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Children's Mercy Hospitals and Clinics
ANNUAL RESEARCH REPORT

2012



Children's Mercy
HOSPITALS & CLINICS

Kansas City





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Michael Artman, MD and Gregory Kearns, PharmD, PhD



Dear Friends and Colleagues,

It is our pleasure to share with you the Children's Mercy Hospital 2011-2012 Annual Research Report. Our researchers, health care professionals and more than 6,000 employees continue to embrace the truth that we must be squarely engaged in scientific discovery and knowledge creation if we are to continue to realize our core mission of improving the lives of our patients and families through the delivery of the best pediatric care in our country and beyond.

As reflected by the information contained within this report, 2011-2012 were years of continued growth for our academic research enterprise at Children's Mercy. During the past two years, our faculty members and staff authored or co-authored hundreds of journal articles, book chapters and review articles. Additionally, our researchers gave several hundred scientific presentations at national and international meetings, thereby spreading the relevance and reach of Children's Mercy far beyond our community. The recruitment of new faculty and work of existing faculty has also resulted in a significant increase in the number of grant submissions and research awards received from NIH, foundations and the private sector.

In addition to these productivity metrics, Children's Mercy has continued to expand several of its research programs, which are recognized worldwide as being nothing short of excellent. These include our exemplary programs in Genomic Medicine, Chronic Renal Disease, Clinical Pharmacology and Therapeutic Innovation, and Developmental/Behavioral Medicine. Also, we have worked diligently to lay the groundwork for the development of two new programs; one focused on health outcomes research, and the other on innovations in pediatric health care delivery. As an academic pediatric health care system, we remain committed to an approach to pediatric research that is not simply translational but, rather, transformational.

Recognizing that success in science requires effective collaboration, investigators at Children's Mercy continue to effectively partner with institutions and colleagues within our region and beyond. In addition to our primary academic affiliate, the University of Missouri-Kansas City School of Medicine, basic and clinical scientists at Children's Mercy work with colleagues at the University of Kansas, the Kansas City University of

Medicine and Bioscience, and the Stower's Institute for Medical Research. As both a health care institution and research entity devoted solely to pediatrics, Children's Mercy figured prominently in the recent National Cancer Institute designation of the University of Kansas Cancer Center and the awarding of the Clinical/Translational Science Award to the University of Kansas School of Medicine. Also, during the past year, we have expanded the reach of Children's Mercy through research activities performed in collaboration with the World Health Organization, which spans the treatment of tuberculosis in pediatric patients to the development of a novel, economical device that can reliably predict the body weight of infants through adolescence.

The report which follows describes the excellence of our research programs and many of our dedicated scientists and clinicians who make them possible. We hope you will take a few moments to read through this report, reflect on it, and most importantly, share in the celebration of success as we work together to continue the evolution of Children's Mercy into a world-class institution for pediatric research. In attaining this goal, we will ensure that the patients we are privileged to care for, and those beyond the boundaries of our institution, will benefit from the very best that new discoveries and knowledge can provide.

Sincerely,

Michael Artman, MD
Pediatrician-in-Chief; Chairman, Department of Pediatrics; Joyce C. Hall Endowed Chair at Children's Mercy; Executive Director for Research Strategy and Implementation; Professor of Pediatrics, University of Missouri-Kansas City School of Medicine

Gregory Kearns, PhD, PharmD
Professor of Pediatrics & Pharmacology, University of Missouri-Kansas City School of Medicine; Chief Scientific Officer; Chair, Research Development and Clinical Investigation; Marion Merrel Dow/Missouri Endowed Chair in Pediatric Medical Research



Research Strategic Plan Keeps Programs

During the past 15 years, research at Children's Mercy has grown in a variety of directions, with a large group of physicians, nurses and allied health professionals involved in a diversity of research.

We've strengthened our infrastructure, recruited additional talent and expanded research opportunities. And like any institution, we've worked to refine our business model.

This past year, we embarked on a new research strategic planning process to assess where we are, where we want to be and what it would take to get there.

"As a comprehensive pediatric medical center, we must be able to move in many directions simultaneously to embrace our patient care mission. We don't have the same luxury with our research program. To succeed in research, it is essential that we remain focused on those areas of excellence that have the greatest possibility of having the most significant impact," says Gregory Kearns, PharmD, PhD, The Marion Merrell Dow/Missouri Endowed Chair in Pediatric Medical Research at CMH and UMKC, and the Chief Scientific Officer and Chair of Research and Development at Children's Mercy.

"Our goal is to move the institution forward by advancing our reputation for excellence in specific areas of research, and selectively developing new ones. We want to be an institution where innovation in research drives discovery which produces the knowledge necessary to make important treatment decisions for our patients. As an ever-evolving institution we are ready to take the next deliberate step."

With more than 48,000 square feet dedicated to research, 200-plus physicians and scientists actively involved in conducting research, and clinical volumes of nearly 500,000 patient encounters per year, Children's Mercy is poised to move forward with a new research plan that will keep the hospital moving forward in redefining and advancing pediatric medicine.

"We have a moral obligation to improve the future for children. It is not enough to provide great care. We want to learn from each patient so we can do better the next time. We need to help contribute to learning and in coming up with better

On The Move

ways to diagnose, treat, cure and hopefully prevent childhood diseases,” said Michael Artman, MD, Joyce C. Hall Endowed Chair in Pediatrics, Professor and Chair, Department of Pediatrics at UMKC School of Medicine.

The research strategic planning process identified four areas of research emphasis:

- **Clinical Pharmacology and Therapeutic Innovations** – We are proud to have the largest and most productive pediatric clinical pharmacology program in North America. We need to continue building on this strength. In 2011 we secured a T32 training grant, one of three training grants in Pediatric Clinical Pharmacology awarded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, to support a pediatric pharmacology training program. We also saw our Phase I and II experimental cancer therapeutics program, which brings our clinical pharmacology and oncology expertise together, grow significantly through increased numbers of clinical trials available to our patients, our leadership roles as the clinical pharmacology core to national consortia in pediatric cancer pharmacology, and the NIH-supported Pediatric Trial Network. During 2012, more than 20 new early-phase clinical investigations were initiated in areas which comprise pediatric cancer, diabetes and infectious diseases. The program is expanding its focus to include discovery and development of new treatment options for unmet therapeutic needs in children.

