American Academy of Pediatrics

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Research Committee Report

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In This Issue

2019 Marshall Klaus Neonatal-Perinatal Medicine

On behalf of the American Academy of Pediatrics (AAP), Section on Neonatal-Perinatal Medicine (SoNPM) and this year's Klaus Neonatal-Perinatal Research Fund supporters, we would like to congratulate the recipients of the 2019 Marshall Klaus Neonatal-Perinatal Research Award! The Research Committee received 37 very strong applications and all applicants deserve recognition for their already strong bios, outstanding mentors, and exciting projects. Thanks to our sponsors, this year we are able to fund the top 12 ranked fellows with the $5,000 research award. The money will be used towards supplies etc. to support the proposed research project.

Special thank you to the award sponsors

Klaus Bench or Clinical Research Award

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Health Services Research Award

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Klaus Bench or Clinical Research Awardees

Maria Estefania Barbian - Emory University

Title: *Effect of Maternal Diet During Pregnancy on Offspring's Gut Development and Response to Intestinal Injury*

Mentor: Rheinallt Jones

Personal Statement: As a future Neonatologist and physician-scientist, my goal is to optimize the outcomes of our most vulnerable patients by developing interventions to prevent necrotizing enterocolitis. My interest in this disease began during my Pediatric residency, where I cared for premature infants, some of whom died from necrotizing enterocolitis. My patients, along with their families, left a lasting impression that has driven me to study this devastating disease. While the etiology of necrotizing enterocolitis is multifactorial, microbial dysbiosis plays an important role in its pathophysiology. Over the last decade, research has shed light on the intricate relationship between the gut microbiome and human health. My interest in the gut microbiome and its relationship to neonatal intestinal disease led to me seek mentorship from Dr. Rheinallt Jones, who is

an expert in the field of host cell and probiotic microbe interactions. Through the guidance of my mentor, the members of his lab, Dr. Patricia Denning and Dr. Ravi Patel, I developed a murine model to study the antenatal effects of maternal diet on the neonatal microbiome and gut development. Since my research interest is in necrotizing enterocolitis, my research specifically focuses on studying the impact of antenatal diet on the offspring's capacity to respond to gut inflammation and injury.

Abstract: Microbial dysbiosis is an important determinant of health. In premature infants, microbial dysbiosis plays an important factor in the pathophysiology of NEC. Unfortunately, premature infants often have microbial dysbiosis and a limited diversity of their gut microbiome. Thus, my research focuses on studying gut and microbiome development. Our preliminary results show that a maternal diet of butyrate protects the adolescent offspring from severe colonic injury in a colitis model. We hypothesize that antenatal consumption of high amounts of butyrate (through a high fiber diet or probiotic supplementation) alters a mother's microbiome diversity, which is passed on to her offspring and has protective effects on the offspring's gut health by enhancing epithelial and immune cell development. The Marshall Klaus Award will allow me to begin the next step in my research which is to study the effects of antenatal diet on neonatal gut injury using a murine model of necrotizing enterocolitis.

Brittany E. Butler – University of Colorado Denver

Title: *The Role of Perinatal Acetaminophen Exposure in Acute Lung Inflammation and Abnormal Pulmonary Development*

Mentor: Clyde Wright

Personal Statement: Despite our advancing knowledge of the risk factors and pathogenesis of bronchopulmonary dysplasia (BPD), we have no safe and effective treatment. However, understanding the inflammatory signaling pathways that lead to abnormal lung development holds the promise to new therapies that will prevent this devastating disease. This is why I joined Dr. Clyde Wright's lab as a second-year pediatric resident and have continued this work in my neonatology fellowship. The overarching goal in our lab is to identify how innate immune NFκB signaling leads to an injurious proinflammatory response in the neonatal lung. I am excited to use the lab techniques I have learned so far studying the expression of proinflammatory cytokines in the neonatal lung and to acquire new skills as I begin to study the effects of acetaminophen in the developing lung. As clinicians are now frequently using acetaminophen in the NICU for patent ductus arteriosus (PDA) closure, I am driven by the potential of this new work to better inform clinical decisions as we strive to provide the best possible care to preterm infants and their families.

