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2008 RESEARCH ANNUAL REPORT



**Children's Mercy
HOSPITALS & CLINICS**
www.childrensmc.org

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Randall L. O'Donnell, PhD
President and
Chief Executive Officer



Gregory Kearns, PharmD, PhD
The Marion Merrell Dow/Missouri
Endowed Chair in Pediatric
Research

Chair, Department of
Medical Research

Associate Chairman,
Department of Pediatrics

Dear Friends,

All parents know that every child is different and unique. In the same way, physicians know that all children with a particular disease don't necessarily react to treatments or respond to medications in the same way.

The newest research program at Children's Mercy is aimed at developing new methods of diagnoses and treatments that are customized to meet the unique needs of each individual child. The Center for Personalized Medicine and Therapeutic Innovation was established in the fall of 2008, and one of the nation's leading experts in this field has joined our medical staff as director of this ground-breaking new program. You can read more about this innovative new center in this annual report.

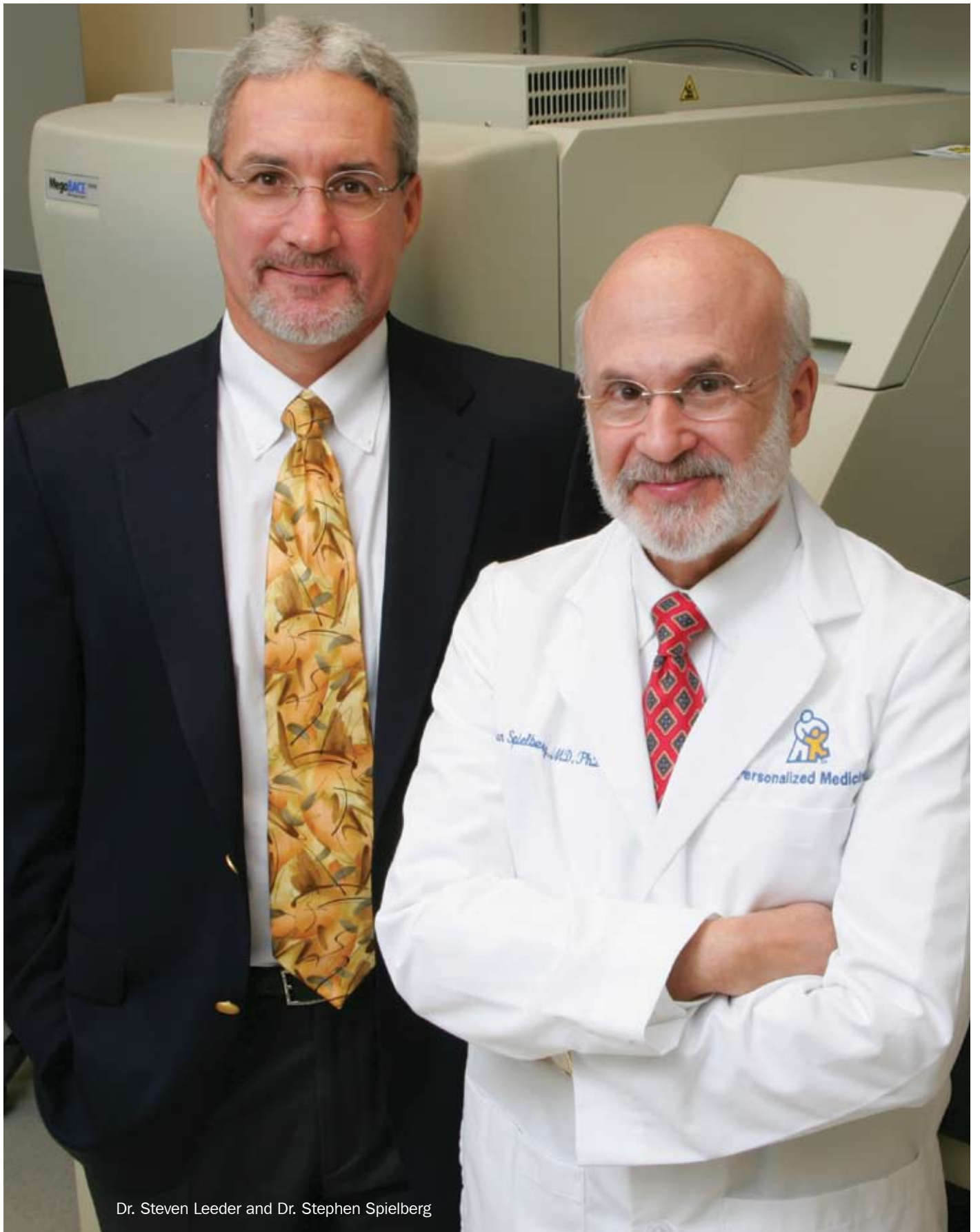
As we continue to expand our initiatives here at Children's Mercy, we also continue to expand our collaborative efforts with other researchers regionally and nationwide. Our academic affiliation with the University of Missouri-Kansas City continues to provide a foundation for our academic endeavors, and our researchers are working actively on collaborative projects with scientists at The Stowers Institute, the University of Kansas, and institutions throughout the nation. We also continue as one of the key stakeholders in the Kansas City Area Life Sciences Institute and are building upon our partnership with them in advancing our work in pediatric drug reformulation.

I hope you will take a few moments to read through this year's annual report and learn more about the exciting work being done by the physicians, nurses and scientists in Children's Mercy's nationally-recognized research programs. The ultimate beneficiaries, of course, are the children worldwide who will benefit from the new knowledge and treatments being developed here.

Sincerely,

A handwritten signature in black ink that reads "Randall O'Donnell".

A handwritten signature in black ink that reads "Gregory J. Kearns".



Dr. Steven Leeder and Dr. Stephen Spielberg

IT'S PERSONAL: New Center Tailors Care to Fit Children's Specific Needs

While the world we live in seems to be growing more impersonal, Children's Mercy is bucking the trend by making its care more personal than ever—as unique as a child's genetic fingerprint.

Stephen P. Spielberg, MD, PhD, director of the new Center for Personalized Medicine and Therapeutic Innovation, and his colleagues have been working across the organization to define areas where they can have an immediate impact in using the latest advances to customize care for children. This new Center is being built upon the success of the pediatric clinical pharmacology program at Children's Mercy and within the next several months, will launch the first pediatric Personalized Medicine Consultation Service in the U.S. Additionally, Dr. Spielberg and faculty working within the Center are creating a unique Personalized Medicine Clinic.

"I believe that the Center for Personalized Medicine will place Children's Mercy squarely at the forefront of optimizing care for sick children using the tools of modern genomics integrated into the best of clinical care," says Dr. Spielberg. "I have been impressed in my short time here with the depth and breadth of the institution, and of the commitment of administration, faculty and staff to making Children's Mercy ever better—a true leader in pediatric research and care nationally."

According to Dr. Spielberg, the complexity of integrating genomics into clinical practice will require an expanded research and education infrastructure, so his team is currently writing grants defining how they can partner throughout the hospital and beyond to drive creative and effective use of new knowledge into patient management and enhanced patient outcomes. The team at Children's Mercy has also been working to support new initiatives within the Institute for Pediatric Innovation, a non-profit organization that was established to develop new medications and products that are specifically designed for children's unique needs. Dr. Spielberg serves as principal investigator for the Institute's Pediatric Pharmaceutical Reformulation Program.

"Our outstanding tradition in pediatric and developmental pharmacology forms the basis for the future of the personalized medicine effort," says Dr. Spielberg. "While our plans and goals are large and will engender change in many areas, I am confident that Children's Mercy is the ideal place to develop pediatric personalized medicine."



Dr. Mara Becker
(center)

COLLABORATIVE EFFORT SEEKS TO IMPROVE ARTHRITIS TREATMENT

Although the word “arthritis” is usually associated with older persons, it strikes a surprising number of young people as well—an estimated 300,000 children in the United States alone.

With new therapeutic approaches of using methotrexate (MTX), an old drug originally developed to treat specific forms of cancer, treatment strategies for Juvenile Idiopathic Arthritis (JIA) have improved over the past couple of decades. While MTX is generally considered to be safe and well tolerated, it only works in about 60 percent of children and can cause side effects such as nausea and liver inflammation in certain patients.

A study by rheumatologist Mara Becker, MD, MSCE, Children’s Mercy Pediatric Rheumatologist and Assistant Professor of Pediatrics at University of Missouri—Kansas City School of Medicine, seeks to better understand who will benefit from MTX and who may be at risk for toxicity. Specifically, Dr. Becker and her colleagues are investigating the function of folic acid, the vitamin that plays a major role in normal cell growth and development.

“Our first step is to establish a baseline for folate levels,” Dr. Becker explains. “Once we have a better understanding of the adjustments that our cells make to adequate or inadequate supplies of folate and how MTX regulates it, we can then branch out and start looking at the factors that affect clinical outcomes.”

These factors include both genetic variations and maturational changes that occur in children as they grow. The goal is to develop a system for identifying patients who could benefit from MTX and those who should pursue other treatment options.

“When we start pulling it all together, we hope to have a lot of really great information about what makes someone more or less responsive to MTX,” says Dr. Becker. “This could ultimately help us to individualize MTX treatment which will make it safer and more effective in children with JIA.”

Dr. Becker notes that one of the keys that makes this research possible is the ability to bring together the expertise of multiple disciplines—including clinical pharmacology, genetics and pharmaceutical chemistry—to focus on this issue

“Today, the technology is so advanced that one person can’t do everything,” says Dr. Becker. “I’ve found some of the best collaborators outside of my own discipline. That’s the kind of environment that Children’s Mercy has fostered here over the past several years.”



Dr. Erica Molitor-Kirsch



Dr. Timothy Apodaca



Dr. Kathleen Neville

K AWARDS

One of the missions of the National Institutes of Health is to provide financial support to foster the development of young physicians and biomedical scientists as members of academic faculties. One of the mechanisms used by NIH to accomplish this goal is the offering of Research Career Development Awards.

These awards, generally referred to as “K-awards” are highly competitive, peer-reviewed grants that must contain both a research plan and a career development plan. Also, each K award application must include a detailed mentoring plan prepared by a senior faculty member who has received NIH research support and has extensive experience in mentoring junior academic faculty members.