- **Genomic Medicine** – All of us in our research enterprise recognize genomic medicine is key to future medical research. Under the leadership of world renowned genomics specialist, Stephen Kingsmore, MD, ChB, BAO, DSc, FRCPath, we have opened the first pediatric genome center located in a children’s hospital dedicated to diagnosing and treating pediatric genetic diseases. Fully integrated into our clinical operations, the Center for Pediatric Genomic Medicine is at the forefront of a new interdisciplinary approach to developing diagnoses of childhood diseases and disorders. And because the center is located within the hospital, we can have an immediate impact on the diagnosis and treatment of patients. We already are making great strides and are preparing to license a single test to identify more than 600 single-gene diseases of childhood.

- **Health Services and Outcomes** – Traditionally in pediatric medicine, we do things because it seems like the right thing – it makes sense. But is it the

most effective or most efficient way to provide care? Our large service area, high volume of patient activity and integrated delivery system provide an ideal setting for conducting health services and outcomes research. We’re well poised to ask those questions and design trials around what’s the best practice. What is the best way to take care of pediatric patients? This research also spans health economics, health literacy and disparity of care. How do we deliver the most value? What is the most cost-effective yet clinically important way to approach a problem? How do we break down barriers to care? How do we make sure children of different racial and ethnic backgrounds receive the same standard of care? These are some of the questions we will address as we build our health services and outcomes research program.

- **Innovation in Health Care Delivery** – Innovations in this area are inextricably linked to outcomes research. Once we determine the best approach for care, how do we then get that out to the community? How do we diffuse those practices to make sure the child in Ellis, Kan. has the same standard of care as the child in Joplin, Mo., and the child in Overland Park, Kan.? How can we as a regional leader make sure children in Kansas, Missouri and surrounding states get the same high quality care? Telemedicine, technology, education programs and enhanced communication tools are just a few of the ways we can improve care, and access to care, for children here and around the world. •

““ These four areas build on our current areas of research strength, as well as our aspirations as a pediatric research leader. ””

Michael Artman, MD





Center for Prospective Clinical Trials Compares Effectiveness of Procedures

The Center for Prospective Clinical Trials at Children's Mercy is dedicated to the innovation and adoption of cutting-edge techniques that may benefit patients needing the most specialized and delicate surgical care. Numerous studies completed by the center from 2011-2012 have been presented to prestigious surgical associations and published in leading journals of medicine. Current and upcoming trials allow the center to continue its dedication to bringing Children's Mercy's patients the best and most innovative surgical care available.

In 2011 the center completed the landmark trial comparing irrigation to no irrigation for perforated appendicitis. The study randomized 220 patients and found no difference in percentage of abscesses, wound infection, length of stay or any other outcome variable. In patients who developed an abscess there was no difference in percentage drained, days of antibiotic use, length of stay, and number or location of abscesses. These results were presented to the American Surgical Association and will be published in *Annals of Surgery*.

The same year, the center completed the largest trial on the emerging technique of single-site appendectomy. The trial concluded there were no differences, apart from a slightly longer operative time with a single-site appendectomy. This trial was presented to the American Surgical Association and published in *Annals of Surgery*.

In 2012 the center completed a trial assessing ad lib versus protocol feedings for pyloric stenosis. The trial concluded ad lib feedings have no disadvantages, which means regulated or non-regulated feeding schedules for infants are equally effective in relation to pyloric stenosis.

"We found significantly less time to goal feedings after laparoscopic pyloromyotomy with ad lib feedings and we have since changed to the new practice," says Shawn St. Peter, MD, Director of Center for Prospective

Clinical Trials; Director, Surgical Scholars Program; Pediatric Surgery Fellowship; Associate Professor of Pediatrics, University of Missouri-Kansas City School of Medicine. Results were presented at the American Physician Scientists Association (APSA) in May 2013.

One of the many upcoming trials for the center includes a novel study of non-operative management of blunt renal trauma in children. "This is our first report on blunt renal trauma," says Dr. St. Peter. "This trial will change the way we manage treatment for these patients."

The center is also enrolling in a new gastroschisis trial that compares forms of immediate treatment for infants born with gastroschisis. The study will compare the effects of immediate surgery on infants with infants who have bedside silos instead. This study is of special interest to the hospital's Elizabeth J. Ferrell Fetal Health Center and the families it serves.

Additional prospective trials for the near future include a comparative study of inguinal hernia repairs in premature infants prior to, versus after, NICU discharge, and an evaluation of the utility of esophageal stitches during laparoscopic fundoplication. •

“As one of the largest and most experienced minimally invasive surgery programs in the country, we are dedicated to advancing the adoption of techniques that bring the most benefit to pediatric patients.”

Shawn St. Peter, MD





Genome Center Reports Breakthrough in Rapid Diagnoses of Genetic Diseases

Thanks to the Children's Mercy Center for Pediatric Genomic Medicine, children in the Kansas City region are now some of the first in the world to have access to advanced genomic testing that can provide faster diagnosis of inherited pediatric diseases and can detect chronic conditions before symptoms appear.

Led by Dr. Stephen Kingsmore, MB, ChB, BAO, DSc, FRCPath, the center provides genome, computation and analytic capabilities that support Children's Mercy's cutting edge research programs in Pediatrics, Neonatology, Hematology/Oncology, Fetal Health, Pharmacogenetics and Personalized Medicine to improve outcomes for affected children here and worldwide.

"The faculty of Children's Mercy has really embraced the idea of Genomic Medicine," says Dr. Kingsmore. "We're already seeing success in implementing new diagnostic tools and treatments for children with genetic diseases."

