2021-2022

THE IMPACT OF YOUR GIVING

PRESENTED WITH GRATITUDE TO THE SUPPORTERS OF PANDA,
THE PHOENIX WOMEN'S BOARD OF THE STEELE CHILDREN'S RESEARCH CENTER

Steele Children's
Research Center

Photo: Brent G. Mathis

You, the supporters of PANDA, are always in my heart.

That's never been more true than during the challenges of 2020 and 2021. Thank you. For more than 20 years, the women of PANDA have helped confront life-threatening diseases that prey on our most vulnerable. Your dedication and commitment inspire all of us at the Steele Children's Research Center. In recognition of your accomplishments, I wanted to remind you of the difference PANDA makes in our work every single day.

This brief report looks at our continued progress in areas PANDA has focused on in the past, as well as how all our work benefits from your investments in our physician-scientists – including my own post as the PANDA Endowed Director for the Steele Children's Research Center.

I hope you'll take a few moments to read this update and recognize the terrific impact you make possible year-round for children and families in our care and around the world. Thank you again for all you do.

With deepest gratitude,

Fayez K. Ghishan, MD
PANDA Endowed Director, Steele Children's Research Center
Chair, Department of Pediatrics
Physician-in-Chief, Banner Diamond Children's Medical Center
Medical Director, Clinical and Translational Sciences Research Center
Horace W. Steele Endowed Chair in Pediatric Research
Alan and Janice Levin Family Endowed Professor in Pediatric

"Severe combined immunodeficiency (SCID) is a disease where children are born with a hole in their immune system. They are unable to fight viral infections and can die from a simple cold. They look completely normal at birth but usually get fatal infections in the first year of life. Early diagnosis and treatment are critical to saving the lives of these children. Bringing newborn screening for SCID to Arizona ensures that these children will be diagnosed quickly, usually in the first week of life. This allows us to quickly isolate them and get to work fixing their immune defect. I'm proud to be part of the newborn screening program in Arizona."
– Michael Daines, MD

EARLY IMMUNODEFICIENCY DIAGNOSES SAVE NEW LIVES

SCID is a disorder characterized by the absence of T cells that affects a baby's immune system. It can result in one or more serious infections in the first few months of life; a simple cold can be life-threatening for an infant with SCID. Babies with SCID often need a bone marrow transplant to replace some of their immune system cells. Ideally, this transplant occurs within the first three months of life. Left undetected and untreated, SCID is uniformly fatal.

Until 2017, Arizona was one of only three states in the US that did not include SCID in newborn screenings to detect rare and serious disorders. Prompted by the work of researchers led by Dr. Michael Daines, who is supported by the PANDA Endowed Faculty Research Fund in Autoimmune Diseases, on August 9, 2017 the Arizona Department of Health Services instituted SCID screening for newborns. Since then, six infants have been diagnosed with SCID and were able to receive treatment that allowed them to manage their disease.

Explore Research by Clicking Below:

Newborn Screening for Severe Combined Immunodeficiency in Arizona

Arizona Department of Health Newborn Screening Information for Parents

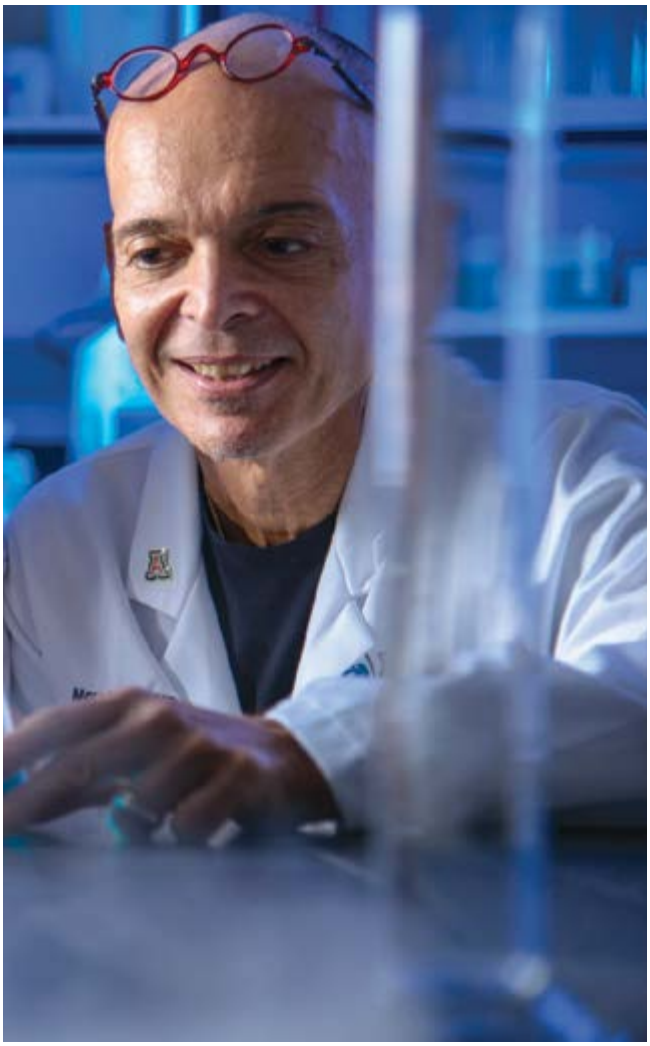
PEDIATRIC HEMATOLOGY-ONCOLOGY UPDATES

In 2020, under the leadership of Emmanuel Katsanis, MD, the Division of Pediatric Hematology-Oncology & Hematopoietic Cell Therapy & Transplantation (HCTT) not only rose to the challenges of a global pandemic but excelled in all areas.

Clinical activities continued to grow in hematology, oncology, cell therapy and transplantation, survivorship, adolescent and young adult cancers. Since 2015, the Division has performed 46 haploidentical bone marrow transplants (haplo-BMT), among the most in the nation, with an incredible survival rate of 91.7 percent. Outstanding accomplishments in research yielded 23 peer-reviewed publications, book chapters and multiple new grants.

Now fully integrated, the Division has three clinical campuses in Tucson, Mesa and Glendale. Four pediatric oncologists and four nurse practitioners in the Phoenix area have joined the six pediatric

oncologists and five nurse practitioners in Tucson under one umbrella, Banner University Medical Group (BUMG), with faculty appointments at the University of Arizona College of Medicine Tucson in the Department of Pediatrics.



Communication and collaboration between the groups continues to increase thanks to weekly divisional clinical teleconferences attended by more than thirty team members. Dr. Katsanis' team also participates in shared educational conferences once a month and joint quarterly morbidity and mortality meetings, all of which strengthen our resources to care for patients and their families across the state of Arizona.

Explore Publications Below:

Bendamustine Conditioning Skews Murine Host DCs Toward Pre-cDC1s and Reduces GvHD Independently of Batf3

T-Cell Replete Myeloablative Haploidentical Bone Marrow Transplantation is an Effective Option for Pediatric and Young Adult Patients With High-Risk Hematologic Malignancies

Bendamustine with total body irradiation conditioning yields tolerant T-cells while preserving T-cell-dependent graft-versus-leukemia

CPAE CENTER OF EXCELLENCE ADAPTS IN PANDEMIC

In August 2016, the University of Arizona Steele Children's Research Center launched the Children's Postinfectious Autoimmune Encephalopathy (CPAE) Center of Excellence, with Dr. Sydney Rice and Dr. Michael Daines – both beneficiaries of PANDA endowed funds – as co-directors. The first facility of its kind in the United States, the CPAE Center of Excellence implemented an integrated model of basic science and clinical research, clinical care and teaching to address a spectrum of neuropsychiatric disorders that are often misdiagnosed, underdiagnosed or undiagnosed in children.

The CPAE clinic treats disorders such as Pediatric Acute-onset Neuropsychiatric Syndrome (PANS), Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infection (PANDAS) and Sydenham chorea. These conditions occur when an infection triggers an autoimmune reaction that targets the brain, leading to changes in neurologic function, mood and behavior. An estimated 4.5 million children in the United States and 138 million worldwide are impacted by CPAE.

Effective assessment and treatment of this complex condition requires multiple specialties, including immunology, developmental and behavioral pediatrics, child and adolescent psychiatry, pediatric psychology/behavior analysis, and pediatric nursing. Families from throughout the United States and Canada seek out our clinical services for this interdisciplinary, multispecialty model of care. Since 2016, the CPAE clinic has helped children from 37 of the 50 states and Canada, Thailand, and Mexico.

“I know that [my son] will always dance to the beat of his own drum, but I just want him to have the proper tools to navigate this world without feeling so anxious. As much as I wish I could take away the pain and stress… it has brought me to you and for that my heart will be forever grateful! Thank you!” - Anonymous grateful patient

“As the COVID pandemic began in March 2020, our teams have had to adapt and get creative in efforts to remain in touch with our patients and keep our project objectives and goals moving forward,” says Dr. Rice, Division Chief, Developmental Pediatrics. “To safely deliver clinical care and meet CDC guidelines during the pandemic, the team dedicated time to duplicate our in-person multispecialty clinic via telemedicine, providing the same quality services virtually.”