Abstract: Acetaminophen (APAP) use in the NICU for closure of the patent ductus arteriosus (PDA) has markedly increased over the last several years. However, acetaminophen used to treat the PDA in preterm infants may be associated with an increased risk for bronchopulmonary dysplasia (BPD). While the potential mechanisms underlying pulmonary APAP toxicity are unknown, APAP-induced liver injury has been well-studied. In response to supratherapeutic APAP exposure, the hepatic cytochrome P450 2E1 (CYP2E1) enzyme converts APAP to its toxic

metabolite N-acetyl-para-benzo-quinone imine (NAPQI). Accumulation of this toxin leads to multiple deleterious effects, including mitochondrial dysfunction and death within the hepatocyte. Released mitochondrial DNA then stimulates Toll-like receptor 9 (TLR9), leading to downstream NFκB activation, proinflammatory cytokine expression, and liver injury. Preliminary data from our lab demonstrate that the murine lung also expresses CYP2E1 and TLR9 at baseline. Thus, the metabolism of APAP into toxic metabolites and activation of pro-inflammatory pathways may also occur in the developing lung. Our hypothesis is that APAP activates CYP2E1 and downstream TLR9/NFκB pro-inflammatory signaling in the developing lung leading to acute inflammation and abnormal development.

Sarah Nicole Cilvik – University of Colorado Denver

Title: *The Role of Exogenous Glucagon in Growth and Metabolism in Late Gestation Fetal Lambs*

Mentor: Paul Rozance

Personal Statement: I am a second-year Neonatal-Perinatal Medicine fellow at the University of Colorado with a research interest in fetal physiology, metabolism, and the hormonal control of development. I have been driven by my love and fascination of infants and science since a very young age, and by my freshman year in college, I was certain I wanted to pursue a career in neonatology. It was through this love of Neonatal-Perinatal Medicine that I discovered my passion for research in Developmental Biology. My past research experiences have explored the effects of the pesticide malathion on zebrafish development (undergraduate honors thesis at Davidson College), as well as the role of fibroblast growth factor signaling in cardiac remodeling in the adult mouse heart (PhD in Developmental Biology at Washington University in St. Louis). The combination of my past research experiences with my clinical training in pediatrics led to an interest in the maternal-fetal relationship, specifically with relation to hormonal control of fetal metabolism and growth in the setting of growth restriction or maternal diabetes. As such, I identified the University of Colorado as the ideal location to complete my fellowship training under the mentorship of Dr. Paul Rozance, a leader in the field of fetal physiology. My research will investigate the impact of chronic hyperglucagonemia, which has been demonstrated in models of growth restriction and other types of fetal stress, on the growth and metabolism of a normally growing late gestation fetal lamb. This project will introduce novel and innovative intellectual concepts to further the understanding of fetal growth and nutrient processing and identify new targets for intervention in the setting of IUGR. The Marshall Klaus Neonatal-Perinatal Research Award will be instrumental to promote my successful transition from Neonatal-Perinatal Medicine Fellow to an independent physician scientist in the field of fetal physiology and metabolism.

Abstract: Intrauterine growth restriction (IUGR) is associated with the development of diabetes, obesity, and cardiovascular disease in adulthood. Glucagon concentrations are increased in IUGR, but limited research has examined the direct role of glucagon in fetal metabolism. The glucagon receptor is expressed in multiple relevant target tissues, including the β-cell, liver, placenta, and adipose tissue, and glucagon has been shown in the adult to have broad metabolic effects through regulation of glucose, amino acid, and lipid metabolism. Our central hypothesis is that in the fetus, glucagon acts as a master regulatory hormone that coordinates fetal growth through a variety of metabolic processes. Studies will utilize an established experimental model of chronically catheterized normally growing late gestation fetal lambs to measure placental nutrient transfer, fetal nutrient metabolism and fetal growth. Fetal lambs will receive a direct IV infusion of glucagon or vehicle control for 8-10 days. Aim #1 will test the hypothesis that chronic hyperglucagonemia will induce glycogenolysis and/or gluconeogenesis in the fetal liver. Aim #2 will test the hypothesis that chronic hyperglucagonemia will stimulate fetal amino acid oxidation, decrease protein synthesis, and result in poor fetal growth. Investigation will involve a combination of both in vivo and in vitro studies. These studies will have significant impact on the field by determining, for the first time, how glucagon regulates fetal metabolism and growth in vivo. It is critical to further delineate hormonal regulators of fetal growth and metabolism in order improve our understanding of IUGR and identify potential therapeutic targets aimed at reversing this phenotype and/or later sequelae.