In the October 2012 issue of the journal *Science Translational Medicine*, Children's Mercy researchers reported a proof-of-concept process, called STAT-Seq®, which used whole genome sequencing to diagnose critically ill infants in two days versus the standard five to six weeks.

This is especially effective for use in the Neonatal Intensive Care Unit, as more than 20 percent of admissions to the NICU are due to congenital abnormalities and genetic disorders. This will have enormous potential in the nearly 20,000 neonatal deaths per year.

The rapid whole genome sequencing approach was named one of TIME magazine's Top 10 Medical Breakthroughs of 2012 and brought honor to Dr. Kingsmore as one of Medscape's best physicians of the year. The breakthrough was not the only early triumph for the Center. There are more than 7,500 single-gene diseases, and about half have a known cause, but clinical testing is only available for some of these and traditional methods take months or years to reach a diagnosis.

"We've developed our first test that allows us to examine about 600 diseases at once to determine which disease is causing the illness," adds Dr. Kingsmore.

These genetic diseases affect approximately three percent of children and account for more than 15 percent of the admissions at Children's Mercy Hospital. •

“We are in a great position because the hospital invested in this so early. The evidence is proving that genomic sequencing will profoundly change medicine.”

Stephen Kingsmore, MB, ChB, BAO, DSc, FRCPath





Bioethics Center Leads Educational Initiatives to Address Difficult Issues

Research in bioethics is different from basic science research. It often involves “thought experiments” in moral reasoning, rather than bench experiments or primary data collection. The motivation, however, is the same as that in basic science research and clinical research — to think carefully about tough questions and to come up with the answers that are most likely to improve patient care and the health of children.

As leaders in the field, the Center for Pediatric Bioethics has implemented two major initiatives to address the difficult ethical issues facing parents and health care professionals.

In conjunction with the journal *Pediatrics*, the center launched “Ethics Rounds” to analyze difficult cases in clinical and research ethics.

“Working closely with colleagues at Children’s Mercy and at other leading children’s hospitals throughout the world, we identify cases that raise complex ethical issues,” says John Lantos, MD, Director. “Those cases are refined into succinct case presentations that lead up to a moment when a decision must be made. We then ask pediatricians and bioethicists who are experts in their fields what they would do and why.”

Nearly a dozen cases have been published during the past two years. The goal of the series is not necessarily to come up with a single right answer or even to present a consensus. Instead, it is to explore the range of reasonable choices and the ethical justifications for each choice. Readers will then have to decide for themselves whether the “experts” made the right decision for the right reasons or not.

The Bioethics Center has also initiated a nine-month pediatric bioethics certificate course, the only one of its kind, to help participants understand common pediatric bioethical issues. The program is targeted to individuals with an interest in pediatric bioethics and to individuals serving on pediatric bioethics committees and Institutional Review Boards for children’s hospitals.

“Students in this program study current and classic articles and books in pediatric bioethics,” says Dr. John Lantos. “They read key legal decisions and discuss all the big issues in pediatric bioethics – fertility, conscience, neonatology, growth hormone and research ethics.”

Launched in 2011, the first installment of the program included students from around the United States and Canada who specialized in medicine, nursing, social work, chaplaincy and hospital administration. •

“ We are training the next generation of leaders in pediatric bioethics. Our students will bring new ways of thinking about complex issues. They will be able to help doctors, nurses and researchers make better decisions, which will improve the care we provide to children and families.”

John Lantos, MD





Early Phase Drug Trials Bring Promise to Pediatric Cancer Patients

The Experimental Therapeutics in Pediatric Cancer Program is quickly gaining recognition as a regional referral center.

Under the direction of Kathleen A. Neville, MD, MS, the program is a collaborative initiative supported by the divisions of Clinical Pharmacology and Hematology/Oncology, and aimed at giving children with recurrent or refractory cancer a local option to pursue experimental treatment with early-phase anti-cancer drugs.

The program has its own investigator-initiated trials and is working with several national consortia, including Therapeutic Advances in Childhood Leukemia & Lymphoma (TACL) and serving as the clinical pharmacology core for both the Pediatric Oncology Experimental Therapeutics Investigators' Consortium (POETIC) and the Neuroblastoma & Medulloblastoma Translational Research Consortium (NMTRC).

“What this means is that when these groups are designing an early-phase study, the Children’s Mercy Hospital team provides support in optimizing the design and expert analysis of the pharmacokinetic data,” says Dr. Neville. “We have also partnered with the Institute for Advancing Medical Innovation at the University of Kansas to conduct some basic science research on refractory or recurrent pediatric tumors and to reformulate older anti-cancer drugs into formulations that are appropriate for children.”

Through its involvement in NMTRC, Children’s Mercy is taking part in an innovative study to evaluate the use of a tumor’s genome-wide expression profile to better understand individual tumors and match them with targeted therapies. The feasibility trial is using molecular-guided therapy for the treatment of refractory or recurrent neuroblastoma. The primary outcome measure is whether this predictive modeling can be used to make real-time treatment decisions.

In collaboration with the Institute for Advancing Medical Innovation (IAMI) and the National Institutes of Health (NIH), the team has begun using high throughput screening of compounds. This is a sophisticated and automated type of technology that can assay the biological or biochemical activity of a large number of chemical libraries of compounds against a wide variety of tumors. Dr. Neville said the team has already seen some compounds that appear promising in this first step in drug development. •

“My hope would be that we will be able to quickly move these compounds into studies. We want to be at the forefront of bringing new or better drugs forward for children with cancer. The goal is that, in 5 or 10 years, treatment will be different, less toxic, better tailored, and we’ll have a better cure rate for these kids.”

Kathleen A. Neville, MD, MS





CKiD Study Redefines Care for Children with Chronic Kidney Disease

The Chronic Kidney Disease in Children (CKiD) study, the largest-ever study of the disease in children in North America, is expanding its scope and cohort of patients to provide researchers with a better understanding of the risk factors for the progression to end-stage kidney disease (ESKD).

