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DEAR COLLEAGUES

The opening of the Children’s Mercy Research Institute (CMRI) research building in February 2021 was a new chapter in the evolution of Children’s Mercy Kansas City (CMKC), fulfilling the dream of the Berry sisters to establish a research facility dedicated to children. It happened amidst the most devastating pandemic in modern times, including 1 million deaths, prolonged lockdown, and the greatest challenge modern health care has ever faced. Through it all, CM team members rose to the enormous task to keep children safe. We learned a great deal, and many of those lessons will be retained in the future state we are now creating.

COVID presented unique challenges in children and it required a rapid response by research teams and caregivers combined. Ultimately, vaccines were invented, utilizing novel synthetic RNA technology. These vaccines were developed, produced and disseminated faster than any in history. Conference rooms in the newly opened research building were adapted to host the many vaccine clinics. Recognizing the risk of future pandemics and the need for continuing research on COVID, in this report we are presenting a new CMRI Area of Emphasis, termed Emerging Infections, led by Rangaraj Selvarangan, PhD. In combination with our other AOEs, Emerging Infections will support the infrastructure and enable research designed to diagnose, prevent and treat diseases that affect all children.

The Annual Report will present several research findings made over the past year, as well as some key events from the calendar. We will celebrate the success of investigators in attracting extramural support and their many recognitions from the scientific community. In recent years, it has become clear that it is essential to address equity, diversity and inclusion, both in research studies and in research teams. Some of our approaches are highlighted here, and we spotlight an exciting new educational program for high school students called STAR. As a prelude of things to come, Rob Lane, MD, MS, will outline a new overarching initiative termed Poised for Life.

The greatest lesson underscored by the events of the past three years is that to promote the health and wellbeing of all children, research must be integrated into all aspects of care at CMKC. We have an obligation, as a free-standing children’s hospital, to learn from every clinical encounter so that future generations of children will benefit. The most important message research can deliver is the hope of a brighter, healthier future for all children.

Tom Curran, PhD, FRS
Senior Vice President, Executive Director, and Chief Scientific Officer, Children’s Mercy Research Institute
Donald J. Hall Eminent Scholar in Pediatric Research
Children’s Mercy has always placed an emphasis on exceptional clinical care, particularly for those most vulnerable. With the establishment of the Children’s Mercy Research Institute, we also set out to transform the future of pediatric research and secure Kansas City as a premier, global research hub dedicated exclusively to the health and wellbeing of all children – not only here in the region, but everywhere.

The collaborations happening inside this world-class pediatric research facility allow us to accelerate even more precise diagnoses and treatments for complex childhood diseases as we bring new learnings from the bedside to the bench and back again.

Through our investment in research, we have been able to attract and recruit top researchers from around the country to the Kansas City community and to Children's Mercy. Our vision is to become a convener and a partner with others in the biomedical research areas — the universities and academic centers — to advance the evolution of children's health care.

Together, we are positioned to cultivate and invest in higher levels of pediatric research, so we can provide groundbreaking care for the most difficult medical cases and give hope to families everywhere.

Paul Kempinski, MS, FACHE
President and Chief Executive Officer, Children’s Mercy

Alice Berry, DDS, and Katherine Berry, MD, Endowed Chair in Executive Leadership

On the journey to improve wellbeing for kids, there are many things to be proud of – our faculty and staff being one of them. The more team members I get to know, the easier it is to appreciate all the ways we positively impact patients, families, the region and our nation. Everything we do matters, from clinical care to education, services to research. But for me, the way our people care is the biggest difference maker of all.

This commitment to caring is what makes programs like the ones you’ll read about in this report possible. It also drives our curiosity to learn and persevere. Research influences our ability to care for kids now and in the future. Today, it impacts the direct care we deliver and offers insights into the pathogenesis of mysterious conditions and diseases. Tomorrow, research becomes answers, hope and healing driven from the findings, knowledge and development of incredible teams. And at any time, it provides a framework for us to educate and train beyond biology and into the administration and execution of a program.

Please enjoy this annual report. It’s a celebration of the last year and the beginning of the vision for the future. And it’s a testament of the CM team members dedicated to promoting the health and wellbeing of all children and their families. Thank you — you truly help lead the way to discover more cures and transform health care.

Robert H. Lane, MD, MS
Executive Vice President/Physician-in-Chief
Schellhorn Family Endowed Chair in Medical Administration
Children in the Kansas City area have different health outcomes based upon the conditions where they live, play and learn. A sobering fact is that there is an estimated 15-year difference in life expectancy based upon where these children live, and the disparities among Kansas City's children can lead to stark differences in their health, educational and behavioral outcomes.

At the root of much of this health disparity are social constructs – also called social determinants of health – that have a significant influence and impact on the lives of children.

Children's Mercy is in the early phases of launching a program dedicated to developing long-term, enterprise-wide community collaborations to address the social determinants of health and health care of children living in the Kansas City area. The Poised for Life Program will integrate research, faculty and staff development, education, advocacy and community partnership to serve not only area children and families but the research interests of Children's Mercy faculty as well.

“If research is part of your culture, as it is at Children’s Mercy, then ultimately our efforts need to include ways to do more for your community and meet them where their needs are,” said Dr. Lane. “We are fortunate that many of our faculty members are passionate about any effort that benefits our community – and their passion is the driver for this program. Integrating research not only into what we do every day at Children’s Mercy but also within our community is critical to making a difference in the lives of the children and families we serve, while also promoting learning and discovery among our faculty.”

Developing and launching the program is an inclusive endeavor involving input and insight from faculty members and the community, Dr. Lane added. At Children’s Mercy, Dr. Lane plans for a variety of working groups to address topics that are critical to the ultimate success of the program, such as the program’s infrastructure and strategies to further strengthen the cohesion of research within the enterprise and with the greater community.

“We are early in our journey with the program, and it is important that our faculty and department leaders have input on our direction during every step of that journey,” said Dr. Lane.

The program, led by Robert H. Lane, MD, MS, Executive Vice President and Physician-in-Chief at Children’s Mercy, aligns with elements of the organization’s strategic plan dedicated to integrating research throughout the enterprise and prioritizing community health improvement efforts that build out a framework for addressing social determinants of health for children.
“As we develop and refine the Poised for Life Program, we also need to ensure that we have strategies in place to educate and support our faculty in how to be better present in our communities and how to advocate in partnership with these communities,” said Dr. Lane. “A cornerstone of this faculty-focused aspect of the program involves creating the infrastructure for their scholarly success through resources like a Research Learning Center, research programs, mentorship and pipelines of research for Children’s Mercy.”

The Poised for Life Program will also work with national scientific experts and external community advisory boards to identify, prioritize and support the most promising collaborative and cross-disciplinary research approaches to enhance health equity in children within the context of social determinants of health.

A key element to this endeavor involves ongoing partnerships with Kansas City and regional communities to foster interactions, inform advocacy, demonstrate mutual benefit, and determine the acceptability of possible research projects and interventions. This initiative also includes integrated community involvement and input for prioritizing, designing and implementing projects, and effectively disseminating the results throughout the community.

The new program offers a palette for further developing Children’s Mercy faculty – some of whom are just beginning their research journeys – in not only research but community service and advocacy as well. Participation in the program will offer faculty members creative opportunities to make an impact on their communities through meaningful, impactful research while simultaneously growing their careers.

As Children’s Mercy continues to develop the Poised for Life Program, Dr. Lane and the program’s work group members are working with community leaders on how the presence of Children’s Mercy in the community can be most beneficial. In addition, the team is developing an infrastructure involving the hospital’s clinical academic departments, the Children’s
Mercy Research Institute, and communities while developing forums throughout the enterprise to encourage cross-departmental and multidisciplinary collaborations, research proposals and training opportunities.

In addition to Dr. Lane, the members of the Poised for Life Work Group at Children’s Mercy include Jeffery D. Colvin, MD, FAAP, director of Research for General Academic Pediatrics (co-chair); Jessica L. Bettenhausen, MD, FAAP, director of Research for Pediatric Hospital Medicine (co-chair); Andrea Bradley-Ewing, MPA, MA, senior director of Community Engagement Research, Health Services Outcomes Research; Jordan A. Carlson, PhD, director of Community Engagement Research for the Center for Children’s Healthy Lifestyles & Nutrition; Kathryn A. Keeler, MD, pediatric orthopedic surgeon; Tolupe A. Oyetunji, MD, MPH, FACS, FAAP, pediatric surgeon and director of Health Outcomes Research and the Quality Improvement & Surgical Equity Research Center; Bridgette L. Jones, MD, MSCR, of the Division of Pediatric Allergy & Immunology; and Kimberly A. Randall, MD, MSc, of the Division of Pediatric Emergency Medicine.