Julie Ann Dillard – Nationwide Children's Hospital

Title: *Effect of Nitric Oxide and Endothelial Cell-Smooth Muscle Cell Cross-talk on the Regulation of Phosphodiesterase 3 in Pulmonary Artery Smooth Muscle Cells*

Mentor: Bernadette Chen

Personal Statement: I am a second-year neonatology fellow at Nationwide Children's Hospital in Columbus, OH. My main research focus is neonatal pulmonary hypertension. Following residency, I spent time overseas as an active duty pediatrician in the US Air Force. During this time, I took care of many term newborns who became critically ill from persistent pulmonary hypertension of the newborn, necessitating transport to a NICU. I developed a special interest in caring for these patients, and eventually applied to complete a neonatal-perinatal medicine fellowship. While my interest in pulmonary hypertension initially stemmed from these patient interactions, it eventually led me to work in the basic science lab of Dr. Bernadette Chen, where I have worked for the past two years of my fellowship. Specifically, we are investigating the regulation of phosphodiesterase 3 by the nitric oxide pathway, and its role in pulmonary hypertension in neonates. I believe that through research we have the potential to impact not only the lives of our current patients, but also of many future generations of patients. My career aspiration is to continue basic science research as a physician-scientist with the ultimate goal of discovering new and effective therapies in the treatment of neonatal pulmonary hypertension.

Abstract: Persistent pulmonary hypertension of the newborn (PPHN) is an important cause of morbidity and mortality in neonates. Often used in combination with hyperoxia, the pulmonary vasodilator inhaled nitric oxide (iNO) is the only FDA-approved therapy for PPHN, although up to 40% of patients are non-responders. In the pulmonary vasculature, NO increases cGMP levels, promoting vasodilation. cGMP competitively inhibits phosphodiesterase 3 (PDE3), thereby decreasing cAMP hydrolysis and further enhancing vasodilation. However, in animal models, NO treatment has been shown to increase PDE3 expression and/or activity and has been postulated to be the reason for rebound pulmonary hypertension upon iNO withdrawal. Furthermore, it has been reported that that addition of a PDE3 inhibitor to iNO enhances pulmonary vasorelaxation. AMP-activated protein kinase (AMPK), a critical regulator of energy homeostasis with downstream effects on NO synthase, has been shown to be regulated by PDE3 isoforms in other cell types and is implicated in PH pathogenesis. We hypothesize that NO regulates the AMPK pathway by modulating PDE3 activity in a cell-type specific manner in the pulmonary vasculature, thereby altering pulmonary artery smooth muscle cell and pulmonary microvascular endothelial cell function.

Kristen Nicole Noble - Vanderbilt University Medical Center

Title: *Defining the Roles of Fetal and Maternal Macrophages in Group B Streptococcal Ascending Chorioamnionitis*

Mentor: David Aronoff

Personal Statement: As a current trainee in the Neonatal-Perinatal Medicine Fellowship program at Vanderbilt University, I am committed to pursue a career in academic medicine with a focus on basic and translational research for a very simple reason: I am determined that health status disparities be minimized. I am an African-American woman and mother who, statistically speaking, is at significantly higher risk of poor health outcomes overall. Unfortunately, despite advancement in health care capabilities, women and infants of color and those of low-income families are more likely to experience worse maternal and neonatal outcomes including significant long-term disability and even death. My intent, as an upcoming physician-scientist in Neonatology, is to contribute to the fundamental understanding of conditions that result in significant morbidity and mortality of neonates. My science career path started with training in cell biology at Meharry Medical College and Vanderbilt University, where I learned to appreciate mechanistic regulation of basic science processes. I then moved to the University of Tennessee Health Science Center in Memphis, TN where I completed my training in general Pediatrics and solidified my clinical interest in caring for the smallest and most fragile babies in the NICU. I have fused my passion with basic science and neonatology to study a problem directly related to maternal-child health, elucidating fundamental mechanisms of fetal membrane macrophages involved in bacterial chorioamnionitis, a significant driver of adverse pregnancy outcomes, particularly in women of color. My long-term plan is to use my experiences from my clinical practice in the NICU to guide my laboratory work towards answering questions that will have the greatest impact on improving neonatal outcomes. My hope is that ultimately, this work will help meet the goal of ensuring that all women, regardless of background, have the