When awarded by a given institute within NIH, K awards generally provide three to five years of support which includes funding (up to 75 percent) of salary and benefit costs, a portion of the funding necessary to support the research and educational costs and support for travel of the awardee to present his/her work at scientific meetings. K-awards also entail a significant institutional investment in that they must assure the NIH that the awardee will have 75 percent of his/her total time and effort protected to execute the research and educational goals of the award.

One of the other goals of the K-award mechanism is to prepare academic investigators for successful attainment of NIH research support as independent investigators (eg., R-series research grants).

In tandem, these awards and the institutional investment represent the bricks and mortar of how successful academic careers and research institutions can be built from the ground up.

At present, three Children’s Mercy faculty members have the distinction of holding active Mentored Patient-Oriented Research Career Development (K-23) awards.

Timothy A. Apodaca, PhD, Assistant Professor of Pediatrics, Division of Developmental and Behavioral Medicine
Grant Number 5K23AA15595-06 (National Institute on Alcohol Abuse and Alcoholism)
Project Title: Identifying Mechanisms of Motivational Interviewing

Erica A. Molitor-Kirsch, MD, Assistant Professor of Pediatrics, Division of Critical Care Medicine
Grant Number 5K23HL073832-05 (National Heart Lung and Blood Institute)
Project Title: rBPI-21 in Children Undergoing Cardiopulmonary Bypass

Kathleen A. Neville, MD, MS, Assistant Professor of Pediatrics, Divisions of Pediatric Clinical Pharmacology and Medical Toxicology, and Hematology/Oncology
Grant Number K23HL077684-03 (National Heart Lung and Blood Institute)
Project Title: Pharmacogenetics of Pediatric Sickle Cell Disease



Dr. Kathleen Neville

ALLEVIATION OF PAIN AND SUFFERING MOTIVATES HEMATOLOGY/ONCOLOGY RESEARCH

In building its cancer research capabilities, Children's Mercy recruited someone who not only had the requisite training, but also a heart for children who are afflicted with it.

Kathleen A. Neville, MD, MS, Assistant Professor of Pediatrics, Divisions of Pediatric Clinical Pharmacology and Medical Toxicology, and Hematology/Oncology, is leading the initiative to develop an experimental therapeutics program in oncology at Children's Mercy, with the goal of obtaining Children's Oncology Group designation as a Children's Oncology Group Phase I Unit.

The initiative is a joint collaboration between Clinical Pharmacology and Hematology/Oncology. Dr. Neville is board-certified in both disciplines and has appointments in both divisions. She had extensive training in experimental therapeutics for children with cancer during her fellowship at Texas Children's Hospital and views her appointment at Children's Mercy as an opportunity to bring all her skills together to address the needs of children facing tough battles.

"The central theme of my research is to help to alleviate suffering," says Dr. Neville. "My background and training have been all about how we can use medications to do that."

In addition to cancer, Dr. Neville has also done a considerable amount of research, supported by her National Institutes of Health K23 award, in the area of pediatric sickle-cell disease. Her work in this area involves both the use of an older anti-cancer medicine, hydroxyurea, and also, medications used to treat pain in patients with sickle-cell disease.

"Developing the Experimental Therapeutics Program will allow us to build on the hospital's outstanding reputation for clinical pharmacology and extend that into additional areas of research," says Dr. Neville. "Obtaining the trial center designation for oncology is especially important because it will mean that we have many more experimental therapies to offer our patients who have disease that is not responsive to existing treatments."



Dr. Timothy Apodaca

DECIPHERING THE CODE: UNDERSTANDING HOW COUNSELING TECHNIQUE ELICITS POSITIVE BEHAVIOR

Helping patients make beneficial health decisions is the focus of a new study led by Timothy R. Apodaca, PhD, Assistant Professor of Pediatrics, Division of Developmental and Behavioral Medicine.

Looking at Motivational Interviewing, a client-centered counseling method that assists people in understanding the consequences of unhealthy behavior, Dr. Apodaca is examining how clinicians guide patients to explore positive alternatives. More specifically, he is seeking to refine the technique by exploring how they elicit verbal commitments to change from patients, leading to subsequent behavior change.

Using audiotapes of brief counseling sessions conducted in a hospital setting, Dr. Apodaca's team is coding every statement by the clinician and patient. These codes are then checked against clinical outcomes, in this case, reductions in alcohol use and injury.

"My goal is to identify specific aspects of clinician behavior and style of communication that serve to enhance patient commitment to change," says Dr. Apodaca. "As a result of these findings, I hope to inform clinicians about ways in which they may be more helpful in facilitating healthy behavior change among their patients."

Dr. Apodaca is also looking at how the participation of a family member in these conversations influences patient commitment and decision-making. His hope is that these findings will illuminate how best to involve family members in the behavior change process.

As the recipient of an NIH K-23 award, Dr. Apodaca credits the training and mentorship he has received through the grant with helping him develop his specific focus on identifying therapeutic mechanisms of action from experts in the field. It also allowed him to receive training at the University of New Mexico on how to develop and run an active coding laboratory.

Ultimately, Dr. Apodaca hopes that this research will have wider applicability that will benefit a variety of patients.

"The use of Motivational Interviewing may be very helpful in other hard-to-change conditions," says Dr. Apodaca. "This could include issues ranging from fostering medication compliance, management of eating disorders among adolescents, treatment of diabetes and facilitating pain management for younger children."



Dr. Erica Molitor-Kirsch

BYPASSING BYPASS COMPLICATIONS: STUDY TESTS NEW DRUG TO IMPROVE HEART SURGERY OUTCOMES

Thousands of infants born with heart defects every year benefit from the dramatic improvements that have been made in the field of heart surgery over the past two decades. However, an essential part of those surgeries—the cardiopulmonary bypass—continues to be a source of concern for the critical care doctors who care for those babies because of complications that can result.

Cardiopulmonary bypass temporarily replaces the functions of the heart and lungs during surgery. While it allows the surgeries to be performed, it can also cause inflammation in the heart and lungs and even lead to kidney problems. While these complications are usually not life-threatening, they do cause patient discomfort and lengthen recovery times.

To address these issues, Erica A. Molitor-Kirsch, MD, Associate Professor of Pediatrics, Division of Critical Care Medicine, and her colleagues are studying the use of the drug Neuprex® to combat the ill effects of cardiopulmonary bypass.

According to Dr. Molitor-Kirsch, some evidence suggests that bacterial byproducts from the intestines called endotoxins, which get released into the bloodstream during bypass, may be the culprits in this process. Neuprex, a naturally occurring protein made by white blood cells to fight off microbial infections, kills gram-negative bacteria and neutralizes gram-negative endotoxins.

“Since Neuprex® has been shown to be effective as an anti-endotoxin in other applications, we’re hoping that it will prove useful in reducing cardiopulmonary bypass complications as well,” says Dr. Molitor-Kirsch.

The team is currently wrapping up a pilot study, supported by a National Institutes of Health K-23 award, and Dr. Molitor-Kirsch is encouraged by the results. The next step will be a multi-center, placebo-controlled trial.

“This study could be an important step forward in the field of congenital heart surgery,” says Dr. Molitor-Kirsch. “Reducing the complications of cardiopulmonary bypass could improve patient comfort following surgery and reduce recovery times”



Dr. Christopher Harrison

INCLUSION IN VACCINE TRIAL NETWORK OPENS NEW OPPORTUNITIES FOR INFECTIOUS DISEASE RESEARCH

Building on its long tradition of excellence in infectious diseases, Children's Mercy has joined the national network of vaccine trial sites. In collaboration with the University of Iowa's adult unit, Children's Mercy has become one of only eight National Institutes of Health Vaccine and Treatment Evaluation Units (VTEU) that perform important vaccine research not sponsored by industry.

Christopher J. Harrison, MD, Director of the Infectious Disease Research Laboratory and Professor of Pediatrics at the University of Missouri—Kansas City, is the principal investigator of the Pediatric Subunit site at Children's Mercy, which is slated to begin studies in the summer of 2009.

The initial two studies will focus on human papillomavirus (HPV) in adolescents and rotavirus vaccine in infants. The studies will compare immune responses when intervals between HPV vaccine doses are longer than recommended and when the rotavirus vaccine series is started with a dose of one of the two available rotavirus vaccines but completed with doses of the other vaccine.

"Being part of this prestigious network puts us in the company of elite pediatric hospitals in this discipline," says Dr. Harrison. "It also means that children of this area may get access to otherwise unavailable vaccines."

Dr. Harrison joined Children's Mercy in 2005, charged with developing the hospital's research capabilities in this field. He notes that the NIH funding will expand the infectious disease infrastructure, adding research coordinators and data managers, while encouraging collaborative vaccine research with members of the adolescent medicine and primary pediatric care sections.

"This designation allows us to have some of the best people work with us at all levels," says Dr. Harrison. "They can be recognized for what they do in vaccine research and their dedicated time to the program will propel it to a new level here at Children's Mercy."

With diseases like H1N1 influenza virus making international headlines, Dr. Harrison notes that vaccine research is very much a part of public consciousness.

"The concepts around these studies can really be cutting edge, allowing us to gain practical knowledge about how to best use vaccines," says Dr. Harrison. "Children's Mercy will now have new opportunities to be a player in developing strategies against not only common infections, but also unusual diseases like pandemic flu."



Dr. Geetha Raghuvier

CHILDREN'S ARTERIES AGING BEFORE THEIR TIME

Parents often lament that their children grow up too fast. When it comes to “vascular age,” however, the consequences of growing up too fast can be tragic.

According to a recent study that made national headlines, the “vascular age” of obese children is about 30 years older than their actual age, greatly increasing their risk of future heart attacks and strokes.