The Poised for Life Work Group is developing a white paper detailing the need for this program in the Kansas City area and will work inclusively with Children’s Mercy faculty, staff and the community on developing, refining and launching the program. This white paper will focus on the “why” of the Poised for Life effort. Subsequent efforts will include faculty and staff from across the Children’s Mercy enterprise and will focus on the “how.”
New Food and Drug Administration labeling warns prescribers and patients of a rare and previously unrecognized—but potentially deadly—pulmonary risk for a decades-old antibiotic, identified by pediatric physicians at Children’s Mercy Kansas City. This summer the FDA’s Office of Pediatric Therapeutics and Center for Drug Evaluation and Research, Division of Pediatric and Maternal Health, Division of Anti-Infectives and Office of Surveillance and Epidemiology approved revised labeling for trimethoprim-sulfamethoxaloe (TMP-SMX) products, known commercially as Bactrim and Septra. The updated labeling advises medical providers to watch for patient reports of cough, shortness of breath or rapid, shallow breathing that could lead to acute respiratory distress syndrome requiring mechanical ventilation, extracorporeal membrane oxygenation (ECMO) or lung transplantation, potentially resulting in death.

The FDA’s action follows June 2019 publication of a case series in which pediatric physicians at Children’s Mercy Kansas City and the University of Missouri-Kansas City School of Medicine described severe acute respiratory failure related to Bactrim treatment in five previously healthy adolescent patients. Additional cases have since been identified now totaling 16 cases, with six—including two international cases—now under active review by pediatric intensivist Jenna Miller, MD, FAAP, and pediatric infectious disease specialist Jennifer Goldman, MD, MS-CR.
Bactrim and Septra are regularly prescribed to treat skin, soft tissue, and urinary tract infections, as well as acne.

Dr. Goldman emphasized the effort to gather data about the drugs’ link to life-threatening respiratory failure in a tiny number of cases is not an effort to deter their use, but rather to alert providers and patients to the symptoms before an adverse reaction becomes severe.

“These are good drugs, and this is a very rare condition, but it’s not commonly known, and needs to be,” Dr. Goldman said. “In medical school we learn about blistering, jaundice and other symptoms of severe reactions to these popular antibiotics, and we want to add ‘difficulty breathing’ to the list and potential for severe reaction considered.

“The group of people who have a severe reaction is rare, and not all those with this genotype have this reaction, but all we have studied who have this reaction have this genotype,” Dr. Miller said. “So, it’s not a sole risk factor, but it is another clue to the puzzle.”

The link between these antibiotics and severe respiratory illness only became suspected in 2018, when Children’s Mercy patient, Zei Uwadia, made national headlines for her extraordinary resolve to walk the halls of the hospital while on ECMO support as she battled a mysterious lung ailment. After the news reports about Zei’s respiratory failure, another patient and parent with a child similarly afflicted reached out to Dr. Miller. It was through review of their medical records that Bactrim emerged as the common thread and the basis for the physicians’ 2019 paper, leading to the larger cohort published in 2021.

Zei ultimately died of the illness shortly after her 17th birthday, but the Children’s Mercy physicians feel her presence acutely as they step up their efforts in the hope that what they learn and share will prevent others from going through similar struggles.

“There’s a window of opportunity to avert serious complications,” she added.

The Children’s Mercy physicians are partnering with Massachusetts General Hospital in identifying pathology markers. In addition, the Children’s Mercy Genomic Medicine Center is performing testing in hopes of identifying genetic predictors of a reaction that, while rare, is fatal to 40% of patients who experience it. They have published two papers with a third currently under peer review describing that all cases evaluated by the Genomic Center have the same HLA genotype.
STAR 2.0 Program Empowers Underrepresented Students to Pursue Science

The current medical and scientific workforce in the United States does not reflect the racial and ethnic identity and diversity in the population or, of particular importance, those who are most impacted by disparities in health care. The cornerstone of health equity therefore relies on developing and maintaining a medical and scientific workforce that reflects the general population as well as those suffering from disparate health care and research benefits.

To help develop a more representative medical and research workforce, Children’s Mercy Research Institute (CMRI) launched the Summer Training in Academic Research (STAR) 2.0 program to give high school students and educators an in-depth opportunity to build their interest and understanding through a high-quality research experience during the summer academic break.

Bridgette L. Jones, MD MSCR, Associate Professor of Pediatrics, who leads the STAR 2.0 program, envisioned and developed the six-week program with an aim toward leveraging the unique opportunities within CMRI to foster interest among high school students in the community who reflect racial and ethnic groups impacted by health-related disparities. Dr. Jones worked with pediatric clinical pharmacology colleagues and collaborators at the Duke Clinical Research Institute to adapt their STAR model and create the STAR 2.0 program at CMRI.

“STAR 2.0 provides unique research experiences and opportunities that reflect many of the strengths we have here in the CMRI such as hands-on experience in genomics, health outcomes and population health, and pediatric clinical pharmacology and precision therapeutics,” said Dr. Jones. “The students...
work directly with research faculty mentors on an original research project and develop a manuscript describing their research findings, with the goal that the students will earn authorship on an academic manuscript.”

In addition to giving students and educators an inside perspective of the world of science and medicine, the unique program at CMRI allows participants to gain hands-on experience in research that will improve the care of real patients and gain valuable contacts in the local medical research community.

The STAR 2.0 program is open to individuals from racial and ethnic groups that are currently underrepresented in medicine and science, including American Indian/Native Alaskan, Black or African American, Hispanic/Latino, Native Hawaiian/Pacific Islander and underrepresented Asian populations such as Vietnamese, Cambodian and Indonesian.

“We work with public and charter high schools on both the Missouri and Kansas sides to recruit students for the program,” said Vickie Yarbrough, MA, BA, who serves as Program Director of STAR 2.0. “During the program, participants not only engage in a unique research project at CMRI but also learn about clinical and translational research methodology, writing, statistics, medical ethics and career development while networking with other students and educators from across the country.”

“STAR 2.0 provides unique research experiences and opportunities that reflect many of the strengths we have here in the CMRI such as hands-on experience in genomics, health outcomes and population health and pediatric clinical pharmacology and precision therapeutics.”

— Bridgette L. Jones, MD
STAR 2.0 launched in the summer of 2021 with five students and an area middle school science teacher (Danielle Farr) and doubled in size for the 2022 program. Within the next three years the program is expected to expand to include 25 students and five teacher participants every summer. STAR 2.0 is made possible through the generous support of Janssen Research & Development, LLC, EMD Millipore Corporation, American Century Investments Foundation and the Carol and Tom Barnett Family.

During its inaugural year, STAR 2.0 participants worked with Elin Grundberg, PhD, and her group in the Genomic Medicine Center at CMRI to analyze whole genome data among children who came to Children’s Mercy with a COVID-19 infection to identify potential genetic susceptibility patterns for the virus. In 2022, STAR 2.0 participants worked with Jordan A. Carlson, PhD, Director of Community Engaged Research at the Center for Children’s Healthy Lifestyles & Nutrition; Paul Hibbing, PhD, of the Center for Children’s Healthy Lifestyles & Nutrition; Jennifer E. Schuster, MD, of the Division of Pediatric Infectious Disease; and Jennifer L. Goldman, MD, of the Division of Pediatric Infectious Disease and the Division of Clinical Pharmacology, Toxicology and Therapeutic Innovation on a research project involving measuring sleep and physical activity and COVID-19 testing in schools.

As a result of the program, Dr. Jones and Yarbrough have observed that STAR 2.0 students have expanded their understanding of medical and science careers as well as their own interest and confidence in their capability to pursue such careers.

“It was fascinating to watch their confidence level improve as they conducted their research project as well as how they thought about their own future in medicine and science,” said Dr. Jones. “One student remarked that she was not aware of a ‘physician-scientist’ as a career choice. She had previously written in her application about her interest in doing work in the future to close Black maternal health disparity gaps. She mentioned that after learning what a physician-scientist is that she now knows what type of career that she wants to have.”

Dr. Jones aims to not only continue to build capacity for the program locally but to continue her robust collaboration with her colleagues at Duke to expand the program to provide summer research opportunities for high school students throughout the country.
While it is understood that diversity and inclusion ultimately benefit everyone, ensuring diversity in research has long presented challenges. Women, ethnic/racial minorities, children, people with disabilities, and those in under-resourced communities who may experience social and educational disadvantages are just a few of the many populations that have been historically underrepresented in research studies. Without including members of diverse populations in research, the results of studies cannot be generalized to historically underrepresented populations, creating a situation that may worsen existing health disparities.

The importance of diversity extends beyond the benefits to underrepresented populations themselves to provide benefits to everyone by ensuring that data and information generated in clinical research studies is accurate. Ensuring representational diversity in clinical trial samples reduces bias in the data generated, leading to more innovative and accurate results and improving the quality of the science. In addition, as datasets are used increasingly to inform health care decisions and policy, it is critical that all datasets include all members of the community. With the increasing use of artificial intelligence analytical strategies, unbiased and inclusive data is essential for all to benefit from the inferences drawn from existing datasets.

Including diverse perspectives and voices at the early stages of research projects helps generate ideas and approaches that strengthen the research itself and ultimately benefit everyone involved. In addition, training and mentoring students from diverse backgrounds helps bring new and important ideas and talents into the health field that will increase the impact of research.
An Unwavering Commitment to Research that Helps Everyone
As the Children’s Mercy Research Institute (CMRI) advances its mission of accelerating transdisciplinary research to improve the health and well-being of children, it continues to explore innovative ways to bolster diversity and inclusion and foster engagement within the CMRI and with research participants, families and community partners.