best possible chance of having healthy babies with promising futures.

Abstract: I have the distinct opportunity of training under Dr. David Aronoff to study the role(s) of both fetally- and maternally-derived fetal membrane macrophages in ascending bacterial chorioamnionitis. Group B Streptococcus (Streptococcus agalactiae, GBS) is a leading bacterial cause of stillbirth, early onset neonatal sepsis (EOS), and meningitis, which commonly result from the in utero inoculation of the fetus before delivery. How GBS ascends from the vagina to infect the fetus is not well defined and represents a critical early step in disease pathogenesis. GBS infects the fetal membranes (causing chorioamnionitis or CAM) en route to the fetus, even in the absence of membrane rupture. Macrophages, with the potential for pathogen recognition and effector function, are a key component to the fetal membrane innate immune system. Interestingly, the fetal membranes include both macrophages derived from the mother (decidual macrophages) and the fetus (placental macrophages, aka Hofbauer cells), though the unique roles for these genetically distinct cells are not well defined. I hypothesize that maternal and fetal macrophages contribute differentially to host protection and to the inflammatory responses to invasive pathogens such as GBS. With the help of the Marshall Klaus Award, I will use an in vivo mouse model of ascending GBS infection in which I can differentially deplete maternal or fetal macrophages to assess for the impact on the natural course of infection. Ultimately, understanding the immunological processes occurring in the fetal membranes will help identify actionable targets of immune system support to better protect against chorioamnionitis.

Leeann Rebecca Pavlek – Nationwide Children's Hospital

Title: *Cardiovascular Contractility Deficits Due to Adverse Perinatal Exposures*

Mentor: Lynette Rogers

Personal Statement: I am currently a second year Neonatal-Perinatal Medicine fellow at Nationwide Children's Hospital in Columbus, Ohio. My clinical interest has always been neonatal cardiology and heart development, and I have been able to conduct basic science research in this field during my fellowship under the mentorship of Dr. Lynette Rogers. Other than structural heart disease, cardiac complications of prematurity are not well-recognized in the neonatal period, but premature birth is associated with higher rates of several cardiovascular morbidities later in life. I am studying the pathophysiology underlying the fetal and neonatal origins of adult cardiovascular disease, using a mouse model to discover molecular and functional changes that can be detected early in life. My project focuses on the increased rates of heart failure seen in former premature infants. My overall objective is to impact the clinical care of patients by identifying methods for early detection of infants at high-risk for heart disease in adulthood, which will allow for targeted surveillance, possible prevention, and prompt treatment of cardiac morbidities. Ultimately, my goal is to become an independent physician-scientist conducting basic and translational research studying the developmental origins of cardiovascular disease.

Abstract: Premature infants have a higher incidence of heart failure, ventricular systolic dysfunction, and cardiac hypertrophy in young adulthood when compared to those who were born full-term. This pathophysiology is triggered, in part, by common adverse exposures including maternal systemic inflammation and postnatal therapeutic hyperoxia use. A mouse model has shown pathologic changes in proteins involved in cardiac contractility and significant in vivo contractile dysfunction in adult mice with a history of perinatal inflammation and hyperoxia exposures. We hypothesize that these abnormalities in heart structure and function can be detected much earlier in life, in the embryonic and neonatal periods. Our initial studies are focused on myosin heavy chain (MHC), which is an important component of the cardiac contractile apparatus. The two isoforms of MHC, α and β, are expressed in specific ratios throughout heart development. Alterations in the α:β-MHC ratio have been associated with heart failure and cardiac hypertrophy. microRNA-208a and -208b regulate the differential expression of α- and β-MHC, and therefore may control the pathologic changes seen after exposure to inflammation and hyperoxia. We are also investigating if alterations in calcium handling within the cardiomyocyte contribute to contractile dysfunction in this population. Through this project, we will develop a better understanding of the link between perinatal exposures and long-term cardiovascular morbidities to allow for more comprehensive clinical care of these patients.