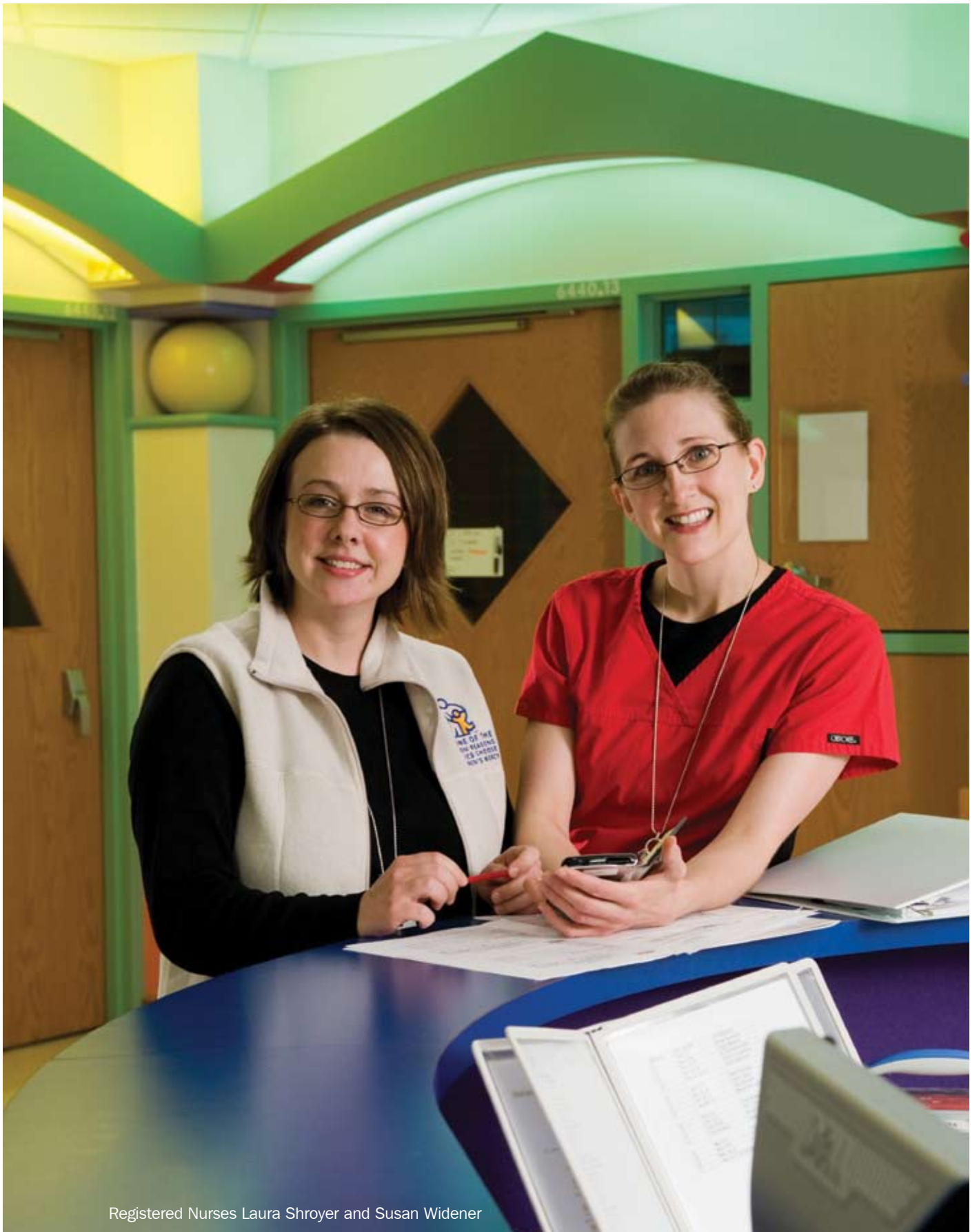
Geetha Raghuvver, MD, MPH, cardiologist at Children’s Mercy Hospital and Associate Professor of Pediatrics at the University of Missouri-Kansas City School of Medicine, led the study. Using ultrasound, her research team determined the thickness of the inner walls of the neck arteries that supply blood to the brain as a measure of atherosclerosis. This non-invasive technique is a “mirror to the coronary arteries,” she says, as previous studies have demonstrated a high degree of correlation between the two.

Increasing carotid artery intima-media thickness (CIMT) indicates the fatty buildup of plaque and atherosclerosis within arteries feeding the heart muscle and the brain. The advanced CIMT scores among children in the study indicate that the epidemic of childhood obesity today may be the harbinger of serious health issues that they could face in the future.

“I was both surprised and alarmed to find that 75% of the obese children we see already have more than three risk factors for coronary artery disease,” says Dr. Raghuvver, who heads the hospital’s Preventive Cardiology Clinic. “But risk factors only tell part of the story. This study gives us an early indication of what could happen to them two decades from now if appropriate interventions are not taken.”

Dr. Raghuvver’s current research focuses on whether these harmful effects can be slowed or even reversed through treatment. Since the buildup in the vessels is not hardened or calcified as yet in children, she is optimistic that they may be reversed through a combination of lifestyle changes and in some instances, the use of medications to lower blood cholesterol and lipid levels.

“Reduction in coronary artery disease cannot be achieved if only adults are targeted for prevention and treatment because the buildup in the blood vessels is in the end stage by then,” says Dr. Raghuvver. “Addressing the behaviors that affect risk factors at an early age will have the maximum potential for preventing and reversing atherosclerosis.”



Registered Nurses Laura Shroyer and Susan Widener

RECLAIMING NURSE TIME FOR THE BEDSIDE TRANSFORMS CARE

Nurses on 6 Henson look forward to bedtime—but not because they are sleepy. As part of a new study called Transforming Care At the Bedside, they are actively searching for ways to spend more quality time with patients at their bedside. Children’s Mercy is one of only three children’s hospitals nationwide participating in the project, which is funded by the Robert Wood Johnson Foundation.

According to 6 Henson co-managers Laura Shroyer, RN, BSN, and Susan Widener RN, BSN, the effort began in 2007 by giving handheld computers called personal digital assistants to nurses on the unit to collect pre-trial data. At random intervals, the nurses were signaled to note what they were doing at that moment in order to establish a baseline.

“What we found was that providing direct patient care accounts for only about 50 percent of a nurse’s shift,” says Shroyer. “The other half of the time, nurses are away from the bedside.”

For this project, all employees on the unit are encouraged to participate in an ongoing series of “deep diving” brainstorming sessions.

“We encourage them to think outside the box and offer extreme ideas,” says Widener. “Then we pare them down to real life ways that we can deliver even better care.”

The suggestions have been wide-ranging, from small things like welcome signs and providing adult-sized toiletries for parents, to discharge follow-up phone calls. The cumulative effect is making a significant impact on satisfaction of patients—and nurses as well.

“Improving care for our children is always our number one goal,” says Cheri Hunt, RN, MHA, CNAA, Vice President and Chief Nursing Officer. “But it’s also clear that the process we have initiated is beneficial for the nursing staff. The patient and family feedback has been so positive that the hospital plans to expand the program to other units. We hope that in the end, we will have more satisfied nurses and better care for patients.”

Since the process began, Widener notes some incremental improvement in the amount of time nurses spend with patients. The big difference, though, has been in the quality of time spent.

“It really only takes a minute to do some things, like writing a goodbye note to a patient who is going home,” says Susan Widener. “We’ve found that just being conscious of it enhances patient care—to break the this-is-how-we’ve-always-done-it mentality.”

AREAS OF RESEARCH



From its inception, the importance of conducting biomedical research has been a cornerstone of the overall mission of Children's Mercy Hospital. As a free-standing, academic pediatric medical center, it has been necessary for Children's Mercy to develop significant laboratory based research programs so that the goal of conducting meaningful translational research in pediatrics could be fully realized.

At Children's Mercy Hospital, approximately 32,000 square feet is dedicated to wet-laboratory research space. Faculty members in the Divisions of Neonatology, Endocrinology and Allergy/Asthma/Clinical Immunology also occupy approximately 6,000 square feet of research laboratory space within the UMKC School of Medicine. Additionally, the research program in Cardiac Surgery has dedicated space in two, off-site research facilities which provide state-of-the-art capabilities required to support the program in tissue engineering.

Research conducted by Children's Mercy laboratories is predominantly translational in that work conducted is focused on diseases / conditions which afflict infants and children and their treatments. A summary of the current Children's Mercy research laboratories and their respective areas of endeavor are contained in the profiles which follow.



Allergy, Asthma and Clinical Immunology Laboratory

Specific Research Interests:

- Dr. Barnes: aerobiology, humeral immunity and protein allergens
- Dr. Chan: immune modulation of inflammation
- Dr. Ciaccio: healthy homes, cellular immunity, clinical trials of allergen/asthma therapeutics
- Dr. Meng: definition of asthma phenotype, genomics of asthma
- Dr. Portnoy: environmental contributions to allergy & asthma, indoor/outdoor allergens, clinical trials allergen/asthma therapeutics
- Dr. Rosenwasser: pharmacogenomics of asthma and role of immune modulation of inflammation



Research Directors: Charles S. Barnes, PhD
Lanny Rosenwasser, MD

Faculty: Christine Ciaccio, MD
Jay Portnoy, MD
Jiafeng Meng, MD, MPH
Marcia Chan, PhD



Overview:

The laboratory conducts basic and applied investigations into all aspects of asthma and allergy with emphasis on environmentally related allergic disease and genotype/phenotype relationships in asthma as associated with inflammation and modulation by the immune system. The goal is to investigate the characteristics of asthma and allergic disease. Investigators employ recognized scientific methods to increase the understanding of asthma and allergic disease and to apply understanding thus gained to the treatment of children. The laboratory is a leading center for the investigation of environmentally related allergic disease and strives to improve scientific understanding in the fields of asthma diagnosis, aerobiology, environmental allergens, building science and asthma education.