This commitment to enhanced engagement aims to ensure that research projects, hospital services, research participants and even the words we use when discussing race and ethnicity appropriately reflect the diversity of the patients and families served by Children’s Mercy.

“Diversity in pediatric research means ensuring all children and families regardless of race, ethnicity, language, economic status, education level, ability, gender identity or sexual orientation have an opportunity to participate in research,” said Andrea Bradley Ewing, who serves as the Director of Community Engaged Research at Children’s Mercy. “This means ensuring communities that have historically been harmed by research or underrepresented in research are adequately represented in all research so the scientific community is more aware of effective interventions and treatments that benefit all children.”

Diversity and Inclusion Are Part of CMRI’s DNA
CMRI incorporates diversity and inclusion into its overall strategic plan to ensure that all patients, families and communities benefit from the scientific breakthroughs that advance treatment and improve care. Some of these efforts include:

- Exploring innovative and effective measures to integrate diversity throughout research through work conducted by the Inclusion and Diversity in Research Work Group.
- Ensuring all facets of work include diversity and inclusion to train the next generation of researchers and scientists (as in the Star 2.0 program).
- Engaging diverse community voices through the CMRI Community Advisory Board on the best ways to develop, implement and disseminate research.
- Recruiting faculty and research coordinator/research assistant candidates from underrepresented communities.
- Recruiting and retaining bilingual research staff who are focused on ensuring non-English speaking patients and families are not excluded from research based solely on language.
- Providing resources for research teams that engage diverse research participants in their projects, like the translation of study documents provided by the Office of Research Integrity.
- Developing mechanisms and tools to enable research teams to track and report their inclusion of diverse races, ethnicities and genders in their research projects.
CMRI’s commitment not only involves efforts to recruit and retain diverse research participants but to also prioritize diversity and inclusion when it comes to implementing studies that enhance community engagement; promoting research that addresses health disparities; and supporting work with businesses that advance diversity, equity and inclusion practices in the communities we serve.

In addition, CMRI’s efforts reflect recent guidance from the American Academy of Pediatrics and the Journal of the American Medical Association on the use of race, ethnicity and inclusive language. To promote a culture that values inclusion, equity and diversity, CMRI leadership are committed to using language that is free from bias and affirms all races, ethnicities, genders, abilities and sexual identities.

Dr. Carlson and his team are working on two projects in the national study – called SOL VIDA and SOL CASAS – that, respectively, investigate the link between sedentary patterns and cardiovascular disease, and test a model of neighborhood environment factors, physical activity, and psychosocial issues like depression and stress on changes in cardiometabolic health in Hispanics/Latinos.

On a more local level, Dr. Carlson leads two community-based studies that focus on structurally disadvantaged communities in the Kansas City area.

A project with Our Healthy KC Eastside (OHKCE) aims to provide residents with tools and support to bolster their levels of physical activity.

“By focusing on diverse perspectives and communities in this research, the outcomes are more likely to lead to improvements in community health that benefit all residents of Kansas City,” said Dr. Carlson.

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Community-based Studies Center on Needs of Hispanic and Latinx Communities
Several current research studies at CMRI aim to directly impact the health and wellbeing of those in the Hispanic and Latinx communities.

Jordan Carlson, PhD, and his team are participating in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL), a national study exploring the role of acculturation in the prevalence and development of disease. The multicenter study is also working to identify those factors playing a role in the health of those in the Hispanic and Latinx communities.
In addition, through an award funded by the National Institutes of Health and the Environmental Protection Agency, Dr. Carlson and Dr. Jannette Berkley-Patton (UMKC) and their teams are collaborating with the University of Missouri-Kansas City, University Health, BikeWalkKC, Kansas City Public Works, and the Kansas City Area Transportation Authority to study a new policy that eliminated bus fare citywide in Kansas City. The team is evaluating the policy’s impact on health factors such as physical activity, healthy eating, weight status and economic barriers to health in order to determine whether the policy could be continued and expanded in other cities across the U.S. as a way to support health in structurally disadvantaged communities.

“Everyone benefits when community environments are designed to support health, and efforts to improve community environments are more likely to be successful when they are inclusive.”
–Jordan Carlson, PhD

Another research project, funded by the Katharine Berry Richardson Foundation and led by Ayanda Chakawa, PhD, is exploring the disparities in seeking help and navigating care access pathways for pediatric behavioral health for youth from Black, Indigenous, and People of Color (BIPOC) groups and socioeconomically disadvantaged backgrounds. The one-year pilot project aims to develop culturally informed pathways that can facilitate families’ care navigation access to behavioral health services for their children. Data collection and care navigation intervention will be provided with English and Spanish language options to account for the majority languages represented among the target sample. Using a community engaged research approach, Dr. Chakawa’s project involves partnership with the Children’s Mercy “El Consejo de Familias Latinas/Hispanas” and “Mental Health” Patient Family Advisory Councils (PFACs) to help maximize the impact of the research based on these PFACs’ diversity, equity and inclusion perspectives and as experts on the needs of children served through Children’s Mercy and challenges faced in accessing needed care.

“Though my study specifically focuses on working to understand disparities in care among BIPOC populations, all patients served through the primary care clinics within the target study age range have the opportunity to participate in the study as the goal is to provide equitable access to care across all groups served,” said Dr. Chakawa.

Fortifying Relationships, Building Trust in the Clinic and in Research
To further support the needs of those in the Hispanic and Latinx communities, Children’s Mercy has three different clinics dedicated to serving Spanish-
speaking families – the Spanish Oncology Clinic, Spanish Epilepsy Clinic and the CHiCoS Clinic. The trusting relationships Children’s Mercy bilingual staff build with these patients and families and the unique focus on their cultural and genetic differences can make a substantial difference in their treatment and outcomes.

Terrie Flatt, DO, Director of the Program for Clinical Oncology Services and Research for Hispanics, established the Spanish Oncology Clinic at Children’s Mercy in 2012 to address genetic differences in the Hispanic population, which has the highest incidence of acute lymphoblastic leukemia and the worst outcomes. While the clinic initially focused on language, Dr. Flatt noted that the focus quickly shifted to the differences in the population related to genetics, disease responses, medication tolerance and toxicity with certain chemotherapies.

Launched in 2017 by Lines Vargas Collado, MD, the Spanish Epilepsy Clinic aims to improve treatment through building trust and understanding the cultural context for any misconceptions in the Hispanic culture about epilepsy. The condition may be seen as a social barrier and assumptions persist about the ability of a person who has epilepsy to have a family or maintain a job. Patients who have epilepsy may experience a stigma and, as a result, feel socially isolated and avoid medical care. Addressing families in a culturally sensitive manner, providing education and communicating in their language help with treatment compliance.

Clínica Hispana de Cuidados de Salud (CHiCoS) translated is the Spanish Health Care Clinic – and it is a lifeline for Spanish-speaking parents looking for care in Kansas City. Established in 2008 by John.
The CHiCoS Clinic serves the primary care needs of the Spanish-speaking community through providers who are linguistically and culturally competent to care for them. The clinic also trains bilingual residents through the Culture and Language Coaching Program at Children’s Mercy, which aims to professionalize the use of Spanish in the health care and social service settings.

The commitment to having bilingual staff available to help build relationships with Hispanic and Latinx communities extends to research as well and the growing number of personnel who earn Qualified Bilingual Staff (QBS) certification.

“Having QBS-certified research personnel is crucial to carry out inclusive projects that will benefit all children,” said Susana Chavez-Bueno, MD, of the Division of Infectious Diseases. “Patients and families need to clearly understand in their own language what a research project is about before deciding to participate. QBS-certified staff facilitate increased representation of children who would otherwise be excluded from participating in research due to language barriers. Their work is essential to obtaining reliable research results that are applicable to broader pediatric populations.”

CMRI recognizes that supporting projects such as these and fostering a diverse and inclusive workforce will not only strengthen trust in the community the institution serves, but it will also advance science and promote the health and wellbeing of children everywhere. “When we root research and clinical work in diversity, equity and inclusion (DEI) efforts, it doesn’t only highlight the needs of those from minoritized or historically disenfranchised groups. It serves as a benefit to all groups because it necessitates developing and implementing efficient and tailored strategies that result in best care for everyone. This can lead to extremely beneficial changes on multiple levels for how medical facilities offer pediatric health care for all people,” added Dr. Chakawa.
As the COVID-19 pandemic slowed or halted services and activities around the world, CMRI investigators stepped up to lead innovative research related to SARS-CoV-2 virus and its impact. To better understand the virus, basic and translational projects kicked off to help bring testing, education and resources into the community.

**Goal: explore age-related differences in COVID-19 infection**

Elin Grundberg, PhD, of the Genomic Medicine Center at the CMRI, and her colleagues found that the population of immune cells in the nasal membrane decreases dramatically with age—a factor that likely contributed to the differences seen in the severity of SARS-CoV-2, the virus that causes the infectious disease COVID-19.

