating host reproduction. Such manipulation has implications for the ecology and evolution of the host organism, and has been reported in all arthropod groups, including beetles. Endosymbiotic bacteria are frequently encountered in insects, and in some species, populations are strongly female-biased; however, a direct relationship between bacterial infection and sex ratio has not been determined for any species of *Nicrophorus*, including populations of the endangered *N. americanus*. The *Nicrophorus* burying beetles are well known for their unique reproductive behaviors that include sequestering vertebrate carrion for use as a food source for developing

offspring and providing bi-parental care. Preliminary data suggests, however, that male parental care is not obligate. This dynamic leads to questions such as, if given the chance to increase fitness, do males decide to leave a developing brood early in order to seek additional matings? If this is the case, could directional selection for female-biased sex ratios be driving polygyny in infected populations? This project will involve field surveys of five sympatric *Nicrophorus* species to determine population level sex-ratio dynamics at The Nature Conservancy's Tallgrass Prairie Preserve, as well as laboratory assays to screen for up to five species of endosymbiotic bacteria (e.g. *Wolbachia* and *Rickettsia*). Data from this study will inform our understanding of mating system selection in wild *Nicrophorus* populations, as well as provide information for husbandry of captive breeding populations of the critically endangered species.

Daniel R. Howard, Ph.D.

Augustana College Biology Department

<http://faculty.augie.edu/~dhoward/>

The goal of this research project is to understand how anthropogenic vibration, acting as an agent of sensory pollution, affects reproductive behavior in animals. The summer SPUR fellow will investigate the effects of wind energy-induced substrate-borne vibration on reproduction in *Nicrophorus americanus* (American burying beetle), an endangered insect species found in South Dakota. Students will use laser Doppler vibrometry to characterize the frequency range and intensity of vibrations induced in the substrate around individual wind turbines and across wind energy arrays and then model the vibrational environment at various scales using a geographic information system (GIS). To determine behavioral thresholds, students will sequester breeding pairs of *Nicrophorus americanus* into treatments subject to varying vibrational intensities corresponding to discrete Euclidean distances from the stimulus source as modeled in the GIS. Reproductive metrics for these treatments will be compared to controls to assess the influence of vibration on fecundity in the species. To experimentally determine the neural sensitivity thresholds to vibration in adult and larval *Nicrophorus americanus*, students will use extra-cellular neurophysiological techniques. Students will then create a physio-spatial model that predicts the effects of vibration on reproductive behavior across varying scales. Data from this SPUR summer research project will inform federal, state and tribal stakeholders on the potential effects of wind energy developments on reproduction in this critically endangered species, and address broader theoretical questions in behavioral ecology, neuroethology and psychoacoustics.

Recent papers by Dr. Howard:

1. Howard, D. R., Lee, N., Hall, C. L. and Mason, A.C. Are Centrally Displaying Males Always the Centre of Female Attention? Acoustic Display Position and Female Choice in a Lek Mating Subterranean Insect. 2010; in press with Ethology.
 2. Howard, D. R. and Hill, P. S. M. 2009. Grassland Botanical Structure Influences Lek Spatial Organization in *Gryllotalpa major* S. (Orthoptera: Gryllotalpidae). American Midland Naturalist 161: 206-218. April 2009.
 3. Howard, D. R., Mason, A. C. and Hill, P. S. M. 2008. Hearing and spatial behaviour in *Gryllotalpa major* Saussure (Orthoptera: Gryllotalpidae). Journal of Experimental Biology 211: 3613-3618. October 2008.
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Meena Jaggi, Ph.D.

Sanford Cancer Biology Research Center

The primary focus of Dr. Jaggi's research is to identify and evaluate the functional significance of cell-cell adhesion molecules known as cadherins and catenins in cancer progression and to understand the regulation of cadherin/catenin complex activity by Protein Kinase D signaling. In-depth knowledge of molecular mechanisms involved in signal transduction of human cancers is critical for the development of biomarker for early detection of cancer and rationalized structure-based drug designing. We have identified a novel interaction between E-cadherin/beta-catenin complex and

Protein Kinase D1 (PKD1), an important modulator of several kinase signal-transduction pathways in benign and malignant human diseases. Downstream signaling of the E-cadherin/beta-catenin and PKD1 interaction alters malignant phenotype of cancer cells. Another project investigates the alteration of signal transduction pathways in prostate, colon, breast and gynecological cancers using genomic and proteomic techniques.

