

Meet the Faculty of the 2023 Summer Child Health Research Internship

*University of Colorado School of Medicine, Department of Pediatrics
Children's Hospital Colorado*

1) Bruce Appel, PhD (Developmental Biology)

We investigate how the nervous system forms during embryonic development, with the hope that that such information will help us repair nervous systems damaged by disease or injury. We use zebrafish embryos as a model system because they are transparent and develop outside the mother, permitting us to use time-lapse microscopy to watch neural cells as they migrate and differentiate into neurons and glia. We also study the effects of mutations that disrupt neural development in zebrafish, with the expectation that they will help us understand the basis of genetic diseases that cause neurological disorders in humans. Finally, we are using zebrafish to learn how to promote regeneration of neural cells that are lost as a consequence of birth defects.

2) Emily Bates, PhD (Developmental Biology)

We study the molecular mechanisms underlying human genetic disorders. For example, we use human genetics to find a mutation that may cause a genetic disorder. We make that same mutation in a mouse or a fly and then we figure out how the mutation could lead to clinical manifestations. We have used this approach to uncover interesting biological principles like how cells signal to one another during embryonic development. Right now, our projects focus on structural birth defects, brain defects, and neurodegeneration.

3) Tim Benke, MD, PhD (Neurology/Neuroscience)

The Benke lab studies the long-term consequences of early life seizures on the developing brain. These changes may not necessarily result in epilepsy but are known to lead to cognitive and behavioral impairments. Understanding the molecular mechanisms leading to cognitive and behavioral impairments is meant to segue into new and novel treatments for all causes of intellectual disability and even autism. Students working in the Benke lab will use animal models of early life seizures to probe these underlying molecular mechanisms. Techniques that will be used include electrical recordings in living rat brain slices, stereotactic injection of interesting antisense viral vectors, electroencephalogram (EEG) and video monitoring in freely moving rats, western blotting and immunohistochemistry.

4) Richard KP Benninger, PhD (Bioengineering/Barbara Davis Center)

The islets of Langerhans are multi-cellular micro organs located in the pancreas which play a central role in maintaining blood glucose homeostasis through secretion of hormones insulin and glucagon. We study the regulation of insulin and glucagon secretion and specifically how different cellular populations within the islet interact to enhance the overall regulation of hormone secretions. We follow an approach whereby precise perturbations in signaling activity are introduced into a well-

defined population of cells in the islet, utilizing transgenic mouse models, microfluidics and optogenetics. Quantitative confocal and two-photon microscopy, together with biochemical and physiological approaches, are applied to measure the effect of these perturbations across the islet and how they manifest in the overall islet dynamical response. Predictive mathematical models are then used to describe these results. We are applying this approach to understand several aspects of how islet connectivity is important for glucose homeostasis and how it is disrupted during the development of diabetes. The overall goal is to be able to manipulate cell-cell communication within the islet to improve the regulation of insulin and glucagon secretion and to optimize islet transplantation approaches to treat and cure diabetes.

5) Petter Bjornstad, MD (Endocrinology and Diabetes)

Dr. Petter Bjornstad is a NIH/NIDDK, NIH/NHLBI, AHA, JDRF and Boettcher funded translational researcher. Diabetic kidney disease remains the leading cause of kidney failure and dialysis in the US. Bjornstad lab (<http://bjornstadlab.org>) focuses on metabolic and hemodynamic mechanisms underlying the development of kidney disease in youth with type 1 and type 2 diabetes, with an emphasis of renal physiology studies, mechanistic clinical trials, mathematical modeling, advanced functional imaging (MRI and PET imaging) as well as research kidney biopsies to better understand structural and functional determinants of kidney disease development.

Dr. Bjornstad has authored over 160 peer reviewed manuscripts and several in high impact journals including NEJM, JCI, Circulation, Lancet Diabetes and Endocrinology, Diabetes Care, Diabetologia, and American Journal of Kidney Disease. Dr. Bjornstad is the principal investigator of several ongoing studies that enroll participants across the lifespan, and students will have the opportunity to gain exposure to a variety of state-of-the-art translational methods, study populations and disease types (obesity, type 1 diabetes, type 2 diabetes, polycystic kidney disease). The research group also has a wet lab that specializes in measurements of iohexol and p-aminohippurate to quantify glomerular filtration rate and renal plasma flow. Therefore, students will have the opportunity to pick bench, translational or clinical research projects according to their interest.