The study offered the first-of-its-kind single-cell atlas that shows the complete cellular landscape of uninfected human nasal samples over a person’s lifespan. The results may illuminate a strategy for future studies to treat respiratory infections.

Other studies had previously pointed to the possibility that, after infection with SARS-CoV-2, those who are younger mount a more robust immune response in the nasal mucosa—the membranes that line the nasal cavity—than those who are older. The question remained, however, whether such age-related disparity was attributed to increased immune activation or the population of immune cells present, also called “immune residency.”

Dr. Grundberg and her colleagues tackled that question by applying single-cell RNA sequencing and measured the composition of the cells as well as the transcriptional profile of the nasal mucosa. The investigators conducted the study in 35 children and adults from four months to 65 years of age who were not infected with SARS-CoV-2.

After analyzing about 30,000 immune and epithelial cells, the investigators found that the population of immune cells inside the nose was found to have decreased as a person’s age increased. There was little evidence that the structure of the cells themselves changed over time.

“We were intrigued by our finding of this clear age association in immune cell residency achieved by applying single-cell technologies on sparse material obtained from nasal swabs,” said Dr. Grundberg, who holds the Roberta D. Harding & William F. Bradley Jr. Endowed Chair in Genomic Research at the CMRI. “This high-resolution cellular investigation also allowed us to narrow it down to a specific immune cell population (CD8+ T cells) that were pronounced in children and express genes with known antiviral functions. Shortly after our report, there was another report from leading investigators in the field validating the signature we observed, which is always reassuring.”
The results of the study helped pave the way for research efforts that include large-scale epigenome investigations using similar nasal mucosal samples from COVID-19 positive children and adults. In these studies, Dr. Grundberg and her colleagues aim to understand population variability in disease outcome and the role of age, sex/gender, race, ethnicity and viral strains.

Dr. Grundberg’s CMRI co-authors on the study, which was published in 2021 in the journal Scientific Reports, were Tomi Pastinen, MD, PhD, Warren A. Cheung, PhD, Boryana Koseva, PhD, Todd Bradley, PhD, and Konner Winkley from the Genomic Medicine Center; and Rangaraj Selvarangan, PhD, and Dithi Banerjee, PhD, MSc from the Department of Pathology and Laboratory Medicine.

**Mission: proactively protect children and public health from infectious diseases**

The world learned from the COVID-19 that infectious diseases can significantly impact lives and public health. Experiences during the pandemic underscored the need for greater preparation to monitor viruses in the community and look for those that may evade detection with current technologies, may not be treatable with available medications, or may not be prevented with existing vaccines. The CMRI aims to get ahead of infectious diseases to protect the health of children everywhere.

To do this, the CMRI’s Emerging Infections Area of Emphasis (AOE) focuses on surveillance, epidemiology and outbreak investigations; in vitro diagnostic evaluation, implementation and outcomes; emergency and pandemic preparedness; vaccine trials and anti-infectives evaluation; antibiotic and laboratory stewardship; and pathogenesis of emerging infections. Much of this work is led by Rangaraj Selvarangan, BVSc, PhD, who serves as director of Clinical Microbiology & Molecular Infectious Disease Laboratories and the vice chair for research, Department of Pathology and Laboratory Medicine at Children’s Mercy.

“We were intrigued by our finding of this clear age association in immune cell residency achieved by applying single-cell technologies on sparse material obtained from nasal swabs.”

– Elin Grundberg, PhD
Other members of the AOE team, Dithi Banerjee, PhD, and Bishnu Adhikari, MSc, PhD, conducted a household COVID-19 transmission investigation called the COVID-19 Diagnostics and Investigations Empowering the Family (CODIEFY) study. This surveillance study took place in the Kansas City metropolitan area and involved the use of molecular testing for the SARS-CoV-2 virus and whole-genome sequencing to characterize the virus and explore whether transmission of SARS-CoV-2 in households was more common from adults to children or vice versa. The investigators also studied if the viral load and duration of viral shedding differed between different clinical samples, such as nasal swab, saliva and stool samples.

SARS-CoV-2 transmission within household members was documented in 80% of enrolled families, with transmission originating at equal rate from both children and adults. The investigators determined that 85% of household members were infected within two weeks of a child’s infection. Whole genomes of SARS-CoV-2 demonstrated that virus detection rates and viral load were higher in patients infected with the SARS-CoV-2 Delta variant. In addition, the research team identified saliva as a convenient alternative specimen type to blood for antibody testing, mainly in children.

**Effort: bring COVID-19 testing and education to schools**

COVID-19 research led by CMRI investigators extended beyond the laboratory and clinic to the Kansas City community, particularly in area schools.
Jennifer L. Goldman, MD and Jennifer E. Schuster, MD, both in the Division of Pediatric Infectious Diseases, spearheaded The School TLC Study, an initiative funded by the National Institutes of Health to offer testing, learning and consultation to Kansas City Public School students and staff to support safe in-person schooling.

During its first year, the study enrolled more than 1,000 participants and provided screening and symptomatic testing in eight schools in the Kansas City Public School District. Drs. Goldman and Schuster and their colleagues oversaw the training of dozens of additional nurses to offer symptomatic, on-demand testing, performing more than 4,000 COVID-19 tests during the school year.

In addition, the study team actively conducted outreach efforts to engage community members who speak different languages and contacted more than 100 local organizations—including businesses, faith-based organizations, non-profits, health centers, libraries, parks and media outlets—to reach diverse populations in the community.

Beyond convenient and free in-school COVID-19 testing, The School TLC Study provided additional benefits to students, parents and school staff including efficient and reliable results, quick turnaround of results, support from Children’s Mercy medical staff, and access to important information about COVID-19 and testing provided in multiple languages.
Genomic Data Accelerates Answers for Kids with Rare Diseases from First-of-its-Kind Repository

The Children’s Mercy Research Institute (CMRI), released more than 2,300 pediatric rare disease genomes through its Genomic Answers for Kids (GA4K) program, making it one of the largest pediatric rare disease whole genomic datasets ever publicly shared. A subset of the data has been recently submitted for publication and is available as a preprint.

GA4K is a first-of-its-kind approach to analyzing and sharing genomic data, with a goal to lead the world in diagnosis rates for pediatric rare diseases. To date, more than 3,160 patients with rare diseases have enrolled in the GA4K program, which has resulted in more than 16,000 new genomic analyses and more than 586 genetic diagnoses. In addition, the program has advanced research genomic analyses for children of 350 families with more common childhood diseases: cerebral palsy and Down’s Syndrome.

“The unfortunate reality is that rare diseases often go undiagnosed for far too long – children typically wait four to six years before being diagnosed,” said Tom Curran, PhD, FRS, Senior Vice President, Executive Director and Chief Scientific Officer, Children’s Mercy Research Institute. “By providing an open and collaborative environment, such as GA4K, we are helping move kids to the forefront of research discoveries much sooner.”

Giving access to our data allows researchers to link their own genetic findings so they can accept or reject hypotheses on their gene discoveries,” said Tomi Pastinen, MD, PhD, Director, Genomic Medicine Center, Children’s Mercy Kansas City. “Data sharing is the only way we’ll make headway in the quicker delivery of results that are non-diagnostic today.”

GA4K would not be possible without the generosity of the Kansas City community. The program has received approximately $18 million in funding from 200 donors.

The unique aspect of GA4K is that the full pediatric data repository will now be shared in a real-time web interface through a comprehensive process, which gives researchers and clinicians low-barrier access to processed data with disease-prioritized genetic changes accounting for more than 10,000 variants per patient. GA4K also periodically deposits full raw sequence data of patients and family members, which is accessible through the National Institutes of Health dbGAP.
“Because of these donors, researchers around the world will be able to understand and diagnose the most challenging pediatric diseases – truly changing the lives of our patients and their families,” said Dr. Curran.

Furthermore, the team prioritized candidate variants for 48% of patients beyond the confirmed clinical diagnoses and showed that some variants are dependent on the sequencing technology used. The results indicate that better systems that accelerate prioritized gene validation and newer sequencing tools, such as long-read genome sequencing (lrGS), are needed.

“Giving access to our data allows researchers to link their own genetic findings so they can accept or reject hypotheses on their gene discoveries. Data sharing is the only way we’ll make headway in the quicker delivery of results that are non-diagnostic today.”

– Tomi Pastinen, MD, PhD

About Preprint Data Publication
In addition to the data release, Dr. Pastinen and colleagues describe their approach in the manuscript “Genomic answers for children: Dynamic Analyses of >1000 pediatric rare disease genomes.” Available in preprint, this manuscript takes a comprehensive look at diagnostics and candidate variant genome analyses in pediatric rare disease patients through the GA4K program.

A total of 1,083 patients with suspected genetic disorders were part of the study. All individuals received short-read exome sequencing (ES) and were followed up by genome sequencing (GS), long-read genome sequencing (lrGS) and machine-learning variant prioritization.

The study revealed that 30% of patients received a diagnosis after the first gene test. Importantly, if earlier testing had failed, an additional 12% of patients were given a conclusive diagnosis – ending diagnostic odysseys that typically last several years.