The virtual platform has allowed more flexibility for supporting clinicians to observe a visit while a RN Navigator moves in and out of each appointment. In addition, follow up care is more accessible, providing effective ongoing services and increasing productivity. Most importantly, each family has access to the vital multispecialty services for their child with minimal disruptions. Even after the pandemic ends, telemedicine will allow the CPAE Center to provide these essential services and help more families.

In other CPAE-related news, Dr. Michael Daines is leading a new clinical study, sponsored by the family-owned pharmaceutical company Octapharma, on the effectiveness of Intravenous Immune Globulin (IVIG) therapy in children. Dr. Daines has found that administering IVIG therapy to CPAE patients can help curtail symptoms in children and bring them back to baseline. The clinical trial is beginning with children in Arizona and will also be conducted at multiple sites across the United States and, eventually, internationally. The anticipated outcomes will provide necessary scientific evidence to convince insurance companies to cover IVIG therapy as an approved CPAE treatment.

Explore Publications Below:

Bringing Services Together: Multispecialty Team Logistics via Telemedicine

Does My Child Have PANS/PANDAS?

MICROBIOME CORE FLOURISHES

The human microbiome is the collection of microscopic organisms which live on all of us, in our skin, our saliva and mouth, our eyes, and in our gut and the rest of the gastrointestinal tract. As startling as that may sound, these bacteria are beneficial. The microbiome is essential for human development, immunity and nutrition. Autoimmune diseases such as diabetes, rheumatoid arthritis, muscular dystrophy, multiple sclerosis, and fibromyalgia are associated with dysfunction in the microbiome.

Established in 2019, the Microbiome Core at Steele Children's Research Center provides end-to-end technical and research support to study microbial communities' structure and function. The Microbiome Core works closely with the CPAE Center of Excellence at the University of Arizona Steele Children's Research Center to better understand the role of gut, nasal and throat microbiome communities in pediatric patients with Postinfectious Autoimmune Encephalopathy. The Microbiome Core, which is led by Director Daniel Laubitz, PhD, also collaborates with the Department of Child Health at the University of Arizona College of Medicine—Phoenix to understand changes in microbial communities after diffuse traumatic brain injury

In its first year of operation, the Microbiome Core performed a total of 43 projects – processing thousands of samples for analysis – for researchers at the University of Arizona, as well as other academic institutions. It also helped in the preparation and execution of two new grants, both co-investigated by the PANDA Endowed Professor in Autoimmune Disease Research, Dr. Pawel Kiela; one studies the role of microbiota and immune responses in colitis, the other examines the role between arsenic in mining waste and diabetes.

Explore Publications Below:

Dynamics and Complexity of Dark Fermentation Microbial Communities Producing Hydrogen From Sugar Beet Molasses in Continuously Operating Packed Bed Reactors

Paneth Cell-Derived Lysozyme Defines the Composition of Mucolytic Microbiota and the Inflammatory Tone of the Intestine

An indisputable role of NHE8 in mucosal protection

Elevating EGFR-MAPK program by a nonconventional Cdc42 enhances intestinal epithelial survival and regeneration

Intestinal Epithelial Expression of MHCII Determines Severity of Chemical, T-Cell-Induced, and Infectious Colitis in Mice

MEET SOME OF OUR RESEARCHERS

Pawel R. Kiela, DVM, PhD

Gastroenterology, Hepatology and Nutrition

Dr. Kiela, who is supported by the PANDA Endowed Professorship in Autoimmune Diseases, focuses on understanding the processes that lead to development of chronic auto-inflammatory disorders of the gut, such as Crohn's Disease and Ulcerative Colitis, collectively known as Inflammatory Bowel Diseases (IBD). A fuller understanding of how these diseases develop will ultimately lead to better prevention, treatments and cures. His current research studies the unappreciated intrinsic roles of the Sodium–hydrogen antiporter 3 (NHE3) protein in colonocytes (epithelial cell of the colon), and how inhibiting NHE3 may positively impact the interaction with commensal and pathogenic bacteria in the gut.

Explore Dr. Kiela's Publications Below:

Intestinal Epithelial Expression of MHCII Determines Severity of Chemical, T-Cell-Induced, and Infectious Colitis in Mice

Paneth Cell-Derived Lysozyme Defines the Composition of Mucolytic Microbiota and the Inflammatory Tone of the Intestine

Vanessa Ribeiro Figliuolo Da Paz, PhD

Gastroenterology, Hepatology and Nutrition

Dr. Figliuolo Da Paz works with the team of Drs. Ghishan and Kiela to study immunology aspects of inflammatory bowel disease (IBD), which can cause nutrient deficiencies, inhibit growth and bone health, and increase the rate of depressive and anxiety disorders in children. Her current study works to define the mechanism involved in the maintenance of steady-state levels of the Disabled homolog 2 gene (DAB2) and its regulation during IBD. The goal is to gain a deeper understanding of how this gene is expressed and modulated in intestinal dendritic cells (iDCs), as well as its impact on the development of mucosal immune response in the gut.

