

**HOPE**  
FROM  
**RESEARCH**

Changing Lives Every Day



## TABLE OF CONTENTS

1	Introduction
2	Mission
3	Letter from the Director
5	Pediatrics
11	Pathology, Psychiatry, Medical Imaging and Anesthesiology Introduction
12	Pathology and Laboratory Medicine
14	Child and Adolescent Psychiatry
16	Medical Imaging
17	Anesthesiology
19	Surgery
22	Centers Of Excellence
24	Research Center and Children’s Memorial Hospital Organizational Chart
27	Children’s Memorial Research Center Introduction
28	Cancer Biology and Epigenomics
30	Developmental Biology
32	Clinical and Translational Research
34	Human Molecular Genetics
36	Neurobiology
38	Mary Ann & J. Milburn Smith Child Health Research Program
41	Research Training Program
44	Core Facilities
46	The Medical Research Institute Council — 60 Years of Extraordinary Philanthropy for Medical Research
47	Summary of Award Activity
48	Research Center Offices and Support

## ACKNOWLEDGEMENTS

DESIGN: Ripple Communications

EDITOR: Peggy Murphy, MILS

EDITORIAL ASSISTANCE: Alexander Fullam

ADDITIONAL WRITING: Francine Blazowski, MSW, Brian Hayes, Julie Pesch, Betsey Pinkert, Marianne Reed, Hilary Sallerson

PHOTOGRAPHY: Children’s Memorial Hospital Audio-Visual Department, Andrew Campbell, Garbo Productions

SCIENTIFIC IMAGES: Daniel Abbott, MD; Carl Backer, MD; Lee Bass, MD; Pauline Chou, MD; Rodney Dale, PhD; Christine DiDonato, PhD; Vasil Galat, PhD; Aleksandra Glavaski-Joksimovik, PhD; Christopher Hamm, PhD; John Lavigne, PhD; Susanna McColley, MD; Pallavi Patwari, MD; Elizabeth Perlman, MD; Jerry Rhee, PhD; Cynthia Rigsby, MD; Arun Sharma, PhD; Santhanam Suresh, MD; Xiao-Di Tan, MD; Jacek Topczewski, PhD; ShanChun Zhang, MD, PhD



# Helping children reach life's **MILESTONES**

The research team at Children's Memorial Hospital is dedicated to reaching one overriding goal: Providing the best medical care for children and their families. In this report, we highlight the many ways in which our medical and research investigators work to help children throughout their young lives.

---

*Children's Memorial Research Center provides hope through research to every parent who wants to hear their daughter's first words, see their son graduate or take their kids on a cross-country road trip.*

In every child's life, families and loved ones eagerly anticipate the milestones that show progress, such as growing an inch taller, learning new words, graduating from 8th grade, driving a car for the first time. But sometimes, obstacles present themselves. Accidents, sudden onset of disease or unexpected diagnoses can create significant roadblocks to achieving life's milestones.

At Children's Memorial we believe strongly in our efforts to place research at the forefront of our patient care program: to prevent accidents from happening; to forestall illness; to improve the process of diagnosing conditions; and to give families hope for better therapies and cures.

Biomedical research is conducted throughout Children's Memorial's departments, divisions, programs and centers of excellence. Indeed, the collaborative spirit that our supportive academic environment engenders makes research progress and biomedical breakthroughs possible. We hope that every child whose medical home is Children's Memorial benefits from our devoted research efforts to provide advanced pediatric healthcare to facilitate life's enchanting milestones.



MARY J.C. HENDRIX, PhD

President and Scientific Director, Children's Memorial Research Center,  
and Medical Research Institute Council Professor,  
Northwestern University Feinberg School of Medicine  
and the Robert H. Lurie Comprehensive Cancer Center

## Achieving Success to Advance Translational Research



On behalf of the faculty, staff and trainees of Children's Memorial Research Center and the academic departments of Pediatrics, Surgery, Pathology, Medical Imaging, Anesthesiology, and Child and Adolescent

Psychiatry, it is my privilege to present our annual report highlighting the basic and translational research discoveries advancing our mission — developing new therapies for pediatric patients and their families.

A little over two decades ago, Children's Memorial charted a course for success by investing in the establishment of a research enterprise that would support the clinical and educational missions of the Children's Memorial Medical Center departments. This strategic decision has had profound implications resulting in the recruitment of top talent and the acquisition of national prominence. Now, with the construction of a world-class children's hospital on the campus of a highly respected medical center and university, we embrace the goal of becoming a top ten research center to support what will surely be a top ten hospital.

Currently, we have 145 funded principal investigators, over 500 staff, \$40.8 million in extramural awards for Fiscal Year 2010, conducting research in approximately 162,000 gross square feet across four campuses. In other words, Children's research is conducted on an "urban" campus. Where do we currently stand? There are 250 children's hospitals in the United States, and one-third of

them operate research centers (approximately 83). When we compare ourselves to other free-standing research enterprises associated with children's hospitals, our NIH-based ranking is 11. Moreover, we would need to acquire an additional \$8 million in NIH funding to tie with #10. Our top 10 goal is driving the research strategic planning process and careful attention is being devoted to the new recruitments, facilities, administrative infrastructure and resources needed to sustain and enhance our enterprise.

I end on a note of deep appreciation for the long-standing partnership we are privileged to share with the Medical Research Institute Council (MRIC), which has raised over \$45 million for the research center since 1991. I would like to especially thank Hilary Sallerson, JoAnn Eisenberg, Ruth Geller, Betsey Pinkert, Joan Brodsky, Malcolm Kamin, Lesli Falk and Seth Prostic for their remarkable leadership contributions to the MRIC during a challenging time in our history. Our special gratitude is also extended to philanthropists Ann Lurie for her extraordinary legacy, David and Denise Bunning whose generosity continues to support the Children's Memorial Food Allergy Study, and to Mrs. Mary Ann Smith who generously continues her commitment to the Smith Child Health Research Program. We are gratefully indebted to all our generous donors who support today's research for tomorrow's cures and make us a premier research enterprise.

*Mary J.C. Hendrix*



## Cracking the **CODE**

### *Life's Milestones*

By using tools that help physicians make sense of complex conditions, the Center for Interdisciplinary Research in Critical Illness and Injury (CIRPCII) is advancing pediatric medicine and creating new knowledge not thought possible before.

# For Families Coping with Health Challenges, Every Milestone Matters

**Research breakthroughs, and their integration into clinical applications help children and their families celebrate important life moments**

The Department of Pediatrics' divisions and programs work individually and collaboratively to improve the health and well being of children and their families through research. We find ways to provide interventions before serious illnesses or injuries happen. We investigate the best methods to treat and offer follow up care for medical conditions. Our physicians are well known for their expertise and accomplishments. Our research seeks to find causes, therapies and cures for many diseases, including those listed to the right.

We accomplish our goals through a combination of laboratory research and clinical trials. In many of our preliminary studies, we look for clues to determine the best course forward. The programs of Children's Memorial Research Center are committed to making discoveries that will improve the lives of children and their families. Clinical trials conducted by our divisions provide opportunities for, and the responsibility of, dramatically improving therapeutics and finding cures.

Note: The research center works closely with the Department of Pediatrics. To read more about our collaborative research in the following areas go to the following pages: Cancer Biology and Epigenomics – page 28, Child Health Research – page 38, Clinical and Translational Research – page 32, Developmental Biology – page 30, Human Molecular Genetics – page 34 and Neurobiology – page 36.

- Respiratory problems and asthma disparities
- Heart failure
- Injuries
- Skin conditions and wounds
- Metabolic syndrome
- Gastrointestinal disorders
- Developmental and behavioral problems
- Genetic diseases
- Cancer and other blood diseases
- Drug resistant infections
- Critical illnesses in newborns
- Epilepsy
- Kidney dysfunction
- Autonomic diseases
- Cystic fibrosis
- Pediatric rheumatic diseases
- and many others

## Breakthrough Research

The research goals of Emergency Medicine encompass the continuum of emergency medical services for children. A broad scope of clinical trials are evaluating the effectiveness of therapeutic interventions, diagnostic tools, clinical decision rules, medical decision making, and the quality and outcome of pediatric emergency care. In the community we serve, we can assess the risk of injury (and illness) in children and measure

the success of prevention strategies. The Injury Prevention and Research Center utilizes a public health model that describes the injury problem, identifies causes and locations, and develops and test interventions to discover best practice and research methods to reduce childhood injury. The KidSTAR high-fidelity simulation center serves as a dynamic laboratory where novel approaches to the measurement of healthcare provider

performance, and unique and effective approaches to professional education are investigated and disseminated. Through support provided by the Grainger Research Initiative in Emergency Medical Services for Children, we plan to build additional capacity and activity in each of these research disciplines and laboratories.



*KidSTAR provides medical simulation experiences, valuable in critical incidents.*

## Research Honors

### CARDIOLOGY

**Katheryn Gambetta, MD** received a Young Investigator Award at the Second International Conference on Cardiomyopathy in Children.

### CRITICAL CARE

**Melissa Brannen, MD** was a 2010 inductee to the Feinberg Academy of Medical Educators. **Conrad Epting, MD** received a Northwestern University Clinical and Translational Sciences (NUCATS) Center for Translational Innovation (CTI) Pilot Grant Award and a Children's Research Foundation Award in 2010.

### EPILEPSY CENTER

**Sarah Ahlm, MA, LCSW** and **Heather Kaplan, LCSW** delivered a Pediatric Highlight platform presentation at the American Epilepsy Society meeting in 2010.

### GENERAL ACADEMIC PEDIATRICS

**Robert Garofalo, MD, MPH** was named to an Institute of Medicine Panel concerning health risks of lesbian, gay, bisexual and transgender youth in 2010.

### HEMATOLOGY, ONCOLOGY AND STEM CELL TRANSPLANTATION

**Seth Corey, MD, MPH** is a member of two study groups at the NIH.

**Alexis Thompson, MD, MPH** was named to the Executive Committee of the American Society of Hematology (ASH).

### PEDIATRIC INFECTIOUS DISEASES

**William Muller, MD, PhD** was awarded the Infectious Diseases Society of America Astellas Young Investigator Award.

### PULMONARY MEDICINE

The CFF TDN Translational Center ranked tenth of 77 sites for research metrics (productivity and quality) in March 2010 and fourth of 77 in September 2010. Furthermore, the Center was chosen as a pilot site for the Clinical Research Ambassador's Program, an initiative to improve knowledge and participation in cystic fibrosis clinical trials.

### RHEUMATOLOGY

**Marisa Klein-Gitelman, MD** was appointed Chair, Committee on Pediatrics, American Society of Rheumatology. **Lauren Pachman, MD** joined the Federation of Clinical Immunology Societies (FOCIS) Center of Excellence Steering Committee.

In 2010, the division was designated a participating center of the national Quality Improvement Collaborative for Pediatric Rheumatology (PR-COIN). Data shared with PR-COIN will serve as a model of multi-center data sharing for other divisions, programs and centers.

**ALLERGY AND IMMUNOLOGY** is actively engaged in childhood asthma research, and is one of ten centers that comprise the Inner City Asthma Consortium. The division has established the Chicago Metropolitan Asthma Consortium with the University of Chicago, Rush University and John H. Stroger Jr., Hospital of Cook County. It was selected to be a site for the AsthmaNet Consortium. Food allergy is another important focus. A productive collaboration with Smith Child Health Research and the CTSA/CRU has produced a database that was used to generate preliminary data, abstract submissions and NIH funding. The division obtained an award to be the genetics site for CoFar (Consortium for Food Allergy Research).

**CARDIOLOGY** conducts clinical and retrospective studies that include collaborations with fellows, residents and faculty in Cardiovascular-Thoracic Surgery and Critical Care. Elfriede Pahl, MD successfully mentors junior faculty, including Jeffrey Gossett, MD and Katheryn Gambetta, and current fellow Steven Kindel, MD. Gossett has submitted grant applications with Sunjay Kaushal, MD, PhD in the area of stem cell research. David Wax, MD and Gossett successfully completed an extended application process to become a center for percutaneous valve implantation.

**CRITICAL CARE's** research is conducted in the CIRPCII, whose projects are chosen on a competitive basis, and serve as educational experiences for junior fellows or starting points in research for junior faculty.

**DERMATOLOGY's** clinical research program includes collaborative studies, prospective research, and one of the largest pharmaceutical research programs in pediatric dermatology in the U.S. The basic science program maintained by Amy Paller, MD, Walter J. Hamlin Professor and Chair of Dermatology, is evaluating oligonucleotide-conjugated gold nanoparticles as a means to suppress gene expression in skin after topical delivery. Anthony Mancini, MD and Sarah Chamlin, MD are members of the Hemangioma Investigator Group, a multi-center collaborative research group. Chamlin is a co-investigator to develop the Hemangioma Severity Scale, which has been tested with high reliability. Mancini and Chamlin will be recruiting patients for the quality-of-life portion of this study.

**EMERGENCY MEDICINE** strives to become a leader in improving the delivery of emergency care to children through the development and validation of new clinical assessment tools, analysis of injury and illness risk and unique prevention strategies, and through the creation and dissemination of novel approaches to healthcare provider education.

Members of **ENDOCRINOLOGY** engage in research related to the metabolic syndrome, type 1 diabetes, and endocrine aspects of brain tumors. Wendy Brickman, MD has demonstrated that the risk of developing glucose intolerance is increased in children with acanthosis nigricans. Jami Josefson, MD studies offspring of obese mothers, and has observed that these infants with normal glucose tolerance tend to have normal body weight but increased fat content. Brickman and Donald Zimmerman, MD, Mae and Benjamin Allen Founder's Board Professor in Endocrinology, participate in the collaborative Diabetes Trialnet, whose studies include treatment of relatives of individuals with type 1 diabetes with oral insulin to determine if such treatment reduces the risk of developing diabetes.

In 2009, the **CHILDREN'S MEMORIAL EPILEPSY CENTER** recruited Anne Berg, PhD who has been instrumental in identifying and developing research studies. A developmental-cognitive-behavioral screening protocol is in use with patients, and will be part of two research studies. The ketogenic diet experience at Children's Memorial is being analyzed, including assessments of the developmental and seizure outcomes of treated children. A charting mechanism to rapidly identify children with specific forms of and causes for epilepsy will allow comparison of practice to developing care guidelines. A study of autism spectrum disorders in children with epilepsy is ongoing. The Center is investigating the relationship between magnetic resonance imaging (MRI) detected brain abnormalities and neuropsychological function among children with febrile seizures.

**GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION** maintains an active research program. Barry Wershil, MD investigates the role of mast cells in GI inflammation and homeostasis. Estella Alonso, MD is a nationally recognized researcher of medical and psychosocial outcomes in children following liver transplantation. Valeria Cohran,

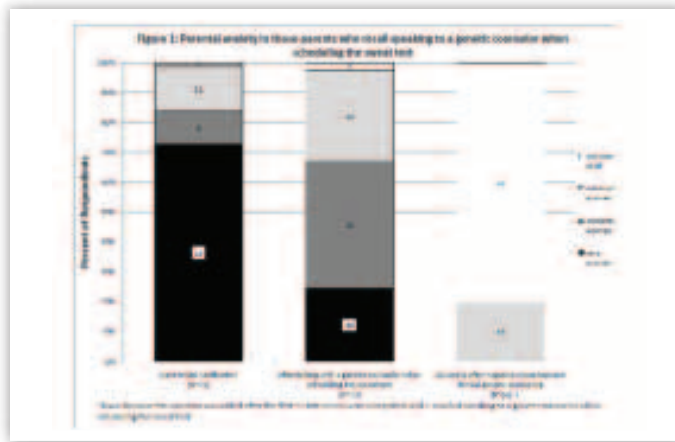


*Erin Allen, MD, Chief resident at Children's Memorial, has organized resident advocacy trips to Washington, D.C.*

MD conducts laboratory research on intestinal stem cell activation and its role in the adaptive process after resection. Udeme Ekong, MD studies immune tolerance in liver transplantation. Mark Fishbein, MD's research includes pediatric feeding disorders. Amir Kagalwalla, MD and Ameesh Shah, MD both study eosinophilic (allergic) gastrointestinal disorders. Maria Greene, MD's research interest is gut immunology and autoimmune liver disease. Peter Whittington, MD, Sally Burnett Searle Professor of Pediatrics and Transplantation, conducts translational research involving immune mechanisms in the pathogenesis of neonatal hemochromatosis and biliary atresia.