“Crowd-sourcing data to advance the course of unsolved rare disease is the ethical and right thing to do,” said Dr. Pastinen. “We are advocating a unique approach and we hope others will actively join us in expanded data sharing.” In parallel with sharing patient and prioritized variant data, the team is making their lrGS “reference” data openly accessible, allowing others to use lrGS in rare disease.
How Genomic Answers for Kids is Making a Difference: Two Patient Stories

“It’s so nice having a diagnosis. Even though we don’t know much about the disorder and there’s not much more we can do treatment-wise, it’s so nice to know what it is that’s causing her delays and challenges. She still doesn’t walk, she doesn’t speak, but she does say, ‘Mom.’ It’s nice to know what it is – we have that info for us, and for our other kids.”

– Teresa, Celia’s mom

A diagnosis for Celia: Genomic Answers for Kids study provides insight into 8-year-old’s medical mystery

Celia’s parents have spent almost her entire life – six of her eight years – trying to solve her medical mystery.

Born a twin, Celia’s brother hit normal developmental milestones right on time, but Celia always lagged behind. At 1 year old, her brother was walking and Celia wasn’t even crawling yet. Then, the painful, odd movements started, and so did the unending doctor appointments.

“We live in Wichita and we went to so many doctors here – urology, acid reflux, neurology, etc. – but no one in Wichita could tell us anything,” said Teresa Cruz-Steele, Celia’s mom. “Finally, we were referred to the Children’s Mercy genetics clinic when Celia was almost 2 years old.”

The Children’s Mercy Neurology Clinic provided a lot of answers for the family, including a diagnosis of dystonia that explained those painful movements. But genetic testing came back normal, time after time, until one day, the neurologist told the family about Genomic Answers for Kids and encouraged them to enroll in the study.

“It’s so nice having a diagnosis. Even though we don’t know much about the disorder and there’s not much more we can do treatment-wise, it’s so nice to know what it is that’s causing her delays and challenges. She still doesn’t walk, she doesn’t speak, but she does say, ‘Mom.’ It’s nice to know what it is – we have that info for us, and for our other kids.”

– Teresa, Celia’s mom
“I thought, sure – why not. We had tried everything at that point – five years of testing – and nothing could find an answer,” said Teresa.

Months went by and Teresa forgot about the study. Until she received an unexpected phone call from their Children’s Mercy genetic counselor and heard the words, “I wanted to let you know that the research team found the diagnosis for Celia.”

“My whole body was shaking. I started crying. It’s been so long, and so many things have been going on with her health over the years. I just couldn’t believe that we now had a reason,” Teresa said.

Celia was diagnosed with a PDE2A disorder. She is one of only five people to have been documented with this disease in the United States. The symptoms of PDE2A align with every challenge Celia has experienced – movement disorder, developmental delays, low muscle tone, epilepsy and more.

“It’s so nice having a diagnosis,” Teresa said. “Even though we don’t know much about the disorder and there’s not much more we can do treatment-wise, it’s so nice to know what it is that’s causing her delays and challenges. She still doesn’t walk, she doesn’t speak, but she does say, ‘Mom.’ It’s nice to know what it is – we have that info for us, and for our other kids.”

Celia continues to receive care from a team of Children’s Mercy doctors who are committed to her wellbeing, and now they have added clarity when treating the symptoms of her rare disease.
Laurel’s daughter, Katie, had battled a compromised immune system and irregular blood levels for nearly 18 years, but it was the spring of 2017 when Laurel, mother of eight, first noticed something was seriously amiss with Katie. She had her tested for thyroid antibodies since autoimmune thyroiditis runs in the family. After seeing her high thyroid levels, Katie went on a dairy and gluten-free diet, and the family went about their day-to-day lives.

But later that year, during a camping trip on Labor Day weekend, what Laurel expected to be a relaxing, fun family trip took a turn for the worse when she noticed Katie was struggling to walk the short trip to the campground. She was pale and had no energy. That’s when it hit Laurel that there was more going on, and it was something they needed to figure out fast.

They cut their camping trip short and took Katie into their doctor the next day. There, they learned she was incredibly anemic, and her white blood cell count was dangerously low. Doctors wanted to do a blood transfusion to bring up her white blood cell count, but they quickly learned that Katie was at too much risk of going into anaphylactic shock given the high levels of antibodies in her system.

Over the next few months Laurel took Katie to doctors across Wichita, where she was prodded and poked many times over by many different specialists. Finally, a rheumatologist recommended they find a hospital where specialists could work together to help Laurel find answers for her daughter.

Laurel recalled a friend telling her many times over the years how wonderful Children’s Mercy had been for their family. So after a year of searching for answers, Laurel and Katie made the drive to Kansas City, where they met with Maxine Hetherington, MD, hematologist/oncology specialist, and began their journey with Children’s Mercy.

Now Katie knows: Roifman syndrome diagnosis provides understanding for teen and her family
After their initial appointment, Dr. Hetherington was able to connect them to other specialists at Children’s Mercy. Katie saw specialists from internal medicine, hematology/oncology, pulmonology and immunology, which turned out to be a huge part of Katie’s health care picture. Doctors across the specialties worked closely together to provide comprehensive care for Katie while also working diligently to find a diagnosis.

Finally, after multiple trials and tests, Katie’s team of doctors referred her to the Genetics Clinic. While clinical testing came back negative for any diagnosis, Katie’s sample was entered into the genetics registry, as were samples provided by her parents.

Laurel and Katie had made the journey to Children’s Mercy many times now in search of an answer for Katie. And little did they know, they were finally going to have one. When the phone rang at home and Laurel answered it, the genetic counselor had good news.

After 18 years of struggling with Katie’s immune system and blood levels, and years of working with doctors across the region to search for answers, they had finally found a diagnosis and an explanation for Katie’s myriad of symptoms. Through a new flagship program of the CMRI, Genomic Answers for Kids, doctors at Children’s Mercy were able to pinpoint Katie’s rare disease: Roifman syndrome. It’s a disease that impacts so few people that any information on it is hard to come by – it is estimated Katie is one of only 50 people in the world affected by Roifman syndrome.

Having a diagnosis – finally – was a relief, but also brought up more questions for Laurel. After Katie’s diagnosis, she had a hunch that Katie may not be the only one in their family with Roifman syndrome, so she worked with Children’s Mercy to run genomic tests on two of her other children as well. Her motherly instincts were correct, and through the Genomic Answers for Kids program, Laurel now has a diagnosis for three of her children.

“It’s really heavy sometimes and can feel overwhelming. But we’re thankful to have a team that has walked us through it and been very steady and persistent in not giving up trying to search for what’s going on beneath the layers,” Laurel said.
As the world has learned over the past two years, infectious diseases have the ability to significantly impact our lives and public health. The world’s experience with the SARS-CoV-2 (COVID) virus has underscored the need for greater preparation by monitoring viruses in the community and looking for those that may evade detection with current technologies, may not be treatable with available medications, or may not be prevented with existing vaccines.

Under Dr. Selvarangan’s leadership, the Emerging Infections AOE focuses on six key areas of investigation:

- Surveillance, epidemiology and outbreak investigations, which includes the longstanding work of Children’s Mercy investigators in the CDC-funded New Vaccine Surveillance Network.
- Clinical trials for evaluation and implementation of in vitro diagnostic tests and measuring their impact on patient outcomes through industry-sponsored studies.
- Emergency and pandemic preparedness, including pandemic viruses such as SARS-CoV-2 and influenza as well as emerging viruses like enterovirus D68 (EV-D68) and its associated complication of acute flaccid myelitis in children.
- Control and prevention of infections by vaccines for pandemic influenza, SARS-CoV-2 and research on the growing problem of antimicrobial resistance.
- Laboratory investigations to support antibiotic and laboratory stewardship efforts to ensure the right drug and testing for the right patient at the right time.
- Pathogenesis of emerging viral and bacterial infections in children, including parechovirus central nervous system infections and invasive bacterial infections in children.
A new Area of Emphasis (AOE) at the Children’s Mercy Research Institute aims to get ahead of infectious diseases in order to protect the health of children everywhere.

“We have built a solid foundation for our research efforts and a fortified, collaborative structure to support it,” said Dr. Selvarangan. “With dedicated support and investment from CMRI leadership and the hospital, we will expand our critical work and enhance our ability to handle any current or emerging infectious disease situation in order to protect children and the public health.”

In addition to working to be ahead of the curve with respect to viruses affecting the local community and the country, the Emerging Infections AOE presents unique opportunities for investigators at CMRI to take part in highly collaborative and cross-disciplinary research projects. Among the departments, divisions and groups currently working with Dr. Selvarangan and the AOE are Infectious Disease, Emergency Medicine, Laboratory Medicine, Genomic Medicine and Immunogenetics, Population Health, Neonatology, Adolescent Medicine, Nephrology, Gastroenterology, and Precision Therapeutics.
Braden’s Hope Support Paves Way for Next Level Childhood Cancer Research

Braden’s Hope for Childhood Cancer’s mission is to raise awareness and funds for research studies of targeted therapies that shut down the activators of childhood cancers.