6) Kristen Boyle, PhD (Nutrition)

In our lab, we study molecular metabolism in umbilical cord stem cells to identify factors that may predispose children to developing obesity or diabetes later in life. We know that mothers' health and pregnancy exposures, such as obesity, diabetes, and environmental pollutants, can increase the child's risk for later disease. However, in humans, little is known about how these exposures may influence child outcomes. We employ various metabolic and molecular biology techniques to identify and characterize epigenetic mechanisms for altered metabolism in umbilical cord mesenchymal stem cells (MSCs), collected at birth. Current projects include: 1) the role of maternal obesity-induced epigenetic signatures on AMP-activated protein kinase signaling and mitochondrial respiration, 2) the role of cell cycle exit on adipogenesis and adipocyte metabolism, and 3) characterizing associations between maternal, MSC, and offspring metabolic phenotypes using multi-omics approaches. Students working in our laboratory will be exposed to a variety of metabolic and molecular biology techniques, including mitochondrial respiration, radiolabeled substrate metabolism, qPCR, luciferase gene

reporter assays, lentiviral transduction, and will have the opportunity to tailor their research toward metabolism, molecular biology, and/or statistical analyses using existing datasets.

7) Martin Breuss, PhD (Human Genetics and Genomics)

We study the phenomenon of 'genetic mosaicism' where some but not all cells within a tissue harbor a unique mutation. It is commonly understood in the context of cancers, where specific mutations within a progenitor cell may cause the disease. However, 'mosaic mutations' occur in every cell of our body during embryonic development and aging. Our laboratory is interested in understanding this phenomenon in term of its general impact on human health and its origin during early development. Current projects include: 1) analysis of mosaicism of the parents that may result in the transmission of disease-causing mutations to multiple children (related to the recurrence risk of 'sporadic' disease); 2) analysis of 'neutral' mosaicism without functional impact that marks the development of cells and allows us to reconstruct development—a feat that is otherwise impossible in humans. In our laboratory, we combine human genetics research where we collaborate with clinical researchers, molecular biology to develop and perform detection assays, and computational approaches to process and analyze a variety of generated data. Find out more about our research and our team at www.breusslab.org.

8) Laura Brown, MD (Neonatology)

Intrauterine growth restriction (IUGR) is a problem that affects 8% of all pregnancies and occurs as a result of placental insufficiency, which restricts nutrient and oxygen delivery to the fetus. In the Brown laboratory, we study the physiological, molecular, and cellular mechanisms that link fetal nutrient availability during pregnancy to skeletal muscle growth and development. We aim to understand how low muscle mass in the IUGR fetus predisposes that individual for long term health problems including sarcopenia, insulin resistance and diabetes. We perform physiological studies using large animal (sheep) models to measure nutrient uptake rates across the fetal hindlimb. We also determine how nutrient supply affects skeletal muscle-specific metabolism using stable isotopic tracer and metabolomic techniques. Finally, in vivo physiological studies are combined with in vitro experiments using muscle tissue and primary fetal myocytes to understand adaptations to nutrient restriction that occur at the cellular level. The overall goal of the Brown lab is to optimize body composition and growth in the IUGR fetus and neonate, which will ultimately preempt the complications of IUGR related to low muscle mass.

9) Child Health Research Biostatistical Core

Claire Palmer, MS

Suhong Tong, MS

Lori Silveira, PhD

Laura Pyle, PhD (Acting Director)

The Child Health Research Biostatistical Core provides statistical support to child health researchers in a variety of disciplines. Our collaborative research includes work in diverse areas such as endocrinology, neonatology and cancer research. Our individual research in statistical methods and applications includes genomics, longitudinal modeling and machine learning. Students who are

placed with our group will have the opportunity to work with multiple faculty members and to participate in study design, creation and execution of analysis plans, data analysis and writing manuscripts. They will also be exposed to statistical programming and have the opportunity to develop communication skills in a collaborative research setting, including working with other students. We will engage with students to tailor their time in the program to their specific interests and encourage them to produce work for presentation at a scientific meeting.