**GENERAL ACADEMIC PEDIATRICS** seeks to develop an exemplary research program regarding HIV (and other STD) infection for high risk youth based at the Howard Brown Health Center under the direction of Robert Garofalo. The division's second research goal is to develop a comprehensive qualitative social science research program regarding parent-professional decision making for children with life threatening illnesses in collaboration with investigators in Critical Care, Neonatology and Cardiology.

**GENETICS, BIRTH DEFECTS AND METABOLISM** strives to further the understanding of the natural history and



From Lang CW et al. Parental knowledge and attitudes about newborn screening for cystic fibrosis and a negative sweat test. Pediatrics 2010.

pathogenesis of rare genetic disorders, and contribute to the development of new therapies for genetic and metabolic disorders. The division is involved in numerous clinical trials of new therapeutic agents and natural history studies, and in developing registries for metabolic disorders. Specific areas of interest include neurofibromatosis, phenylketonuria, Gaucher disease, Fabry disease, Pompe disease and the mucopolysaccharidoses.

The research mission of **HEMATOLOGY, ONCOLOGY AND STEM CELL TRANSPLANTATION** is to understand the causes of cancer and non-malignant blood disorders, and to develop new approaches for treatment and cures. We follow the long-term effects of therapies and strive to improve outcomes in children. David Walterhouse, MD, George M. Eisenberg Research Scholar in Developmental Systems Biology, studies the role of the GLI gene in rhabdomyosarcoma. William Tse, MD, PhD's basic research involves the mechanisms of stem cell division. Seth Corey, Sharon B. Murphy, MD and Steven T. Rosen, MD Research Professor in Cancer Biology and Chemotherapy, focuses on the pathogenesis of marrow failure syndromes, myelodysplastic syndromes and leukemia. Morris Kletzel, MD, MBA, Meryl Suzanne Weiss Distinguished Professor in Hematology, Oncology and Stem Cell Transplant investigates minimal residual disease in leukemia and neuroblastoma. Kimberley Dilley, MD, MPH studies osteoporosis and fractures in children undergoing therapy for acute lymphoblastic leukemia. Alexis Thompson, A. Watson and Sarah Armour Endowed Chair in Childhood Cancer and Blood Diseases, is involved

in new approaches for the treatment of sickle cell anemia and thalassemia. Robert Liem, MD's work focuses on acute lung injury in patients with sickle cell anemia. Jennifer Schneiderman, MD, MS and colleagues are developing an animal model to study the effects of photopheresis in graft rejection for solid organ transplants.

**PEDIATRIC INFECTIOUS DISEASES** strives to develop research programs related to the epidemiology, prevention, pathogenesis, diagnosis and therapy of infections and post-infectious conditions that affect children and adolescents. Studies to find the cause of Kawasaki disease (KD), the leading cause of acquired heart disease in children, and to understand how herpes infections develop, are ongoing. We are also involved in practical projects to improve the treatment of HIV infection in children, infections that cause strep throat or pneumonia, and to better understand chronic fatigue syndrome and other infectious diseases. Our research goal is to answer many of the mysteries regarding infections of children that can lead to serious outcomes. Particularly exciting are promising findings that may reveal the cause of KD and generate improved diagnostic tests and treatment, and possibly prevention.

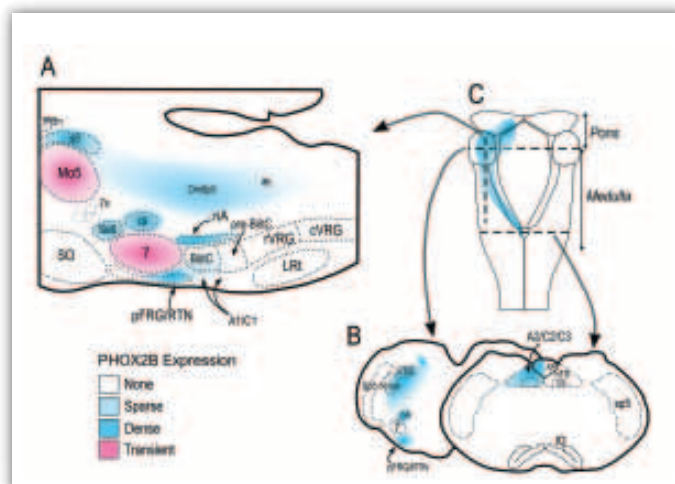
The research of **KIDNEY DISEASES** seeks to understand the pathogenesis, diagnosis, prevention and treatment of chronic kidney diseases during stages of growth and development. Studies involve the basic mechanisms of kidney fibrosis, a common pathway for loss of function in progressive chronic kidney diseases; innovative proteomic markers of disease progression in monogenic and polygenic kidney stone diseases; childhood precursors of cardiovascular and bone diseases of adulthood; relationships between the burden of cardiovascular disease in chronic kidney disease with disordered nitric oxide metabolism; the meaning of vitamin D deficiency for transplant function and related infections; obesity in childhood chronic kidney diseases; sleep dysfunction that occurs in chronic kidney disease; new uses for existing drugs in inflammatory kidney diseases; and fundamental drug studies in kidney diseases.

**NEONATOLOGY'S** research team, including physicians and full-time investigators uses a bench-to-bedside approach to understand the causes of pulmonary

hypertension and other conditions, and to develop new therapies. Some of the conditions under intense scrutiny are: necrotizing enterocolitis, for which basic research is being conducted by Isabelle De Plaen, MD; hypoxic-ischemic encephalopathy, studied by Karen Mestan, MD; and persistent pulmonary hypertension, involving research by Stephen Black, MD, Robert Dettman, PhD, Kathryn Farrow, MD, PhD and Robin Steinhorn, MD, Raymond and Hazel Speck Berry Professor of Neonatology. James Collins, Jr., MD, MPH studies reproductive outcomes disparities among minority and low income women in Illinois. Maria Luz V. Dizon, MD studies perinatal hypoxic-ischemic brain injury and its impact on white matter development. Paul Schumacker, PhD, Patrick M. Magoon Distinguished Professor of Neonatal Research, investigates oxygen metabolism, tissue responses to hypoxia, oxidative stress, and molecular mechanisms of oxygen sensing by mitochondria.

**NEUROLOGY** seeks to advance the field of child neurology through lifelong education and sound basic and translational research. Mark Wainwright, MD, PhD, Bernard L. Mirkin, PhD, MD Research Scholar, investigates biomarkers and mechanisms of brain inflammation following traumatic or ischemic brain injuries. Charu Venkatesan, MD, PhD studies signaling pathways to harness neural precursor cells for repair and regeneration. Sookyong Koh, MD, PhD conducts research on the long-term cellular and molecular consequences of early-life seizures, and inflammation and immunity in the epileptic brain. Leon Epstein, MD, Derry A. and Donald L. Shoemaker Professor of Pediatric Neurology, focuses on the role of human herpesviruses as a cause of febrile status epilepticus and subsequent temporal lobe injury and recurrent seizures. A new research initiative will study concussion in high school football players using innovative MRI-based techniques.

**PULMONARY MEDICINE** aims to increase knowledge and improve practice in the care of pediatric respiratory system disease through research. We are leaders in the development and oversight of clinical research professional staff. The division houses the Cystic Fibrosis Foundation Therapeutic Development Translational Center, one of 13 in the U.S. that have special capabilities to perform studies



From Patwari PP et al. Congenital central hypoventilation syndrome and the PHOX2B gene: a model of respiratory and autonomic dysregulation. Respiratory Physiology and Neurobiology 2010.

that could result in new therapies for CF. Clinical trials in progress include therapies that target the underlying defect and novel antimicrobial agents. Epidemiologic research of CF includes early risk factors for morbidity and mortality, and outcomes disparities in Hispanic patients. Our CF research program collaborates with Human Molecular Genetics, and we work with Allergy and Immunology in clinical trials of asthma. We also have an active clinical research program in sleep medicine.

**RHEUMATOLOGY** strives to develop better clinical tools and laboratory biomarkers of disease activity to improve outcomes and quality of life for children with rheumatologic diseases. Megan Curran, MD is collecting data on how rheumatology is taught in residency programs, and plans to design a curriculum for pediatric residents. Michael Miller, MD has placed extractable data elements within the electronic medical record and will use this data to track treatment efficacy and quality indicators of care. Marisa Klein-Gitelman's collaborative program for the study of pediatric lupus focuses on developing robust criteria for disease flare and remission, biomarkers, genetics and improved diagnostics. Lauren Pachman has an international reputation in the field of juvenile dermatomyositis. Her research efforts include factors that modify disease presentation and outcome, and potential biomarkers of disease activity.



Achieving our  
**BIGGEST**  
goals

*Life's Milestones*

We are conducting research to improve diagnostics, treatment and support for patients and their families, helping kids graduate to a bright tomorrow.

# We know that children are not small adults

## Studies to optimize dosages, improve diagnoses and enrich life experiences benefit our patients

The Departments of Anesthesiology, Medical Imaging, Pathology and Psychiatry provide support, services and knowledge that offer tremendous benefits to children and families. All of these departments also conduct research in their respective areas of experience in order to improve care, enhance diagnoses, offer safer techniques and develop more targeted therapies. Collaboration is a critical component of these research programs. For example, a pathologist will be called upon to examine research specimens with a team of cancer biologists. Investigations of the cardiac system often require imaging studies conducted and interpreted by a radiologist. Research protocols initiated by members of these departments aim to answer questions such as “What is the best way to administer anesthesia to a newborn?” or “How do we prevent and treat depression in Latino youth?” Explorations of these and many other questions will lead to better care for our babies, children and teens, and brighten their families’ hopes for achieving important milestones in the future.

### Breakthrough Research

**Santhanam Suresh** received first prize in the Scientific and Educational Exhibits for “Regional anesthesia education in infants: a novel computer-based visual learning technique to improve confidence and performance in anesthesia residents” at the American Society of Anesthesiologists annual meeting in 2009.

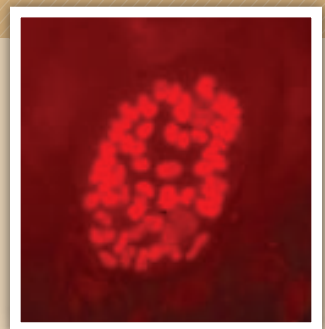
As Illinois’ first and only pediatric hospital to offer 64-slice CT technology,

the Medical Imaging Department creates high resolution images of any part of a patient’s body in a matter of seconds. These advances in imaging technology reduce the patient’s radiation dose by up to 68 percent without compromising image quality.

The treatment of Wilms tumor is one of the great success stories of pediatric oncology, with improved cure rates and decreased treatments.

Prior to cooperative research, only about 40 percent of these children were cured, as compared to 85 to 90 percent today.

**Jill Weissberg-Benchell** is serving on the Safe at School committee of the American Diabetes Association. She is helping to develop policy and legislation to create state-specific laws to protect children with diabetes in the school system.



Human embryonic stem cell CM5 expressing pluripotency marker Oct4. (Vasil Galat)

# Pathology and Laboratory Medicine

The mission of the Department of Pathology and Laboratory Medicine is to provide the highest quality, most advanced testing in anatomic pathology and laboratory medicine by providing expertise, cutting edge technology, education and training, research and development.

The department actively participates in the research effort of Children's Memorial Medical Center in the following ways:

## PROVISION OF CORE FACILITIES AND SERVICES

The **Research Clinical Laboratory Services** provided research phlebotomy, processing, storage and shipping for 114 studies this year and handled 3,861 research specimens under the direction of Shannon Haymond. During this time, 4,067 research clinical laboratory analyses were performed, reflecting a 30 percent increase over the previous year. The **Research Histology** facility, led by Samantha Gadd, PhD, processed immunohistochemical stains, hematoxylin and eosin stains, unstained sections and electron microscopic analyses for research samples. **Special Research Histology** worked up specialized antibodies for analyses and performed Affymetrix gene expression analyses. The **Tissue Bank**, directed by Veena Rajaram, functions under the direction of the Institutional Review Board and was a resource for multiple research studies this year.

## PROVISION OF CUTTING EDGE TECHNOLOGY

The department successfully brought in-house comparative genomic hybridization array technology for clinical and research practice, and supports this with Multiplex Ligation Probe Amplification Analysis (MLPA). MLPA can simultaneously detect copy number changes of multiple loci in one simple PCR reaction, making it an attractive alternative to fluorescent in situ hybridization (FISH). Tandem mass spectrometry has been expanded and is utilized for both clinical and research practice.

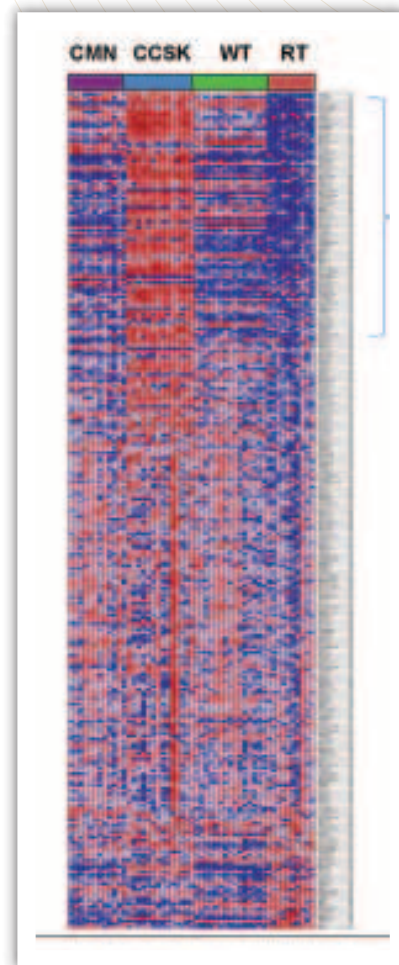
## COLLABORATIVE RESEARCH

A large part of the department's mission is to contribute the specialized expertise of those in clinical and anatomic pathology to research across the institution. Particular funded efforts include the following: Rajaram plays a large role in the investigation of brain tumors through the Falk Brain Tumor Center, and Larry Jennings is a key collaborator in the studies of the Center for Autonomic Medicine in Pediatrics. Maurice O'Gorman has long-standing collaborations in support of HIV investigations with Steven Wolinsky, MD

in the Division of Infectious Diseases at the Feinberg School. Hector Melin-Aldana is a critical contributor to the considerable efforts devoted to liver disease at Children's Memorial.

## INDEPENDENT RESEARCH

Studies in the laboratory of Elizabeth Perlman are aimed at defining biological markers that shed light on the pathogenesis and/or aid in the therapeutic stratification of pediatric renal tumors and pediatric sarcomas in collaboration with the Children's Oncology Group (COG). Vasil Galat focuses on the differentiation lineages and utilization of stem cells in the study of human disease.



*Gene expression analysis of the most common malignant renal tumors of childhood. (Elizabeth Perlman)*

## FEATURED RESEARCH

Rhabdoid tumors (RT) are highly malignant and lethal tumors for which no effective treatment is available. These tumors are characterized by genetic loss of SMARCB1, a component of a complex that facilitates gene expression by helping transcription factors gain access to their targets. A study by the Perlman laboratory sought to shed light on the SMARCB1-mediated pathogenesis of RT and to discover potential therapeutic targets. Analysis of gene expression showed differential expression of a number of genes known to cause tumor suppression or tumor progression. The authors concluded that RTs arise within early progenitor cells during a critical developmental window in which loss of SMARCB1 directly results in repression of neural development, dysregulation and differential expression of a number of prominent genes that are known to promote malignant behavior.