Partnering with Children’s Mercy and The University of Kansas Cancer Center, Braden’s Hope funds collaborative pediatric research projects that are uniquely positioned to find cures for our community’s children and bring hope to our heroes with cancer. Since 2017, this funding includes three $1 million research projects led by teams of investigators from Children’s Mercy and KU Cancer Center. One of the studies, led by Tomoo Iwakuma, MD, PhD, (awarded 2017) examines p53, one of the most important genes that stops the growth of osteosarcoma tumors in children. Another study, led by Midhat Farooqi, MD, PhD, (awarded 2019) investigates children’s solid tumors and why some don’t respond to treatments using their own immune cells (T cells) to kill cancer cells. A third study, led by John Perry, PhD, (awarded 2018) now in a pilot clinical trial, uses a standard chemotherapy drug in a new way to eliminate leukemia cancer stem cells and provoke an immune response that will effectively vaccinate children against relapse.

Dr. Iwakuma’s study, “Capitalizing on p53 Loss/Mutations in Osteosarcoma by Novel Compounds,” is targeting osteosarcoma cells that lack p53 with a new drug development strategy. The goal is to discover and characterize small-molecule drugs that specifically suppress progression of osteosarcoma and ultimately to test the compound(s) in clinical trials. The team has been testing their hypothesis

“The support of Braden’s Hope has really allowed us to hit the ground running and take our research to the next level. Many researchers are initially surprised by our findings. The more researchers see our data, the more our results make sense to them.”

– John Perry, PhD
that KU0171032 analogs induce mitotic arrest and cell death specifically in p53-deficient cells as a single agent through the dual effects of increasing ROS production and inhibiting ATM-mediated DNA damage response (DDR), offering a novel approach to treating cancers with p53 deletions or mutations. The findings of biological effects of KU0171032 and the mechanism of action have been summarized and will be submitted to a high-impact journal. Meanwhile, the study team continues to improve metabolic stability and pharmacological properties of KU0171032 analogs for study in future clinical trials.

“Discovery of novel compounds targeting vulnerabilities imposed by p53 deficiency is significant, since such compounds would inhibit progression of highly malignant and therapy-resistant cancers deficient in p53 and because completion of this proposal would accelerate development of a novel p53-deficiency-targeted anti-cancer therapy. These compounds are also expected to cause minimal side effects, since normal cells do not usually have p53 deletions or mutations,” said Dr. Iwakuma.

Dr. Farooqi’s study, “Targeting Solid Tumors with Multi-antigen Specific T-cells by Identifying the Genetic and Epigenetic Determinants of Therapeutic Response,” supports an ongoing clinical trial at Children’s National Medical Center in Washington, D.C. In this trial, pediatric patients with relapsed or treatment-resistant solid tumors, such as sarcomas, neuroblastoma, and Wilms’ tumors, are being treated with T cell infusions. This therapy is created by harvesting the patient’s own T cells, which are then grown in the lab. These immune cells are then exposed to multiple markers found on the surface of solid tumors and injected back into the patient to kill cancer cells. Dr. Farooqi’s team seeks to understand how a tumor’s genetic makeup affects its response to T cell therapy. His team has begun sequencing pediatric solid tumors collected at Children’s Mercy, as well as other sites across the country such as Children’s Health in Dallas, Texas, and Cook Children’s in Fort Worth, Texas. Thanks to the Genomic Medicine Center and the Children’s Mercy Research Institute, the most cutting-edge sequencing technologies—long-read sequencing and HiC sequencing—are being used to study these tumors with the goal of uncovering novel genetic drivers of pediatric cancer as well as specific biomarkers that predict response to immune therapy.

“I am deeply grateful to Braden’s Hope for Childhood Cancer for their generous support. We were able to establish important collaborations with other children’s hospitals across the United States directly because of it, as well as build and expand upon our library of pediatric tumor genomes at Children’s Mercy. This, in turn, allowed us to participate in national data sharing
efforts around childhood cancer, together with The University of Kansas Cancer Center and through support from the National Cancer Institute,” said Dr. Farooqi. “Like Braden’s Hope, our larger goal is not only to improve treatment but ultimately provide a life-long cure for children with cancer; Braden’s Hope gives us hope of making that a reality!”

Dr. Perry’s study, “Targeting the Therapy-Resistant Cancer Cells that Cause Relapse,” examines leukemia stem cells or cancer stem cells and their ability to hide from immune recognition. They found that administering one of the major backbone chemotherapeutic agents to leukemia stem cells at a very low dose knocks down the camouflage that hides the stem cells from the immune system, allowing the immune system to come in and eliminate the cells that are responsible for relapse.

Dr. Perry’s team is also exploring the potential of a new drug that may combine the positive effects of the repurposed old drug without the negative effects. The mechanism underlying the positive and negative effects is being investigated using whole genome CRISPR screens along with single-cell genomic and proteomic analysis. This will allow them to improve the positive immunological effects while preventing negative effects. Ultimately, the team’s goal is to eliminate the cancer cells that are resistant to current treatments by provoking an immune response that will effectively vaccinate patients against relapse.

“The support of Braden’s Hope has really allowed us to hit the ground running and take our research to the next level,” said Dr. Perry. “Many researchers are initially surprised by our findings. The common view is that old chemotherapy drugs work by killing rapidly dividing cells at a high dose. The idea that they can have more subtle, targeted effects seems surprising. However, the more researchers see our data, the more our results make sense to them.”

Thanks to Braden’s Hope, these studies, and others to follow, are redefining cancer care for children here at home and across the globe. We look forward to continued partnership with Braden’s Hope to create a world of wellbeing for children facing a cancer diagnosis.
National Institutes of Health (NIH) Awards

KL2 Career Development Program Award, Frontiers CTSI at the University of Kansas, NIH
Barral, Romina [PI]
Ramaswamy, Megha (Primary Mentor)
Miller, Melissa [Co-Mentor]
Staggs, Vincent [Co-Mentor]
Brindis, Claire, University of California San Francisco [Co-Mentor]
Miller, Elizabeth, University of Pittsburgh [Co-Mentor]

$143,494
07/01/2021 - 06/30/2023
Decreasing teen reproductive health disparities in rural Latino immigrant communities
Click here to read more.

R01 DK132350, NIDDKD, NIH
Carlson, Jordan [PI]
Staggs, Vincent [Co-I]
Feldman, Keith [Co-I]

$2,665,578
04/14/2022 - 01/31/2026
Health impacts of city wide zero-fare bus transit: A natural experiment
Click here to read more.

R21 HD098086, NICHD, NIH
Miller, Melissa [PI]
Randell, Kimberly [Co-PI]

$389,828
05/01/2021 - 04/30/2022
A novel community intervention to reduce disparate impact from COVID-19 on vulnerable adolescents
Click here to read more.

K23 DA055736, Mentored Career Development, NIAD, NIH
Masonbrink, Abbey [PI]
Catley, Delwyn [Primary Mentor]
Miller, Melissa [Co-Mentor]
Richter, Kimber, The University of Kansas Medical Center [Co-Mentor]

$50,000
07/01/2021 - 06/30/2022
Eating disorders individualized therapeutics-naltrexone neuroimaging (EDIT-N2)
Click here to read more.
IAMI Trailblazer Award, Frontiers CTSI at the University of Kansas, NIH  
Vivian, Jay (PI)  
$25,000  
07/01/2021 – 06/30/2022  
A cell-based platform for screening for therapeutics for Vici syndrome and other diseases of autophagy  
Click here to read more.

T32 HD069038, NICHD, NIH  
Wagner, Jonathan (PI)  
Goldman, Jennifer (Co-PI)  
$1,292,338  
05/01/2021 - 04/30/2026  
Postdoctoral research in pediatric clinical pharmacology

U01 DK066143, NIDDK, NIH  
Warady, Bradley (PI)  
$155,238  
8/1/2021 - 7/31/2022  
Administrative supplement for research and capacity building efforts related to bioethical issues (admin supp clinical trial optional)

Research Grants

Crohn’s & Colitis Foundation of America  
Bass, Julie (PI)  
$60,000  
01/01/2021 - 12/31/2023  
CAPTURE IBD- Deputy Director Agreement

American Thrombosis and Hemostasis Network  
Carpenter, Shannon (PI)  
$1,500 per patient enrolled  
09/30/2020 – 09/29/2025  
ATHN transcends: A natural history cohort study of the safety, effectiveness, and practice of treatment in people with non-neoplastic hematologic disorders

American College of Cardiology  
Erickson, Lori (PI)  
$8,350  
12/01/2021 - 11/30/2022  
Evaluating pediatric physiologic monitoring for infants with complex congenital heart disease

Masonic Cancer Alliance  
Flatt, Terrie (PI)  
Iwakuma, Tomoo (Co-I)  
Ahmed, Atif (Co-I)  
Gonzalez Dominguez, Elizabeth (Co-I)  
$250,000  
12/01/2021 - 12/31/2023  
The activity of metarrestin: An investigational anti-cancer agent that reduces perinucleolar compartment prevalence in pediatric Ewing sarcoma

University of Kansas Medical Center  
Flatt, Terrie (PI)  
Ahmed, Atif (Co-I)  
Gonzalez Dominguez, Elizabeth (Co-I)  
$24,000  
01/01/2022 - 12/31/2022  
The role of the perinucleolar compartment and eEF1A2 in pediatric and young adult sarcoma
Masonic Cancer Alliance
Guest, Erin (PI)
Perry, John (Co-I)
$249,801
12/01/2021 - 12/31/2023
Evaluating the impact of rare, clinically detected germline variants in MLL-AF4 leukemia: A bedside-to-bench translational model of infant ALL

Midwest Cancer Alliance
Iwakuma, Tomoo (PI)
$250,000
11/01/2019 - 10/31/2022
Role of a sugar (O-GlcNAc) modification of EWS-FLI1 in malignant progression of Ewing’s sarcoma and its therapeutic potential

2021 Research Catalyst, Alex’s Lemonade Stand Foundation
Iwakuma, Tomoo (PI)
$25,000
05/17/2021 - 05/16/2022
Identifying drugs that kill overexpressing MDM2 gene in pediatric cancers
Click here to read more.