10) eXtraordinary Kids Program

Nicole Tartaglia, MD, MS

Shanlee Davis, MD, MSCS

The eXtraordinary Kids program is focused on improving the lives of youth affected by sex chromosome aneuploidies through excellent clinical care and research. 1 in 400 babies are born with an extra or missing sex (X or Y) chromosome, but only a handful of centers around the world are conducting research to learn more about these conditions and how best to care for them. Our clinical-translational research program applies multiple methodologies (intervention trials, retrospective and prospective observational studies, neurodevelopmental studies, translational science, secondary data analyses, surveys, qualitative methods, etc.) to answer important clinical questions with the goal of improving patient outcomes in these genetic conditions, with a focus on neurodevelopmental, endocrine, and health outcomes. Our interdisciplinary team includes Developmental Pediatrics (Dr. Tartaglia), Pediatric Endocrinology (Dr. Davis), neuropsychology, psychology, genetic counseling, speech and occupational therapy, and study coordinators. Students play a crucial role on our team with a project suited to their experience and goals. In addition to identifying and completing a project, students will have the opportunity to assist with patient visits for our ongoing studies focused on neurodevelopment and early cardiometabolic health in infants and toddlers with sex chromosome aneuploidies.

11) Nick Foreman, MD (Hematology/Oncology)

The goal of the Foreman laboratory is to better understand the biology of pediatric brain tumors. In particular, we are interested in identification of biological characteristics of these tumors that have clinical relevance, such as drug sensitivity, diagnosis and prognosis. To identify novel clinically relevant factors, we screen patient surgical samples using gene expression microarray tools. Gene expression microarray technology allows us to simultaneously measure tens of thousands of genes in a tiny sample of tumor, an extremely powerful and efficient approach that provides huge amounts of novel data. Analysis of this microarray data is performed by our laboratory, and students working in the Foreman lab would be encouraged to be involved with this. Students would then further explore the results of microarray analyses using protein expression analyses including flow cytometry, Western blot and immunohistochemistry.

12) Craig Forester, MD, PhD (Hematology/Oncology)

The Forester lab studies a unique approach to understanding how early blood development is controlled. Our lab seeks to understand why the bone marrow in certain children stops functioning leading to failed blood maturation and production; a collection of diseases known as the Inherited

Bone Marrow Failure Syndromes (IBMFS). Historically, much focus has been devoted to the consequences of mutations in DNA and RNA giving rise to changes in gene expression. However, mutations discovered in these children focus on the protein synthesis machinery and delineates a clear need to study how genes can be controlled by translation in early hematopoiesis. Why mutations in the translation machinery leads to failed blood production is still poorly understood. Our lab seeks to determine how this process is able to quickly and specifically target RNA messages for translation and how this becomes dysregulated with mutations found in children with IBMFS. To this end, we have developed novel tools to identify waves of new gene expression shortly after cells encounter an array of pharmacologic inhibition and growth stimuli using mass spectrometry. Our lab employs mouse models and tissue culture models that recapitulate red blood cell production to identify specific sets of expressed genes that are aberrantly expressed with patient mutations. We then utilize RNA sequencing techniques to delineate nucleotide and structural elements encoded in the mRNA message that mechanistically yields insight into how specific mRNA are recognized by the protein synthesis manner to allow normal blood production. The overall goal of the lab is to identify how the ribosome can rapidly and specifically translate specific mRNA to allow for normal blood production in response to stresses such as growth and injury and how this process is impaired with mutations we discover in children.

13) Masanori Hayashi, MD (Solid Tumor Program)

The main goals of the Hayashi lab is to investigate the biology of pediatric sarcoma metastasis in order to develop specific anti-metastasis therapy, as well as develop biomarkers to identify who will fail conventional therapy and relapse with metastasis. We have a robust program focused on liquid biopsies, such as circulating tumor cell and circulating tumor DNA detection in pediatric sarcoma patients. Our preclinical investigation projects focus on specific targets to interrupt the metastatic cascade in high grade sarcomas, as well as strategies to modulate the immune environment in sarcomas to enhance the effect of various immunotherapies.