DenYelle Baete Kenyon, Ph.D.

Sanford Health Disparities Research Center

Dr. Kenyon engages in social/behavioral research using quantitative and qualitative research methods to examine various adolescent health and development issues. Students would have the opportunity to be involved in several ongoing projects, which include adolescent reproductive health, American Indian ethnic identity and mental health, obesity prevention, and parent-adolescent relationships during the transition to adulthood. Students interested in adolescent health/development and health disparities are encouraged to apply.

Two recent papers written by Dr. Kenyon:

1. Kenyon, D. B., & Carter, J. (2011). Ethnic identity, sense of community, and psychological well-being among Northern Plains American Indian youth. *Journal of Community Psychology*, 39, 1-9.
 2. Kenyon, D. B., Sieving, R. E., Jerstad, S. J., Pettingell, S. L., & Skay, C.L. (2010). Individual, interpersonal, and relationship factors predicting hormonal and condom use consistency among adolescent girls. *Journal of Pediatric Health Care*, 24, 241-249.
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Mary Kinkel, Ph.D.

Sanford Children's Health Research Center

<http://www.sanfordresearch.org/ResearchCenters/SanfordChildrensHealth/KinkelLab/Index.cfm>

My lab studies developmental biology of the pancreas, using the zebrafish as a model. We are focused on the beta-cells of the pancreatic islet, which are responsible for secreting insulin to control blood sugar. We study genes that are important for patterning the endoderm, and for controlling the number of beta-cells that differentiate during development to make an appropriately-sized organ. Currently we are focused on the role of canonical Wnt signaling. To study Wnts, one of our strategies is to block Wnt signaling, or to activate Wnt signaling, at specific timepoints during endoderm patterning. The results of these disruptions are analyzed by performing in situ hybridization to detect changes in gene expression patterns of genes of interest. For example, analyzing the expression pattern of the *insulin* gene tells us whether a particular manipulation to Wnt signaling has altered the location of the beta-cells or has altered the number of beta-cells. In other studies, we are investigating the function of the endocrine pancreas in adult zebrafish. We study zebrafish that carry insulin mutations that cause neonatal diabetes in humans. For these studies, we analyze the histology of the adult pancreatic islets using immunostaining and electron microscopy. We measure beta-cell function by performing blood glucose tests and by measuring circulating insulin levels. If you are interested in these studies, see my webpage for more information.

Michael Kruer, M.D.

Sanford Children's Health Research Center

<http://www.sanfordresearch.org/ResearchCenters/SanfordChildrensHealth/KruerLab/Index.cfm>

The overall goal of the Kruer lab is to improve diagnostic and treatment options for children affected by neurological disease. Our group's primary focus is the characterization of new disease genes that lead to neurodegenerative diseases in children. We use a combination of massively parallel DNA sequencing, microarray analysis, human neuropathological studies, and biochemical and molecular biological approaches to understand the mechanisms that lead to cell death. An additional research focus is the identification of novel autoantibodies and emerging viruses that cause encephalitis in order to improve treatment outcomes for patients.

Mark Larson, Ph.D.

Augustana College Biology Department

<http://faculty.augie.edu/~mklarson/>

Platelets are a critical cellular component for maintaining normal blood flow and distribution by forming clots in response to blood vessel damage. We aim to elucidate some of the extracellular and intracellular signals that influence the activity of existing blood platelets and the formation of new platelets. Specifically, my lab has two main projects. The first is to determine what signals promote the formation of new platelets from platelet precursor cells called megakaryocytes. The second is to understand how dietary omega-3 fatty acids affect platelet function, a project that is run in collaboration with Dr. Greg Shearer at Sanford Research. Please visit Dr. Larson's Web site (above) for more information.

John Lee, M.D.

Sanford Cancer Biology Research Center

Dr. Lee's lab goal is to improve cure rates for the treatment of Head and Neck cancer. His lab uses a variety of basic science approaches to better understand mechanisms of invasion and mechanisms of immune related clearance of head and neck cancer. He works to translate these findings into the clinic by using a mouse model of head and neck cancer that they have developed. He also works to develop new therapies by the initiation of clinical trials for the patients that he treats with cancer.