Children's Mercy Hospitals and Clinics is one of two clinical coordinating centers for the study. Principal Investigator Bradley Warady, MD, Senior Associate Chair for Children's Mercy's Department of Pediatrics and Chief, Division of Nephrology, says recent funding from the National Institutes of Health has allowed CKiD to increase its original patient population of almost 600 children by about 50 percent.

"Our main focus is to look at the factors that influence the progression of chronic kidney disease and its impact on children's growth, cognitive development and cardiovascular disease," Dr. Warady says. "The increased size of our patient cohort will most definitely enhance the productivity of the study."

As CKiD was originally designed when it began in 2003, once a child needed dialysis or a transplant, the child was no longer in the study.

"We recognized that we were missing an opportunity to better understand what was occurring in the patients who experienced the most rapid worsening of their kidney disease, after they were transplanted or had been started on dialysis," Dr. Warady says. "The NIH agreed this was a population that required study, and that we needed to take advantage of our unique situation of having extensive clinical and laboratory information about each patient that preceded their development of end-stage kidney disease."

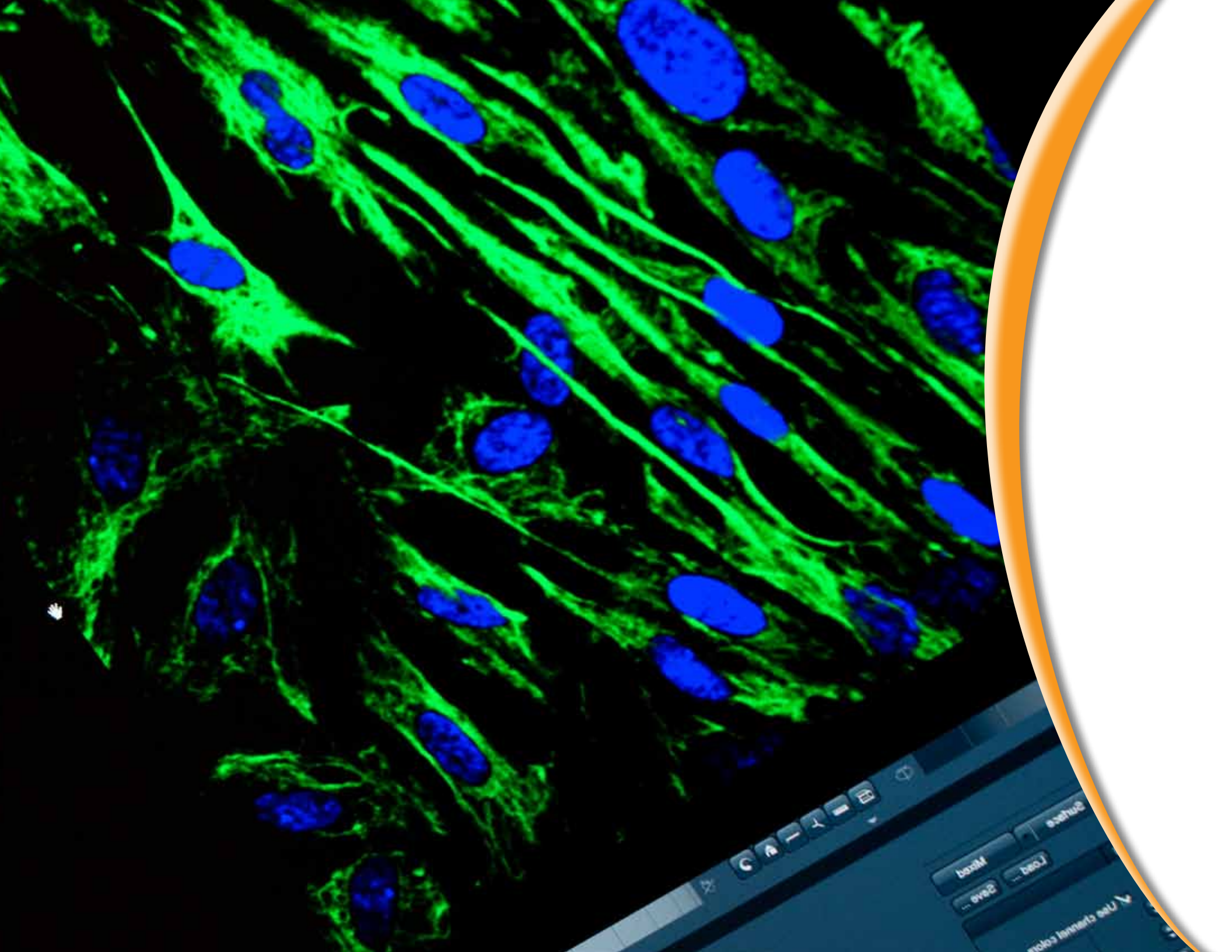
Children who had phased out of the study are being re-enrolled. To better understand the status and risk for progression of heart disease among children with ESKD, all of the dialysis patients and those being re-enrolled, as well as any current participants who progress to end-stage kidney disease, will undergo spiral CT scans of their hearts to look for calcification within the coronary arteries.

"We know from other studies that people with advanced chronic kidney disease can have calcification of the coronary arteries that can contribute to significant cardiovascular disease and decreased life expectancy," says Dr. Warady. "However, there haven't been any studies that have followed a large number of children on a long-term basis prior to these types of cardiovascular radiologic studies. We're now going to have the opportunity to do so and to define important risk factors for this significant complication."

The team is currently analyzing data gathered on the children whose kidney disease progressed to end-stage, and Dr. Warady hopes CKiD investigators will soon be able to more definitively identify factors, such as protein loss in the urine or high blood pressure, that appear to influence the disease's progression. •

“If we can define these factors, we could begin to design interventional studies. Ultimately, effective intervention early in the course of the disease will be what helps us prevent the development of ESKD for other children in the future.”