Vasil Galat and colleagues investigated the developmental potential of rat extraembryonic stem cells. Extraembryonic tissues have various roles in protecting, nourishing and patterning embryos. Extraembryonic endoderm precursor (XEN-P) cells display a unique molecular signature sharing some of the characteristics of embryonic stem cells, trophoblast stem cells and extraembryonic endoderm stem cells. “The inner cell mass of the very early embryo is the source of embryonic stem cells. We now know this is a heterogeneous population of three types of cells with different potentials. Our work establishes the last of these cell types in tissue culture, allowing experiments that will help us understand how stem cells differentiate,” says Galat. XEN-P cells provide a tool for comparative studies that can be used to improve understanding of basic stem cell biology, including properties that make cells therapeutically relevant.

The ability to reliably distinguish between positive and negative populations of cells is an essential aspect of clinical flow cytometry. Accurate measurement of antigen-positive cells can be hampered by background fluorescence of antigen-negative cells and other particles. O’Gorman and colleagues from Boston, Seattle, Toronto and the Netherlands performed a critical review of considerations for the

## Faculty

**Elizabeth Perlman, MD** *Pathologist-in-chief; Arthur C. King Professor of Pathology and Laboratory Medicine*

Molecular classification of pediatric renal tumors. Diagnostic signatures of pediatric sarcomas. Central pathology review of pediatric renal tumors.

**Pauline Chou, MD** *Division head, Anatomic Pathology*

Pediatric tumors. Neuroblastoma drug resistance.

**Shannon Haymond, PhD** *Director, Clinical Chemistry*

Evaluation of new clinical chemistry biomarkers for the diagnosis and prognosis of pediatric disease states. Development of mass spectrometry assays.

**Lawrence Jennings, MD, PhD** *Director, HLA and Molecular Diagnostics*

Translational research and molecular assay development for patient diagnosis, prognosis, and monitoring.

**Maurice O’Gorman, PhD** *Director, Diagnostic Immunology*

Clinical and applied research in immune deficiency and autoimmunity. Diagnostic test design. Immune pathogenesis in autoimmune disease.

**Veena Rajaram, MD** *Neuropathologist*

Molecular aspects and pathogenesis of brain tumors.

**Xiaotian Zheng, MD, PhD** *Director, Microbiology*

Antimicrobial resistance testing, molecular diagnostics for infectious agents.

**Katrin Leuer, PhD** *Director, Cytogenetics*

Recurring abnormalities in leukemia/lymphoma, novel chromosome abnormalities resulting in congenital malformations. COG cytogenetics review.

**Maria Proytcheva, MD** *Director, Hematology and Hematopathology*

Diagnostic pediatric hematopathology. Stem cell polarity and childhood lymphoblastic leukemia. Expression of GLI1 in Burkitt lymphoma.

**Hector Melin-Aldana, MD** *Pediatric Anatomic Pathologist*

Pathology and pathogenesis of pediatric liver disease.

**Vasil Galat, PhD**

Study of genetic regulation of stem cell lineages, directed differentiation, and utilization for therapy.

control of background fluorescence in clinical flow cytometry. The authors presented a set of recommendations that will enable users to develop an optimized cell labeling protocol that minimizes background and maximizes the ability to reliably distinguish between a positive and a negative population of cells. These recommendations are also intended to augment existing guidelines designed to aid in the formulation of a consensus regarding the utility of flow cytometry for the analysis of clinical samples.

# Child and Adolescent Psychiatry

The mission of the Department of Child and Adolescent Psychiatry includes providing state-of-the-art family-centered clinical services and national leadership in the education of pediatric mental health care professionals and advancing knowledge through research. Our research is focused primarily on mental health problems seen by primary care pediatricians and by subspecialists in the tertiary care pediatric setting.

## GRANTS

Mina Dulcan is co-investigator with members of the Department of Psychiatry and Behavioral Sciences, Preventive Medicine and Infectious Diseases at the Feinberg School on a grant from the NIH and other federal agencies. The study will examine how incarceration, release and re-entry into the justice system affects drug use behaviors, HIV/AIDS sex risk behaviors and injection risk behaviors, and the relationship between patterns of drug use and disorder and HIV/AIDS risk behaviors. The grant is a new focus for the Northwestern Juvenile Project, the largest longitudinal epidemiological study of mental health needs and outcomes of delinquent youth.

Colleen Cicchetti designed and implemented a model program for the delivery of mental health services in two underserved Chicago public schools, and is evaluating the effectiveness of universal, targeted and clinical services delivered in both a school-based and community-linkage model. She has also received funding from Chicago Public Schools to provide consultation to various offices, including the Illinois State Board of Education.

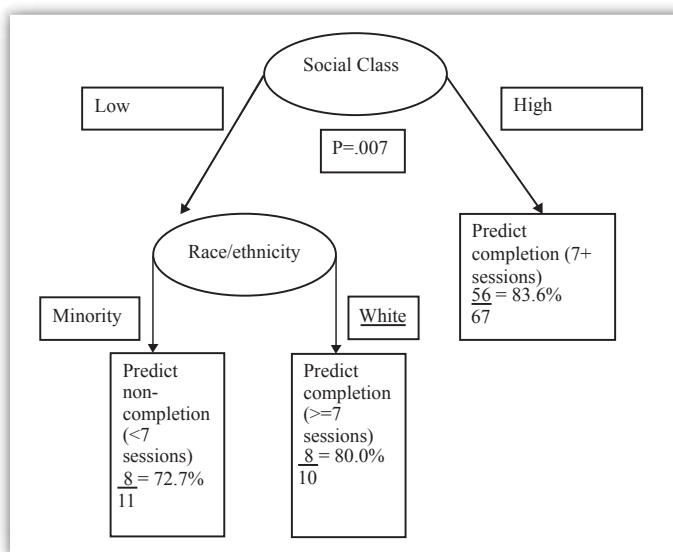
Rebecca Ford-Paz is the 2010 recipient of the Alliance for Research in Chicagoland Communities (ARCC) faculty development mini-grant. She will use the funds to support the conduct of the ARCC Partnership-Building grant she received with Healthcare Alternative Systems. This project aims to reduce mental health disparities for Latino youth and families by targeting prevention of adolescent

depression. She is also principal investigator of a study intended to develop culturally appropriate, evidence-based treatment of depression in Latino adolescents (Van Buren Research Fund Grant, Department of Child and Adolescent Psychiatry).

John Lavigne is leading a project funded by the Grant Healthcare Foundation endowment to Children’s Memorial that is studying the evaluation and prediction of outcome in outpatient pediatric mental health treatment. This project has resulted in a published outcome measure.

Kelly Lowry is a KL2 scholar through the NUCATS Clinical and Translational Sciences Award. Her study is entitled “Exploring effects of parent feeding styles on child eating and weight in early childhood”.

Sigita Plioplys is co-investigator for a study entitled “Multiple pathway models of attention deficit hyperactivity disorder (ADHD)”. The principal investigator is James Booth of the School of Communication at Northwestern University. Plioplys is also the recipient of the American Epilepsy Foundation Targeted Research on Youth grant for



From Lavigne JV et al. Predictors and correlates of completing behavioral parent training for the treatment of oppositional defiant disorder in pediatric primary care. Behavior Therapy 2010. Copyright 2010 by the Association for Behavioral and Cognitive Therapies. Reprinted by permission of the publisher.

the study “Risk factors for pediatric psychogenic nonepileptic seizures”.

Lisa Sorensen is co-investigator on several NIH-funded studies of pediatric liver transplantation and pediatric acute liver failure, functional outcomes in adolescents following liver transplantation, and immunosuppression withdrawal for pediatric living donor transplant recipients.

Deli Wang has been involved in 23 grant proposals as primary statistician this year. The Medical Research Junior Board Foundation, a component of the Medical Research Institute Council (MRIC) selected the BRC to fund this year.

## FEATURED RESEARCH

For the last 20 years, John Lavigne and colleagues have been engaged in a line of research that involves studying ways to improve the psychological care provided by pediatricians in their offices. Many children with emotional and

*“Many children with emotional and behavioral problems never reach mental health professionals for service, and pediatricians are the first-line providers of medication management for ADHD.”*

behavioral problems never reach mental health professionals for service, and pediatricians are the first-line providers of medication management of ADHD. Studies have shown, however, that many children with ADHD are not treated optimally. The group has recently completed data collection on a study in which pediatricians were trained to improve their care of children treated by medication for ADHD. They are comparing the children treated by the doctors who provided special care with those who received usual care to see if the children in the special care group show better behavior at school and home.

## Faculty

**Mina Dulcan, MD** is the *Margaret C. Osterman Professor of Child Psychiatry*, Chief of Child and Adolescent Psychiatry at the Feinberg School, head of the Department of Child and Adolescent Psychiatry at Children’s Memorial, and Chief of Adolescent Psychiatry at Northwestern Memorial Hospital. She is a member of the Accreditation Council for Graduate Medical Education (ACGME) Residency Review Committee for Psychiatry. Dulcan has expertise in ADHD and child psychiatric epidemiology. She is the author of *Dulcan’s Textbook of Child and Adolescent Psychiatry*, published in 2010.

**Colleen Cicchetti, PhD** is director of Advocacy and Community Linked Mental Health Services Program at Children’s Memorial, which develops, implements and evaluates sustainable models for delivery of mental health services through community partnerships with schools and other community settings.

**Rebecca Ford-Paz, PhD** studies the cultural adaptation of evidence-based mental health treatment to improve treatment retention and outcomes for Latino youth.

**John Lavigne, PhD** has long-standing interests in ways to improve the delivery of mental health services in primary care pediatrics, the behavior problems of preschoolers, and outcomes of child psychotherapy. He is on the leadership team of the Pediatric Practice Research Group (PPRG) of the research center.

**Kelly Lowry, PhD** is involved with the Consortium to Lower Obesity in Chicago Children (CLOCC), PPRG and NUCATS. She studies parent-child interactions in mealtime behaviors and school-based opportunities for healthy eating and exercise.

**Sigita Plioplys, MD** has expertise in the psychiatric aspects of children with neurological disorders, and psychosocial difficulties in children with epilepsy or nonepileptic seizures.

**Tali Raviv, PhD** works with the Community Linked Mental Health Services Program. Her responsibilities include staff training and consultation, curriculum development and implementation, parent education and outreach.

**Lisa Sorensen, PhD** conducts research with Estella Alonso of the Division of Gastroenterology,

Hepatology and Nutrition on outcomes of children following solid organ transplant, with a focus on their cognitive development and school performance.

**Deli Wang, MD, PhD** directs the Biostatistics Research Core (BRC) of the research center, whose primary objective is to serve as the resource from which Children’s Memorial investigators may draw statistical knowledge for study planning, management and analysis. Wang has expertise in a wide range of data analysis methodologies and conducts statistical methodology research.

**Jill Weissberg-Benchell, PhD** studies children with diabetes, including patient and family adaptation to chronic illness and improving adherence to medical regimens. She also evaluates patients and families prior to solid organ transplants.

**Frank Zelko, PhD** is participating in multi-site studies of the cognitive sequelae of sickle cell disease, pediatric lupus, childhood absence epilepsy, chronic kidney disease, liver transplantation, pediatric cancer, and phenylketonuria. His primary focus is on attention and executive skills deficits in pediatric epilepsy.

# Medical Imaging

The Department of Medical Imaging is committed to providing tailored service to each patient, minimizing radiation doses and using cutting-edge technology in order to eliminate delays. The department promotes and supports institution-wide research efforts by scientists in many disciplines. It does this by supplying the state-of-the-art imaging and interpretation required for research studies. The Medical Imaging Research Committee reviews and catalogs all research proposals involving imaging, including those projects internal to the department as well as those by investigators in other departments. There are currently 180 active research studies that involve imaging, 25 of these originating from Medical Imaging. Our faculty present many papers, posters, and lectures at a variety of scientific meetings.

In 2009, Children's Memorial, which leads the country in best practices when it comes to medical imaging in children, joined a nationwide initiative of the Alliance for Radiation Safety in Pediatric Imaging called Image Gently. The campaign, a coalition of health care organizations dedicated to providing safe, high quality pediatric imaging worldwide, was created to increase awareness in the medical imaging community on how children should receive lower doses of radiation than adults. The Society for Pediatric Radiology, which counts among its members medical staff from Children's Memorial, is a participant in this coalition, which also includes 33 other societies.



Image of a normal coronary artery tree. (Cynthia Rigsby)

“Children are much more sensitive to radiation and are not just smaller adults. Their bodies are different and require a different approach to imaging,” said James Donaldson. “Children come to our department, and their outside facility CT scans show that they were given high doses of radiation when they needed half that amount. It is our job to educate the medical community that in this case, less is better. The Image Gently campaign is a way for us to work with different physician groups and let them know that we use ‘child size’ techniques to reduce unnecessary exposure to radiation.”

## Faculty

**James Donaldson, MD**, *Earl J. Frederick Professor of Radiology*, is department chairman whose primary interest is in interventional radiology.

**Cynthia Rigsby, MD** conducts research involving pediatric body imaging, especially CT and MRI, with a specialty interest in cardiovascular imaging.

**Eugene Anandappa, MD** Nuclear medicine imaging.

**Tamar Ben-Ami, MD** Chest and abdominal imaging.

**Ellen Benya, MD** Abdominal imaging and education.

**Corey Bregman, MD** Head trauma imaging.

**Delilah Burrowes, MD** Cochlear implant imaging, tumor imaging, epilepsy imaging.

**Jie Deng, PhD** MRI research with a focus on optimizing pediatric MR imaging techniques.

**Stanley Kim, MD** Interventional radiology procedures.

**Robert MacDougall, MS** CT imaging.

**Brian Mitchell, MD** Abdominal imaging.

**Jackson Norman, III, MD** Chest and musculoskeletal imaging.

**Francis Prendergast, MD** Interstitial lung disease chest imaging.

**Maura Ryan, MD** Stroke and brain trauma imaging.

**Martha Saker, MD** Foreign body imaging.

**Ali Shaibani, MD** Vascular brain imaging and interventional procedures.

**Richard Shore, MD** nuclear medicine imaging.

**Jessica Stern, MD** Stroke imaging.

**Mary Wyers, MD** Abdominal imaging and education.

## Anesthesiology

The department is a national leader of research into drugs, equipment and techniques to increase the safety of administering anesthesia to children. Medical staff members serve on national and international committees, contribute to and edit anesthesiology textbooks.

### RESEARCH HONORS

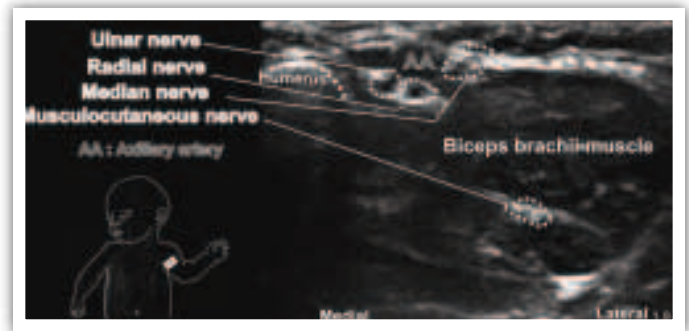
Santhanam Suresh received first prize in the Scientific and Educational Exhibits for “Regional anesthesia education in infants: a novel computer-based visual learning technique to improve confidence and performance in anesthesia residents” at the American Society of Anesthesiologists annual meeting in New Orleans, October 2009.

### GRANTS

Suresh is a co-investigator with the University of Colorado on a NIH grant to develop a small volume sampling technique for fentanyl pharmacokinetic, pharmacodynamic and pharmacogenetic analysis in preterm and term neonates. With Children’s Hospital Boston, he is involved in a federal grant to assess long-term neurodevelopmental outcomes in pediatric patients administered regional and general anesthesia as neonates and infants.