Explore Dr. Figliuolo Da Paz's Publication Below:

Emerging Roles of Disabled Homolog 2 (DAB2) in Immune Regulation

Katri V. Typpo, MD, MPH

Critical Care

A scholar in the Pediatric Critical Care and Trauma Scientist Development Program (PCCTSDP), Dr. Typpo examines non-nutritive benefits of enteral and parenteral nutrition on intestinal epithelial barrier function and microbiome diversity in critically ill children, including those who require mechanical ventilation. Severe Pediatric Acute Respiratory Distress Syndrome (PARDS) is a life-threatening condition with a high mortality rate (33%).

The PROSpect study, a multi-center, NIH-funded clinical trial, will randomize 1,000 children with severe PARDS to compare positioning and ventilation strategies to improve patient outcomes. This clinical trial presents a unique opportunity to investigate potential mechanistic underpinnings of early enteral nutrition (EEN) as a targeted approach to improve outcomes for children with severe PARDS. As an ancillary study to PROSpect, Dr. Typpo's lab will be investigating whether crosstalk between the lung and gut microbiome may be a potential mechanism by which EEN may reduce PARDS mortality.

Explore Dr. Typpo's Publications Below:

Early Enteral Nutrition Is Associated With Improved Clinical Outcomes in Critically Ill Children: A Secondary Analysis of Nutrition Support in the Heart and Lung Failure-Pediatric Insulin Titration Trial

Outcomes of Day 1 Multiple Organ Dysfunction Syndrome in the PICU

Nahla Zaghloul, MD

Neonatology

An Assistant Professor of Pediatrics at the University of Arizona College of Medicine and attending Neonatologist at Banner Diamond Children's Medical Center, Dr. Zaghloul's research interests involve improving outcomes among premature infants with brain injury – including Periventricular Leukomalacia, the most common cause of cerebral palsy in premature infants. From now until the end of January 2022, Dr. Zaghloul's research is supported by a University of Arizona Health Sciences Career Development Award (UAHS-CDA).

Dr. Zaghloul is currently investigating how the administration of the natural therapeutic Allopregnanolone after hypoxia ischemia (when insufficient blood flow to cells and organs, combined with a lower-than-normal concentration of oxygen in arterial blood, inhibits normal function) can ameliorate this devastating white matter brain injury by promoting neuro-regeneration, oligodendrogenesis (a vital process in ongoing brain development), and reducing neuro-inflammation.

Explore Dr. Zaghloul's Publications Below:

Caffeine inhibits hypoxia-induced nuclear accumulation in HIF-1α and promotes neonatal neuronal survival

Neonatal lung ultrasound exam guidelines

Jennifer Andrews, PhD

Developmental Pediatrics

Pain that first appears as "growing pains" in young children can be one of the symptoms of Ehlers-Danlos Syndrome (EDS), a rare genetic connective-tissue disorder which can be manifested by joint hypermobility, intestinal fragility, skin elasticity, and underlying tissue fragility. Complications from EDS may include chronic joint pain, joint dislocation, early onset arthritis, slow healing of wounds (leading to prominent scarring), and surgical wounds that have a hard time healing. Dr. Andrews, who serves as Director of Research for the Division of Genetics and Developmental Pediatrics, conducts gene sequencing and metabolomics studies of this under-researched disease.

In 2019, Dr. Andrews received $2.4 million through a five-year CDC cooperative agreement to examine survival, health care utilization, other health conditions and outcomes over time for a variety of geographically, culturally and socioeconomically challenged subpopulations of Arizona children, adolescents and adults living with congenital heart defects.

Explore Dr. Andrews' Publications Below:

Diagnostic Accuracy of Phenotype Classification in Duchenne and Becker Muscular Dystrophy Using Medical Record Data1

Subtle differences in autonomic symptoms in people diagnosed with hypermobile Ehlers-Danlos syndrome and hypermobility spectrum disorders

Keith Hazleton, MD, PhD

Gastroenterology, Hepatology and Nutrition

Dr. Hazleton is researching interactions between complex systems as it relates to the gut microbiome, which converts the food we ingest to extract vitamins, fiber, and other nutrients. Currently, he seeks to determine how a Western-style diet influences infection from C. difficile (C. diff), a bacterium that lives in the intestines and can cause symptoms ranging from diarrhea to life-threatening inflammation of the colon. Dr. Hazleton, who joined the division of Pediatric Gastroenterology, Hepatology and Nutrition as an assistant professor last fall, is currently the only board certified pediatric hepatologist in Arizona.