Ehlers-Danlos Society
Jones, Jordan (PI)
$50,000
05/03/2021 - 05/02/2022
Care and management of children with Ehlers-Danlos syndrome: A survey of primary care providers

Childhood Arthritis and Rheumatology Research Alliance
Jones, Jordan (PI)
$490
12/01/2021 - 11/30/2022
Down Syndrome–associated arthritis cohort in the new childhood arthritis and rheumatology research alliance (CARRA) registry: Clinical characteristics, treatment and outcomes

BioNexus KC (KCALSI)
McLaughlin, Matthew (PI)
$50,000
07/01/2021 - 06/30/2022
BioNexus KC - Patton Trust Research Grant

Noah’s Bandage Project
Myers, Gary (PI)
$250,000
11/01/2021 - 10/31/2024
Development of a novel chimeric antigen receptor for the treatment of pediatric solid tumors

MO Dept. of Health and Senior Services
Oermann, Christopher (PI)
$69,180
06/01/2021 - 05/31/2022
Newborn Cystic Fibrosis screening services
Basic Science Grant Award, The Ehlers-Danlos Society
Pastinen, Tomi (PI)
Rush, Eric (Co-I)
$200,000
08/16/2021 – 08/16/2023
Hidden genome in hEDS resolved by 3rd generation sequencing
Click here to read more.

University of Missouri - Columbia
Schuster, Jennifer (PI)
Friedman, Elizabeth (Co-PI)
Goldman, Jennifer (Co-PI)
$22,946
10/01/2021 - 06/30/2022
Show-Me ECHO COVID kids

The Ray E. Helfer Society
Segal, Rachel (PI)
$6,380
03/01/2021 - 02/28/2023
Understanding home visitor attendance at well child checks: A qualitative study
Click here to read more.

U01 IP001154, CDC
Selvarangan, Rangaraj (PI)
Bradley, Todd (Co-PI)
Dinneen, Laura (Co-PI)
Harrison, Christopher (Co-PI)
Moffatt, Mary (Co-PI)
Pahud, Barbara (Co-PI)
Grundberg, Elin (Co-PI)
Purandare, Amol (Co-PI)
Schuster, Jennifer (Co-PI)
Weddle, Gina (Co-PI)
Weltmer, Kirsten (Co-PI)
$1,441,647
09/01/2021 - 08/31/2026
U.S. enhanced surveillance network to assess burden, natural history and effectiveness of vaccines to prevent enteric and respiratory viruses in children
Click here to read more.

Investigator Studies Program Award, Organon
Stancil, Stephanie (PI)
Adelman, William (Co-I)
Hurley, Emily (Co-I)
Miller, Melissa (Co-I)
Yeh, Hung-Wen, (Co-I)
$383,165.57
07/01/2021 – 06/30/2023
A prospective, quasi-experimental study to evaluate the feasibility of CHOICE-AYA for unintended pregnancy prevention in adolescents and young adults (AYA) experiencing homelessness
Click here to read more.

Paul Patton Charitable Trust
Stancil, Stephani (PI)
Leeder, J. Steven (Co-PI)
$75,000
01/01/2022 - 12/31/2022
Patton Trust Research - Antidepressant study
Children’s Trust Fund
Terreros, Amy (PI)

$441,176
07/01/2021 - 06/30/2025

*Child abuse prevention projects: Safe sleep initiative grant*

Training/Mentored Research

**Young Investigator Award, NASPGHAN**

Chevalier, Rachel (PI)
Catley, Delwyn (Primary Mentor)
Miller, Melissa (Co-Mentor)

Richter, Kimber, The University of Kansas Medical Center (Co-Mentor)
Wilson, Karen, ICAHN-Mount Sinai (Co-Mentor)
Richardson, Troy, Children’s Hospital Associations (Co-Mentor)

$150,000
12/15/2021 - 12/15/2023

*Mucosal CYP3A4 and P-gp mediated drug metabolism of budesonide in patients with eosinophilic esophagitis (EoE)*

[Click here to read more.]

**Postdoctoral Fellowship Research Grant in Pediatric Psychology from the Society of Pediatric Psychology**

Fornander, Mirae (PI)
Moser, Christine (Mentor)
Egan, Anna (Mentor)

$10,000
01/01/2022 – 12/31/2022

*A mixed-methods examination of transgender youth desistance*

Postdoctoral Fellowship Award, American Diabetes Association

Materia, Frank (PI)
Catley, Delwyn (Co-Mentor)
Goggin, Kathy (Co-Mentor)

$195,396
04/01/2022 – 03/31/2025

*Understanding African Americans’ adoption and engagement with mobile health for lifestyle modification to prevent type 2 diabetes*

Additional Awards

University of Missouri - Columbia

Beck, Amy (PI)

$5,524
06/15/2021 - 06/14/2022

*SHOW-ME ECHO AGREEMENT*

REACH Healthcare Foundation

Cowden, John (PI)

$100,000
12/01/2021 - 12/31/2022

*Adelante - Spanish language behavioral health capacity building project*

Health Forward Foundation (HCF KC)

Cowden, John (PI)

$45,000
10/01/2021 - 10/01/2022

*Adelante KC-Health Forward Foundation*
Cystic Fibrosis Foundation
Escobar, Hugo (PI)
Singh, Alvin (Co-I)
$254,699
04/01/2022 - 03/31/2023
Cystic Fibrosis Foundation: 2022-2023 TDN Renewal

University of Missouri - Columbia
Friedman, Elizabeth (PI)
$3,840
10/01/2021 - 09/30/2022
SHOW-ME ECHO

University of Missouri - Columbia
Hampl, Sarah (PI)
$134,122
03/01/2021 - 06/30/2022
SHOW-ME ECHO

GlaxoSmithKline
Humiston, Sharon (PI)
$50,000
05/15/2021 - 05/14/2022
Comprehensive Vaccine Education from Training to Practice
Click here to read more.

Janssen Research and Development
Jones, Bridgette (PI)
$224,800
04/11/2022 - 04/10/2026
Janssen support of Summer Training in Academic Research (STAR) 2.0 Program
Click here to learn more.

Healthcare Coalition Partners of KS, LLC
Kolleda, Kristen (PI)
$4,975
02/01/2022 - 03/15/2022
KS Metro Healthcare Coalition Mini Grant

Healthcare Coalition Partners of KS, LLC
Kolleda, Kristen (PI)
$4,975
02/17/2022 - 03/15/2022
KS Metro Healthcare Coalition Mini Grant #2

Children's Hospital Association
Long, Desiree (PI)
$14,366
09/20/2021 - 05/31/2022
Child’s Play - Grants for Play Projects in Children’s Hospitals

MO Dept. of Health and Senior Services
Quiriconi, Margo (PI)
$62,500
06/06/2022 - 08/12/2023
Summer Food Service Program 2022
Children's Trust Fund
Sielaff, Amy (PI)
$25,000
05/16/2022 - 06/30/2023
CBCAP Supplemental Funding for Immediate Needs

Veteran's Affairs Medical Center
Staggs, Vincent (PI)
$21,772
10/01/2021 - 02/28/2022
VA IPA

Jackson County COMBAT
Templeton, Oneta (PI)
$65,000
01/01/2022 - 12/31/2022
2022 COMBAT Substance-Use Disorder Treatment for TIES

Intramural Awards

CMKC Internal Grants Program
Five Children’s Mercy researchers received CMKC internal grant awards in 2021 through the CMKC Internal Grants Program which has been active for the last 15 years. Each spring, the five opportunities are announced internally, along with the different criteria for submission. Their availability each year is dependent on several factors. The Katharine Berry Richardson Foundation (KBR) grant nurtures new researchers by giving them the time, infrastructure, and mentorship necessary to begin their careers as investigators. The Kenneth & Eva Smith Foundation has donated funds to support Clinical Scholar Awards to help researchers establish or expand their research programs. The Tom Keaveny Endowed Fund supports pediatric cancer research. The Connolly Research Scholar Endowment continues Ed Connolly Jr.’s interest in pediatric excellence by advancing research, particularly in genomic medicine, to find answers, better treatments and cures for childhood illness and disease.