### RESEARCH HIGHLIGHT

Suresh and colleagues longitudinally evaluated the epidemiological characteristics of headaches in a school-based, community setting to determine the impact of headache symptoms on the health of children. A prospective cohort study was conducted at two Chicago public schools for a period of six months. Members of the research team surveyed both schools weekly for headache and other pain symptoms. The students rated each pain symptom on a five-point scale. Demographic information was collected at the time of enrollment, and all participants were asked to complete age-appropriate and validated pediatric surveys to assess the severity of concurrent somatic complaints, anxiety symptoms, functional limitations and quality of life



From Tsui B, Suresh S. *Ultrasound imaging for regional anesthesia in infants, children, and adolescents: a review of current literature and its application in the practice of extremity and trunk blocks.* Anesthesiology 2010.

issues. Of the participating children, 89.5 percent reported at least one headache during the study period. Females experienced more frequent headaches compared with males. The researchers concluded that school-aged children commonly experience headaches, and those who do are more likely to report other somatic symptoms, feelings of anxiety, functional limitations and quality of life impairments.

### Faculty

**Steven Hall, MD**, *Arthur C. King Professor of Anesthesiology*, studies anesthesia exposure and neurodevelopment in infants and children.

**Patrick Birmingham, MD** studies anesthesia in neonates and infants.

**Richard Dsida, MD** investigates regional anesthesia.

**Narasimhan Jagannathan, MD and Kenneth Langen, MD** study difficult airway management.

**Dawn Belvis, MD, Aisha Siddiqui, DO, Carmen Simion, MD, Lisa Sohn, MD and Jeffrey Steinfeldt, MD** investigate various aspects of pain management.

**Santhanam Suresh, MD** is the director of research for Anesthesiology and liaison for research to Children’s Memorial Research Center. He studies regional anesthesia and pain management in children.

**Tetsu Uejima, MD** conducts clinical research involving all aspects of pediatric anesthesia care. His foci are on safety, organ transplantation and the use of ultrasound in the operating room.

**Polina Voronov, MD**’s clinical research involves pain mechanisms and regional anesthesia.



Practicing for  
**THE BIG**  
recital

*Life's Milestones*

Our Surgery Department is conducting research that prevents devastating diseases before they happen. By constantly testing and exploring, we're ready for the big breakthrough moments.

# Children who are undergoing surgery need the best care possible

**We conduct research focused on significantly improving procedures and outcomes, or making surgery unnecessary**

The Department of Surgery aims to develop substantive research programs to achieve our goal of becoming a national leader in academic, clinical and research activity. We pursue a wide-range of research initiatives throughout our ten surgical divisions aimed at advancing pediatric surgical care. We place special emphasis on multidisciplinary and collaborative research efforts to reflect, foster and enhance our multidisciplinary and collaborative approach to clinical care.

The department's active research programs reflect our core belief that productive research enriches our clinical practices in addition to enhancing our position as a national leader in pediatric surgery. A focused approach to identifying and pursuing funding opportunities has strengthened our ability to attract top-tier faculty and trainees. We are also committed to exploring opportunities for interdisciplinary collaborations and to faculty recruitment efforts that support academic as well as clinical productivity, such as our surgeon-scientist program and recent academic grant initiatives.

## Breakthrough Research

Led by **Carl Backer, MD, A.C. Buehler Professor of Surgery**, several of the Cardiovascular-Thoracic Surgery division's recent protocols have been tested in the laboratory and applied in the operating room.

Members of the Neurosurgery division pursue research that will translate to a better understanding of pediatric brain tumors. Division head **Tadanori Tomita, MD** has made a substantial commitment to nanotechnology.

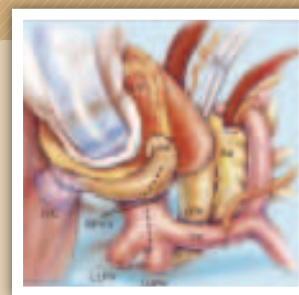
In the Orthopaedic Surgery division, the Knee Injury Prevention Program (KIPP®) established by **Cynthia LaBella, MD** is a preseason, neuromuscular training program designed for female teenage athletes who are at a much higher risk for anterior cruciate ligament (ACL) injuries compared to boys in similar sports.

**Nancy Young, MD** in the Otolaryngology Division plans to work with the

research center on the genetics of hearing loss.

The Urology Division's **Earl Cheng, MD** has an active research program with a focus on urinary bladder regeneration using tissue engineering techniques.

The kidney transplant program is developing a transplant immunobiology research effort that would allow doses of immunosuppressive medications tailored to each child.



*From Kelle AM et al. Total anomalous pulmonary venous connection: Results of surgical repair of 100 patients at a single institution. Journal of Thoracic and Cardiovascular Surgery 2010.*

Cardiovascular-Thoracic Surgery is the most productive surgical division in terms of external funding and academic activities. As the division's designated surgeon scientist, Sunjay Kaushal, MD, PhD is pursuing exciting transplantation-related research which is directed towards the understanding of mechanisms in chronic rejection, establishment of tolerance and xenotransplantation. Research to create better approaches to the surgical management of patients with congenital cardiac birth defects is under way.

Members of the Neurosurgery division are committed to research that will translate to a better understanding of pediatric brain tumors. Division head Tadanori Tomita, Yeager Professor in Pediatric Neurosurgery, serves on numerous national and international committees. He is a full member of the internationally recognized Pediatric Oncology Group's Brain Tumor Core Committee. Shekhar Mayanil, PhD is the lead investigator for spina bifida research including neural tube and neurobiology research. Hydrocephalus studies are ongoing. Arthur DiPatri, Jr., MD is researching neurorestoration following brain injury.

Ophthalmology division head Marilyn Mets, MD is conducting a population study of the Hutterites in South Dakota to determine if there are specific genetic markers associated with strabismus, exotropia, and esotropia. The Hutterites are a genetically homogenous group of European origin. Janice Lasky-Zeid, MD is researching strabismus and NF-1 associated pathway glioma.

## Research Honors

**Carl Backer** was appointed to the Accreditation Council for Graduate Medical Education (ACGME) Review Committee for Thoracic Surgery.

**Joseph Janicki, MD** was the recipient of the 2010 Angela S.M. Kuo Memorial Award presented at the annual meeting of the Pediatric Orthopaedic Society of North America (POSNA). The award recognizes an outstanding young investigator who is a member of POSNA and provides funding to help promote a long-term research career for that individual.

**Cynthia LaBella** won the "Best Overall Research" award at the American Medical Society for Sports Medicine 2009 annual conference. She presented her research results showing that KIPP® warm-up reduced ACL injuries by 80 percent among female soccer and basketball athletes in Chicago public schools.

Led by division head John Sarwark, MD, Martha Washington Foundation for Handicapped Children Professor in Pediatric Orthopedics, Orthopaedic Surgery is actively involved in numerous research initiatives. Joseph Janicki, the designated surgeon-scientist, has a multi-year grant for bone-mass studies related to fractures in children and adolescents. He also mentors the Feinberg School's resident research program. Erik King, MD is researching a normative database for upper extremity motion. The division plans closer collaboration with their colleagues in the nanosciences/cartilage regeneration program at the Feinberg School, and with the Developmental Biology Program at the research center for spine development and embryology studies. The division is also pursuing an Adolescent Idiopathic Scoliosis Etiology project that will study DNA arrays using research center technology.

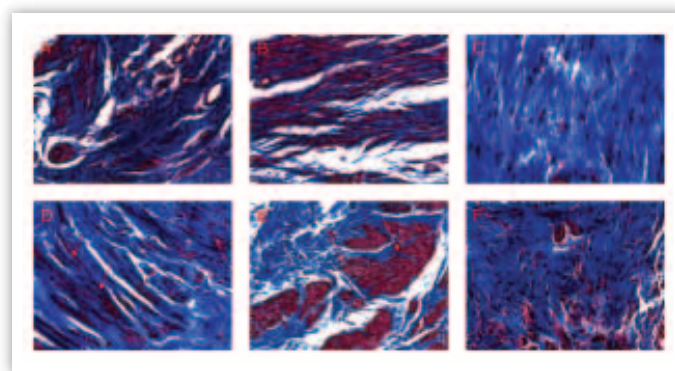
The Otolaryngology division, led by Lauren Holinger, MD, Paul H. Holinger, MD Professor in Pediatric Otolaryngology, is growing its research initiatives. Nancy Young, The Lillian S. Wells Chair in Pediatric Otolaryngology, studies cerebral anatomic factors as predictors of cochlear implant outcomes. She anticipates a study with the current PhD investigator at the Feinberg School who is developing a new type of cochlear implant system using laser technology. James Schroeder, Jr., MD is coordinating the development of an administrative structure for a more robust clinical research program, which includes the recent addition of a research coordinator. Their work has resulted in a proposal to investigate the use of salivary amylase levels in pediatric tracheobronchial secretions.

Under the leadership of division head and Surgeon-in-Chief Marleta Reynolds, MD, Lydia J. Fredrickson Professor in Pediatric Surgery, Pediatric Surgery is home to long-standing research projects as well as more recent clinical initiatives. Mary Beth Madonna, MD, the division's surgeon-scientist, researches the behavior of neuroblastoma, focusing on two main areas. The first is drug resistance, in particular specific proteins that may be important in transferring resistance to chemo-sensitive cells; epigenetic changes that are present in resistant neuroblastoma cells; and, in conjunction with the chemistry department of Northwestern

University, research to find better drug delivery systems and to produce a nanoparticle containing doxorubicin. The second is the importance of nerve growth factor (NGF) and its two receptors in the survival or death of neuroblastoma cells.

In the clinical realm, Katherine Barsness, MD has prospective studies evaluating the efficacy of antibiotics after surgical drainage of a skin and soft tissue infection, and of foam dressings to reduce the incidence of granulation tissue after gastrostomy tube placement. Marybeth Browne, MD, David Rothstein, MD and Erin Rowell, MD all have ongoing clinical studies, including a retrospective review of lung biopsies performed at Children's Memorial to determine indications, outcomes, and whether biopsies changed management; a retrospective review of gastrostomy tubes placed at Children's Memorial to determine whether pre-operative upper GI series x-rays are necessary; a pilot study to provide neuropsychiatric testing after minimal head trauma to help determine return-to-sports policies for pediatric patients; and descriptive analysis of pediatric surgical patients within the Indian Health Service, with comparison to national benchmarks for disease incidence and treatment outcomes. Anthony Chin, MD has led several research studies, including "Acute pancreatitis in children and adolescents: spectrum of disease and predictors of severity", and "CT features of acute pancreatitis in children: utility of the Balthazar CT Severity Index in predicting outcome".

Led by William Kaplan, MD, the Urology division is active in both clinical and pedagogical research initiatives. Max Maizels, MD was granted funding for a sabbatical to further develop his Computer-Enhanced Visual Learning (CEVL) system. A computer-based approach to surgical and medical education, CEVL has shown great promise in advancing the training of residents as well as hospital staff. Collaborations with numerous services at both Children's Memorial and the Feinberg School have led to diverse applications of the technology. Arun Sharma, PhD and Earl Cheng sought to evaluate the potential uses of autologous sources of bone marrow mesenchymal stem cells and endothelial progenitor cells as alternatives to cells currently used for bladder tissue regeneration. Preliminary data suggest that these



*Masson's Trichrome staining of 4 week poly(1,8-octanediol-co-citrate) elastomeric thin film augmented tissues. (Arun Sharma)*

stem cells provide a robust source of cells that may be substituted for the smooth muscle cell component in the bladder. Also, endothelial progenitor cells showed the potential to provide vascularization for developing tissue.

In Transplant Surgery, Children's Memorial is one of 15 centers in North America participating in the Pediatric Intestinal Failure Consortium (PIFCON). This study aims to retrospectively and prospectively study the pediatric intestinal failure population, including medical, surgical, nutritional and therapeutic management. Another aim of this collaborative effort is to create a multi-center registry of patients with intestinal failure. Riccardo Superina, MD, division head, co-director of the Siragusa Transplantation Center, and Robert E. Schneider Chair in Transplantation, is site-principal investigator for this study.

Kidney transplant research includes Children's Memorial as a major contributor to the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS), a cohort of 130 centers from the U.S., Canada and Mexico that maintains the largest transplant database for children. NAPRTCS is completing its first trial of transplant induction medications, and is starting a second study involving a medication to help prevent chronic rejection.

The physician-researchers on our staff in liver transplant research have pioneered influential new methods of studying pediatric liver disease and transplantation. Our commitment to clinical and laboratory research allows the Siragusa Transplantation Center to lead the way in improving the health of children with liver disease.

# Centers of Excellence

The Centers of Excellence focus on specific child health issues, and represent areas that either lie outside of programmatic scope or cross program boundaries. Members may choose to affiliate with one or more program, or with a center.

## **CENTER FOR INTERDISCIPLINARY RESEARCH IN PEDIATRIC CRITICAL ILLNESS AND INJURY (CIRPCII)**

Director: Mark Wainwright, MD, PhD

CIRPCII's mission is to advance our understanding of the fundamental mechanisms of diseases producing critical illness, and to apply this knowledge to the advancement of care and improvement of outcomes for critically ill children, through a combination of research and education. The XenoBase-Critical Care Project at Children's Memorial is designed to apply the tools of bioinformatics to pediatric critical care medicine. Originally designed for the management and analysis of genetic and clinical data, XenoBase is currently being used to apply these analysis methods to clinical and physiological data generated from patients admitted to the Pediatric Intensive Care Unit (PICU). This is a

novel approach to data mining in critical care, and has the potential to permit studies of fundamental questions related to the cost of critical care, outcomes, physiologic management, biochemical predictors of outcomes and epidemiologic factors.

The dataset encompasses all PICU admissions from 1994 to 2008, and contains data from multiple sources in addition to geocoded census tract data. This is a unique set of data that incorporates information ranging from detailed physiologic values to ICD-9 procedure codes, laboratory studies and indicators of socioeconomic status. Investigators have the opportunity to apply the methods of genetic analysis such as cluster analysis and multidimensional scaling to test or generate hypotheses in a dataset including over 14,000 de-identified subjects.

*“CIRPCII's mission is to advance our understanding of the fundamental mechanisms of diseases producing critical illness, and to apply this knowledge to the advancement of care and improvement of outcomes for critically ill children.”*

## **CENTER FOR NEUROBLASTOMA RESEARCH**

Director: Morris Kletzel, MD, MBA



Morris Kletzel

The Center for Neuroblastoma Research brings all Children's Memorial related investigators with common interests in neuroblastoma into an interdisciplinary center that can guide the research and lead to national extramural funding. Its special foci are the areas of drug resistance, neuroblastoma, stem cells, epigenomics alterations, altered microRNA expression, phase I clinical trials, and surgical and radiation therapeutic approaches.

## **CENTER ON OBESITY MANAGEMENT AND PREVENTION (COMP) / CONSORTIUM TO LOWER OBESITY IN CHICAGO CHILDREN (CLOCC)**

Director: Katherine Kaufer Christoffel, MD, MPH

Executive Director of CLOCC: Adam Becker, PhD, MPH

Please see page 38.

**CHILD HEALTH DATA LAB (CHDL) / CENTER FOR COMMUNITY PARTNERSHIPS AND HEALTH PROMOTION (CCPHP)**

Co-Directors: Jenifer Cartland, PhD, Maryann Mason, PhD, and Karen Sheehan, MD, MPH

Please see page 38.

**CHICAGO CITY-WIDE FOCIS (FEDERATION OF CLINICAL IMMUNOLOGY SOCIETIES) CENTER OF EXCELLENCE IN CLINICAL IMMUNOLOGY (FCE)**

Director: Lauren Pachman, MD

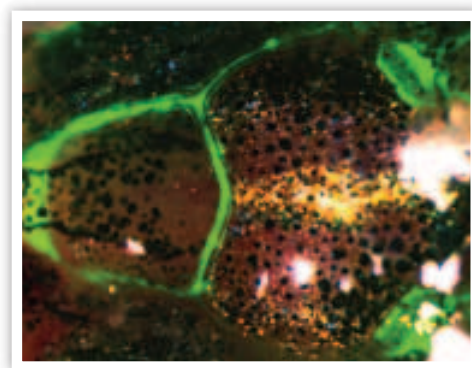
FOCIS Center of Excellence in Clinical Immunology is committed to providing a venue for communication and education in the field of clinical and basic immunology and fostering interdisciplinary collaboration. In 2010, FOCIS held several events, including a workshop entitled “Response to infectious agents”, featuring J.J. Oppenheim from NIH and Anne Rowley from Children’s Memorial. The center organizes city-wide workshops and hosts a journal review club. It encourages research by trainees from immunology programs by holding an annual competition and sponsoring the winners to attend the annual international FOCIS meeting.