14) Ken Maclean, PhD (Clinical Genetics and Metabolism)

The Maclean lab studies the etiology and pathogenesis of cystathionine beta-synthase deficient homocystinuria (HCU), Down syndrome and a range of hepatic disorders. Our research uses a range of transcriptomic and proteomic platforms coupled with, biochemical, behavioral, genetic and molecular approaches to study mouse models of these diseases with a view towards delineating pathogenic mechanisms and the rational design of novel treatment strategies. With regard to HCU we have generated a novel transgenic mouse model of the disease and using behavioral analysis, hippocampal microarrays and proteomic analysis have elucidated a number of novel pathogenic mechanisms that we have subsequently confirmed in human HCU tissue samples. This work has led to the discovery of a novel treatment for HCU, for which an FDA funded clinical trial is currently running at the Children's hospitals of Denver and Philadelphia.

15) Shelley Miyamoto, MD (Cardiology)

Pediatric Cardiovascular Research Laboratory (PCRL)

Shelley Miyamoto, MD

Anastacia (Tasha) Garcia, PhD

Brian Stauffer, MD
Kika Sucharov, PhD

Stephanie Nakano, MD
Katie Chatfield, MD, PhD

The mission of this multidisciplinary research group is to perform translational and molecular research focused on children with heart disease. Expertise within the laboratory spans the cardiovascular field from pediatric to adult disease and from basic molecular biology to cardiovascular physiology and clinical translation. Our research utilizes a pediatric and adult heart tissue bank as well as animal and primary cell culture models. Our current projects include study of: (1) the study of mitochondrial function in the failing hearts of children with cardiomyopathy and single ventricle heart disease; (2) regulation of phosphodiesterase expression and activity in pediatric heart failure; (3) tissue and circulating microRNA profiling; and (4) myocyte mechanics of the failing heart. Currently, treatment of pediatric heart failure is largely extrapolated from the results of trials performed in adults with heart failure. Our results demonstrate that children with heart failure have a unique molecular adaptive response that warrants specific targeted therapy. Students working in our laboratory would be exposed to a variety of molecular biology techniques including RT-PCR, Western blotting, various activity assays and basic biostatistics.

16) Jean Mulcahy Levy, MD (Hematology/Oncology)

I have a broad background in oncology research with specific training and expertise in pediatric brain tumors. My research is focused on the development of new brain tumor therapies with a special interest in therapy resistance mechanisms. One goal of my lab is to determine how to utilize autophagy, a cellular recycling program, to improve therapy for patients with central nervous system (CNS) tumors. As a Fellow and early investigator, I laid the groundwork for targeting autophagy in CNS tumors, identifying the connection between BRAF pathway alterations and autophagy addiction in brain tumors. My work demonstrated the effectiveness of autophagy inhibition when tumors become resistant to BRAF/MEK inhibitors. A *first in pediatrics multi-institutional trial* of autophagy inhibition based on my work opened in 2019 in collaboration with the Pediatric Brain Tumor Consortium and Novartis. We also recently published the largest series of paired pediatric CNS tumor samples used to investigate other resistance mechanisms to BRAF/MEK inhibitors. Together, we are using this work as a basis for additional work in my lab focused on the development of novel, rapidly translatable treatments for pediatric CNS tumors. Our work has continued to identify biologically driven therapies for AT/RT and other tumors using genome and pharmacologic screening. Here we combine these techniques and identified CDK7 as a key vulnerability in AT/RT. We will build on these findings to investigate the mechanistic relationship of CDK7 and the SWI/SNF complex in AT/RT and the potential for inhibiting CDK7 alone and in combination with available AT/RT chemotherapies.