Cynthia Nichole Schreiner- Children's Hospital Colorado

Title: *Placental Proteins and Prematurity*

Mentor: Theresa Powell

Personal Statement: I am currently a fellow in the Neonatal-Perinatal fellowship program at Colorado Children's Hospital. Throughout my career, clinical research has been an integral part in my overall development, but it was not until I started to study at Colorado Children's that the placenta, an organ which has recently received attention for being more than just a bystander during pregnancy, sparked my interest. Under the direction of Drs. Theresa Powell and Thomas Jansson, I developed and received IRB approval for a novel project that hypothesizes that the mortality and morbidities seen with prematurity today is due to the loss of factors secreted from the placenta to the fetus following discontinuation of the umbilical circulation with preterm delivery. We are currently undergoing active recruitment of mothers with infants 23 to 32 gestational weeks and collecting both cord blood at birth and neonatal blood at 2-3 days of life to evaluate this hypothesis. Once all samples have been collected we will use a proteomic platform that will evaluate >1300 proteins to determine if proteins are secreted from the placenta at varying gestational ages. If this is seen, we will next evaluate if their concentration is significantly decreased following delivery. With the funding provided by this grant, my goal is to continue to advance my career in academics through strengthening my written and laboratory skills, ultimately leading to future investigations in medical research.

Abstract: Extreme prematurity (23 to <28 weeks) continues to be a leading cause of infant morbidity and mortality and increases the risk of significant long-term sequelae such as cerebral palsy, respiratory and neurodevelopmental disease. Emerging evidence from animal experiments indicates that factors secreted by the placenta are critical for normal fetal organ development. One fundamental difference between fetal and postnatal life is the instantaneous discontinuation of the umbilical circulation. As a result, the premature infant is deprived of placental factors potentially critical for fetal organ development. We recently reported that 341 proteins are secreted by the term human placenta into the fetal circulation. Using bioinformatic approaches, we found that these proteins were involved in neurogenesis (18%), angiogenesis (11%), inflammatory processes (19%), embryogenesis (6%), and lung development (1%) implicating a role in fetal organ development and maturation. However, it is currently unknown if these proteins are expressed earlier in gestation and if the preterm neonate can produce these proteins once separated from the placental circulation. We hypothesize that 10 or more placentally derived proteins with actions associated to angiogenesis, lung, eye, and/or brain development decrease significantly (>50%) in the premature infant following delivery. Using the SOMAlogics proteomic platform, we intend to determine the change in the concentration of >1300 proteins between fetal life (represented by umbilical vein blood at delivery) and the preterm infant (23 to <32 gestational weeks) 48-72 hours after birth to identify candidate proteins. We subsequently will confirm these candidate proteins are placentally derived by determining the differences in levels of candidate proteins in umbilical vein and artery plasma using the SOMAlogics proteomic platform as well as assessing placental expression using qPCR and western blot. Our current proposal represents an important first step to identify proteins secreted by the human placenta that may be essential for the development and maturation of multiple organs in the premature infant and could potentially lead to therapies that improve preterm infant health.

Julie Du Thai - Brigham and Women's Hospital

Title: *The Role of Intestinal Inflammation on the Premature Intestinal Microbiome and Postnatal Growth*