Lance Lee, Ph.D.

Sanford Children's Health Research Center

<http://www.sanfordresearch.org/ResearchCenters/SanfordChildrensHealth/LeeLab/Index.cfm>

Research in Dr. Lee's Lab focuses on understanding cilia biology through identification and characterization of genes required for motile cilia function in mouse models of the pediatric disorder Primary Ciliary Dyskinesia (PCD). PCD affects approximately 1 in 16,000 newborn children worldwide. It results from dysfunction of motile cilia and flagella, and it is commonly characterized by chronic sinusitis (sinus infection), male infertility, situs inversus (a reversal of left-right asymmetry), and hydrocephalus ("water on the brain"). We use positional cloning approaches to identify mutations causing PCD in mouse models. We are also interested in functional characterization of the proteins encoded by the mutated genes, as well as the molecular mechanisms that regulate the function of motile cilia and flagella in the respiratory system, the reproductive system, and the brain.

Qiangrong Liang, M.D., Ph.D.

Sanford Cardiovascular Health Research Center

Research in my laboratory is devoted to understanding the molecular events and intracellular signaling mechanisms that underlie heart failure, a clinical syndrome that occurs in virtually all cardiovascular diseases and is one of the major causes of mortality in human population. Using an approach that combines cell culture system and genetic altered animal models, we are currently conducting research in three major areas: 1. Explore mechanisms of myocardial protection by caloric restriction and develop drugs that mimic the beneficial effects of caloric restriction. 2. Investigate why diabetic patients and animals are predisposed to heart failure and suggest mechanism-based approach to reduce the susceptibility. 3. Investigate why the anti-cancer drug doxorubicin can cause heart failure and how myocardial homeostasis can be restored by coordinately promoting survival mechanisms and blocking cell death pathways.

Steven Matzner, Ph.D.

Chair, Augustana College Biology Department

www.augie.edu/dept/biology/Web/faculty/Matzner/Matzner.htm

Epigenetic regulation refers to modifications to the chromatin or DNA that can affect which genes are expressed. Epigenetic regulation has recently emerged as an additional layer of regulation acting at the interface between the genotype and the environment, creating phenotypes sensitive to environmental inputs. The overall goal of this research is to look at epigenetic regulation in known water-related genes and determine if water stress induced epigenetic alterations occur for these genes in tomato. Specifically, we have use the recently completed tomato genome sequence to identify genes that are likely to be under epigenetic control and are known to have an impact on water-use-efficiency. Initially, we are looking to see if DNA methylation patterns are correlated with gene regulation changes in response to drought. Ultimately we will be looking at additional epigenetic mechanisms. With the threat of global warming and projections of higher drought frequency coupled with greater urban, recreational, and environmental demands on water resources; our need to understand how plants respond to their hydraulic environment has dramatically increased.

Jared R. Mays, Ph.D.

Augustana College Chemistry Department

<http://faculty.augie.edu/~jmays>

Consumption of fruits and vegetables has been associated with reduced incidence of cancer, especially in the gastrointestinal tract. The *Brassica* vegetables are rich sources of glucosinolates; evidence suggests that these phytochemicals are indirectly responsible for the observed cancer chemopreventive properties of cruciferous vegetables. Although glucosinolates themselves have no known bioactivity, they are converted to isothiocyanates through by the enzyme myrosinase; many of their corresponding organic isothiocyanates are well-documented chemopreventive agents. In particular, the isothiocyanate L-sulforaphane is the primary chemopreventive agent found in broccoli. The Mays research group is interested in exploiting the myrosinase/glucosinolate enzymatic processes as a means of achieving selective drug or drug candidate activation. This multi-disciplinary research program bridges the boundaries between chemistry and biology and offers students the opportunity for training in several fields of research. Multiple student projects are available with differential and cross-emphases including multi-step organic synthesis, cell culture, molecular biology, enzymology, and computational modeling.

A recent paper written by Dr. Mays:

1. Mays, J.R.; Hill, S.A.; Moyers, J.T.; Blagg, B.S.J. "The synthesis and evaluation of flavone and isoflavone chimeras of novobiocin and derrubone." *Bioorg. Med. Chem.* **2010**, *18*, 249-266.
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Cecelia Miles, Ph.D.