17) Kristen Nadeau, MD, MS (Endocrinology and Diabetes)

Dr. Kristen Nadeau is a Pediatric Endocrinologist and the Director of Research for Pediatric Endocrinology, who performs clinical-translational research on reducing long-term complications of pediatric obesity, type 1 diabetes, type 2 diabetes, and prediabetes. The focus of her group's work is better understanding early contributors to cardiovascular disease (CVD), including mechanisms of insulin resistance, cardiovascular and muscle dysfunction. Dr. Nadeau's lab performs human studies

including measures of insulin sensitivity and pancreatic function (IV hyperinsulinemic clamps with isotopes, hyperglycemic clamps, arginine stimulation tests, hypoglycemic clamps, mixed meal tolerance tests and oral glucose tolerance tests); assessment of liver, visceral and muscle fat deposition via MRI/MRS; heart function via resting and exercise-stress echocardiography and cardiac MRI; measures of endothelial function, arterial stiffness, blood flow and arteriosclerosis via MRI and other vascular techniques; exercise function via VO₂max and physical activity monitoring; sleep and circadian rhythm monitoring; carbohydrate oxidation via metabolic cart; and muscle mitochondrial function via exercise MRI/MRS. Dr. Nadeau's research also includes several large longitudinal studies, including studies in youth and young adults with type 2 diabetes (TODAY), a trial to improve pancreatic function in youth and adults with prediabetes/early type 2 diabetes (RISE), and medication trials to reduce cardiovascular disease and improve insulin sensitivity in youth and young adults with type 1 diabetes. Finally, Dr. Nadeau's work includes several studies of American Indian youth with obesity, including a gestation diabetes prevention project. Thus, students would have a rich exposure to clinical/translational research in youth with obesity and diabetes.

18) Maki Nakayama, MD, PhD (Barbara Davis Center for Childhood Diabetes)

Type 1 diabetes is an organ-specific autoimmune disease caused by lymphocytes that mistakenly destroy cells in the pancreas, called "beta cells." Pancreatic beta cells secrete insulin to regulate the blood glucose level, and as a result of beta cell destruction, patients develop hyperglycemia. We have discovered that a peptide contained in insulin itself is an essential antigen targeted by autoreactive lymphocytes causing type 1 diabetes in the animal model. If we can identify such essential antigens required for the development of human type 1 diabetes, blocking or regulating lymphocytes targeting those antigens will enable us to prevent diabetes. Thus, one of our current goals is to define antigen specificity of human autoreactive lymphocytes that target pancreatic beta cells in patients having type 1 diabetes and to elucidate whether and how antigen specificity determines the fate of lymphocytes (i.e. pathogenic or regulatory). Techniques used in in my laboratory include molecular biology techniques (e.g. high-throughput sequencing), cellular engineering (e.g. transfection), and immunoassays (e.g. ELISA) using both animal models and human samples. Our long-term goal is to understand the molecular mechanism of beta cell autoimmune-destruction and ultimately to develop robust diagnostic and therapeutic tools for type 1 diabetes.

19) Eva Nozik, MD (Critical Care/Developmental Lung Biology)

The overall mission of the Nozik lab is to understand the mechanisms responsible for the development of diseases of the lung and blood vessels in infants and children, and to develop better tools to detect and treat these lethal diseases. Our work focuses on an important antioxidant enzyme, extracellular superoxide dismutase (EC-SOD), which is highly expressed in the lung and vessels under normal conditions and is impaired in diseases such as acute lung injury and pulmonary hypertension. We predominantly utilize a series of genetically engineered mouse strains with alterations in EC-SOD expression to test how EC-SOD modulates inflammation and vascular injury in disease models. Ultimately our long-term goal is to provide a foundation for the development of novel diagnostic tools and cell-targeted antioxidant therapies to treat life-threatening pediatric lung diseases including acute lung injury and pulmonary hypertension.