Mentor: Katherine Gregory

Personal Statement: My early training in basic science led me to develop a keen interest in how the microbiome influences health outcomes during early life. This interest was magnified while I was a pediatric resident at UCSF Benioff Children's Hospital Oakland. Now, as a neonatology fellow at Boston Children's Hospital, I am working to develop new means to study overall gut health during infancy, with a focus on how the microbiome influences clinical outcomes, such as preterm infant growth. Preterm infant growth outcomes, and in particular, growth failure, is one of the most common problems among preterm infants, impacting half of all preterm infants born today. Not only is this a common problem, it is one that has been persistent across decades, despite improved nutritional strategies. Focusing on gut health and intestinal biology, my overall goal is to identify novel therapeutic targets to optimize growth outcomes in this vulnerable population. Under the mentorship team led by Katherine Gregory, PhD at Brigham and Women's Hospital and Harvard Medical School, I will analyze fecal and urine biospecimens as well as clinical metadata from a previously hospitalized group of preterm infants to assess the influence of intestinal inflammation and the microbiome on growth outcomes. The Marshall Klaus Award will not only aid in the successful completion of this ambitious project but will also enable my goal in transitioning to an autonomous physician scientist.

Abstract: Premature infants, who account for approximately 10% of all births in the United States, are disproportionately at risk for a unique set of pathologies, primarily due to immature and underdeveloped organ systems. This results in not only short-term, but also long-term morbidities that can endure throughout the infant's lifetime. Of particular significance is sub-optimal postnatal growth, a problem most notable among very low birthweight (VLBW) infants. Postnatal growth failure (PNGF), defined as discharge weight less than the 10th percentile, has been estimated to affect approximately half of VLBW infants. Severe PNGF, discharge weight less than the 3rd percentile, affects one quarter of these infants. This early growth faltering has been known to extend across the lifespan and has recently been associated with poorer neurodevelopmental outcomes in later childhood. Though PNGF is a major problem in the preterm population, the etiology and mechanism remain unclear. Despite accounting for illness and optimizing nutrition strategies over the years, PNGF rates continue to be high, suggesting that other physiologic characteristics of the premature infant are involved. Intestinal inflammation has been shown to be associated with suboptimal growth outcomes in many pediatric and adult populations, though its association with preterm postnatal growth outcomes remain unexplored. Many studies have shown the importance of the infant intestinal microbiome in specific health outcomes, including immune development, inflammation regulation, nutrient absorption, metabolism and growth. My overall goal is to investigate how intestinal inflammation impacts

postnatal growth in premature infants. I hypothesize that intestinal inflammation is a mechanism by which the intestinal microbiome influences preterm postnatal growth. I will leverage previously collected and analyzed biospecimens (fecal and urine specimens), as well as clinical metadata to assess the influence of intestinal inflammation and the microbiome on preterm infant growth outcomes. I will add an additional measure of intestinal inflammation (fecal calprotectin measured via ELISA), to more fully assess these associations. This work will not only advance our understanding of the premature intestinal microbiome, specifically its interactions with intestinal inflammation and postnatal growth, but will also contribute to the development of new microbial therapies that may optimize premature infant growth, representing a critically important opportunity to improve the health of preterm infants.

Christopher Stephen Thom- Children's Hospital of Philadelphia

Title: *Computational and Biochemical Investigation of Tropomyosin 1 and Other Genetic Regulators of Platelet Development*

Mentor: Benjamin Voight

Personal Statement: My long-term goal is to become a productive physician-scientist engaged in clinical neonatology, laboratory research, and teaching. I aim to use computational methods to rigorously analyze human genetic data, and test computationally-driven hypotheses using cellular and molecular approaches. Ultimately, I want to use genetic insights to make translational discoveries that improve human health. My current focus aims to identify genetic determinants of hematopoiesis. I used machine learning to identify putatively active genetic variation that impacts human platelet traits, and validated my findings in cellular models. Specifically, I found that Tropomyosin 1 deficient stem cells yield at least twice as many blood cells as controls. Going forward, I will (i) use computational analysis of human genetics and functional genomics data to identify modulators of hematopoiesis, (ii) develop cellular models and model systems to study modulators of hematopoietic development, with TPM1 as an exemplar candidate, and (iii) use these two experimental workflows to identify novel translational gene targets and therapeutic approaches to ameliorate hematopoietic disorders. Support from a Marshall Klaus Perinatal Research Award will help me pursue this research.