Selected 2008 Publications:

1. Ciaccio CE, Portnoy JM. Strategies for primary prevention of atopy in children. *Curr Allergy Asthma Rep.* Nov;8(6):493-9, 2008
2. Portnoy JM, Sampson H. Management of allergic rhinitis. *Lancet.* Sep 20;372(9643):1037, 2008
3. Barnes CS, Kennedy K, Gard L, Forrest E, Johnson L, Pacheco F, Hu F, Amado M, Portnoy JM. The impact of home cleaning on quality of life for homes with asthmatic children. *Allergy Asthma Proc.* Mar-Apr;29(2):197-204, 2008
4. Portnoy JM, Barnes CS, Kennedy K. Importance of mold allergy in asthma. *Curr Allergy Asthma Rep.* Mar;8(1):71-8, 2008
5. Horner WE, Barnes C, Codina R, Levetin E. Guide for interpreting reports from inspections/investigations of indoor mold. *J Allergy Clin Immunol.* Mar;121(3):592-597, 2008

Cardiac Surgery Research

Research Director: Richard A. Hopkins, MD

Faculty: Gabriel L. Converse, PhD
William B. Drake, III, MD
Stephen L. Hilbert, PhD, MD
Gary K. Lofland, MD
James E. O'Brien, BSE, MD



Overview:

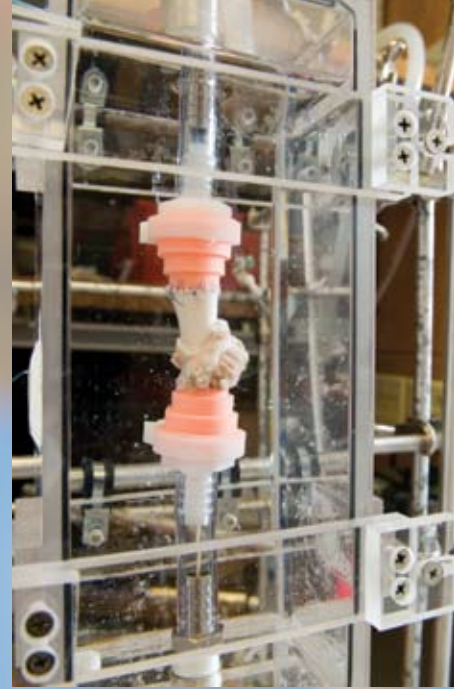
Researchers utilize the intersection of the field of reconstructive cardiac surgery with biotechnology, bioengineering, tissue engineering and regenerative medicine for the development of novel therapeutic options, treatments and devices especially based on tissue, cell and gene therapy strategies for patients with congenital and structural heart defects needing treatment by cardiac surgeons and cardiologists. These core competencies provide a unique platform for industry support, patent and intellectual property development, as well as traditional grant support (eg, NIH, AHA, NSF, etc.). Combining excellence in clinical surgery with translational research and development generates unique research projects and collaborations including discovery, development and FDA regulatory preclinical testing that lead to multicenter cutting edge clinical trials, leadership and a role in defining regulatory criteria. Multidisciplinary team research and dynamic collaborations enhance the clinical programs and results in an attractive intellectual and interactive research environment for scientists, engineers and clinicians.

The Cardiac Surgery Research Laboratories of The Ward Family Center for Congenital Heart Disease are dedicated to the translation of fundamental scientific research into therapeutic strategies for the treatment of congenital and structural cardiac disorders, fostering focused research and the development of collaborations by leveraging expertise in the fields of cardiac surgery, cardiology, cardiac anesthesiology, cardiac imaging, bioengineering, tissue engineering, cell biology, developmental biology, molecular biology, cardiovascular pathology, biotechnology and regenerative medicine. The governing commitment is to develop and share knowledge that improves the care of patients with congenital cardiac disease through innovative translational research.



Specific Research Interests:

- Dr. Converse: predictive models of assessing tissue stress in situ
- Dr. Drake: normative models of human cardiac growth, left ventricular mass index
- Dr. Hilbert: explant pathology related to bioengineered human tissues
- Dr. Hopkins: tissue engineering; allograft heart valves
- Dr. Lofland: genomic factors contributing to congenital heart disease
- Dr. O'Brien: conotruncal defects, congenital heart disease



Selected 2008 Publications:

1. Hopkins RA. Fleur de Lys repair of posterior Mitral Valve leaflet. Operative Techniques in Thoracic and Cardiovascular Surgery – A Comparative Atlas 13(2): 68-73, Summer 2008.
2. Hopkins RA, Gitter H, Stave J, Bert A, Atalay M. Stable Partial Dehiscence of Aortic Homograft Inserted Freehand Using Subcoronary Intra-Aortic Root Noncoronary Sinus Ross Scallop Inclusion Technique. Journal of Thoracic and Cardiovascular Surgery 135: 214-216, 2008.



Pediatric Clinical Pharmacology and Medical Toxicology

Research Director: J. Steven Leeder, PharmD, PhD

Faculty: Susan Abdel-Rahman, PharmD
Chengpeng “Charlie” Bi, PhD
Andrea Gaedigk, PhD
Roger Gaedigk, PhD
Bridgette Jones, MD
Gregory Kearns, PharmD, PhD
Kathleen Neville, MD, MS
Robin Pearce, PhD
Stephen Spielberg, MD, PhD
Carrie Vyhlidal, PhD



Specific Research Interests:

- Dr. Abdel-Rahman: developmental pharmacokinetics and pharmacodynamics
- Dr. Bi: bioinformatics and intelligent computing
- Dr. A. Gaedigk: pharmacogenetics of drug metabolism and disposition
- Dr. R. Gaedigk: genotyping, drug metabolism enzymes
- Dr. Jones: genotype/phenotype associations in asthma, development of pharmacodynamic biomarkers
- Dr. Kearns: developmental pharmacogenetics and pharmacodynamic biomarker development
- Dr. Leeder: pharmacogenomics, adverse drug reactions
- Dr. Neville: genomics of Sickle Cell disease, evaluation of analgesic response in children
- Dr. Pearce: impact of development on drug metabolism
- Dr. Spielberg: developmental pharmacology and pharmacogenomics, adverse drug reactions
- Dr. Vyhlidal: developmental regulation of drug metabolizing enzyme activity

Overview:

Researchers tailor the use of medications to the unique needs of each individual pediatric patient through the use of cutting edge genomic tools and information. The goal of the Clinical Pharmacology research program is to explore the extent of variability in the response to medications across all fields of pediatric medicine, and to ascertain the relative contributions of genetics and development. To achieve this mission, “translational teams” are created in which clinicians identify important, clinically significant medication-related problems are paired with basic science faculty members with the expertise necessary to develop solutions to those problems. The ultimate goal of the program is to improve clinical care by increasing both the safety and efficacy of medications in children. A secondary goal is to provide a learning environment conducive to developing clinician-scientists who will subsequently provide leadership for integrating personalized pediatrics into standard clinical care.



Selected 2008 Publications:

1. Adams DM, Zhou T, Berg SL, Bernstein M, Neville K, Blaney SM. Phase 1 trial of O6-benzylguanine and BCNU in children with CNS tumors: a Children's Oncology Group study. *Pediatr Blood Cancer* 50: 549-53, 2008
2. Adjei AA, Gaedigk A, Simon SD, Weinshilboum RM, Leeder JS. Interindividual variability in acetaminophen sulfation by human fetal liver: Implications for pharmacogenetic investigations of drug-induced birth defects. *Birth Defects Res A Clin Mol Teratol* 82: 155-65, 2008
3. Bi CP. Data augmentation algorithms for detecting conserved domains in protein sequences: A comparative study. *Journal of Proteome Research*; (7), 192-201, 2008
4. Bi CP, Vyhlidal C, Leeder JS. A comparative study on structured motif detection: algorithms and applications. *Molecular Pharmaceutics*; (5), 3-16, 2008
5. Gaedigk A, Coetsee C. The CYP2D6 gene locus in South African Coloureds: unique allele distributions, novel alleles and gene arrangements. *Eur J Clin Pharmacol* 64: 465-75, 2008
6. Gaedigk A, Simon SD, Pearce RE, Bradford LD, Kennedy MJ, Leeder JS. The CYP2D6 activity score: translating genotype information into a qualitative measure of phenotype. *Clin Pharmacol Ther* 83: 234-42, 2008
7. Grossman I, Sullivan PF, Walley N, Liu Y, Dawson JR, Gumbs C, Gaedigk A, Leeder JS, McEvoy JP, Weale ME, Goldstein DB. Genetic determinants of variable metabolism have little impact on the clinical use of leading antipsychotics in the CATIE study. *Genet Med* 10: 720-9, 2008
8. Kang P, Liao M, Wester MR, Leeder JS, Pearce RE, Correia MA. CYP3A4-Mediated carbamazepine (CBZ) metabolism: formation of a covalent CBZ-CYP3A4 adduct and alteration of the enzyme kinetic profile. *Drug Metab Dispos* 36: 490-9, 2008
9. Kennedy MJ, Davis DA, Smith N, Gaedigk A, Pearce RE, Kearns GL. Reduced activities of cytochrome P450 1A2 and xanthine oxidase in children with growth hormone deficiency. *Clin Pharmacol Ther* 84: 674-8, 2008
10. Kennedy MJ, Davis DA, Smith N, Gaedigk A, Pearce RE, Kearns GL. Six-month, prospective, longitudinal, open-Label caffeine and dextromethorphan phenotyping study in children with growth hormone deficiency receiving recombinant human growth hormone replacement. *Clin Ther* 30: 1687-99, 2008
11. Leeder JS, Pearce RE, Gaedigk A, Modak A, Rosen DI. Evaluation of a [13C]-dextromethorphan breath test to assess CYP2D6 phenotype. *J Clin Pharmacol* 48: 1041-51, 2008
12. Neville KA, Szeffler SJ, Abdel-Rahman SM, Lahu G, Zech K, Herzog R, Bethke TD, Gleason MC, Kearns GL. Single-dose pharmacokinetics of roflumilast in children and adolescents. *J Clin Pharmacol* 48: 978-85, 2008
13. Pearce RE, Lu W, Wang Y, Uetrecht JP, Correia MA, Leeder JS. Pathways of carbamazepine bioactivation in vitro. III. The role of human cytochrome P450 enzymes in the formation of 2,3-dihydroxycarbamazepine. *Drug Metab Dispos* 36: 1637-49, 2008
14. Shroba J, Olson-Burgess C, Preuett B, Abdel-Rahman SM. A large outbreak of *Trichophyton tonsurans* among health care workers in a pediatric hospital. *Am J Infect Control* May 16, 2008
15. James LP, Capparelli EV, Simpson PM, Letzig L, Roberts D, Hinson JA, Kearns GL, Blumer JL, Sullivan JE. Acetaminophen-associated hepatic injury: evaluation of acetaminophen protein adducts in children and adolescents with acetaminophen overdose. *Clin Pharmacol Ther* 84:684-690, 2008



Fungal Genomics Laboratory



Research Director: Susan M. Abdel-Rahman, PharmD

Overview:

Researchers conduct the highest quality basic, translational, clinical and epidemiologic research aimed at predicting, preventing and mitigating diseases in children with an emphasis on diseases that are disproportionately distributed among the underserved minorities. The goal of the laboratory is to use state-of-the-art molecular and pharmacologic techniques to explore the genotypic and phenotypic characteristics of humans and pathogens that may offer insight into disease processes and treatment response. The laboratory will aim to ensure that the passion for, and commitment to, biomedical research focused on children becomes self-sustaining by training and mentoring future clinician-scientists in general pediatrics and the pediatric subspecialties.