20) Sarit Polsky, MD (Barbara Davis Center for Childhood Diabetes)

Dr. Polsky is the director of the Pregnancy & Women's Clinic at the Barbara Davis Center (BDC) for Diabetes. The BDC is a specialty center for type 1 diabetes. The main focus of Dr. Polsky's work is to improve the health of women with diabetes through clinical research trials and excellence in clinical care. Pregnancies associated with type 1 diabetes are increased risk of adverse health outcomes, such as fetal loss (miscarriage, stillbirth), abnormal fetal size (babies born too large or too small), pre-term delivery, cesarean delivery, gestational hypertensive disorders, and babies being born with low glucose (sugar) levels, low oxygen, and/or needing admission to the neonatal intensive care unit. In order to reduce the risks of the adverse outcomes, it is recommended that women obtain and maintain normal to near-normal blood glucose levels throughout pregnancy, which is challenging for women on intensive insulin therapy. Dr. Polsky's research examines how advanced diabetes technologies (insulin pumps, continuous glucose monitors, and artificial pancreas systems) impact glycemic control and health outcomes in pregnant women with type 1 diabetes. Dr. Polsky also examines how some adverse maternal outcomes in pregnancy (such as preeclampsia) impact long-term cardiovascular and renal health in women with type 1 diabetes. Students working with our group will take part in research team meetings, learn about and participate in data collection and reporting, learn responsible research conduct for human clinical trials, and may have an opportunity to help prepare abstracts for scientific meetings.

21) Tamim Shaikh, PhD (Human Genetics and Genomics)

The Shaikh lab investigates the genetic basis of neurodevelopmental and neuropsychiatric disorders. Their main focus is on identifying the genetic mutations that underlie multiple congenital anomaly syndromes (MCAS), which includes phenotypes like global developmental delay, intellectual disabilities and deficits, other neurological phenotypes such as seizure disorders, behavioral issues, etc., cranio-facial differences, cardiac defects and/or defects in other tissues and organs. Dr. Shaikh's group uses state-of-the-art high resolution genomic technologies including high-throughput short and long-read sequencing and optical genome mapping to identify genetic mutations in these patient samples. They have identified novel, pathogenic mutations in several candidate genes and are now beginning to analyze the effect of mutations in these genes using functional genomics approaches in cellular and animal models, including patient-derived induced pluripotent stem cells.

22) Stacey L. Simon, PhD (Pulmonary & Sleep Medicine)

Dr. Simon is a pediatric sleep psychologist with a research focus on mechanisms underlying the negative cardiometabolic consequences of insufficient sleep and circadian misalignment in adolescents. Short sleep duration and circadian misalignment are believed to contribute to health problems, including obesity and insulin resistance. Adolescence is a time of chronic short sleep duration and a propensity for delayed circadian phase. However, imposed early school start times mean that adolescents are often unable to avoid going to bed late, yet are woken early in the morning and out of synchronization with their circadian rhythm. Dr. Simon's current projects are evaluating the impact of increased sleep duration on insulin resistance in short-sleeping adolescents; and examining associations between sleep and glycemic control in youth with type 1 diabetes.

23) Lori Sussel, PhD (Islet Biology/Diabetes)

Our research program combines advanced molecular biology techniques with mouse embryology, genetics and physiology to understand the molecular mechanisms that contribute to pancreatic islet function in health and disease. We are interested in understanding how the pancreas forms during fetal development and how insulin-producing beta cell function is maintained in the adult. These studies have identified several novel proteins and molecular mechanisms that are involved in islet cell fate decisions during pancreas development; human mutations in these genes cause neonatal diabetes. We have also identified several regulatory pathways that are important for maintaining the function and/or identity of the insulin-producing beta cell in mice and humans. Current research in the lab continues to explore how pancreas development and function are regulated by transcriptional and epigenetic modifications. In addition, the lab has embarked on a set of ground-breaking studies to identify and characterize pancreas-specific long non-coding RNAs (lncRNAs) and alternative splicing events in physiological and pathophysiological conditions, including diabetes and pancreatic cancer.

24) Johan Van Hove, MD, PhD (Medical Genetics and Metabolism)

The field of medical genetics is rapidly advancing with the advent of whole exome sequencing. My laboratory examines disorders that affect the mitochondrion. The mitochondrion contains about 1000 proteins, and performs a very large number of biochemical reactions. We examine patients with genetic disorders of mitochondrial enzymes with an emphasis on either disorders of energy generation, or disorders of neurochemistry such as infantile seizures. We identify new genetic causes of disease, we then examine the way in which the gene leads to the symptoms, and develop new treatments focused on the specific cause. Students have been involved in either the identification and proof of a new genetic cause for a mitochondrial disease, or in the development of a new treatment for a specific neurological disorder affecting babies.