Abstract: Allogeneic platelet transfusions can treat thrombocytopenia, but associated complications and potential inadequacy of the donor-derived platelet supply has sparked interest in generating transfusable platelets in vitro. A better understanding of the genetic mechanisms augmenting hematopoiesis and megakaryocyte (MK) yield are necessary and could increase the cost-effectiveness of in vitro cultures. Using available genome-wide association data sets, I applied a machine-learning framework to identify genomic features enriched at established platelet trait associations and score variants genome-wide to identify biologically plausible gene candidates. I found that high-scoring SNPs marked relevant loci and genes, including an expression quantitative trait locus for Tropomyosin 1 (TPM1). CRISPR/Cas9-mediated TPM1 knockout in human induced pluripotent stem cells (iPSCs) unexpectedly enhanced early hematopoietic progenitor development, identifying a novel strategy to augment in vitro hematopoiesis and MK production. My focus is now to explore related biochemical mechanisms and pursue other genetic leads that may synergize with TPM1-deficiency to further augment in vitro hematopoiesis.

Beth Israel Deaconess Neonatology Education Research Award

Kinsey Marie Roth - University of Pittsburgh Medical Center

Title: *Letting Parents be Parents: A Medical Education Curriculum to Facilitate Parent Bedside Engagement and Family Integrated Care*

Mentor: Karena Lawrence

Personal Statement: I am a second year Newborn Medicine fellow at the University of Pittsburgh Medical Center as well as a candidate in the Master of Medical Education program. A native of Colorado, I attended the University of Colorado as an undergraduate and later as a graduate student at the school of medicine. During these years, I cultivated a passion for education and an appreciation of its power as a social determinant and vital aspect of health. In medical school, I immediately joined our leadership, education, and advocacy track and dove into an issue rife with complex interplay of social determinants: insurance coverage. Under the mentorship of Dr Mark Earnest and Dr Steve Federico, I worked with the Colorado Consumer Health Initiative during the construction of Colorado's statewide health insurance marketplace. It was important for me that those who were uninsured, underinsured, or not receiving their due benefits (eg-children eligible but not yet covered by the Children's Health Insurance Program) would have easy access to information and guides to get them through the process. This experience led me into pediatrics, and I completed my general pediatrics residency at the University of Pittsburgh Medical Center. During residency I carried out a scholarly project entitled "Roadmap to the NICU." Using key informant interviews of current NICU parents, I created a graphic-heavy workbook for families to track progress through the NICU and have a visual sense of closing in on the requirements for discharge. This extended time interviewing parents made me keenly aware of opportunities to improve the support of our NICU families. For me, taking care of my patient's family is part of providing care for my patient. Through education of staff and caregivers, my career goal is to advance the application of family integrated care practices and improve parental-self efficacy in the NICU.

Abstract: More than many subspecialty fields in pediatrics, neonatal-perinatal medicine is deeply involved in the development and health of our patient's families in addition to the patient themselves. Specifically, admission to the neonatal intensive care unit (NICU) represents a traumatic event to parents, a disruption in caregivers' identify formation as parents, and an independent health risk for the infant after discharge. Mitigating these negative effects is most evident when interventions focus on the principles of parental engagement, empowerment, and education collectively referred to as "family-integrated-care." Internationally, entire units that are structured around this care model demonstrate improvements in parental stress, weight gain, breastfeeding and length of stay. However, this data represents countries where families are available for 8-10 hours daily at the bedside and physical space is built to

accommodate a family's long-term presence. Alternatively, educational programs collectively described as COPE (creating opportunities for parent empowerment) which focus on teaching families more about development and behavioral cues have made similar strides, but require copyrighted, literacy heavy materials and trained staff for administration.

Klaus Health Services Awardee

Delia Marie Horn – University of Vermont Medical Center

Title: *Association Between Antenatal Ultrasound Findings and Neonatal Outcomes in Rural Uganda*