Augustana College Biology Department

The Miles lab studies the dynamics and mechanisms of differential nuclear migration in the preblastoderm *Drosophila* embryo, which involves using confocal microscopy in *Drosophila melanogaster* to examine nuclear migration during mitotic cycles 10-14 in both fixed and live embryos. Timing and control of cellular migration is a fundamental question in developmental biology. During early development *D. melanogaster* embryos undergo 13 nearly-synchronous mitotic divisions before cellularization occurs. During this syncytial period nuclei migrate from the yolky center out to the periphery of the developing embryo and form a monolayer. Fellows will use two inbred fly lines that have fast-maturing fluorescent proteins as live-cell nuclear markers, as well as fixed specimens, to examine aspects of the differential recruitment of nuclei to the embryonic surface in these two fly lines with different numbers of nuclei at the blastoderm stage.

Keith Miskimins, Ph.D.

Director, Sanford Cancer Biology Research Center

Our laboratory examines the molecular mechanisms that regulate proliferation and survival of cancer cells. Neoplastic cells undergo metabolic reprogramming that may make them sensitive to drugs that target specific metabolic pathways. We have found that certain metabolism-modulating compounds are able to selectively promote cell cycle arrest and cell death of cancer cells. We are examining the molecular pathways that mediate these effects and characterizing the effects of the compounds in preclinical mouse models of cancer.

Timothy O'Connell, Ph.D.

Sanford Cardiovascular Health Research Center

Dr. O'Connell's lab goal is to understand the role of adrenergic receptors in the pathogenesis of heart failure. His lab is studying the physiologic role of alpha-1-adrenergic receptors in preventing heart failure using transgenic mouse models as well as the basic biochemical and biophysical aspects of alpha-1-adrenergic signaling in cardiac myocytes.

David A. Pearce, Ph.D.

Director, Sanford Children's Health Research Center

Vice-President, Sanford Research

Neuronal Ceroid Lipofuscinoses is caused by autosomal recessive inheritance of mutations in the genes CLN1-10. Juvenile Neuronal Ceroid Lipofuscinosis (Batten Disease) is the most common neurodegenerative disease of childhood resulting from mutations in CLN3. This devastating disease results in loss of vision around 5 years of age, followed by slow decline in cognitive and motor function and a progressively increased frequency of seizures. Batten disease is

universally fatal. The Pearce lab uses cell biology, biochemistry, molecular genetics, and neuroscience to investigate the underlying pathological mechanisms of Batten disease.

Kyle J. Roux, Ph.D.

Sanford Children's Health Research Center

<http://www.sanfordresearch.org/ResearchCenters/SanfordChildrensHealth/RouxLab/Index.cfm>

Defects in a cellular structure called the nuclear envelope are associated with a myriad of diverse diseases that clinically manifest during the first two decades of life and include muscular dystrophy, cardiomyopathy, lipodystrophy, dystonia, neuropathy, skeletal defects, and progeria. The nuclear envelope is situated at a critical juncture in the cell, both intimately associated with the genome and responsible for connecting it to the rest of the cell. While it is clear that mutations in genes encoding protein constituents of the nuclear envelope underlie these diseases, the exact mechanisms remain largely unknown. Our laboratory investigates the structure and function of the mammalian nuclear envelope in health and disease.

Alexei Savinov, M.D.

Sanford Project

The development of human type 1 diabetes (T1D) involves autoimmune destruction of insulin-producing β -cells of the pancreatic islets. This destruction is done by T cells. In order to kill β -cells, T cells first should travel from the bloodstream into these pancreatic islets. This process of activated lymphocytes migration from the bloodstream into the underlying target tissue is called homing. Homing takes place in the small blood vessels called capillaries. Homing of diabetogenic T cells into pancreatic islets consists of several steps of interaction between a migrating T cell and cells comprising the capillary wall – endothelial cells. In essence, during their homing, autoimmune T cells, freely disseminated in the bloodstream, first attach themselves to the endothelial cells of pancreatic capillaries, and then make their way through the endothelial cell layer into the underlying islets. Our previous studies using mice of non-obese diabetic (NOD) strain have demonstrated that homing of autoimmune T cells into the islets depends on a certain molecule - T cell proteinase, called MT1-MMP. Unfortunately, the potentially serious side-effects of these drugs prevented small-molecule synthetic inhibitors of MT1-MMP from being used in clinical trials in T1D patients. Our proposed study will explore a novel, alternative approach for regulating T cell MT1-MMP, and thus, impeding the homing of diabetogenic T cells. We believe that reduced level of homing will support the restoration of the β cell mass in the pancreas, and at least partial reversal of T1D.