**FALK BRAIN TUMOR CENTER**

Co-Directors: Tadanori Tomita, MD and Marcelo Bento Soares, PhD

The Falk Brain Tumor Research Center seeks to make discoveries that lead to improved diagnosis, prognosis and treatment of pediatric brain tumors. The center’s research program focuses on multiple translational studies of ependymomas and brain stem gliomas in a highly collaborative environment led by Tomita, Soares and Stewart Goldman, MD, Gus Foundation Chair in Neuro-oncology.

*Expression of green fluorescent protein reporter in the zebrafish sutures of an adult animal. (Rodney Dale)*



**MOLECULAR EPIDEMIOLOGY AND BIOINFORMATICS (MEpi)**

Faculty members: Xiaobin Wang, MD, MPH, ScD, Mary Ann and J. Milburn Smith Research Professor; Ruchi Gupta, MD, MPH; Binyan Wang, MD, PhD; Xin Liu, MD, PhD; Xiumei Hong, MD, PhD; and Lester Arguelles, PhD

Please see page 39.

**PEDIATRIC PRACTICE RESEARCH GROUP (PPRG)**

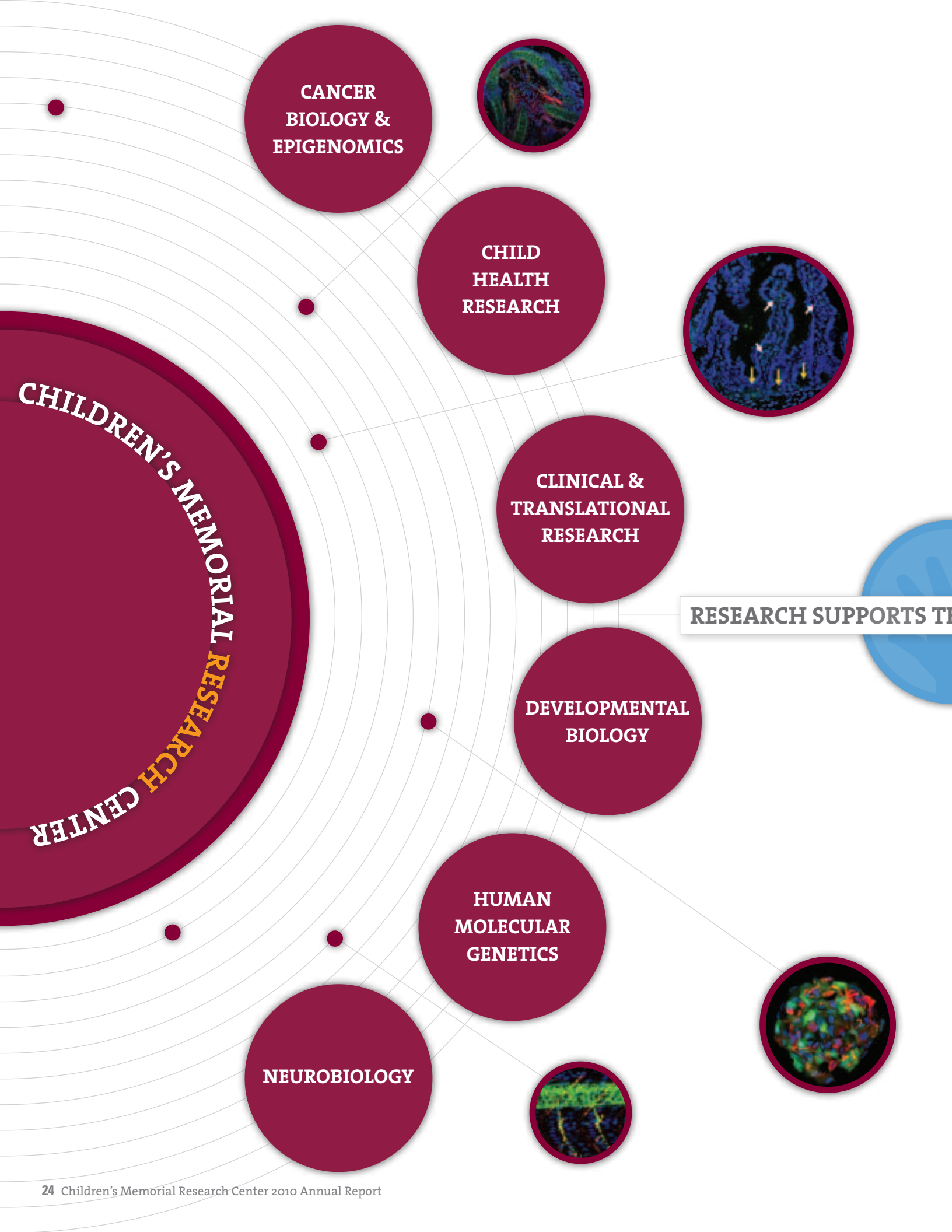
Director: Helen Binns, MD, MPH  
Associate Director: Adolfo Ariza, MD

Please see page 39.

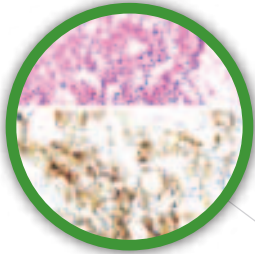
**RETINOBLASTOMA CENTER OF EXCELLENCE**

Faculty members: Nikia Laurie, PhD; Marcelo Bento Soares, PhD; Marilyn Mets, MD; Joanna Weinstein, MD; and Paul Bryar, MD

The Retinoblastoma Center of Excellence, formed in 2010, is a translational collaboration between scientists and physicians at the research center, Children’s Memorial Hospital, and the Feinberg School. Currently, we are working together to elucidate the role of microRNAs in retinoblastoma progression for the identification of new therapeutic targets.



THE CLINICAL MISSION



PEDIATRICS

PATHOLOGY &  
LABORATORY  
MEDICINE

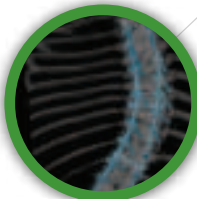
CHILD &  
ADOLESCENT  
PSYCHIATRY

SURGERY

ANESTHESIOLOGY

MEDICAL  
IMAGING

CHILDREN'S MEMORIAL MEDICAL CENTER





## Navigating the **TERRITORY**

*Life's Milestones*

Children's Memorial Research Center scientists start from basic bench research to uncover the mysteries, develop therapies and find cures for pediatric conditions.

We're designing the roadmaps that will lead to healthier lives for children.

# Discovering underlying mechanisms of disease will help future generations

## The best biomedical minds combined with advanced technology can result in life-changing breakthroughs

As a leader in pediatric research, Children's Memorial Research Center is dedicated to preventing childhood illness, treating pediatric conditions for which cures are not available and promoting healthier lifestyles. As the research arm of Children's Memorial Hospital, the research center is responsible for prioritizing, promoting and managing the research efforts of the medical center. It is also one of the interdisciplinary research centers and institutes of the Feinberg School.

Over 140 investigators, 500 staff and numerous trainees contribute to the six programs in basic research and translational medicine and ten centers of excellence. A primary goal of the research center is to facilitate the ability of its membership to perform research leading to the most advanced pediatric health care.

In the past year, the research center has embraced the opportunity and challenge of the hospital's move to its new location in 2012. This has involved a rigorous strategic planning process in which research priorities have been developed by leaders, including program directors, department chairs and division heads. This process is concurrent with the remarkable research efforts our members are generating.

### Breakthrough Research

**Marcelo Bento Soares, Vasil Galat and John Crispino** are analyzing gene expression profiles to determine what contributes to the predisposition to leukemia in infants and children with Down syndrome.

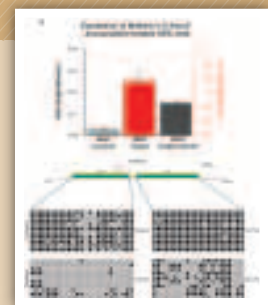
**Ram Yogev** has been appointed to the NUCATS Leadership Committee to represent the Children's Memorial research community. The committee is working to synchronize priorities and strategies.

A study by **Rajesh Kumar** and colleagues has found that genetic ancestry significantly affects performance on tests used to diagnose conditions like asthma.

A team led by **Arun Sharma and Earl Cheng** has developed human stem cells seeded onto special thin films for partial bladder regeneration. The augmented bladders show tremendous promise.

The laboratory of **Ann Harris** has found that CFTR, the underlying cystic fibrosis gene, adopts a specific conformation in cells that are affected by the disease.

**Mark Wainwright** and colleagues have reported that traumatic brain injury alters susceptibility to seizure. A drug developed at Northwestern University that prevents increased seizure risk is in clinical trial.



From Hamm CA et al. Global demethylation of rat chondrosarcoma cells after treatment with 5-aza-2'-deoxycytidine results in increased tumorigenicity. PLoS One 2009.

# Cancer Biology and Epigenomics

The scientific objectives of the Cancer Biology and Epigenomics Program include the identification of molecular mechanisms underlying tumorigenesis, metastasis and development of drug resistance. The program is strengthened by its members' multidisciplinary expertise in clinical, translational and basic cancer research.

The program conducts translational research using high powered computing, clinical-laboratory-industry collaborations and basic bench science. Recent studies involving pediatric brain tumors have uncovered new prognostic markers and novel targets for therapeutic intervention. In addition, these studies have identified certain genes that are dysregulated during cancer progression.

## **EurekaAlert! ESC & iPSC News Top Story • June 18, 2010**

*Are stem cells ready for prime time?*

The therapeutic potential of embryonic stem cells has been an intense focus of study and discussion in biomedical research and has resulted in technologies to produce human induced pluripotent stem cells (hiPSCs). Derived by epigenetic reprogramming of human fibroblasts, these hiPSCs are thought to be almost identical to human embryonic

stem cells (hESCs) and provide great promise for patient-tailored regenerative medicine therapies. However, recent studies have suggested noteworthy differences between these two stem cell types which require additional comparative analyses.

The Hendrix laboratory investigated the expression of key members of the Nodal embryonic signaling pathway, critical to maintaining pluripotency, in hiPSC and hESC cell lines. Nodal is an important morphogen — a soluble molecule that can regulate cell fate — in embryological systems that requires tight regulatory control of its biological function. These data demonstrate cancer hallmarks expressed by hiPSCs, which will require further elucidation for their impact on clinical applications, especially with respect to the fate of precancerous stem cells.

## **Adapted from *Northwestern News* • October 6, 2009**

Think of a protective fence that blocks the neighbor's dog from charging into your backyard. The body, too, has fences — physical and biochemical barriers that keep cells in their place. When breast cancer spreads or metastasizes, it crashes through the body's protective fences. The disease becomes fatal when it travels outside the mammary ducts, enters the bloodstream and spreads to the bones, liver or brain. Until now, drugs that try to stem the uncontrolled division of cancer cells within the ducts existed, but no drugs specifically targeted the invasion and spread of breast cancer to the organs. Seth Corey has found a way to strengthen the breast's "fence" to prevent cancer from metastasizing. He has discovered that when the leukemia drug dasatinib is combined with the breast cancer drug doxorubicin, the potent mix inhibits cell invasion by half in breast cancer cells.

## **BioEssays —“Non-coding RNAs: Meet thy masters”**

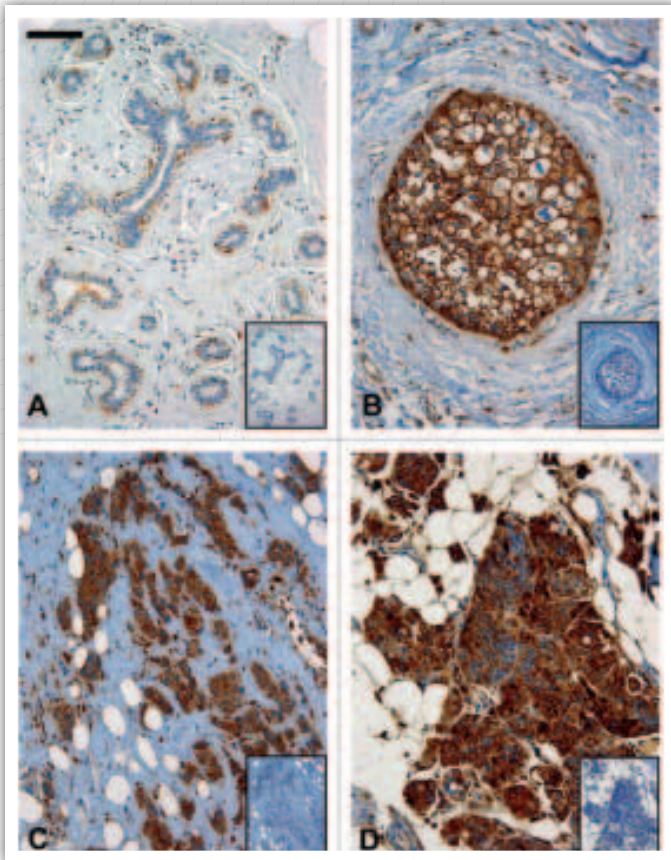
Fabrizio Costa reviewed the already huge, but rapidly expanding, diversity of non-coding RNAs (ncRNAs). The review describes the most recent discoveries in the ncRNA field that implicate these molecules as key players in the

## **Research Honors**

**John Crispino** was named Associate director of Education and Training for the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

**Seth Corey** was appointed to the Leukemia and Lymphoma Society Specialized Center of Research, and to the American Society of Hematology Scholar Committee.

The University of Alabama at Birmingham Department of Pathology honored **Mary J.C. Hendrix** with the 2010 Paulette Shirey Pritchett Endowed Lectureship Award. The lecture is named for the late Paulette Shirey Pritchett, MD, renowned faculty member whose research advanced the fields of pathology, dermatopathology and electron microscopy. Hendrix's presentation, "Targeting a novel embryonic pathway to suppress the metastatic phenotype" addressed the ways in which genes and regulatory molecules interact during the development of cancer metastasis, and the role of tumor classification in the search for new targets in cancer therapeutics.



From Abbott DE et al. *Reevaluating cathepsin D as a biomarker for breast cancer: serum activity levels versus histopathology*. Previously published in *Cancer Biology and Therapy* 2010.

epigenome. Costa's work was also featured on the cover of the journal issue. Costa is a research scientist in the laboratory of Marcelo Bento Soares.

### Prognostic indicators for aggressive tumors

The Soares group studied the pattern of hypomethylation in the cancer genome. Global loss of DNA methylation is known as an epigenomic aberration associated with carcinogenesis and cancer progression. This loss affects predominantly repetitive elements, which encompass over 50 percent of the CpG dinucleotides present in the human genome. To precisely determine the CpG sites with methylation loss during progression of pediatric intracranial ependymomas, the group exploited a high-throughput bisulfite sequencing approach that generates methylation profiles for thousands of Alu elements and their flanking sequences. They demonstrated that methylation losses in Alu elements are insignificant in primary nonaggressive ependymomas but increase in aggressive primary tumors

## Faculty

**Marcelo Bento Soares, PhD**, *Rachelle & Mark Gordon Endowed Professor in Cancer Biology & Epigenomics*

Maria F. Bonaldo, PhD, Fabrício Costa, PhD, *Maeve McNicholas Memorial Foundation Scholar*, Sergey Malchenko, PhD, Simone Sredni, MD, PhD, Elio Vanin, PhD, Min Wang, PhD, Hehuang Xie, PhD

Define protein networks and signaling pathways that are functionally compromised in pediatric brain tumors. Develop effective and safe individualized targeted therapies. Analyze the genome, epigenome and transcriptome of these tumors to map structural/functional alterations to protein networks and cellular processes.