Specific Research Interests:

- Dr. Abdel-Rahman: genomics of *T. tonsurans* and other fungal pathogens, molecular diagnosis of fungal infection



Selected 2008 Publications:

1. Abdel-Rahman SM. Strain Differentiation of Dermatophytes. *Mycopathologia*;166:319-33, 2008
2. Abdel-Rahman SM, Talib N, Solidar A, Nopper AJ, Wyckoff GJ. Examining *Trichophyton tonsurans* genotype and biochemical phenotype as determinants of disease severity in tinea capitis. *Med Mycol*; 46:217-223, 2008
3. Shroba J, Olson-Burgess C, Preuett B, Abdel-Rahman SM. A large outbreak of *Trichophyton tonsurans* among healthcare workers in a pediatric hospital. *Am J Infect Control* 2008; May 16 [Epub ahead of print]
4. Abdel-Rahman SM. Strain differentiation of dermatophytes. *Mycopathologia* 166: 319-33, 2008

Genetics and Genomics Research

Research Director: Wayne V. Moore, MD, PhD

Faculty: Douglas C. Bittel, PhD
Daniel Heruth, PhD
Nataliya Kibiryeve, MD
Zohreh Talebizadeh, PhD
Robert A. White, PhD

Overview:

This multifaceted group of investigators conducts and supports biomedical research in the field of genomics as it relates to diseases that affect infants and children. State-of-the-art approaches are used to investigate both the molecular and epigenetics of developmental disorders, autism spectrum disorders, hematologic diseases and neuromuscular disorders. Laboratory approaches are facilitated by demonstrated capabilities in molecular modeling and the application of genomics computing.





Specific Research Interests:

- Dr. Bittel: application of molecular genetic tools to study genomic and epigenetic factors contributing to developmental disabilities
- Dr. Heruth: development of murine models of human disease
- Dr. Kibiryeve: assessment of genomic variability in developmental disabilities
- Dr. Talebizadeh: genetics and epigenetics of autism spectrum and neurodevelopmental disorders
- Dr. White: mouse genetics, muscular dystrophy therapy, muscular regeneration, Prader-Willi syndrome mouse model studies and hereditary anemias in mouse and man

Selected 2008 Publications:

1. Bazeley P, Shepelev V, Talebizadeh Z, Butler MG, Fedorova L, Filatov V, Fedorov A. SnoTARGET shows that human orphan snoRNA targets locate close to alternative splice junction. *Gene* 408:172-179, 2008
2. Bittel DC, Theodoro M, Kibiryeve N, Fischer W, Talebizadeh Z, Butler MG. Comparison of X chromosome inactivation patterns in multiple tissues from human females. *J Med Genet*; 45:309-313, 2008
3. Bittel DC, Theodoro MF, Kibiryeve N, Fischer W, Talebizadeh Z, Butler MG. Comparison of X-chromosome inactivation patterns in multiple tissues from human females. *Journal of Medical Genetics* 45:309-313, 2008
4. Butler MG, Fischer W, Kibiryeve N, Bittel DC. Array comparative genomic hybridization (aCGH) analysis in Prader-Willi syndrome. *American Journal of Medical Genetics A* 146A:854-860, 2008
5. Newkirk HL, Bittel DC, Butler MG. Analysis of the Prader-Willi syndrome chromosome region using quantitative microsphere hybridization (QMH) array. *American Journal of Medical Genetics A* 146A:2346-2354, 2008
6. Talebizadeh Z, Butler MG, Theodoro MF. Feasibility and relevance of examining lymphoblastoid cell lines to study role of microRNAs in autism. *Autism Research* 1: 240-250, 2008
7. Wang YP, Gunampally M, Chen J, Bittel DC, Butler MG, Cai WW. A comparison of fuzzy clustering approaches for quantification of microarray gene expression. *Journal of Signal Processing Systems* 50:305-320, 2008

Endocrinology and Diabetes Research

Research Director: Wayne V. Moore, MD, PhD

Faculty: Ghufraan Babar, MD
Mark Clements, MD, PhD
Jill D. Jacobson, MD
Karen Kover, PhD
Scott Sands, PhD

Overview:

The section has a multifaceted group of investigators that conducts and supports biomedical research in the field of Endocrinology as it relates to diseases that affect infants and children. State-of-the-art approaches are used to investigate the underlying causes of disease, discover new biomarkers predictive of disease and to develop new treatments for endocrine associated diseases such as diabetes and obesity. The ultimate goal of the program is to improve clinical care by increasing both the safety and efficacy of treatments in children. A secondary goal is to provide a learning environment conducive to developing clinician-scientists, who will subsequently provide leadership for integrating personalized pediatrics into standard clinical care. In addition opportunities are provided to medical, undergraduate, and high school students to participate in research activities facilitating their understanding of basic/clinical research and its translation into clinical care.



Specific Research Interests:

- Dr. Clements: glycemic variability on the risk for loss of micro- and macro-vascular complications in diabetes; glycemic variability on the risk for loss of residual beta cell mass in type I and type II diabetes; glycemic variability on the evolution of oxidative stress and endothelial cell dysfunction in diabetes.
- Dr. Moore: immunology of diabetes related specifically to the prevention of diabetes and islet transplantation.
- Dr. Jacobson: sexual dimorphism of autoimmunity. sexual dimorphism of autism. role of G proteins in the sexual dimorphism of human disease. role of epigenetics in the sexual dimorphism of human disease.
- Dr. Kover: islet biology and transplantation, immunomodulation strategies for treatment of type 1 diabetes:
- Dr. Sands: exploring hormonal effects on G protein expression using PCR.
- Dr. Babar: the impact of glycemic control on the evolution of endothelial dysfunction and vascular disease early in the course of type I diabetes
- Dr. Ugrasbul: clinical and metabolic phenotype of obese children and adolescents with normal glucose tolerance and type 2 diabetes.

2008 Publications:

1. Alemzadeh R, Kichler J, Babar G, Calhoun M. Hypervitaminosis D in obese children and adolescents: Relationship with adiposity, insulin sensitivity, ethnicity, and season. *Metabolism* 57(2):183-91, 2008
2. Alon US, Levy-Olomucki R, Moore WV, Stubbs J, Liu S, Quarles LD. Calcimimetics as an adjuvant treatment for familial hypophosphatemic rickets. *Clin J Am Soc Nephrol* May 3(3):658-64, 2008 [Epub 2008 Feb 6]
3. Block RC, Harris WS, Reid KJ, Sands SA, Spertus JA. EPA and DHA in blood cell membranes from acute coronary syndrome patients and controls. *Atherosclerosis* 197: 821-828, 2008
4. Moore WV, Dana K, Frane J, Lippe B. Growth hormone responsiveness: peak stimulated growth hormone levels and other variables in idiopathic short stature (ISS): data from the National Cooperative Growth Study. *Pediatr Endocrinol Rev* 08 6(1):5-8, 2008
5. Ugrasbul F, Moore WV, Tong PY, Kover KL. Prevention of diabetes: effect of mycophenolate mofetil and anti-CD25 on onset of diabetes in the DRBB rat. *Pediatr Diabetes* 9: 596-601, 2008



Infectious Diseases Laboratory

Research Director: Christopher J. Harrison, MD

Faculty: Hooi Yew, PhD
Douglas Swanson, MD
Raj Selverangan, PhD



Overview:

Research consists of quality translational, clinical and epidemiologic research into the pathogenesis, immunology and outcome of viral and bacterial diseases in children focusing on selected pathogens' responses to vaccines and treatments, and new potential interventions. One of the primary goals of this program is to investigate innate immune responses to CMV as a basis for variable outcomes of congenital CMV infections. TLR and SRA signaling is being investigated as well so that we might establish a pathogen library for ongoing surveillance of antibiotic susceptibility changes and strain variability in pediatric respiratory pathogens. Another goal of this laboratory is to develop and validate new molecular diagnostic tests for a variety of bacterial and viral pathogens that are common in pediatric patients. Researchers provide support for other Investigators interested in TLR signaling and provide a bench experience in ID for students, residents and fellows.

Specific Research Interests:

- Dr. Harrison: candidiasis, vaccinations, antibiotic resistance, cytokines influence on CMV disease, gram-positive pathogens
- Dr. Swanson: tuberculosis, pneumococcal conjugate vaccine
- Dr. Yew: biology of cell signaling regarding toll-like receptor response
- Dr. Selverangan: molecular diagnosis of viral and bacterial infections





Selected 2008 Publications:

1. Harrison CJ, Bratcher D. Cephalosporins: A Review. *Pediatrics in Review*, Vol 29, No. 8, pp 264-273, August 2008.
2. Pelton SI, Black S, Kohl S, and Harrison CJ. Reducing the burden of Pertussis: Diagnostic Advances and New vaccine Strategies. *Hayworth ME. MPR 10: 3-12, 2008.*
3. Julie. L Wei, J. Bond, K. Sykes, R. Selvarangan and MA. Jackson. Treatment outcomes for nontuberculous mycobacterial cervicofacial lymphadenitis in children based on the type of surgical intervention. *Otolaryngol Head Neck Surg.* 138 (5): 566-71, 2008.