Bradley Warady, MD



Pathology

A federal study proposed by the Center for Disease Control and Prevention has selected Children's Mercy as one of six pediatric hospitals to form the New Vaccines Surveillance Network. Clinical principal investigator Rangaraj Selvarangan, BVSc, PhD, D (ABMM), Director of Pathology and Laboratory Medicine, along with co-investigators Christopher Harrison, MD, Director of Infectious Disease Research Laboratory, and Mary Moffatt, MD, Pediatric Emergency Medicine Specialist, are aiming to understand the epidemiology of vaccine preventable infectious diseases by examining norovirus, acute gastroenteritis, and acute respiratory illness. The specimens are collected from emergency departments and outpatient clinics for laboratory testing to assess the effectiveness of both the influenza and rotavirus vaccines. Over a period of five years, Children's Mercy will receive a total of \$3.6 million from the CDC.

Dr. Selvarangan is involved in an additional study regarding the Human Parechovirus infection in infants aged 90 days to 6 months old. Appropriating a grant contributed by the Marion Merrell Dow Clinical Scholar Award, Dr. Selvarangan has established a pediatric network of four hospitals to examine our country's current meningitis testing procedures in hopes of mandating a specific diagnostic routine test for the virus. The study is the first in the United States to determine the indicators for pediatric "outbreak years" by understanding compartments, risk factors and mother-to-infant transfers.

Cardiology

The addition of new Cardiology Section Chief Girish Shirali, MBBS, has brought notable expertise in echocardiography to the Heart Center with a research focus on measurements of cardiac structures and validation of advanced echocardiographic measurements.

Dr. Shirali's work is directed toward developing new methods to validate echo measurements compared to gold standard techniques such as cardiac MRI. Dr. Shirali believes this approach will help identify technologies that are relevant and effective, and make a meaningful difference to outcomes.

Dr. Shirali is also medical co-director of The Ward Family Heart Center and the Melva and Randall L. O'Donnell Chair in Pediatric Cardiology at Children's Mercy Hospitals and Clinics. The endowed chair was created by a \$1 million donation from Children's Mercy President and CEO Randall L. O'Donnell and his wife, Melva.

Cardiac Surgery

The Cardiac Regenerative Surgery Research Laboratories (CRSRL) of The Ward Family Heart Center at Children's Mercy are dedicated to the translation of fundamental scientific research into therapeutic strategies for the treatment of congenital and structural cardiac disorders. Groundbreaking tissue-engineered heart valve research is moving through the FDA-approval process and is currently being tested with clinical trials in sight. Once fully developed and approved, the living, growth-capable valve will eliminate the need for multiple reoperations, as is currently required for available valve prosthetics.

The team - which works out of the academic and discovery laboratory at Children's Mercy and through multiple collaborations with university partners in the Kansas City area, as well as with a full-time Good Laboratory Practices (GLP) compliant testing facility located in Maryland - is also working on projects that include a range of cell, tissue, polymer, drug eluting and gene engineered constructs for surgical- and catheter based cardiovascular repairs. •





Research of Note...continued

Pediatric Urology

Children's Mercy is taking strides in the surgical correction of ureteropelvic junction obstruction, the most common cause of hydronephrosis in children. The preliminary reports of a ground-breaking pediatric urology study led by John Gatti, MD, Director of Minimally Invasive Urology, has identified laparoscopic pyeloplasty as a safe and effective alternative to the traditional open procedure.

Under the umbrella of the hospital's nationally recognized Center for Prospective Clinical Trials, the study is the first of its kind to evaluate the effectiveness of the two methods. Dr. Gatti aims to continue the study throughout next year with hopes to increase his sample size. If trends continue, the study will demonstrate that the laparoscopic method has less associated pain, quicker post-operative recovery and superior cosmesis, as opposed to the open procedure.

Otolaryngology

Robert A. Weatherly, MD, Chief for the Section of Otolaryngology at Children's Mercy, partnered with the University of Kansas School of Engineering to uncover an effective material that could be used for the correction of tracheal stenosis, a rare condition causing breathing difficulties in approximately 2,000 infants worldwide.

Dr. Weatherly and his collaborators identified a polycaprolactone (PCL) biodegradable synthetic patch capable of dissolving when the trachea can sustain on its own, possibly proving to be a superior alternative to the current technique of excavating cartilage from a donor site. The School of Engineering contributed a portion of their \$400,000 National Science Foundation Career Award, as well as other department funds to jumpstart the project. Presently, the team's preliminary findings support the formulation of a strong case in regards to moving toward FDA approval with this advanced technology.

Neurology

Recognizing a need to increase pediatric neurological research opportunities, the Division of Neurology at Children's Mercy serves as a pediatric resource for the NIH-funded Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT). Created in 2011, NeuroNEXT is a network of 25 clinical sites across the nation that collaborate to increase the efficiency for identifying new treatments and protocols for both adult and pediatric neurological disorders. In the Greater Kansas City region, Children's Mercy partners with the University of Kansas Medical Center in Kansas City, Kan., and KU's Life Span Institute and Child Development Center in Lawrence, Kan.

Vaccines Research

A federal study conducted by the Vaccine Treatment and Education Unit included Christopher Harrison, MD, Director of Infectious Disease Research Laboratory and a Professor of Pediatrics at UMKC School of Medicine, and his colleagues in the investigation of Human Papillomavirus immunizations and their effectiveness with discrepancies in the series schedule. The study elevated awareness of the 70 percent of females who are inconsistent in receiving their vaccinations.