Gregory Shearer, Ph.D.

Sanford Cardiovascular Health Research Center

We investigate the role of fat metabolism in cardiovascular disease. Generally fat is considered to promote cardiovascular diseases such as atherosclerosis and heart failure however some fats, such as polyunsaturated fatty acids, are associated with lower risk. Polyunsaturated fatty acids are unique because they are used by cells in the body to generate signals, or hormones, that regulate fundamental physiology such as inflammation, blood vessel reactivity, and heart muscle contraction. Unfortunately there are many conflicting reports on how these fatty acids work. We think there are two reasons: first, most studies focus on a single polyunsaturated fatty acid (arachidonate) and so miss the biology of complex mixtures that occur in real life, and secondly because there is an important reservoir of these

hormones that has not been characterized well. This reservoir is found in lipoproteins which are fat packages transported in the blood. While lipoproteins such as HDL and LDL are well known as the 'good' and 'bad' cholesterol, their effect on cardiovascular disease has surprising overlap with the function of the hormones they transport, providing another mechanism by which fat metabolism contributes to disease. We use animal and human studies to investigate these dynamics.

William C. Spanos, M.D.

Sanford Cancer Biology Research Center

A subset of head and neck cancer is caused by human papillomavirus (HPV). We found that an immune response is required for the clearance of HPV positive cancer in mice during treatment with chemotherapy and radiation. My lab is currently focused on determining the components of the immune system important for this tumor clearance. One exciting treatment utilizes the CD40 and CD40 ligand interaction to improve tumor removal with decreased conventional treatment. We are determining how this interaction improves immune recognition of the tumor and looking at the best mechanism for drug delivery.

A recent article written by Dr. Spanos:

1. Spanos, W.C. et al. Immune response during therapy with cisplatin or radiation for human papillomavirus-related head and neck cancer. *Arch. Otolaryngol. Head Neck Surg* **135**, 1137-1146(2009).
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Kamesh Surendran, Ph.D.

Sanford Children's Health Research Center

<http://www.sanfordresearch.org/ResearchCenters/SanfordChildrensHealth/SurendranLab/Index.cfm>

Nephrons are tubular structures composed of an epithelial monolayer, and are the functional units of the mammalian kidney. One of our interests is to understand the cellular and molecular mechanisms that regulate nephron formation by using mouse models of cystic kidney diseases, and cell culture systems that model aspects of tubule formation. In other words we wish to determine the genes and cell processes that ensure that the correct diameter, length and thickness of the different nephron segments are formed during kidney development. A second interest is to decipher the molecular mechanisms that specify the different cell fates of the collecting ducts in the kidney. How do cells in the collecting ducts with the same genetic composition gain different characteristics and functions as they mature?

Two recent papers written by Dr. Surendran on these two topics:

1. Surendran K, Selassie M, Liapis H, Krigman H, Kopan R. Reduced Notch signaling leads to renal cysts and papillary microadenomas. *J Am Soc Nephrol*. 2010 May;21(5):819-32.
 2. Surendran K and Kopan R. Chromatin mediated mechanisms of epithelial differentiation. *J Am Soc Nephrol*. 2011 Jul;22(7):1208-12.
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Peter Vitiello, Ph.D.

Sanford Children's Health Research Center

<http://www.sanfordresearch.org/ResearchCenters/SanfordChildrensHealth/VitielloLab/Index.cfm>

The Vitiello lab investigates growth, injury, and repair in the developing lung. Premature infants exposed to supplemental oxygen (hyperoxia) often develop Bronchopulmonary Dysplasia (BPD), a form of chronic lung disease characterized by impaired alveolar growth. To investigate the molecular basis of BPD, we utilize multiple approaches including tissue culture, animal models, and biochemical methods. We specifically focus on the role that thiol oxidoreductase proteins, such as thioredoxin, play in regulating redox-sensitive developmental pathways. The overall goal of our research is to apply biochemical, molecular, cellular, and system biology approaches to understand signals which regulate normal lung development and how environmental stresses, such as hyperoxia, affect these signals and alter the human condition.