Developmental Lung Biology

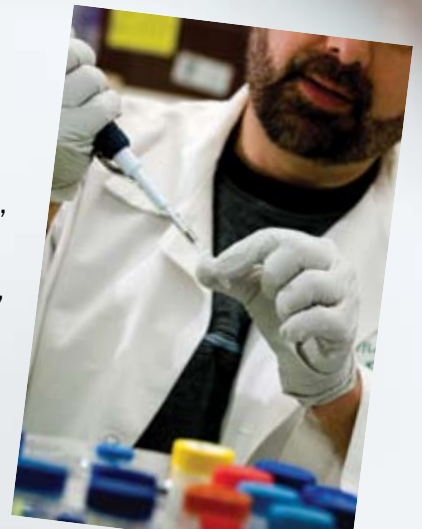


Research Director: William Truog, MD

Faculty: Ikechukwu Ekekezie, MD
Dong Xu, MD
Lisa Castro, MD
Maria Navarro-Olmo, PhD

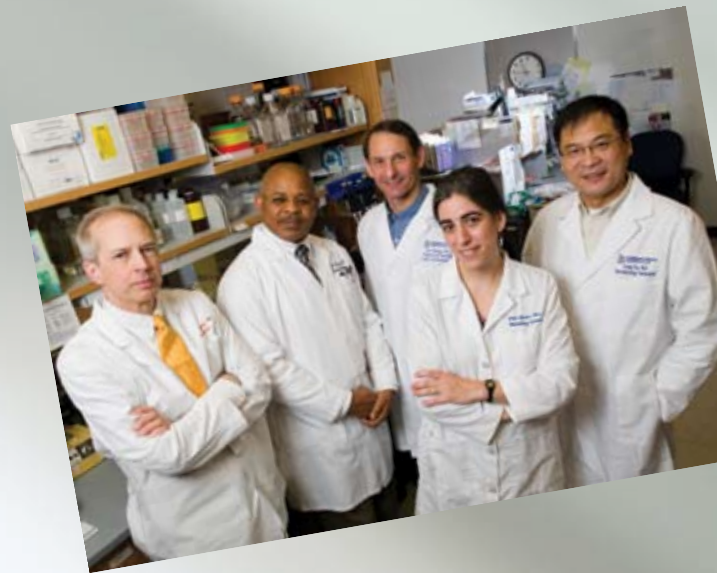
Overview:

The research interest of investigators in the Donald W. Thibeault Neonatal Research Laboratory at Children's Mercy Hospitals/University of Missouri at Kansas City School of Medicine revolves around lung development and disease. In addition to the principal investigators, Drs. Truog and Ekekezie, there are two research scientists with similar interests, Drs. Dong Xu and Angel Maria Navarro-Olmo, as well as three research technicians. The lab, now more than 30 years in existence, functions to provide the mandated research training requirements for completion of the Neonatology fellowship program.



Selected 2008 Publications:

1. Navarro A, Perez RE, Rezaiekhalthigh M, Mabry SM, Ekekezie II. T1alpha/podoplanin is essential for capillary morphogenesis in lymphatic endothelial cells. *Am J Physiol Lung Cell Mol Physiol* 295(4): L543-51, 2008
2. Truog WE, Xu D, Ekekezie II, Mabry S, Rezaiekhalthigh M, Svojanovsky S, Soares MJ. Chronic hypoxia and rat lung development: analysis by morphometry and directed microarray. *Pediatr Res* 64(1):56-62, 2008
3. Xu D, Perez RE, Ekekezie II, Navarro A, Truog WE. Epidermal growth factor-like domain 7 protects endothelial cells from hyperoxia-induced cell death. *Am J Physiol Lung Cell Mol Physiol* 294(1): L17-23, 2008



Specific Research Interests:

- Dr. Ekekezie: BPD; lung development and injury; role of metalloproteinases and their inhibitors in hyperoxia/ventilator-induced lung injury
- Dr. Truog: genomics; lung development and chronic lung disease; nitric oxide biology
- Dr. Xu: BPD; hyperoxia induced apoptosis; vascular angiogenesis and lymphangiogenesis
- Dr. Castro: developmental pharmacology, genomics of inflammatory cytokines in BPD
- Dr. Navarro-Olmo: angiogenesis and inflammation

Nephrology Research

Research Director: Bradley Warady, MD

Faculty: Uri Alon, MD
Tarak Srivastava, MD
Douglas Blowey, MD
Stanley Hellerstein, MD
René VanDeVoorde, MD

Overview:

Investigations conducted by faculty members focuses on clinical/translational, basic and epidemiological research as it relates to children with chronic kidney disease (CKD) and end-stage renal disease. Clinical investigation focuses on the development of accurate methods to assess kidney function, the detection of factors that influence the progression of CKD, and the prevention and treatment of complications associated with CKD, dialysis and transplantation. Unique approaches to modulate calcium and phosphorous balance as it relates to both kidney stone formation and the development of rickets are additional key areas of study. Basic research conducted in the Nephrology laboratory focuses on the structure and function of the glomerulus in children who suffer from nephrotic syndrome.

Specific Research Interests:

- Dr. Alon: fluid and electrolytes/minerals/acid-base disorders, metabolic bone disease, kidney stones
- Dr. Blowey: hypertension, fetal urinary tract abnormalities, pediatric pharmacology, extracorporeal drug clearance
- Dr. Hellerstein: methods to assess kidney function
- Dr. Srivastava: nephrotic syndrome, bone and mineral disorders, osteogenesis imperfecta
- Dr. Warady: chronic kidney disease, peritoneal dialysis, hemodialysis, kidney transplantation





Selected 2008 Publications:

1. Alon US, Levy-Olomucki R, Moore WV, Stubbs J, Liu S, Quarles LD. Calcimimetics as an adjuvant treatment for familial hypophosphatemic rickets. *Clin J Am Soc Nephrol* 3:658-364, 2008
2. Flores FX, Brophy PD, Symons JM, Fortenberry JD, Chua AN, Alexander SR, Mahan JD, Bunchman TE, Blowey D, Somers MJ, Baum M, Hackbarth R, Chand D, McBryde K, Benfield M, Goldstein SL. Continuous renal replacement therapy (CRRT) after stem cell transplantation. A report from the prospective pediatric CRRT Registry Group. *Pediatr Nephrol* 23:625-630, 2008
3. Flynn JT, Mitsnefes M, Pierce C, Cole SR, Parekh RS, Furth SL, Warady BA; Chronic Kidney Disease in Children Study Group. Blood pressure in children with chronic kidney disease: a report from the Chronic Kidney Disease in Children study. *Hypertension* 52:631-637, 2008
4. Freundlich M, Alon US. Bisphosphonates in children with hypercalciuria and reduced bone mineral density. *Pediatr Nephrol* 12:2215-2220, 2008
5. Toyoda M, Moudgil A, Warady BA, Puliyaanda DP, Jordan SC. Clinical significance of peripheral blood Epstein-Barr viral load monitoring using polymerase chain reaction in renal transplant recipients. *Pediatr Transplant* 12:778-784, 2008

Department of Pathology and Laboratory Medicine Research

Laboratory Director: David Zwick, MD

Faculty: Atif Ahmed, MD
Linda Cooley, MD, MBA
Angela Ferguson, PhD
Uttam Garg, PhD
Marilyn Hamilton, MD, PhD
Alex Kats, MD
Carol Saunders, PhD
Lei Shao, MD
Vivekanand Singh, MD
Eugenio Taboada, MD
Shihui Yu, PhD
Lei Zhang, PhD
David Zwick, MD

Overview:

The department provides comprehensive clinical laboratory testing services in support of all pediatric subspecialty care areas of the institution including toxicology, endocrinology, clinical chemistry, microbiology, cytogenetics including clinical array copy number variation testing, molecular genetic and molecular infectious disease testing, and histopathology. Departmental research is largely applied and deals mainly with defining usefulness of clinical diagnostics and monitoring techniques used in the care of pediatric patients. Departmental faculty support clinical studies of impact of laboratory testing on patient outcomes and aggregate health care costs. Certain subsections of the laboratory also support more basic investigations by providing technical support to institutional investigators in using high complex laboratory testing resources including instrumentation and skilled personnel (e.g. toxicology, flow cytometry).

Specific Research Interests:

- Dr. Cooley: molecular genetics, diagnosis of rare disorders
- Dr. Garg: biochemical genetics, clinical chemistry, therapeutic drug monitoring and drug metabolism, and metabolic disorders
- Dr. Hamilton: laboratory utilization ordering/interpretation of common laboratory tests, test development facilitating proper testing utilization
- Dr. Saunders: molecular genetics, pharmacogenetics
- Dr. Singh: Hirschsprung's disease, celiac disease, functional dyspepsia and inflammatory bowel disease
- Dr. Zwick: flow cytometry; hematopathology



Selected 2008 Publications:

1. Brandau DT, Lund M, Cooley LD, Sanger WG, Butler MG. Autistic and dysmorphic features associated with a submicroscopic 2q33.3-q34 interstitial deletion detected by array comparative genomic hybridization American Journal of Medical Genetics 146A(4)521-524, 2008
2. Brandau DT, Theodoro M, Garg U and Butler M. Follicle stimulating and leutinizing hormones, estradiol and testosterone in Prader-Willi syndrome. American Journal of Medical Genetics 146A(5)665-9, 2008
3. Ferguson, A.M., Ford, B., and Gronowski, A.M. Method validation for cerebral spinal fluid human chorionic gonadotropin measurement with the ADVIA® Centaur. Clinical Chemistry 54(8): 1408-9, 2008
4. Hamilton, M.S., Singh V., Warady, BA. Additional case of acute cellular kidney rejection associated with the presence of antibodies to the red blood cell Kidd antigen. Pediatric Transplantation 12(8) 918-9, 2008.
5. Selvarangan. R, Abel, D., Hamilton M. Comparison of BD Directigen EZ RSV and Binax NOW RSV tests for Rapid detection of Respiratory Syncytial virus from nasopharyngeal aspirates in a pediatric population Diagnostic Microbiology and Infectious Disease 62 (2): 157-61, 2008
6. Shao L, Manalang M, Cooley L. Juxtaglomerular cell tumor in an eight-year-old girl. Pediatric Blood and Cancer 50(2):406-9, 2008
7. Shao L, Singh V, Cooley L. Angiomatoid fibrous histiocytoma with t(2;2)(q33;q12.2) and EWSR1 gene rearrangement. Accepted for publication Pediatric and Developmental Pathology 2008 Jul 30:1 [Epub ahead of print]

Surgical Research

Research Director: Shawn St. Peter, MD

Faculty: Walter Andrews, MD
George W. Holcomb, III, MD, MPH
J. Patrick Murphy, MD
Daniel Ostlie, MD
Donna Pacicca, MD
Nigel Price, MD
Richard Schwend, MD
Susan Sharp, PhD



Overview:

Research conducted by the Department of Surgery reflects a comprehensive program which embraces both clinical/translational and outcome research. Laboratory-based efforts reflect work in the areas of spinal embryogenesis and the biology of bone remodeling during development. As well, the department houses an active program that prospectively evaluates a variety of surgical interventions required to care for infants and children.