Additionally, Pfizer presented the 2011 Junior Investigator Award in Pediatric Vaccine Research to Barbara A. Pahud, MD, MPH, a Pediatric and Infectious Disease Specialist at Children's Mercy and an Assistant Professor of Pediatrics at the UMKC School of Medicine. The grant — the first competitive grant of its kind awarded by peers — contributes \$40,000 to Dr. Pahud's research on lowering the barriers for obtaining pediatric immunizations through community based initiatives. •



Research Assets

Children's Mercy Hospitals and Clinics continues to dedicate and develop resources to support both translational and clinical research. At our Children's Mercy Hospital campus, more than 48,000 square feet of actively used research space provides an environment where clinical and basic investigators interact, discover and develop new approaches to the diagnosis and treatment of a multitude of disorders that affect infants, children and adolescents. A summary of these research assets is as follows:

Genome Center Laboratory at Crown Center

The new Center for Pediatric Genomic Medicine laboratory, located in Crown Center, occupies approximately 3,500 square feet, and markedly increases our capacity to perform genome sequence analysis and research. Most importantly, this state-of-the-art facility, unique to children's hospitals in the U.S., allows us to perform a far greater number of diagnostic testing and genome analyses for our patients – a new service available inside a children's hospital for the very first time.



Pediatric Clinical Research Unit

The new Pediatric Clinical Research Unit located in the hospital's new Hall Tower is a state-of-the-art, 5,000 square foot facility dedicated to the support of clinical-translational research. This unit and its staff of experienced



research nurse coordinators support the activities of our Experimental Therapeutics in Pediatric Cancer program, the hospital's pivotal role as the Pediatric Clinical Pharmacology core of the NIH-funded Pediatric Trials Network, and an expanded institutional clinical trial

program, which is focusing on therapeutic drugs and devices developed for children with both acute and chronic medical conditions.

The Center for Children's Healthy Lifestyles and Nutrition

This joint program with the University of Kansas School of Medicine occupies approximately 14,000 square feet on the first floor of the Children's Mercy Hospital Don Chisholm Center. This facility supports both health outcome and translational research associated with pediatric obesity and other nutritional disorders. The Center is unique in that it combines an exercise facility, a metabolic kitchen, rooms dedicated to evaluation, and sophisticated nutritional assessment, a 500 square foot laboratory equipped for the preparation and analysis of biological samples obtained as part of translational research, and dedicated space for data analysis.



Health Sciences Library

The Health Sciences Library's collections include 5,300 print books, 240 online texts, and 400 currently subscribed medical journals. Three medical librarians support research efforts with expert literature searches and other assistance. Library services include participation in both the Docline and OCLC interlibrary loan networks, and document delivery from UMKC's library collections.



The Pediatric Research Center

Approximately 40,000 square feet of wet laboratory space supports translational research being conducted by 13 different laboratories representing the Children's Mercy Departments of Pediatrics and Surgery. This includes NIH-supported work in Nephrology, Fungal Biology, Neonatology, Genetics, Clinical Pharmacology and Pharmacogenomics. It also houses the Children's Mercy Cardiac Regenerative Surgery Research Laboratory. •





Strategic Partnerships and Collaborations

The increasing complexity of biomedical science and the ability to effectively address research questions, which are important for the health of children, increasingly requires collaboration among disciplines. At Children's Mercy Hospitals and Clinics, such collaboration occurs within our institution and with other institutions, large and small, across the United States and beyond.

Within the Kansas City region, researchers at Children's Mercy continue to enjoy robust, growing collaborations with partner institutions such as the University of Missouri-Kansas City, the University of Kansas, the Stowers Institute and the Kansas City University School of Medicine and Biosciences. Children's Mercy investigators continue to pursue discovery and make critical programmatic contributions to both the Cancer Center at the University of Kansas and Frontiers, the Clinical Translational Science Award supported by the National Institutes of Health, housed at the University of Kansas Medical Center. These collaborations leverage complementary expertise across several disciplines and areas of biomedical research, and in particular, enable us to explore the complex interaction between human development, disease and its treatment throughout the span of life, from birth through old age.

In addition to our regional research collaborations, more than 50 Children's Mercy investigators are actively working with counterparts in institutions across the globe. Specific examples include the following:

- Bradley Warady, MD, Nephrology Division Director at Children's Mercy, continues to lead the research efforts of the NIH-funded CKID Network, which studies the treatment of chronic renal disease in children.
- The Children's Mercy Division of Pediatric Pharmacology and Therapeutic Innovation, with leadership provided by J. Steven Leeder, PharmD, Kathleen Neville, MD and Gregory Kearns, PharmD, PhD, continues to serve as the core clinical pharmacology resource for the NIH Pediatric Trial Network; a national collaborative involving more than 30 pediatric institutions studying therapeutic drugs in children,

and the Pediatric Oncology Experimental Therapeutics Consortium, an international network which conducts early phase trials in pediatric patients with cancer. Collaborators within the Children's Mercy program in pediatric clinical pharmacology also support NIH-funded programs at the University of Utah and Harvard University which study the impact of growth and development on the metabolism of therapeutic drugs.

- Timothy Apodaca, PhD, supported by funding from the NIH and in collaborations with colleagues at Brown University, is studying methods to improve communication between clinicians and adolescents who are being treated for high-risk alcohol abuse.
- In collaboration with the World Health Organization, Susan Abdel-Rahman, PharmD, is working across four countries on three continents to validate the clinical application of the Mercy TAPE, a device invented by Dr. Abdel-Rahman which can accurately determine the body weight of infants, children and adolescents irrespective of body habitus.
- Raj Selvarangan, BVSc, PhD, D(ABMM), from the Children's Mercy Department of Pathology continues to lead an effective national collaboration funded by the U.S. Centers for Disease Control to study the prevalence of human parechoviruses – viruses which recently were recognized as the cause of serious central nervous system infections in children.
- Douglas Myers, MD, from the Children's Mercy Division of Hematology/Oncology, with support from the Midwest Cancer Alliance, is collaborating with investigators from the University of Kansas Cancer Center and the Center for Cell and Gene Therapy at Baylor College of Medicine to perform groundbreaking research to treat neuroblastoma in children. Their approach uses patient derived, gene-modified T cells which target and destroy tumor cells.
- The flagship project for the Cardiac Regenerative Surgery Research Laboratories has been, and remains, the development of a tissue engineered heart valve that can grow and adapt in pediatric patients, eliminating the need for multiple reoperations. The base approach is to utilize decellularized allogeneic heart valves from organ and tissue harvests as a scaffold for autologous cell seeding.