Katharine Berry Richardson Foundation
Chakawa, Ayanda (PI)
$39,998
10/01/2021 – 09/30/2023
Disparities in pediatric behavioral health help-seeking: Developing culturally informed pathways to facilitate service access

Tom Keaveny Endowed Fund
Perry, John (PI)
$35,000
10/01/2021 – 09/30/2023
Ex vivo maintenance and expansion of healthy hematopoietic versus leukemia stem cells
Kenneth & Eva Smith Foundation  
Shakhnovich, Valentina (PI)  
$50,000  
10/01/2021 – 09/30/2022  
*Effect of steatosis on hepatic drug metabolism in children*

Kenneth & Eva Smith Foundation  
Shook, Robin (PI)  
Yeh, Henry (Co-I)  
Hurley, Emily (Co-I)  
Ries, Daniel, Sandia National Laboratories (Co-I)  
$50,000  
10/01/2021 – 09/30/2022  
*Fitbit teens: A measurement error approach to estimating energy balance in free-living adolescents*

Marion Merrell Dow Fund/Ed Connolly Research Scholar Endowment  
Smail, Craig (PI)  
$15,000  
10/01/2021 - 09/30/2023  
*Rare disease diagnosis beyond the exome: Computational approaches to interpret the effects of rare noncoding variants on disease processes*

**Mercy Research Partners**  
Mercy Research Partners was formed with the goal of bringing together emerging philanthropists to provide a uniquely immersive research funding experience and create an annual investment pool to advance pediatric research at Children’s Mercy – ultimately unlocking solutions that advance our mission to create a world of wellbeing for all children. This exciting, shark-tank-style model allows donors to connect with and fund research in a new way and brings Children’s Mercy researchers face-to-face with potential funders for coaching and investment. Researchers were selected to pitch their projects to the Mercy Research Partners members at a Pitch Party held on the evening of June 3, 2021. At the end of the evening the Members voted to select five research projects to receive funding from their investment pool of more than $540,000.

Mercy Research Partners  
Bradley, Todd (PI)  
$75,000  
06/01/2021 – 05/31/2022  
*Project Description:*

Diffuse large B-cell lymphoma describes a highly variable form of cancer with survival outcomes that vary widely from patient to patient. Molecular profiling can aid in identifying patients that have a high risk for treatment failure thereby empowering providers to seek out alternative treatment options. Dr. Bradley and his team have identified unique gene signatures around which they are developing clinical diagnostic assays that can be used to improve outcomes in patients with this unique form of cancer.
Mercy Research Partners
Chavez-Bueno, Susana [PI]

$67,439
06/01/2021 – 06/30/2022

Project Description:
Countless newborn babies across the globe suffer from bloodstream infections that place their lives at risk. The pathogens that cause these infections typically reach the baby through the genital tract of the mothers. There are currently few options to prevent these infections; however, Dr. Chavez-Bueno and her team believe that they have discovered a new therapeutic strategy that will help to prevent infections with a common bacterium responsible for these infections, Escherichia coli.

Mercy Research Partners
Haney, Eric [Co-PI]
Reading, Brenton [Co-PI]

$124,693
06/03/2021 – 01/31/2023

Project Description:
To adequately care for some patients, such as those with cancer or kidney disease, long-term access to their blood stream is needed. Tunneled central venous catheters safely and effectively provide this access, but they are very difficult to remove and often require general anesthesia. Taking a cue from nature, Eric Haney and Dr. Brenton Reading have developed a modification to these catheters that will make it easier to secure and remove these devices.

Mercy Research Partners
Oyetunji, Tolulope [PI]

$22,500
06/01/2021 – 06/30/2022

Project Description:
Various conditions require that bowel contents be diverted outside the body to a bag that is connected through an opening in the skin. However, these bags can leak causing severe irritation to the surrounding skin. These bags also restrict a patient's freedom to engage in various activities and have a significant impact on body image. Dr. Oyetunji and his team are creating a less bulky, leak-free stoma device that promises to significantly improve quality of life for patients.

Mercy Research Partners
Vivian, Jay [PI]

$155,429
06/03/2021 - 08/02/2022

Project Description:
Vici syndrome is a devastating genetic disorder that often robs children from making it to their 5th birthday. At present, there are no treatment options for these children. A team led by Dr. Vivian is designing new cell lines that will allow researchers to screen large libraries of compounds in the hopes of accelerating the identification of treatment options for children with Vici syndrome and other deadly rare diseases.
Appointed Endowed Chairs FY21-FY22
Children’s Mercy invested 15 endowed positions in 2021 and 2022 to honor outstanding clinicians, researchers and leaders who are committed to transforming the health, wellbeing and potential of children across the region and world.

“Established through the generosity of committed donors, endowed positions are the highest academic award one can achieve – it is an incredible honor to be the named holder of the appointment and an enduring tribute to the donor who creates it,” said Paul Kempinski, Children’s Mercy President and CEO, Alice Berry, DDS, and Katharine Berry, MD, Endowed Chair in Executive Leadership. “Now, more than ever, endowed positions are crucial for recruiting and retaining world-class talent. They provide the recipient time and funding to focus on their work. It truly is an investment in the future of children’s health.”

Aliessa Barnes, MD
Melva & Randall L. O’Donnell Chair in Pediatric Cardiology

Denise Bratcher, DO
Dr. Sidney F. Pakula Endowed Chair in Graduate Medical Education

Mark Clements, MD, PhD, CPI, FAAP
Rick and Cathy Baier Family Endowed Chair in Endocrinology

William Douglas, MD
Jerry Smith Chair in Pediatric Cardiac Surgery

Jeanne M. James, MD, MBA, FAAP
Joyce C. Hall Eminent Scholar in Pediatrics

Robert Lane, MD
Schellhorn Family Endowed Chair in Medical Administration

James E. O’Brien Jr., MD, FACS
Joseph Boon Gregg/Missouri Endowed Chair in Cardiac Surgery

Steve Olsen, MD
Swatek Family Endowed Chair in Neonatology

Eric T. Rush, MD, FAAP, FACMG
Underdown/Yeomans Family Endowed Professorship in Connective Tissue Disorders Care

Venkatesh Sampath, MD, MBBS, MRCPCH
Sosland Chair in Neonatal Research

Rangaraj Selvarangan, BVSc, PhD, D(ABMM), FIDSA, F(AAM)
William R. Brown/Missouri Endowed Chair in Medical Genetics and Molecular Medicine

Sarah Soden, MD
Nick Timmons Endowed Chair in Developmental and Behavioral Health

Tangula Taylor, MBA, BSN, RN, NE-BC
Bernell Hevner O’Donnell, RN Endowed Chair – Chief Nursing Officer
CMRI Biorepository (CRIB) receives CAP Accreditation.
In June 2021, JD Nolen, MD, PhD, MSPH, Director of the Children’s Mercy Research Institute Biorepository (CRIB) was informed that the biorepository had received accreditation status from the College of American Pathologists (CAP) Biorepository Accreditation Program (BAP).

The CAP Biorepository Accreditation Program is the first accreditation program designed to improve the quality and consistency of biorepositories. Pioneered in 2012, the program’s goal is to establish guidelines and requirements for the standardization of processes that will result in high-quality human specimens and genetic materials used to support research. The program helps ensure confidence in specimen provenance, collection integrity, and pre-analytical variable tracking by reviewing over 400 requirements.

To date, the CAP has accredited around 70 biorepositories across the United States. The accreditation announcement of the CRIB makes it only the fifth pediatric biorepository to achieve this status.

National Honors and Recognitions During FY22

Accepted into the American Pediatric Society
Tarak Srivastava, MD, FASN

Accepted into the Society for Pediatric Research (SPR)
Alain Cuna, MD

Elected as an American Academy Microbiology Fellow
Rangaraj Selvarangan, BVSc, PhD, D(ABMM), FIDSA, F(AAM)

Elected to the Association for Molecular Pathology (AMP) Infectious Diseases Program Committee
Rangaraj Selvarangan, BVSc, PhD, D(ABMM), FIDSA, F(AAM)

Named as one of Modern Healthcare’s class of Top 25 Innovators
Tomi Pastinen, MD, PhD

2021 Highly Cited Researcher – Pharmacology and Toxicology, Institute for Scientific Information, Clarivate
Andrea Gaedigk, PhD

J. Steven Leeder, PharmD, PhD
Total Grant Expenditures: 2018 – 2022

- FY 2018: $18,041,451
- FY 2019: $20,583,502
- FY 2020: $21,216,276
- FY 2021: $25,693,226
- FY 2022: $29,109,630
$29,109,630 Total

- Federal: $16,572,137
- Foundation (Prime and Sub): $4,192,535
- Other: $5,053,243
- Industry Clinical Trials: $3,291,715
Learn more how Children’s Mercy Research Institute accelerates groundbreaking therapies and treatments to transform the potential of children.

childrensmercy.org/research