**Pauline Chou, MD**

**Fei Chu, MD, PhD**

Biological processes that regulate adaptation of malignant tumor cells to stressful environments, and permit their survival in the presence of agents that would normally kill them.

**Seth Corey, MD, MPH**

Oncogene signaling, Src family protein kinases and PI 3'kinase that regulate cellular functions such as proliferation and cytoskeletal reorganization.

**John Crispino, PhD**

Regulatory mechanisms governing normal and malignant blood cell development.

**Kimberley Dilley, MD, MPH**

**Mary J.C. Hendrix, PhD**, *Medical Research Institute Council Professor, President and Scientific Director at Children's Memorial Research Center*

Zhila Khalkhali-Ellis, PhD, Dawn Kirschmann, PhD, Naira Margaryan, DVM, PhD, Richard Seftor, PhD, Luigi Strizzi, PhD

Identify genes that contribute to cancer metastasis as well as related diseases that exhibit similar biological activities. Define important structure/function relationships and provide the biological basis for new therapeutic strategies.

**Nobuko Hijiya, MD**

**Nikia Laurie, PhD**

Molecular mechanisms associated with retinoblastoma progression.

**Mary Beth Madonna, MD**

**Elizabeth Perlman, MD**

**Veena Rajaram, MD**

**Tadanori Tomita, MD**

and further yet in relapsed ependymomas. In particular, the data suggest that the methylation status of some Alu elements may serve as prognostic factors for a subset of aggressive ependymomas. The study was conducted with the Falk Brain Tumor Center of Children's Memorial Hospital.

# Developmental Biology

The Developmental Biology Program focuses on mechanisms of genetic fate specification in early human development. We examine pattern formation, the process by which cells organize to form structures that develop into a normal body; stem cell biology; and allocation and assortment of cells in organ development.

Our scientists are exploring several key aspects of signal transduction, the method by which protein signals outside a cell cause changes in gene expression inside the nucleus. These signals are critical to normal development. Studying them allows us to uncover and understand disturbances and disruptions in genes during development that may cause birth defects, cancer and other diseases.

## TRAINEES

A confocal microscopy image created by postdoctoral fellow Rodney Dale and Jacek Topczewski was featured by Visage Imaging, Inc<sup>®</sup>. The image, which highlights the nucleus and cells of an embryonic zebrafish cartilage element, was rendered with Amira visualization software by Visage Imaging.

## Research Honors

**Philip Iannaccone** received a distinguished service award for contributions from 1998 to 2008 as Child Health Editor, Associate Editor and Advisory Board Member for *Environmental Health Perspectives*, the leading environmental health sciences journal, in appreciation for significant contributions made to the advancement of knowledge in environmental health sciences.

**Shekhar Mayanil** was honored by the Spina Bifida Association with a SBAA Young Investigator award. His work identifies microRNA as a candidate in mediating the effect of folic acid in prevention of neural tube defects. This work points to mechanisms of action that are likely to enhance prevention strategies for children.

**David Walterhouse** is the Children's Oncology Group (COG) Study Chair for "Vincristine, dactinomycin, and lower doses of cyclophosphamide with or without radiation therapy for patients with newly diagnosed low-risk embryonal/botryoid/spindle cell rhabdomyosarcoma".



*The graduation ceremony for the 2009–10 Searle Fellows Program. Yong-Chao Ma (back row, second from right) was among the graduates.*

At the spring 2010 meeting of the Center for Genetic Medicine's Mouse Genetics Group, Northwestern University, Diana Himmelstein, Kohtz laboratory, received second place in the poster competition. Himmelstein is in the Northwestern University Interdepartmental Neuroscience (NUIN) Program.

Tyler Schwend, Integrated Graduate Program in the Life Sciences (IGP) student in the laboratory of Sara Ahlgren, defended his thesis on December 18, 2009. Schwend is now a postdoctoral research fellow at Kansas State University.

The Hedgehog (Hh)-signaling pathway plays a critical role in craniofacial development. Disruption of this pathway in humans can lead to Holoprosencephaly (HPE), which is often characterized by a variety of craniofacial defects. Recently, Schwend and Ahlgren showed that inhibiting the Hh-signaling pathway at early developmental stages selectively reduces anterior facial cartilages, while blocking the pathway at later stages selectively inhibits posterior cartilage development. These findings may help explain the spectrum of human facial phenotypes characteristic of HPE.

PDZ-LIM proteins have wide-ranging cell functions during development and homeostasis. Recent work in the laboratory of Hans-Georg Simon has revealed that the protein family member Pdlim7 mediates signals between the nucleus and the cytoskeleton, with significant impact on organ development. The group has integrated current

**“CenterPiece, a magazine about research scholarship, collaboration, and outreach at Northwestern University, highlighted the zebrafish work of Jacek Topczewski, who studies craniofacial defects.”**

knowledge about the PDZ-LIM protein family and proposed a new role: sequestering nuclear factors in the cytoplasm. First author Jennifer Krcmery is an IGP student.

Jorge Cantu and Barbara Sisson, both in the laboratory of Jacek Topczewski, received Ruth L. Kirschstein National Research Service (NRSA) awards in 2010. Cantu is studying the role of Notum in axon guidance through a NRSA Predoctoral Fellowship. Sisson's research involves the role of RhoA and its targets in craniofacial cartilage morphogenesis through a NRSA Postdoctoral Fellowship.

## RESEARCH HIGHLIGHTS

Tbx5, a transcription factor that controls developmental pathways, is involved in congenital heart disease. However, the mechanisms leading to organ malformation are largely unknown. The laboratory of Hans-Georg Simon has

shown an essential role of the Tbx5 binding protein Pdlim7 in controlling nuclear/cytoplasmic shuttling and function of the transcription factor, and in regulating cardiac formation. Pdlim7/Tbx5 interactions affect the expression of two Tbx5 target genes at the atrio-ventricular boundary, and their domains of misexpression correlate with the identified defects.

About 30 percent of all human cancers show activation of the GLI1 transcription factor. This indicates that GLI1 plays an important role in disruptions that result in cancer. Now, targeted therapies are being developed. David Walterhouse is studying GLI1 biochemistry in medulloblastoma, rhabdomyosarcoma, Burkitt lymphoma and basal cell carcinoma. Says Walterhouse, “The more we understand about the regulation of GLI1, the greater our chances of targeting it in cancer therapy. We are still addressing basic questions, but this research is moving closer to the clinic.”

## Faculty

**Philip Iannaccone, MD, PhD** *George M. Eisenberg Professor*

GLI transcription factors, genetics and biochemical mechanisms in normal development and disease states. Stem cell allocation in organ development.

**Sara Ahlgren, PhD** *Crown Family Research Scholar in Developmental Systems Biology*

Sonic Hedgehog signaling pathway. Gene expression changes produced by embryonic exposure to ethanol.

**Robert Dettman, PhD**

Cardiac development, coronary arteries, vasculogenesis, smooth muscle, signaling and cell fate.

**Vasil Galat, PhD**

Genetic regulation of stem cell lineages. Development of a stem cell repository.

**Sunjay Kaushal, MD, PhD**

Cardioprotective effects of celastrol against toxicity induced by doxorubicin. Tissue engineering for vascular repair with stem cells.

**Jhumku Kohtz, PhD**

Mechanism of action of Evfs, non-coding RNAs that are essential for proper GABAergic interneuron development.

**Marilyn Lamm, PhD**

Interaction between prostate cancer cells and bone cells via the hedgehog signaling pathway.

**Craig Langman, MD, Isaac A. Abt, MD**  
*Professor of Kidney Diseases*

Stem cell based tissue engineering in kidney.

**Yong-Chao Ma, PhD**

Differentiation of stem cells into neurons that degenerate in Parkinson's disease, and spinal motor neurons that are lost in spinal muscular atrophy and amyotrophic lateral sclerosis.

**Shekhar Mayani, PhD**

Gene regulatory and microRNA networks during neural tube development.

**Arun Sharma, PhD**

Tissue engineering for urinary bladder repair with stem cells.

**Hans-Georg Simon, PhD** *Bernard L. Mirkin, PhD, MD Research Scholar*

Regulatory genes that play key roles in limb development. Common genetic pathways in limb and heart development and disease.

**Jolanta Topczewska, PhD**

Signaling pathways in zebrafish development.

**Jacek Topczewski, PhD**

Craniofacial cartilage morphogenesis, neural tube patterning and muscle specification.

**David Walterhouse, MD**

Soft tissue sarcoma, rhabdomyosarcoma, regulation and function of the GLI1 oncogene and Hedgehog-GLI1 signal transduction pathway.

**Catherine Webb, MD**

**Joon Won Yoon, PhD**

Cancers that show dysregulated Hedgehog signaling activities.

---

# Clinical and Translational Research

The mission of the Clinical and Translation Research Program (CTR) is to provide a synergistic mechanism for the entire Children's Memorial research enterprise to accelerate the delivery of translational and clinical research to our patients. CTR provides support to multidisciplinary teams from all departments at Children's Memorial Hospital and the research center who are involved in translational and clinical research.

Under the leadership of Ram Yogev, MD, Susan B. DePree Founders' Board Professor in Pediatric, Adolescent and Maternal HIV Infection, and with over 115 members, the program provides a home for investigators engaged in both clinical trials and bench-to-bedside research. Complementing the core programs and centers of the research center and working in tandem with the Clinical Research Unit (CRU) and Clinical Trials Research Center (CTRC), we assist researchers as they progress from innovation to patient treatment.

Our goal is to develop a culture of translational and clinical research by fostering collaboration, training researchers, identifying funding resources, and facilitating delivery of innovative therapies through coordination of services.

The program works to:

- Expand the breadth of clinical and translational studies conducted at Children's Memorial and to assure the highest scientific standard for all such studies.
- Improve upon the current infrastructure for conducting clinical research trials.
- Encourage the development of multi-center patient groups to participate in therapeutic trials. This is a crucial asset for translational initiatives, serving as a vital bridge between drug/device discovery in laboratories and the needs of our pediatric populations.
- Train residents, fellows and other investigators in experimental and biostatistical methodology through an educational program. Topics covered include

study design, conduct, and analysis of clinical trials related to pediatric and adolescent disorders as well as research ethics and the protection of human subjects.

- Help investigators develop and evaluate treatment and prevention measures for pediatric disorders and adult-onset disorders with childhood antecedents. By giving our patients and other children an opportunity to participate in clinical trials of novel or modified therapies for a range of serious childhood disorders, we ultimately will be able to give all children the benefit of new, better and less toxic medications. As scientists reveal information leading to innovations in detecting and treating childhood diseases, we will be able to test these promising new treatments and ensure they reach those who most need them.

## **XENOBASE: A POWERFUL TRANSLATIONAL RESEARCH TOOL**

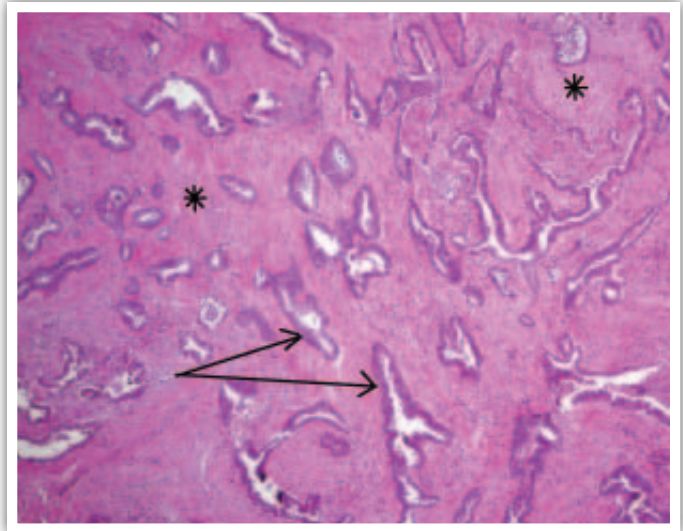
There are many reasons researchers need to identify patient cohorts. For example, they may be investigating if a particular population is large enough for a study, exploring preliminary data for grant proposals, gathering data for analysis, or extracting data for inclusion in a registry. XenoBase, an advanced bioinformatics system that integrates data analysis across the translational research work flow, is being used for this purpose. Children's Memorial's Clinical & Translational Research Data Mart, included in XenoBase, allows clinical researchers to generate and refine complex queries in a self-service, on demand fashion with the support of the research center Information Technology staff. The Data Mart contains information on more than 900,000 Children's Memorial patients, all of which has been de-identified to ensure patient confidentiality. Additional historical data continue to be incorporated. An example of a recent clinical query using XenoBase's self-service cohort identification capability was a request by Anthony Chin, MD to identify all patients diagnosed with pancreatitis between 2004–2009, with an analysis of their labs, demographics, vitals, comorbidities, procedures and medications.

XenoBase will continue to grow as an easily accessible and intuitive reference tool in assessing the viability of data to support or develop potential investigations.

## RESEARCH HIGHLIGHTS

In 2010, the American Thoracic Society issued a new official clinical policy statement on congenital central hypoventilation syndrome (CCHS), a disorder of respiratory and autonomic nervous system (ANS) regulation. The ANS regulates reflexive acts, including heart rate and blood pressure, digestion, body temperature and pain perception. In 2003, a gene called PHOX2B was found to be the disease-defining gene for CCHS. The specific manner in which the gene mutates predicts the severity and form of the disease. Debra Weese-Mayer, MD, who chaired the committee that wrote the guidelines, said “The discovery that PHOX2B is the gene that defines CCHS offers endless opportunities in terms of basic science inquiry and clinical care — all with the long-term goal to improve quality of life for these patients.”

Praveen Kumar, MD is the lead author of a recently published American Academy of Pediatrics (AAP) statement: [Hospital Stay for Healthy Term Newborns](#), AAP Committee on Fetus and Newborn. The hospital stay of the mother and her healthy term newborn infant should be long enough to allow identification of early problems and to ensure that the family is able and prepared to care for the infant at home. The length of stay should also accommodate the unique characteristics of each mother-infant dyad, including the health of the mother, the health and stability of the infant,



From Bass LM et al. Pancreatic adenocarcinoma in type 2 progressive familial intrahepatic cholestasis. BMC Gastroenterology 2010.

the ability and confidence of the mother to care for her infant, the adequacy of support systems at home, and access to appropriate follow-up care.

Chronic fatigue syndrome (CFS) is a complex and controversial condition involving severe fatigue and disabling musculoskeletal and cognitive symptoms. Chronic fatigue accounts for marked functional impairment and educational disruption among adolescents. Ben Katz, MD and colleagues reported the results of a prospective study of CFS after acute infectious mononucleosis (IM) in adolescents. The goal was to characterize the course and outcome of CFS in these patients during a two-year period after IM. Their study found that IM may be a risk factor for CFS in adolescents, and that female gender and greater fatigue severity are associated with the development of CFS.

## Research Honors

**Estella Alonso, MD** was appointed chair of the Studies of Pediatric Liver Transplantation (SPLIT) Consortium research committee.

**Kathryn Farrow, MD, PhD** received a Young Investigator Award during the 2009 American Heart Association Resuscitation Science Symposium.

**Amy Paller, MD** was honored with the Urs Schnyder Award from the European Society for Pediatric Dermatology, recognizing her work in genetic disorders of skin.

**Catherine Powers**, research manager of the Cystic Fibrosis Center, received the Judy Williams Award from the Cystic Fibrosis Foundation.

**Stanford Shulman, MD**, *Virginia H. Rogers Professor of Pediatric Infectious Diseases*, was selected as Clinical Mentor of the Year by the Feinberg School.

**Cynthia Stack, MD** was named Outstanding Teacher by the medical students of the Feinberg School.

**Peter Whittington, MD**, *Sally Burnett Searle Professor in Pediatrics and Transplantation*, was the recipient of the Canadian Liver Foundation / Canadian Association for the Study of the Liver Sass-Kortsak Award for sustained excellence in pediatric liver-related research.

The American Academy of Pediatrics granted its Special Achievement Award to **Ram Yogev** for advocacy efforts related to making Illinois a leading state in prenatal and newborn HIV testing.