Under the direction of Richard Hopkins, MD, the CRSRL has quickly emerged as a recognized leader in decellularization technology. This has led to active collaborations with regenerative researchers at the University of Kansas in both the School of Medicine and the School of Engineering. The CRSRL team has modified decellularization techniques shown to be effective for heart valve tissue to optimize the effectiveness for other tissues. Working with Omar Aljitalawi, MD, and Lisa Stehno-Bittel, PhD, and others at the KU Medical Center, Dr. Hopkins' laboratory has developed methods to decellularize human umbilical cord Wharton's Jelly, the gelatinous tissue that protects umbilical blood vessels in utero. Numerous applications are being investigated for this porous tissue, including direct use as a scaffold for cell seeding and as a bioactive additive in composite scaffold materials.

Similarly, the CRSRL is collaborating with Michael Detamore, PhD, at the KU School of Engineering to decellularize cartilage tissue. Other collaborations include researchers at the UMKC Dental School (bone and muscle) and Department of Pharmaceutics (coronary stents), Kansas State Veterinary School (human umbilical cord derived mesenchymal stem cells), Kansas University Biotechnology Center (multiscale investigations of scaffold material properties), Children's Mercy Otolaryngology (tissue engineered trachea), and Brown University (bioactive surgical sutures for tissue engineering clinical applications).



2011-2012 Awards

Children's Mercy Hospital Cancer Center

2011 - Gerald Woods, MD

"COMPARE – Choosing Opioid Management for Pain and Analyzing Acute Chest Syndrome (ACS) Rates Equally"

Cross Foundation Clinical Scholar Award

2012 - Sara Tsai, MD

"Motivational Interviewing in Adolescents with Type I Diabetes: A Randoized control Trial"

Dee Lyons Research Scholarship

2011 - Rolanda Peterson, RN, CPN, Jennifer Meade, RN, BSN, Kristin Stegenga, RN, PhD, CPN, Jacqueline Bartlett, MSN, MBA/HCM, RN

"Perception of the Implementation of Ultrasound Guided Peripheral Intravenous Catheter Insertion in the Emergency Department"

CMH Clinical Fellowship Research Award

2011 - Michael Nyp, MD

"TIMP-3 Modulates Chronic Hypoxia Induced Pulmonary Arterial Remodeling and Inhibition of Alveolar Development"

Keaveny Cancer Research Fund

2012 - Sanket Shah, MD

"Non-Invasive Evaluation of Cardiac Function in Pediatric Cancer Survivors"

Katharine B. Richardson Award

2011

Keith August, MD, MS

"Effects of Intrathecal Methotrexate on Folate Metabolism in the Cerebrospinal Fluid of Children with Acute Lymphoblastic Leukemia"

Jeffrey Colvin, MD, JD

"Innovation & Defusion: Improving Physicians' Ability to Detect Critical Social Factors"

Adrianus Domen, PhD

"Tolerance Induction Using Myeloid Progenitors: Are Lymphoid Cells Essential?"

Kimberly Gandy, MD

"Computer Fluid Dynamic Modeling of the Aortic Arch after Stage I Palliation in HL"

Cindy Hensley, RD

"In Vitro Study of Bacterial Growth in Powdered Reconstituted Pediatric Enteral Formula at 4, 6 and 8 Hours"

Michelle Herzer, PhD

"Evaluating the Efficacy of a Multicomponent Adherence-Promoting Intervention Package in Youth with IBD: A Replication-Extension Study Using Single-Case Methodology"

Stephanie Page, MD

"A Trial of Montelukast for Maintenance Therapy of Eosinophilic Esophagitis in Children"

2012

Seth Septer, DO

"Hippo Kinase Signaling in APC/Min Mice, an Animal Model for Familial Adenomatous Polyposis"

Kreamer Research Excellence Award

2012 - Mara Becker, MD, MSCE

Marion Merrell Dow Clinical Scholars Award

2011 - Keith Mann, MD

"Febrile Infant Clinical Practice Guideline: Implementation and Assessment"

2011 - Rangaraj Selvarangan, BVSc, PhD, D(ABMM)

"Epidemiology of Human Parechovirus Infections in Children"

2012 - Jennifer Goldman, MD

"Variation of Bioactivation and Detoxification of Trimethoprim in Children"

2012 - Craig Friesen, MD

"Effects of Obesity of Pharmacokinetics on Pantoprazole in Children and Adolescents"

Paul Henson Endowment Clinical Scholar Award

2011 - Marcia Chan, PhD

"SNP in CD23 (Low Affinity IgE Receptor): Mechanism of B Cell Asthma Exacerbation"

Young investigator Awards in Clinical/Translational Research

2011 - Neil Mardis, DO

"Cartilage Damage Determined by 3Tesla MRI Analysis in a Pediatric Population with Acute ACL Injuries"



Areas of Research

Children's Mercy has been conducting clinical investigations since its inception more than 100 years ago. We have participated in industry-sponsored clinical trials for more than 25 years. During this time, we have worked with nearly 60 top pharmaceutical sponsors in the areas listed below.