Specific Research Interests:

- Dr. St. Peter: surgical outcome research
- Dr. Andrews: solid organ transplantation
- Dr. Holcomb: outcome associated with minimally invasive surgery
- Dr. Murphy: surgical outcome research
- Dr. Ostlie: outcome research associated with surgical intervention and devices
- Dr. Pacicca: developmental biology of bone formation
- Dr. Price: embryogenesis of spinal development
- Dr. Schwend: outcome research associated with surgical intervention and devices





Selected 2008 Publications:

1. Barsness KA, St.Peter SD, Holcomb GW III, Ostlie DJ, Kane, TD: Laparoscopic fundoplication after previous open abdominal operations in infants and children. *J Laparoendosc Adv Surg Tech A*, Nov 4, 2008 [e pub ahead of print]
2. Keckler SJ, Tsao K, Sharp SW, Holcomb GW III, Ostlie DJ, St. Peter SD: Blood utilization in children managed non-operatively for blunt solid organ injury. *J Surg Research*, 147:237-239, 2008
3. Keckler SJ, St. Peter SD, Spilde TL, Ostlie DJ, Snyder CL: The influence of Trisomy 21 on the incidence and severity of congenital heart defects in patients with duodenal atresia. *Pediatr Surg International*, 24:921-923, 2008
4. Keckler SJ, Ostlie DJ, Holcomb GW III, St. Peter SD: The progressive development of pyloric stenosis: a role for repeat ultrasound. *European J of Pediatr Surg*, 18:168-170, 2008
5. Kelly RE Jr, Cash TF, Shamberger RC, Holcomb GW III, et al: Surgical repair of pectus excavatum markedly improves body image and perceived ability for physical activity: multi-center study. *Pediatrics*, 1218-1222, 2008
6. Spilde TL, Keckler SJ, St. Peter SD, Tsao K, Holcomb GW III, Ostlie DJ: Open versus laparoscopic repair of congenital duodenal obstructions – a concurrent series. *J Pediatr Surg*, 43:1002-1005, 2008
7. St. Peter, SD, Weesner KA, Spilde TL, Sharp RJ, Sharp SW, Ostlie DJ, Holcomb GW III: Is epidural anesthesia truly the best pain management strategy after minimally invasive pectus excavatum repair? *J Pediatr Surg*, 43:79-82, 2008
8. St. Peter SD, Sharp SW, Holcomb GW III, Ostlie DJ: An evidence-based definition for perforated appendicitis derived from a prospective randomized trial. *J Pediatr Surg*, 43:2242-2245, 2008
9. St. Peter SD, Ostlie DJ: Pyloric Stenosis: from a retrospective analysis to a prospective clinical trial: the impact on surgical outcomes. *Current Opinion in Pediatr*, 20:311-314, 2008
10. St. Peter SD, Tsao K, Sharp SW, Holcomb GW III, Ostlie DJ: Predictors of emesis and time to goal intake after pyloromyotomy: analysis from a prospective trial. *J Pediatr Surg*, 43:2038-2041, 2008

AWARD WINNERS



Paul Henson Immunology Research Award



Mara Becker, MD

Rheumatology

Assistant Professor of Pediatrics, UMKC School of Medicine

“Impact of Genomic Variation on Intracellular Methotrexate Polyglutamate Concentrations in Juvenile Idiopathic Arthritis.”

The Paul Henson Endowment Fund for Pediatric Research in Immunology was established to support education and research pediatric immunology.

Paul Henson, a member of the Children’s Mercy Hospital board of trustees from 1990 until his death in 1997, is remembered for his desire to fully develop the hospital’s teaching and research capabilities. Through the endowment fund, Mr. Henson’s legacy continues to touch children through the advances it makes possible in immunology research.

The Paul Henson Pediatric Immunology Research Award is presented yearly to a Children’s Mercy researcher to further promising, ongoing research in pediatric immunology.

Paul Henson Pediatric Immunology Award

- 2007 Tarak Srivastava, MD
- 2006 Susan Abdel-Rahman, PharmD
- 2005 Lanny Rosenwasser, MD
- 2004 Wayne Moore, MD
- 2003 Wayne Moore, MD
- 2002 Wayne Moore, MD
- 2001 Wayne Moore, MD
- 2000 Jill Jacobson, MD
- 1999 Jill Jacobson, MD
- 1998 Jill Jacobson, MD

Kenneth and Eva Smith Award



Gina Calarco - 2007

Infectious Diseases

“Acceptance of Maternal Postpartum Tdap Vaccine: Maternal Attitude and Impact on Mother and Infant Vaccine Coverage Rates”



Meredith Dreyer, PhD - 2008

Developmental and Behavioral Medicine

Assistant Professor of Pediatrics, UMKC School of Medicine

“Parenting Skills and Nutrition Education Intervention for Treatment of Overweight/Obesity in Young Children”

The Kenneth and Eva Smith Foundation instituted this Research Award in 2005. The purpose of the award is to fund current research at Children’s Mercy Hospitals and Clinics with defined areas of focus. The intention of this award from the Smith Foundation is that data generated from the investigation(s) performed will produce publications in peer-reviewed biomedical literature and will also provide sufficient proof-of-principle/concept to support related grant applications to the NIH or a research foundation. These awards will be made to a member of the Children’s Mercy faculty, fellows, or professional staff based upon the scientific merits of a peer-reviewed research proposal.

Kenneth and Eva Smith Award

2005	Susan Abdel-Rahman, PharmD
2006	Susan Abdel-Rahman, PharmD

William Randolph Hearst Endowment



Doug Swanson, MD

Infectious Diseases

Associate Professor of Pediatrics, UMKC School of Medicine

“Detection and Differentiation of Nontuberculous Mycobacteria from Children with Cystic Fibrosis by Real-Time PCR and DNA Sequencing of the hsp65 and 16S and 23S Intergenic Gene Region”



Karen Kover, PhD

Endocrine Research Laboratory

“Bone Marrow Cavity, An Intriguing New Site for Islet Transplantation”

Each spring and fall, an internal competition is held for the Katharine Berry Richardson (KBR) awards. Among the proposals submitted for the competition, the two top-rated projects are designated the William Randolph Hearst Endowment Fund awardees and receive a portion of their support from this fund.

William Randolph Hearst Endowment

- 2007 Mark Connelly, PhD
Ben Pieters, DO
- 2006 Roger Gaedigk, PhD
Chengpeng Bi, PhD
Heather Newkirk, PhD
- 2005 Chetanbabu Patel, MD
Kathleen Neville, MD, MS
- 2004 Mary Moffatt, MD
Heather Newkirk, PhD

Marion Merrell Dow Clinical Scholar Award

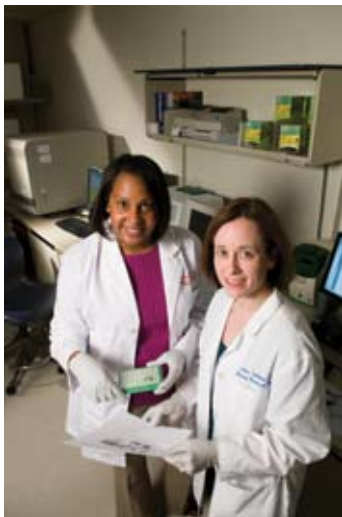


Donna Pacicca, MD

Orthopaedic Surgery

Assistant Professor of Orthopaedic Surgery, UMKC School of Medicine

“Hematopoietic Stem Cells Can Differentiate Along an Osteogenic Lineage”



Bridgette Jones, MD

Asthma, Allergy and Immunology

Assistant Professor of Pediatrics, UMKC School of Medicine

and

Carrie Vyhldal, PhD

Pediatric Pharmacology & Medical Toxicology

Assistant Professor of Pediatrics, UMKC School of Medicine

“A Non-Invasive Approach to Predict Steroid Sensitivity in Patients with Asthma”

The Marion Merrell Dow Clinical Scholar Award supports new or existing Medical and Research Staff who are expanding their research or establishing a new research program. To be eligible for this award, an applicant must hold an MD or PhD, and may not be a previous recipient of a Clinical Scholar award. Consideration is given to new investigators in the first five years of faculty appointment at Children’s Mercy.

Research Days Award Winners



As part of the hospital’s ongoing commitment to pediatric research and education, each year Children’s Mercy hosts Research Days presentations by residents and fellows. A panel of judges confers Research Days awards on the presenters of the best papers.

Shayna Smith, MD

Faculty Mentors: John Cowden, MD; Sara Pyle, PhD; Lynette Poolman, MD; Denise Dowd, MD

“Connected Kids at Head Start: Taking Office-based Violence Prevention to the Community”



Bridgette Jones, MD

Faculty Mentors: R.E. Pearce, PharmD; Susan Abdel-Rahman, PharmD; Craig Friesen, MD; Gregory Kearns, PharmD, PhD

“Validation of the ¹³C Acetate Breath Test to Measure Liquid Gastric Emptying in a Pediatric Population”



Dena Hubbard, MD

Faculty Mentors: Daphne Reavey, NNP; Tracy Sandritter, PharmD; Barbara Haney, CPNP; Eugenia Pallotto, MD; William Troug, MD

“Continuous Opioid Infusions in NICU Patients: Too Much or Not Enough”

Hospital Leadership

Children's Mercy Hospital Senior Management

Randall L. O'Donnell, PhD

President/Chief Executive Officer

V. Fred Burry, MD

Executive Medical Director/Executive
Vice President

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Executive Vice President/Co-Chief
Operating Officer

Sandra A.J. Lawrence

Executive Vice President/Chief
Financial Officer

Jo Stueve

Executive Vice President/Co-Chief
Operating Officer

David Westbrook

Senior Vice President of Strategy and
Innovation

Lonnie Breaux

Vice President, Facilities

Kimberly Brown

Vice President, Audit and Compliance

Warren Dudley

Vice President, Market Development
and Outreach

Robert Finuf

CEO, Children's Mercy Family Health
Partners

Joe Galeazzi

Vice President, Medical Affairs

Cheri Hunt, RN, MHA, CNAA

Vice President/Chief Nursing Officer

Laurisa Jackson

Vice President, Revenue Cycle and
Supply Chain

D. Bradley Leech

Vice President/Chief Development
Officer

Barbara Mueth

Vice President, Community Relations

Genny Nicholas

Vice President, Government Relations

Charles Roberts, MD

Associate Executive Medical Director/
Vice President

Sally SurrIDGE

Vice President/General Counsel

Terry Weathers

Vice President of Finance/Controller

Dan Wright

Vice President, Human Resources

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Summer Scholars

Through the Summer Scholars program, Children's Mercy provides college students with experience in pediatric research.

During the summer of 2008, 10 scholars worked with researchers in the sections of Genetics Research, Clinical Pharmacology and Medical Toxicology, Endocrinology, Allergy/Asthma/Immunology, Infectious Disease, and Cardiac Surgery Research. Their experience culminated in a public symposium wherein they presented their research. We are glad to provide these students with the opportunity to explore their interest in research careers.