Mentor: Danielle Ehret

Personal Statement: My interest in improving resource management and allocation in the low and middle-income country (LMIC) setting preceded my entry into medical training, and has remained a driving force behind my academic pursuits. In medical school I was awarded a Schweitzer Fellowship to design a curriculum introducing the American health care system to new Americans, which I then taught to Nepali-American refugees. In residency I participated in a pilot concordance study evaluating the utility of basic protocoled ultrasound sweeps for use in the LMIC setting. As a neonatal-perinatal medicine fellow and physician scientist in-training, I remain dedicated to initiatives that will improve the care provided to infants and families where resources are scarce. Throughout my career I hope to combine technological advances with quality improvement work in order to elevate the care that is available to LMIC residents, as well as those living in resource-limited areas within middle and high income countries. During my fellowship at the University of Vermont I have had the privilege to work with Dr. Danielle Ehret, Director of Global Health for Vermont Oxford Network, as my mentor. Guided by her experience and expertise, I intend to explore the utility of prenatal ultrasounds when performed in the LMIC setting. The goal of this work is to determine if certain ultrasound findings, when identified prenatally in the LMIC, are predictive of neonatal outcomes at delivery.

Abstract: More cost-effective ultrasound (US) devices have been developed in recent years, and this has led to a proliferation of their use in the low- and middle-income country (LMIC) setting. Several studies have verified the validity of basic ultrasound sweeps and protocols used by low- or mid-level providers with limited training for the reliable identification of certain findings, such as fetal position, multiple gestation, placental position, and fetal growth estimates. However, this use of US in LMICs has not yet been tied to demonstrable improvement in maternal or neonatal outcomes. The aim of this study is to determine if findings on basic prenatal ultrasound combined with maternal demographic information in the LMIC setting are associated with adverse neonatal outcomes at delivery. This will be a secondary analysis of data gathered prospectively at Nawanyago Health Center III in Kaguli District, Uganda, including over 1000 pregnant women and their neonates from July 2010-August 2018. If such an association can be identified, we will partner with our Ugandan team members on how to prospectively incorporate this information into antenatal counseling, with the goal of providing evidence to guide caregivers and families as they continue to strive to reduce neonatal morbidity and mortality.

Kathleen E. Hannan – University of Colorado

Title: *Characterization, Disparities, and Prediction of Medical Complexity in VLBW Infants Discharged from the NICU*

Mentor: Sunah Susan Hwang

Personal Statement: As a current first year fellow at the University of Colorado, my research interests stem from caring for high-risk neonates, notably those with medical complexity and technology dependence. My passion in this area began in medical school and continued through residency, where I gained experience by working with NICU graduates with high medical needs through my weekly continuity clinic at our hospital's complex care clinic. As I now continue to expand my research skills using population-level databases focusing on neonatal outcomes through pursuing a Master of Science in Clinical Science degree, I have become even more interested in applying these skills to define and characterize neonates with medical complexity, with a particular focus on how disparities affect their medical risk at NICU discharge. I hope to use this information as an early step towards disentangling the complex interactions of social, clinical, and hospital-level factors on discharge outcomes of VLBW infants. Not only will the Marshall Klaus Award help me to advance my current research, but it will also provide opportunities for education to support me on my path to becoming an academic neonatologist and an avid health services researcher

Abstract: Advances in maternal and neonatal care have led to improved survival of very low birthweight (VLBW, <1500g) infants, however there has also been an increase in the number of children living with significant morbidities. Currently little is known about the overall prevalence and predictors of ongoing medical complexity and the need for medical technology among preterm infants at the time of hospital discharge. Further, significant racial/ethnic disparities exist in preterm birth rates, with Non-Hispanic Black (NHB) mothers having 1.5 times the risk of preterm birth compared to their Non-Hispanic White (NHW) counterparts, leading to an over-representation of NHB infants in the U.S. preterm population. The presence and magnitude of racial/ethnic disparities in the burden of ongoing medical risk after NICU discharge remains unknown.

The overall goals of this project are 1) to characterize VLBW infants with medical complexity, defined as the presence of complex chronic conditions (CCC) and/or technology dependence (TD), discharged from the NICU using a large, nationally representative sample, and 2) to assess racial/ethnic disparities in the prevalence of CCC/TD, with the hypothesis that disparities exist in the prevalence of CCC/TD beyond what may be attributed to the higher preterm birth risk among NHB infants. The results of this study will allow health care providers, policy makers, and maternal and child health researchers to better understand the extent of complex medical needs of VLBW infants with CCC/TD, particularly focused on racial/ethnic disparities in ongoing medical risk at the time of NICU discharge.