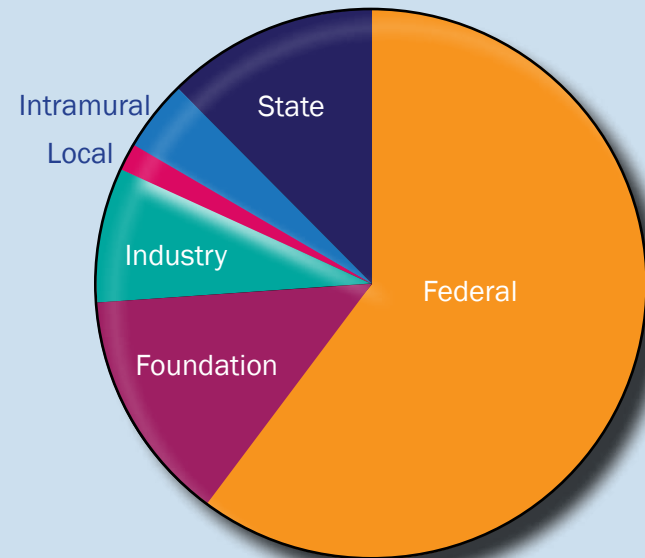
Acid Reflux Disease	Dyspepsia	Migraine
Adrenal Gland Disorders	Eczema	Muscular Dystrophy
Allergies and Allergic Rhinitis	Endocrinology	Neonatal Nutrition
Anemia	Epilepsy	Obesity
Anti-Emetic Therapy	Fecal Retention	Organ Transplantation
Antigen Challenge Testing	Gender Differences in Systemic Lupus	Otitis Media
Anti-Fungal Treatment	Genetic Disease	Pain Treatment, Post Surgical
Attention Deficit Hyperactivity Disorder	Genetics	Partial Liquid Ventilation
Asthma	Genotyping	Patients and Newborns
Autism	Glaucoma	Pharmacogenetics
Bladder Disorder	Graft vs. Host Disease	Pharmacokinetics
Bone Marrow Transplant	Growth Factors	Pneumonia
Bronchiolitis	Growth Hormone Deficiency	Psychiatry and Behavioral Disorders
Catheter Flow	Gynecomastia	Pulmonary Disease in Critical Care
Childhood Cancers	Hepatitis	Pulmonary Hypertension in Newborns
Chronic Abdominal Pain in Children	Hemophilia	Quality of Life Scale
Chronic Lung Disease	Hormone Deficiency	Rehabilitation & Physical Therapy
Chronic Pain	Hypertension	Renal Disease
Coagulation Disorders	Ideopathic Nephrotic syndrome	Renal Transplantation
Constitutional Delay of Growth & Puberty	Immune Tolerance Induction	Respiratory Disease in Newborns
Cystic Fibrosis	Infectious Diseases	Respiratory Tract Infections
Cytogenetics	Influenza	Sedation in Critical Care Patients
Device Studies	Intra-Ocular Lens	Seizure Disorder
Diagnostic Imaging	Iron Metabolism	Sepsis
Diabetes Mellitus Types I & II	Irritable Bowel Syndrome	Sickle Cell Disease
Dialysis	Juvenile Rheumatoid Arthritis	Skin and Soft Tissue Infections
Diagnostic Kits	Lymphomas	Turner Syndrome
Dietetics	McCune Albright Syndrome	Ulcerative Colitis
Digestive Disorder	Meningitis	Visual Acuity
Drug Metabolism	Metabolic Disorders	

Research Facts and Figures

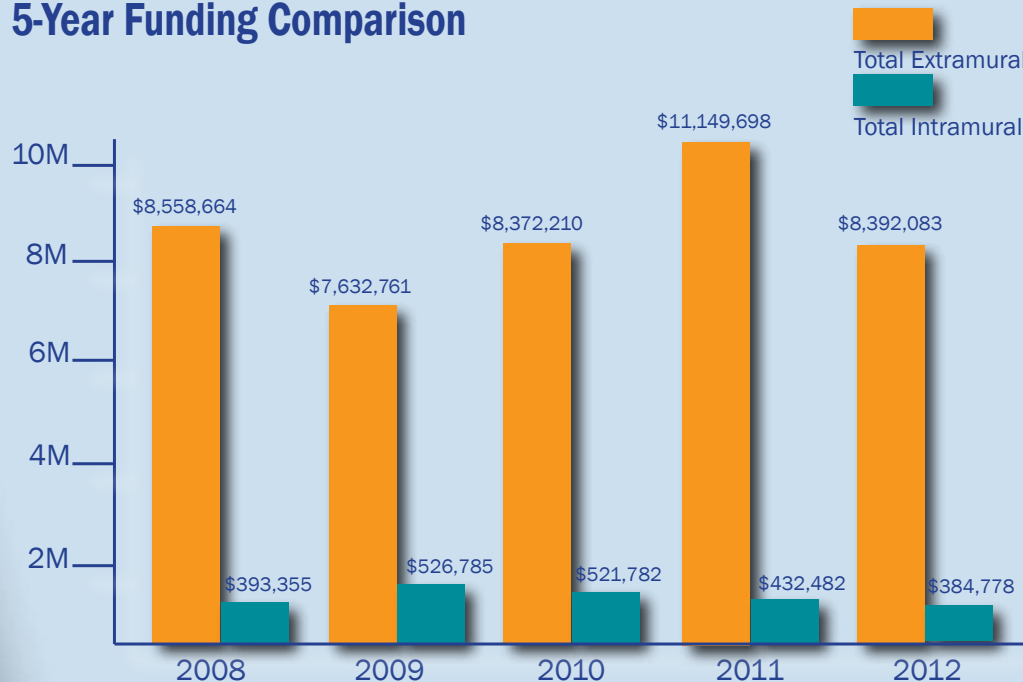
Detailed Total Expenditures

	2011	2012
Federal:	\$6,686,195	\$7,020,143
Foundation:	\$1,516,177	\$845,564
Industry:	\$1,153,392	\$394,985
Local:	\$184,723	\$0
State:	\$1,609,211	\$131,391
TOTAL EXTRAMURAL:	\$11,149,698	\$8,392,083
TOTAL INTRAMURAL:	\$432,482	\$384,778

2011-12 Sources of Research Funds



5-Year Funding Comparison



Research Facts and Figures

By the Numbers

Total Number of Researchers	90
Number of Active Clinical Trials	112
Number of Active Industry Studies	46

Institutional Review Board

	2011	2012
New Projects	273	304
Continuing Oversight	315	389
Other Activity	787	2,407
Total Reviews	1,375	3,100



 **UMKC School
of Medicine**



Children's Mercy
HOSPITALS & CLINICS

Kansas City

2401 Gillham Road
Kansas City, MO 64108
(816) 234-3000
www.childrensmercy.org