Seasson P. Vitiello, Ph.D.

Augustana College Biology Department

The focus of Dr. Vitiello's research is to use the model organism *Saccharomyces cerevisiae* to study the human disease cystinosis, an autosomal recessive pediatric lysosomal storage disorder characterized by the accumulation of cystine in the lysosomes of patient cells. It is caused by mutations in *CTNS*, which encodes the lysosomal cystine transporter Cystinosin. Although the causative gene and the primary biochemical defect have been identified, it is still unclear what pathways could be contributing to the cell death that is observed in cystinosis patient cells. The yeast model is useful for identifying pathways that have been altered due to lack of a functional cystine transporter by studying phenotypes that occur when the ortholog of Cystinosin, Ers1p, is absent in *ers1-Δ* cells. By exploiting the relative ease of yeast genetic manipulation and the organism's highly annotated genome, Dr. Vitiello and her students use molecular genetics, functional genomics, cell biology, and biochemistry to understand the role of Ers1p in the cell.

Jill M. Weimer, Ph.D.

Sanford Children's Health Research Center

<http://www.sanfordresearch.org/ResearchCenters/SanfordChildrensHealth/WeimerLab>

The research objective of the Weimer lab is to understand novel mechanisms controlling the development of the cerebral cortex, with an emphasis on events regulating neural stem cell proliferation and neuronal differentiation. Disruption in various aspects of neuronal proliferation and placement have been shown to contribute to an array of neurodevelopmental migration defects, including leptomeningial heterotopias, subcortical band heterotopias, and periventricular heterotopias. These defects can lead to severe mental retardation, developmental delays and moderate to severe epileptic seizures and are thought to contribute to developmental disorders such as Lissencephalies, Autism, and Schizophrenia. Our current work focuses on understand the developmental role of two proteins: 1) Myristoylated alanine-rich C-kinase substrate protein (MARCKS), an actin-cross-linking protein and prominent cellular substrate of PKC, which is required for proper proliferation and placement of cortical neurons in the developing cerebral cortex and 2) CLN6, the protein mutated in variant late-onset neuronal ceroid lipofuscinosis (vLINCL), a childhood neurodegenerative disorder resulting from aberrant neuronal cell loss and pathological accumulation of lysosomal autofluorescent storage material in the central nervous system.

Casey Wright, Ph.D.

Sanford Cardiovascular Health Research Center

The focus of the Wright lab is the development of a new alpha1-AR antagonist for the treatment of hypertension and benign prostate hyperplasia. Clinical trials have shown that blockade of alpha-1 adrenergic receptor activation can lead

to increased incidence of heart failure in patients with hypertension and/or benign prostate hyperplasia. Current projects include localization of alpha1-AR subtypes in vascular and prostate smooth muscle cells versus cardiac myocytes and the signal transduction differences between alpha1-AR at the plasma membrane and a1-AR inside the cell.

Haotian Zhao, Ph.D.

Sanford Children's Health Research Center

One of the common childhood cancerous diseases is medulloblastoma (MB) that usually forms in the cerebellum at the lower back part of the brain. MBs tend to spread to other parts of brain and the spine in early stages of illness, which necessitates preventative irradiation of the brain and spine, except in very young children, chemotherapy and surgery. However, patients going through these conventional treatments have a high risk of developing long-term neurological defects including hormonal, hearing and learning impairment, whereas patients with tumors that relapse and/or spread to other sites have very poor outcome due to resistance to therapies. Knowledge of what causes tumor cells to grow and migrate may hold the key to the development of innovative strategies to more safely and effectively prevent MB growth and spreading. In our research, we will utilize mouse models of MB to examine the migratory behaviors of tumor cells. Specifically, we would like to find out how tumor cells migrate, how cytoskeletal elements affect their migration and what signals attract or repulse tumor cells. We are also interested in evaluating different therapeutic agents targeting tumor growth and invasion in our model system. Our study will shed light on the mechanisms governing the spreading of MB.