# Human Molecular Genetics

The Human Molecular Genetics Program strives to nurture a world-class center of translational genetic medicine, with innovative basic science generating new routes to therapy for inherited diseases.

We benefit greatly from close collaborations with other research center programs, and are an integral part of the Northwestern University genetics community. Our investigators study genetic diseases that affect the function of the brain, nervous and neuromuscular systems; the lungs and digestive system; and that cause cancer.



Christopher Payne

Christopher Payne joined the program as a new faculty member in October 2009. Payne's research focuses on the identification of the male germline stem cell niche. He currently holds a prestigious NIH Pathway to Independence Award. The research center is indebted to the Medical Research Institute Council (MRIC) for its funding of

this faculty position and continuing support of the center's research mission and commitment to excellence.

## Research Honors

**Elfriede Pahl** has been elected Secretary Treasurer of the Pediatric Heart Transplant Study (PHTS) steering committee. The PHTS is a not-for-profit organization dedicated to the advancement of the science and treatment of children during listing for and following heart transplantation. The purposes of the group are to establish and maintain an international, prospective, event driven database for heart transplantation; to use the database to encourage and stimulate basic and clinical research in the field of pediatric heart transplantation; and to promote new therapeutic strategies. Data collection began in 1993. Currently, PHTS has 36 member institutions, with over 3,475 listed and 2,491 transplanted patients in the database.

Pahl has also been elected vice-chair of the International Society for Heart and Lung Transplantation's Scientific Council on Pediatric Transplantation.

## TRAINEES

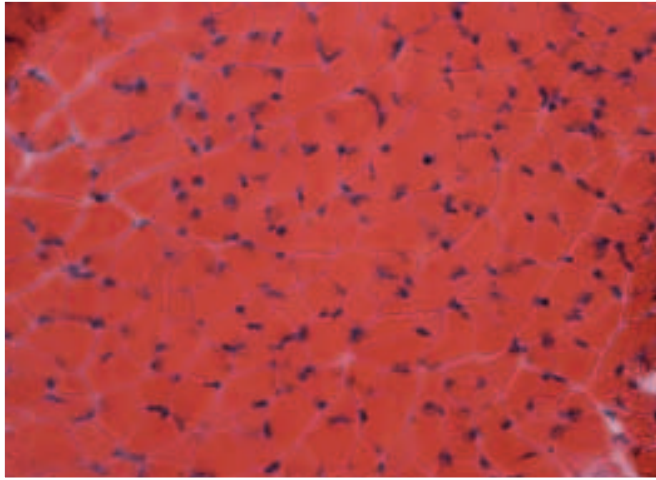
At the spring 2010 meeting of the Center for Genetic Medicine's Mouse Genetics Group, Northwestern University, Christopher Heier, an IGP student in the DiDonato laboratory, received first place in the poster competition.

Christopher Ott, a graduate student in the laboratory of Ann Harris, defended his thesis in May 2010. He is a graduate of IGP. In her introduction Harris said that Ott developed and applied state-of-the-art technologies to his work on the cystic fibrosis transmembrane conductance regulator (CFTR) gene, and has moved the field forward. She added that in making many important contributions to the research center training program and in his other leadership roles, Ott has inspired others. In September 2010 he began a postdoctoral fellowship at the Dana Farber Cancer Institute of Harvard Medical School.

Kathryn Meyer, a graduate student in the laboratory of Jill Morris, defended her thesis in March 2010. She is a graduate of NUIN. Among her other accomplishments, Meyer was first author of a seminal research study using in-utero electroporation of the developing mouse hippocampus in *Human Molecular Genetics*, 2009. A figure from the research was featured on the cover of the journal. She is a postdoctoral fellow at Weill Cornell Medical College.

Suzan Hammond, IGP student in the laboratory of Christine DiDonato, defended her thesis in December 2009. Hammond is a postdoctoral fellow at the University of Oxford, UK.

Catherine Willis, IGP student in the laboratory of Michael Klüppel, was first author on a study of Chondroitin-4-sulfotransferase-1(C4ST-1)/carbohydrate sulfotransferase 11 (CHST11), an enzyme involved in the biosynthesis of the glycosaminoglycan chondroitin sulfate. The sulfation pattern of chondroitin is tightly regulated during development, injury and disease. The laboratory previously showed that a mutation in C4st-1 leads to severe skeletal abnormalities during mouse embryogenesis. In addition, they described



Skeletal muscle sections stained with hematoxylin and eosin. (Christine DiDonato)

a highly specific temporal and spatial expression pattern of C4st-1. However, the transcriptional regulatory mechanisms that control C4st-1 gene expression remain unexplored. The laboratory used a bioinformatical approach to identify a functional C4ST-1 promoter, as well as a number of cis-regulatory modules. Moreover, the lab identified TGF $\beta$  responsive regulatory modules that can function in a cell type-specific fashion.

## MEDIA COVERAGE

*CenterPiece*, a magazine about research scholarship, collaboration, and outreach at Northwestern University, highlighted the zebrafish work of Jill Morris, who studies the Disrupted-in-Schizophrenia-1 (DISC1) gene.

The Brain Research Foundation featured the Morris laboratory in its 2008-2009 annual report. The foundation is dedicated to making a positive difference in the lives of children, adolescents and adults who are touched by neurological disorders. Through the Fay/Frank Seed Grant Program, the foundation provides start-up funds to researchers conducting new investigations that have the potential to lead to understanding and treatments of neurological disorders. The title of Morris' grant is "Deciphering the roles of DISC1 isoforms in embryonic brain development". Kathryn Meyer, PhD, a former member of the Morris laboratory and graduate student, was pictured on the cover of the report.

## Faculty

### PRIMARY FACULTY

**Ann Harris, PhD** *Valerie and George D. Kennedy Research Professor in Human Molecular Genetics*

Tissue-specific regulation of gene expression, chromatin structure and modification in the context of the CFTR gene, that when mutated causes cystic fibrosis. Identified and are characterizing intronic and extragenic elements that control CFTR gene expression, modulate the 3D structure of the locus and mediate tissue specificity. The role of secreted proteoglycans in initiation, invasion and metastasis of human pancreatic adenocarcinoma.

**Christine DiDonato, PhD**

Survival motor neuron gene function within nerve and muscle, the two tissues affected in spinal muscular atrophy.

**Laura Herzog, PhD** *Ann Marie and Francis Klocke, MD Research Scholar in Human Molecular Genetics*

Epigenetics, or how changes in gene expression can impact neurodevelopmental disorders such as autism, epilepsy, Rett and Angelman syndromes; and in how general or specific environmental factors such as fetal alcohol exposure can work through epigenetics to impact outcome.

**Michael Klüppel, PhD**

Functional roles of chondroitin sulfates and chondroitin sulfotransferase genes in mammalian development and disease, including cancer.

**Jill Morris, PhD** *Eloise and Warren Batts Research Scholar*

Cellular mechanisms by which DISC1, a schizophrenia susceptibility gene, affects neurodevelopment. Role of DISC1 in development, particularly the migration of cells to their proper location in the brain and subsequent differentiation into their intended fate.

**Christopher Payne, PhD**

How genetic and epigenetic modulators promote the development and maintenance of adult stem cells. Goal is to identify and characterize the genetic and epigenetic mechanisms utilized by both stem cells and their surrounding niche in supporting the stem cell program.

### ASSOCIATED FACULTY

**Brad Angle, MD**

Dysmorphology and chromosome abnormalities in 22q11 deletion syndrome.

**Joel Charrow, MD**

Natural history of genetic disorders, with concentration on neurofibromatosis, Gaucher disease and other lysosomal storage disorders, developing optimal strategies for treating lysosomal storage diseases, and studying the methods and pitfalls of population screening for genetic disorders.

**Nina Gotteiner, MD**

Fetal cardiology: Fetal arrhythmias, congenital heart disease and pulmonary hypertension in the neonatal period.

**Elfriede Pahl, MD**

Heart transplant, cardiomyopathy, heart failure in children, Kawasaki disease, coronary abnormalities in children.

**Kimberly Watts, MD**

Health outcome disparities in cystic fibrosis, focusing on the Latino CF population.

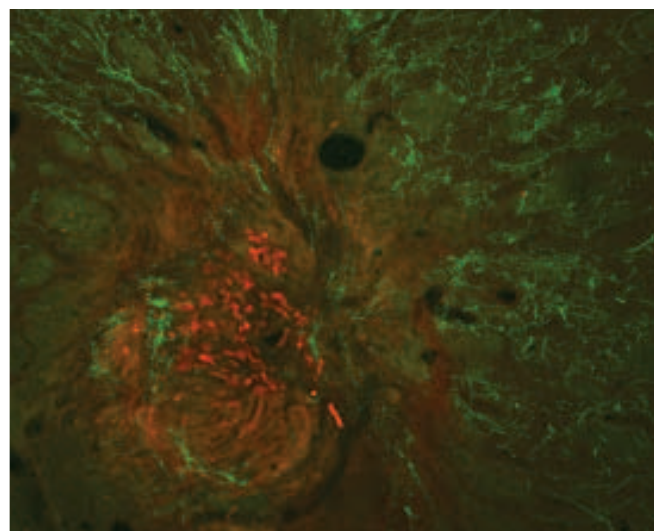
# Neurobiology

Scientists in the Neurobiology Program engage in research to define molecular processes critical to development, degeneration and regeneration of cells in the nervous system, with the aim of developing novel therapies for diseases and injuries of the human nervous system.

The program continues to thrive in its activities designed to mesh basic neuroscience with clinical studies in pediatric neurology and neonatology. The weekly research hour fosters interactions among members with diverse interests and backgrounds. In addition, the program hosts the Chicago Neural Repair Club, which features prominent neuroscientists speaking on topics such as stem cells, gene therapy, re-wiring the brain and novel approaches for epilepsy and neurodegenerative diseases. Program investigators employ leading stem cell and gene therapies, molecular neurobiology, computerized imaging and bioinformatics to advance our understanding of brain development and the basis for neurological disorders. The XenoBase Critical Care initiative, directed by Mark Wainwright, has completed its data acquisition and entry phase, and is now applying powerful tools to discover novel associations and therapeutics.

## **Maria Dizon** PHYSICIAN-SCIENTIST

The benefits of combining clinical practice with laboratory research are evident in the work of Maria Dizon. As a neonatologist at Prentice Women's Hospital and Children's Memorial, Dizon encounters babies at risk for brain injury. She is completing a Mentored Clinical Scientist Research Career Development Award from the National Institute of Neurological Disorders and Stroke. Dizon's research with John Kessler, head of the Ken & Ruth Davee Department of Neurology at the Feinberg School, focuses on developing novel therapies for cerebral palsy, a non-progressive disorder of motor control that can affect both full term and prematurely born babies. This disorder results from injury to white matter (myelin) in the brain. Work done in conjunction with Francis Szele suggests that neural progenitors found within injured areas may be appropriate targets. Dizon seeks to manipulate these progenitors to produce new oligodendrocytes, the cells that produce myelin. She is completing studies showing that downregulation of bone morphogenetic proteins results in protection and even increased production of myelin after hypoxia-ischemia. This is relevant to an important clinical problem in which white matter is lost in the preterm baby. Dizon has demonstrated rescue of neurons and neuronal function.



*From Glavaski-Joksimovic A et al. Reversal of dopaminergic degeneration in a parkinsonian rat following micrografting of human bone marrow-derived neural progenitors. Cell Transplantation 2009. Reprinted with permission of Cognizant Communication Corp.*

## RESEARCH HIGHLIGHTS

Scientists in the laboratory of Martha C. Bohn have reported on a potential use of bone marrow derived neuroprogenitor cells for the treatment of Parkinson's disease (PD). PD is a neurodegenerative disease characterized by the extensive loss of dopaminergic (DA) neurons in the midbrain, resulting in debilitating movement disorders. Following collection of bone marrow from healthy human adult volunteers, mesenchymal stem cells (MSC) were genetically modified to create SB623 cells. These cells express genes characteristic of neuroprogenitor cells derived from brain. Microdeposits of SB623 cells were surgically placed into the rat brain near the terminals of DA neurons that had previously been damaged. In rats that received these cells, dense rejuvenated host DA axons were observed. These results suggest that MSC could be developed as a novel therapy for ameliorating the degeneration of DA neurons in PD patients. This study was done in collaboration with a stem cell biotechnology company, SanBio Inc. The first co-authors of the study are Aleksandra Glavaski-Joksimovic and Tamas Virag, PhD, a former postdoctoral fellow in the Bohn laboratory.

Sookyong Koh and colleagues at the Children's Memorial Epilepsy Center quantified cell death, astrocyte proliferation, microglial activation and cytokine release in brain tissue from patients who underwent epilepsy surgery. They found that neuroinflammation and ongoing cell injury were extensive in patients with intractable epilepsy. The results suggest that active neuroinflammation and marked cellular injury may play a common pathogenic role, or be the result of childhood epilepsy of diverse etiologies. Their findings support the concept that immunomodulation which targets activated microglia and astrocytes may be a novel therapeutic strategy to reduce neurological morbidity and prevent intractable epilepsy.

#### Adapted from *ConNEXTions* Newsletter • April 2010

Mark Wainwright has been involved with the XenoBase project since its inception, beginning with a pilot study regarding children with traumatic brain injury. He is now expanding the breadth of the XenoBase data warehouse for the entire Pediatric Intensive Care Unit (PICU). "As of now, the data have been de-identified, organized and entered into the system, which gives us a great tool for feasibility studies," remarked Wainwright. "We are asking XenoBase

to expand its initial parameters, so that we can include laboratory reports, physiologic data as well as genetic information — and it seems to be doing everything we ask. Ultimately, our goal is to enable real time entry of data for all of the 43 beds in the PICU and have that information available for analysis immediately."

While Wainwright admits this is an ambitious goal, he's encouraged by the performance of XenoBase and the cooperation of the team from Van Andel Research Institute, always meeting the challenges he puts before them and getting XenoBase to perform beyond its initial projections.

## PATENTS

Martha Bohn, Lixin Jiang, PhD, Neva West, PhD, and Elio Vanin, PhD were awarded an amended claim to "Tetracycline-regulated adeno-associated viral (AAV) vectors for gene delivery to the nervous system".

Martha Bohn and Mohan Sapru, PhD were awarded European Patent No: 1 799 826, "siRNA-mediated gene silencing of synuclein" in August 2009. The invention relates to methods and systems for siRNA gene silencing of the alpha-synuclein gene and gene family members.

## Faculty

### PRIMARY FACULTY

**Martha C. Bohn, PhD** *Medical Research Institute Council Professor in Neurobiology*

Gene and stem cell therapies for Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS) using experimental rodent models of these diseases.

**Maria Dizon, MD**

Mechanisms leading to newborn brain injury, especially preterm brain injury. Impact of hypoxia-ischemia on the development of cells of the oligodendroglial lineage.

**Leon Epstein, MD** *Derry A. and Donald L. Shoemaker Professor in Pediatric Neurology*

Impact of viral infections on the developing nervous system. Biomarkers of neurological status in HIV infection.

**Aleksandra Glavaski-Joksimovic, PhD**

Studies of bone marrow derived neural stem

cells for brain repair in Parkinson's disease and traumatic brain injury.

**Sookyong Koh, MD, PhD**

Novel treatments for children with epilepsy. Research to minimize the detrimental effects of seizures.

**Honglin Li, PhD**, *Eleanor Clarke Research Scholar in Developmental Neurobiology*

Molecular mechanisms that regulate cellular stress response and cell death signaling.

**Charu Venkatesan, MD, PhD**

Mechanisms involved in the formation of white matter pathways in the developing brain.

**Mark Wainwright, MD, PhD**

Research to improve the therapy available for acute brain injury in children, principally perinatal asphyxia, early-life seizures and traumatic brain injury.