Another part of the laboratory examines new treatments for a rare condition called nonketotic hyperglycinemia. This condition causes infantile seizures and cognitive delays and has no effective treatment. We have developed a mouse model and are evaluating several new treatments for this condition, to which the student can participate.

25) Sujatha Venkataraman, PhD (Peds Neuro-Oncology)

Dr. Venkataraman's lab research is focused on identifying novel therapeutic strategies for a fatal brain tumor in children called DIPG (Diffuse Intrinsic Pontine Glioma). Treatment options for DIPG are limited as chemotherapy is largely ineffective and surgical resection is not possible due to the tumor's location in the pons, a region of the brain responsible for multiple vital functions like heartbeat and respiration. Ionizing radiation is the current standard of care for DIPG but provides only a temporary relief as the tumor becomes resistant to radiation at recurrence. Our lab is currently studying the radiation resistant mechanisms at the single cell level to identify new targeted treatments that are directed towards enhancing radiation efficacy in DIPG. In addition, Dr. Venkataraman lab have also been working on immunotherapy, both CAR-T cell and antibody-based therapies to effectively target DIPG, which is otherwise a refractory disease.

26) Rajeev Vibhakar, MD, PhD, MPH/MSPH (Hematology/Oncology)

The Vibhakar lab is interested in studying the Biology of childhood brain tumors and in particular Medulloblastoma and ATRT. We have several projects underway. The overarching theme is to understand how chromatin biology and epigenetic changes regulate tumors and how these may be targeted for therapeutic strategies.

27) Christine Vohwinkel, MD, PhD (Critical Care)

Our lab is housed in the Division of Critical Care. The lab is focused on acute lung injury-its clinical manifestation, the acute respiratory distress syndrome (ARDS), which is a highly-morbid critical illness characterized by acute onset of hypoxemia, pulmonary edema, and chest X-ray with bilateral opacities. We are specifically interested how metabolism is regulating inflammation that is central of the pathogenesis of acute lung injury and how the lung epithelium “communicates” with macrophages. We work with several mouse models of acute lung injury (ventilator induced acute lung injury, acid aspiration and pneumonia) and in cell cultures (mouse cells and cells donated by human patients). Other techniques we use in our lab are PCR, Western Blotting, ELISA and enzyme activity assays and histology.

28) Stephanie Wesolowski, PhD (Neonatology)

Our lab studies how altered nutrient supply programs fetal metabolism and how these changes may persist after birth and increase susceptibility to adult metabolic disease. Our primary research is aimed to understand the effects of intrauterine growth restriction (IUGR) on liver metabolism and function using integrative approaches in physiology and metabolism combined with novel molecular techniques in cell biology, epigenetics, and metabolomics. Current studies in our research program are focused on understanding the mechanisms for the early activation of fetal hepatic glucose production and development of hepatic insulin resistance, specifically the role of reduced glucose versus oxygen supply to the fetus, both key features of placental insufficiency and resulting IUGR. This is important in understanding why IUGR offspring have increased susceptibility to diabetes across their lifespan. We also have projects investigating the effects of maternal high fat diet and obesity on offspring metabolism, specifically the early development of non-alcoholic fatty liver disease (NAFLD) and immune cell reprogramming.

29) Clyde Wright, MD (Neonatology)

Dr. Wright’s lab investigates how inflammatory insults encountered in the perinatal period contribute to various morbidities observed in babies born prematurely. Through studying cell-specific innate immune pathways, we hope to identify therapeutic targets to improve the outcomes of these vulnerable patients. We use in vitro and in vivo approaches to evaluate the impact of manipulating innate immune signaling setting of clinically relevant stressors (infection, oxidative stress) in hopes of attenuating inflammatory injury. Students will learn the scientific method, including developing and testing a hypothesis, and will be mentored through data analysis and presentation.