The 2008 Summer Scholars are:

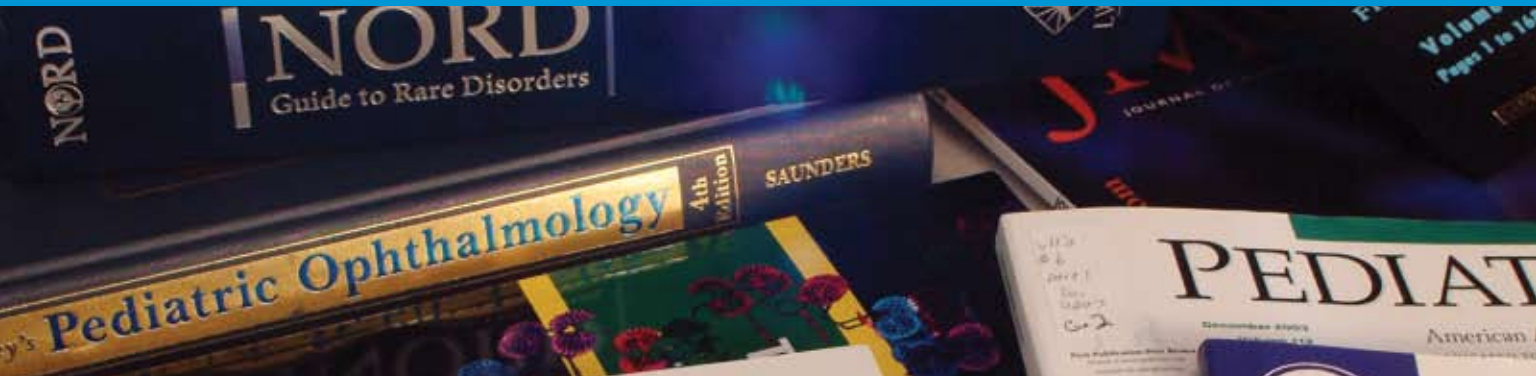
- **David Berg, Evangel University**
- **Jacob Brown, Creighton University**
- **Suzanne Fox, University of Notre Dame**
- **Alex Heisler, Indiana University**
- **Katherine Klockau, University of Kansas**
- **Erica Levorson, University of Nebraska-Lincoln**
- **Derek Logsdon, Evangel University**
- **Brittanie Martin, University of Missouri-Columbia**
- **Audrey Southard, Georgia Institute of Technology**
- **Whitney Wells, University of Missouri-Columbia**

RUDOLPH'S PEDIATRICS

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Textbook of Pediatric Infectious Diseases

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The American Thoracic Society
Next Meeting: April 18-22, 2008
Headquarters: Meeting Center, Tennessee, Chattanooga, TN
(See page 1120)
The Western Thoracic Surgical Association
Next Meeting: June 18-22, 2008
Headquarters: La Costa, California
(For Program see page 1120)

The Journal of Thoracic and Cardiovascular Surgery

The NEW ENGLAND JOURNAL of MEDICINE

- 1105 THIS WEEK IN THE JOURNAL
- 1115 ORIGINAL ARTICLES
- 1115 Expression of Pulmonary C.D. Cook
 - 1123 Withdrawal of Death in O. Cook
 - 1133 A Comparison for the Prevention with the Anti M.A. Crowder
 - 1139 Brief Report: Associated with E.M. Kolford
- REVIEW ARTICLE
- Concepts

CLINICAL PHARMACOLOGY & THERAPEUTICS

American Society for Clinical Pharmacology and Therapeutics
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In December of 2008, the lead article in *Pediatrics* (Vol. 22, No. 6, pp. 1165-1170), the official journal of the American Academy of Pediatrics, described the results from a study conducted by Drs. Jane Knapp and Vidya Sharma which examined the quality of care for common pediatric respiratory illnesses seen by Emergency Departments in the United States. This manuscript reported a critical, highly significant finding: effective therapies for asthma and croup were being grossly underutilized in favor of treatments that had been shown to be either ineffective or unproven.

Publications such as this one do not simply represent a form of academic currency, but most importantly, represent the vehicle for communication and dissemination of new knowledge that when applied, can improve our understanding of pediatric diseases and their proper treatment. During 2008, faculty members in almost all of the academic departments at Children's Mercy Hospital published scholarly works which described original research, reviewed important topics and/or informed the greater medical community about interesting cases. The listing of faculty publications for 2008 which follows chronicles the accomplishments of our faculty and reflects the importance of their scholarly endeavors.

MANUSCRIPTS PUBLISHED IN PEER-REVIEWED JOURNALS

Adolescent Medicine

Duffy K, **Lynch D**, Santinelli J. (Santelli) Government Support for Abstinence-Only-Until-Marriage Education. *Clinical Pharmacology and Therapeutics* 84: 746-748 (2008)

Cardiovascular Surgery

Grist GE. Preface: General Introduction. *Progress in Pediatric Cardiology* 24(2):88 (2008)

Grist GE. Oxygen Pressure Field Theory: A Detailed Description of Vital Gas Exchange, at the Capillary Level for Perfusionists. *Progress in Pediatric Cardiology* 24(2): 89-99 (2008)

Grist GE. The Viability Index: A Survival Score for Perfusion Patients. *Progress in Pediatric Cardiology* 24(2): 101-111 (2008)

Grist GE. Extracorporeal Membrane Oxygenation (ECMO) or Extracorporeal Cardiopulmonary Resuscitation (ECPR): A Critical Life or Death Choice. *Progress in Pediatric Cardiology* 24(2): 113-116 (2008)

Hoffman TL. The Clinical Process and Quality Process in Pediatric Perfusion. *Progress in Pediatric Cardiology* 24(2): 123-126 (2008)

Hopkins RA. Fleur de Lys repair of posterior Mitral Valve leaflet. *Operative Techniques in Thoracic and Cardiovascular Surgery – A Comparative Atlas* 13(2): 68-73 (2008)

Hopkins RA, Gitter H, Stave J, Bert A, Atalay M. Stable Partial Dehiscence of Aortic Homograft Inserted Freehand Using Subcoronary Intra-Aortic Root Noncoronary Sinus Ross Scallop Inclusion Technique. *Journal of Thoracic and Cardiovascular Surgery* 135: 214-216 (2008)

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Swihart JA. Medical Device Regulation and the Conduct of Clinical Trials in the United States. *ACRP The Monitor* June 2008

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Witherspoon KA. ECMO for Resuscitation of an Infant Immediately Post-Op VSD Closure and RVOT Repair: A Case Report of Possible Malignant Hyperthermia. *Progress in Pediatric Cardiology* 24(2): 131-135 (2008)

Clinical Pharmacology and Medical Toxicology

Abdel-Rahman SM. Strain differentiation of dermatophytes. *Mycopathologia* 166: 319-33 (2008)

Abdel-Rahman SM, Benziger DP, Jacobs RF, Jafri HS, Hong EF, **Kearns GL**. Single-Dose Pharmacokinetics of Daptomycin in Children With Suspected or Proved Gram-Positive Infections. *Pediatr Infect Dis J* 27: 330-334 (2008) [supported in part by funding from NICHD]

Abdel-Rahman SM, Talib N, Solidar A, Nopper AJ, Wyckoff GJ. Examining Trichophyton tonsurans genotype and biochemical phenotype as determinants of disease severity in tinea capitis. *Med Mycol* 46: 217-23 (2008) [supported in part by funding from NIAMS]

Adams DM, Zhou T, Berg SL, Bernstein M, **Neville K**, Blaney SM. Phase 1 trial of O6-benzylguanine and BCNU in children with CNS tumors: a Children's Oncology Group study. *Pediatr Blood Cancer* 50: 549-53 (2008)

Adjei AA, **Gaedigk A**, Simon SD, Weinshilboum RM, **Leeder JS**. Interindividual variability in acetaminophen sulfation by human fetal liver: Implications for pharmacogenetic investigations of drug-induced birth defects. *Birth Defects Res A Clin Mol Teratol* 82: 155-65 (2008)

Algren DA. Management of the Poisoned Patient. *Missouri Medicine* 105: 47-52 (2008)

Algren DA. Review of N-Acetylcysteine for the Treatment of Acetaminophen (Paracetamol) Toxicity in Pediatrics. World Health Organization Subcommittee of the Expert Committee on the Selection and Use of Essential Medicines. (2008) Available at http://www.who.int/selection_medicines/committees/subcommittee/2/acetylcysteine/en/index.html.

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- Montgomery EJ, **Wasserman GS.** Toxicity and Use of Over-the Counter Cough and Cold Medication in the Pediatric Population. *Missouri Medicine* 105(6): 514-517 (2008)
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- Wible Jr. JH, Tata PN, Napoli AM, Lowe LH, Kearns GL.** Pharmacokinetics of gadoversetamide injection, a gadolinium-based contrast agent, in pediatric patients. *Magn Reson Imaging* Sept 22 (2008)
- Zhang Y, Zhang L, Abraham S, Apparaju S, Wu TC, Strong J, Xiao S, Atkinson Jr A, Thummel K, **Leeder JS, Lee C, Burckart G, Lesko L, Huang SM.** Assessment of the Impact of Renal Impairment on Systemic Exposure of New Molecular Entities: Evaluation of Recent New Drug Applications. *Clin Pharmacol Ther* Nov 19 (2008; online ahead of print)

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Bittel DC, Theodoro MF, **Kibiryeveva N**, Fischer W, **Talebizadeh Z**, Butler MG. Comparison of X-chromosome inactivation patterns in multiple tissues from human females. *Journal of Medical Genetics* 45:309-313 (2008) [Regarding NIH support, in this study we received tissues from the BTB which is supported by NIH. Funding: This study was partially supported by the Hall Foundation of Kansas City and a Physician Scientist Award (MGB) and the Fraternal Order of Eagles of the State of Kansas (DCB). Human tissues were obtained from the NICHD Brain and Tissue Bank for Developmental Disorders, University of Maryland, Baltimore, MD under contracts NO1-HD-4-3368 and NO1-HD-4-3383]

Brandau DT, **Lund M**, **Cooley L**, Sanger W, Butler MG. Autistic and dysmorphic features associated with a submicroscopic 2q33.3-q34 interstitial deletion detected by array comparative genomic hybridization. *Am J Me Genet Part A*. 146A:521-524 (2008)

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Infectious Disease

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Neonatology

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