### ASSOCIATE FACULTY

**Rajesh Awatramani, PhD**

**Lise Eliot, PhD**

**Laura Herzing, PhD**

**Philip Hockberger, PhD**

**Jhumku Kohtz, PhD**

**Shekhar Mayanil, PhD**

**Richard Miller, PhD**

**Jill Morris, PhD**

**Hande Ozdinler, PhD**

**Daniel Peterson, PhD**

**Francis Szele, PhD**

**Sheila Wang, PhD**

**Jane Wu, MD, PhD**

---

# Mary Ann & J. Milburn Smith Child Health Research Program

The scientific mission of the Mary Ann and J. Milburn Smith Child Health Research Program (CHR) is to address important clinical and public health problems of children, using state-of-the-art epidemiological, clinical, and laboratory methodology and interdisciplinary collaborations.

The program engages in both population and clinic based research to advance knowledge about the natural history, causes and psychosocial impacts of common and important child health problems and to identify childhood precursors of adult diseases. We are actively engaged in translating scientific knowledge into effective clinical and public health interventions and policy that can benefit children, their families and their communities. We partner with policy makers and the general public to address child health problems. In addition, we train a new generation of child health professionals and researchers. The program is striving to become a leading national center for child health research. The ultimate goal is to foster healthy children today and healthy adults tomorrow.

CHR consists of four core centers that possess unique expertise and resources.

## **CHILD HEALTH DATA LAB (CHDL) / CENTER FOR COMMUNITY PARTNERSHIPS AND HEALTH PROMOTION (CCPHP)**

Co-Directors: Jenifer Cartland, PhD, Maryann Mason, PhD and Karen Sheehan, MD, MPH

CHDL is a repository of information on child and adolescent health in Chicago and Illinois. CHDL supports investigators and program planners who focus on injury prevention and community-based efforts to improve the health of youth. In the belief that many of the health problems facing children are related to a broad range of socioeconomic factors, CHDL seeks to pinpoint public policy solutions to the prevention of unintentional and violent injury to children and to

the improvement of children's health. CHDL conducts epidemiologic research and evaluates interventions designed to reduce injuries. <http://www.chdl.org>

CCPHP, a Center of Excellence within CHR, is a hub of interdisciplinary research. Its two primary goals are to build a community of scholars that will optimize the commitment of Children's Memorial, the research center and Northwestern University-affiliated researchers to build excellent community-based public health interventions; and to improve the health of children and adolescents in Illinois by expanding local and state governments' capacity to make data-driven decisions in support of child health. <http://www.centerforcommunitypartnerships.org>

## **CENTER ON OBESITY MANAGEMENT AND PREVENTION (COMP) / CONSORTIUM TO LOWER OBESITY IN CHICAGO CHILDREN (CLOCC)**

Director: Katherine Kaufer Christoffel, MD, MPH  
Executive Director of CLOCC: Adam Becker, PhD, MPH

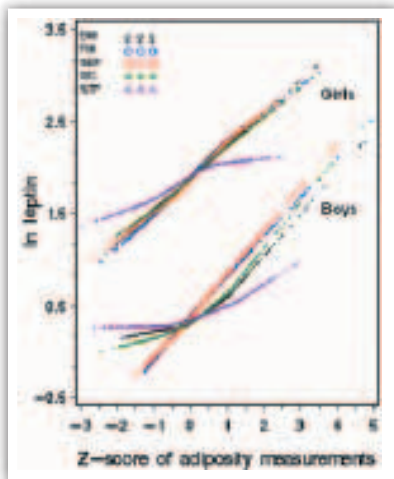
COMP coordinates and expands research on childhood obesity, and integrates this research with the clinical and public education/advocacy aspects of obesity-related work at Children's Memorial. COMP provides educational opportunities and facilitates the development of collaborative research projects. <http://www.childrensmrc.org/comp>

CLOCC, COMP's community arm, is a nationally recognized model whose mission is to confront the childhood obesity epidemic by promoting healthy and active lifestyles for children throughout the Chicago metropolitan area. A data-driven effort that brings together over 1,200 organizations and over 2,600 participants, CLOCC fosters and facilitates connections between childhood obesity prevention researchers, public health advocates and practitioners, and children, families and communities. CLOCC has been identified as a leading community model by the Institute of

Medicine (IOM), the American Medical Association (AMA), and the Centers for Disease Control and Prevention (CDC). Today, CLOCC supports the Chicago Interdepartmental Task Force on Childhood Obesity. CLOCC's work includes documentation of the prevalence of obesity and obesity-related knowledge, attitudes and behaviors, as well as program evaluation. It recently received a two-year \$5.8 million grant from the U.S. Department of Health and Human Services (DHHS) to lead Chicago efforts under the Communities Putting Prevention to Work initiative. <http://www.clocc.net>

### MOLECULAR EPIDEMIOLOGY AND BIOINFORMATICS (MEpi)

Faculty members: Xiaobin Wang, MD, MPH, ScD, the Mary Ann & J. Milburn Smith Research Professor; Ruchi Gupta, MD, MPH; Binyan Wang, MD, PhD; Xin Liu, MD, PhD; Xiumei Hong, MD, PhD; and Lester Arguelles, PhD



From Zhang S et al. Association of plasma leptin concentrations with adiposity measurements in rural Chinese adolescents. *Journal of Clinical Endocrinology and Metabolism* 2009.

The MEpi core bridges epidemiological, clinical and bench research through interdisciplinary collaborations and application of advanced methods in molecular biology, population genetics, bioinformatics and biotechnology. Its research focus is to elucidate the role of environmental/community factors, genetic and epigenetic factors, and gene-environment interactions in the development of complex human diseases. Ongoing studies focus on adverse reproductive outcomes, food allergy and related conditions, and obesity and metabolic syndrome. These studies are supported by grants from the NIH and foundations, including the March of Dimes Birth Defects Foundation and the Food Allergy Initiative. <http://www.childrensmrc.org/childhealthresearch/bioinformatics>

### PEDIATRIC PRACTICE RESEARCH GROUP (PPRG)

Director: Helen Binns, MD, MPH  
Associate Director: Adolfo Ariza, MD

PPRG is a well-established, practice-based research network with over 450 Chicago-area clinicians from more than 75 primary care practices. PPRG provides the research center community with the supporting systems and expertise necessary to partner with community clinicians to study topics in primary care settings. Its extensive partnerships allow for a laboratory to test ideas of relevance to primary care. Our goal is to improve and refine child health care through determining best practices, delivering ongoing clinical education to providers, and evaluating the outcomes. In the past year, PPRG has been moving to a partnership model, in which community clinicians are fully engaged in research processes. Additionally, PPRG is strengthening ties with the newly-established Northwestern University internal medicine practice-based research network through the Community-Engaged Research Center (CERC) of NUCATS. Binns and Ariza are leaders of practice based research nationally. <http://www.childrensmrc.org/pprg>

### Research Honors

**Helen Binns** is chair of the American Academy of Pediatrics (AAP) Council on Environmental Health and AAP liaison to the CDC Advisory Committee on Childhood Lead Poisoning. She serves on the Practice-Based Research Advisory Committee, which advises the Agency for Healthcare Research and Quality.

**Jenifer Cartland** has been appointed to the 2011 Illinois State Health Improvement planning team.

**Katherine Kaufer Christoffel** serves on the National Advisory Committee of the National Initiative for Child Health Quality for obesity issues, and on the Chicago Mayor's Pedestrian Advisory Council. She was invited to a White House meeting during planning for the First Lady's Let's Move! initiative. Christoffel has been selected as the Feinberg School Dean's 2011 Daniel Hale Williams Award winner for Distinguished Service to Underserved Communities.

**Xiaobin Wang** serves on a steering committee of the National Institute of Allergy and Infectious Diseases Consortium of Food Allergy Research, and on the Genomic and Proteomic Network for Premature Birth Research advisory board, National Institute of Child Health and Human Development (NICHD). She also is a member of the NICHD Epigenetics/Genetics/Genomics Working Team for the National Children's Study.



Mastering  
**COMPLEX**  
skills

*Life's Milestones*

We work with scholars at all stages of their careers to prepare them for the next steps. We believe that by introducing young people to science, we help them succeed in a complicated world.

# The children we treat today can become tomorrow's leaders

Just as we strive towards improving pediatric health care, we prepare young people for careers in science

The Children's Memorial Research Center Training Program is a dedicated and distinguished endeavor, developing our brightest graduate and postgraduate scientists for prolific careers. Not only does the training prepare them for individual success, but under the guidance of our faculty members, the students and fellows contribute breakthrough research and technologies that aid in the application of basic science discoveries to clinical practice.

The program provides a learning and mentoring environment for graduate students, postdoctoral and clinical fellows working in research center laboratories. Currently, there are 16 graduate students, 19 postdoctoral fellows and 11 clinical fellows working in 21 laboratories. The graduate students typically belong to the three graduate programs of the Feinberg School: Integrated Graduate Program (IGP) in the Life Sciences; Northwestern University Interdepartmental Neuroscience (NUIN) Program; and Medical Scientist Training Program (MSTP).

The trainees play an active role in the training program, organize themselves into different committees and coordinate a number of activities. They hold monthly meetings to discuss science and other issues important to a trainee's life. They run a peer-reviewed travel award program to attend scientific meetings, and invite outside speakers for career-planning discussions and research talks.

This year's achievements include:

- Five graduate student thesis defense presentations;
- Six first author publications by graduate students;
- Eight first author publications by postdoctoral fellows;
- Six first author publications by clinical fellows; and
- 30 publications.

## Breakthrough Research

### Biomedical Research Symposium

Research center trainees organized and hosted an event dedicated to research. Guests from Chicago area universities, including new graduate students from NUIN, IGP and MSTP listened to short talks, viewed posters and interacted with other members of the biomedical science community.

### Highlights

Research staff, graduate students and postdoctoral fellows selected for

the excellence of their work gave oral presentations.

**Kenneth Cadigan, PhD** from the University of Michigan presented the Bernard L. Mirkin honorary lecture.

Trainees participated in the poster session, showing the diversity of studies conducted at the research center.

Award presentations and a reception completed the day.

### Poster winners

**Staff:** **Kristin Kalita**, Payne laboratory (Human Molecular Genetics).

**Junior graduate students:** **Austin Gillen**, Harris laboratory (Human Molecular Genetics); **Catherine Willis**, Klüppel laboratory (Human Molecular Genetics). **Senior graduate students:** **Diana Himmelstein**, Kohtz laboratory (Developmental Biology); **Grant Parker Flowers**, Topczewski laboratory (Developmental Biology). **Postdoctoral**



Poster presentation at the Biomedical Research Symposium.

**fellows:** **Rudyard Sadleir, PhD**, Simon laboratory (Developmental Biology); **Rodney Dale, PhD**, Topczewski laboratory

## PhDs AWARDED

Suzan Hammond, IGP student in the laboratory of Christine DiDonato, defended her thesis in December 2009. The title of her talk was “Characterizing the effect of mutations within exon 7 of the murine survival motor neuron gene to model spinal muscular atrophy in the mouse”. Hammond is a postdoctoral fellow in the laboratory of Matthew Wood at the University of Oxford, UK.

Yongsoo Kim, a graduate student in the laboratory of Francis Szele, Neurobiology Program (now at the University of Oxford), defended his thesis in February 2010. The title of his talk was “Cell migration and proliferation in postnatal murine subventricular zone neurogenesis: roles of the epidermal growth factor receptor and dopamine receptor 3”. He is a graduate of NUIN. Kim continues his research in the Szele laboratory.

Kathryn Meyer, a graduate student in the laboratory of Jill Morris, Human Molecular Genetics Program, defended her thesis in March 2010. The title of her talk was “Expression and function of Disrupted-In-Schizophrenia 1 in the developing mouse hippocampus”. She is a graduate of NUIN. Meyer is a postdoctoral fellowship in the laboratory of Samie Jaffrey, MD, PhD at Weill Cornell Medical College.

Christopher Ott, a graduate student in the laboratory of Ann Harris, Human Molecular Genetics Program, defended his thesis in May 2010. The title of his talk was “Chromatin structure and conformation of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene”. He is a graduate of IGP. Ott is a postdoctoral fellow at the Dana Farber Cancer Institute of Harvard Medical School in the laboratory of James E. Bradner, MD.

Tyler Schwend, IGP student in the laboratory of Sara Ahlgren, Developmental Biology Program, defended his thesis in December 2009. The title of his talk was “Elucidating the spatiotemporal requirement for zebrafish Hh-signaling in craniofacial skeleton development”. Schwend is a postdoctoral research fellow at Kansas State University.

## EVENTS

### BIOMEDICAL RESEARCH SYMPOSIUM

In 2010, the trainees organized the second annual Biomedical Research Symposium, a day of science that highlights research opportunities to incoming Northwestern graduate students and provides peer-to-peer discussions and scientific exchange for the Chicago biomedical community.

### GRANTSMANSHIP WORKSHOP

A two day workshop, “Grantsmanship for the research professional” was taught by Holly Falk-Krzesinski, PhD, director of NUCATS Research Team Support & Development, in August 2010. Falk-Krzesinski, an expert in all phases of the funding process, instructed trainees on successful grant writing. This included providing a solid definition of the project, considering the audience and interacting with various agencies. She provided many details on how to write each section of a proposal, what goes into a review and much more.

## Awards

**Rosa Carrasco, MD**, a second year fellow working in the laboratory of Isabelle De Plaen, MD, received a Thrasher Early Career Award for her study entitled “Role of Vascular Endothelial Growth Factor in necrotizing enterocolitis”. The purpose of this program is to encourage the development of medical research in child health by awarding small grants to new researchers. De Plaen is a member of the Clinical and Translational Research Program.

At the 15th annual Drug Discovery Symposium hosted by the Center for Molecular Innovation and Drug Discovery of Northwestern University, **Rocco Gogliotti** from the DiDonato laboratory won the scientific poster session in the graduate student category. Gogliotti is an IGP student.

At the spring 2010 meeting of the Center for Genetic Medicine’s Mouse Genetics Group, Northwestern University, two research center graduate students won top awards in the poster competition. **Christopher Heier**, DiDonato laboratory, Human Molecular Genetics Program, received first place. Second place went to **Diana Himmelstein**, Kohtz laboratory, Developmental Biology Program. Heier is an IGP student; Himmelstein is in the NUIN Program.

**Sarah Mercer**, a third year IGP student in Hans-Georg Simon’s laboratory, received third place for best student presentation at the 49th Annual Midwest Developmental Biology Meeting. Mercer also received an invitation to participate in the Pan-American Advanced Studies Institute Regenerative Biology short course in Santiago, Chile.

## RESEARCH HIGHLIGHTS

The Hedgehog (Hh)-signaling pathway plays a critical role in craniofacial development. Disruption of this pathway in humans can lead to Holoprosencephaly (HPE), which is often characterized by a variety of craniofacial defects. In *BMC Developmental Biology*, Tyler Schwend and Sara Ahlgren studied chameleon mutants that display reduced and dysmorphic mandibular and hyoid arch cartilages, and lack all ceratobranchial cartilage elements. The study showed that inhibiting the Hh-signaling pathway at early developmental stages selectively reduces anterior facial cartilages, while blocking the pathway at later stages selectively inhibits posterior cartilage development. These findings may help explain the spectrum of human facial phenotypes characteristic of HPE.

In their review article “Fishing for the signals that pattern the face” in the *Journal of Biology*, Thomas F. Schilling and Pierre Le Pabic discussed the findings in the Schwend *BMC Developmental Biology* paper.

The laboratory of Michael Klüppel, PhD previously showed that a mutation in an enzyme called chondroitin-4-sulfotransferase-1 (C4ST-1) leads to severe skeletal abnormalities during mouse embryogenesis. In addition, they described a highly specific temporal and spatial expression pattern of C4st-1. However, the mechanisms that control C4st-1 gene expression remained unexplored. The laboratory used a bioinformatics approach to identify a C4ST-1 promoter, as well as a number of regulatory modules. Moreover, they identified regulatory modules that can function in a cell type-specific fashion. The study was published in *Genetics and Molecular Research*. First author Catherine Willis is an IGP student.

PDZ-LIM proteins have wide-ranging and multicompartamental cell functions during development and homeostasis. Facilitating the assembly of protein complexes, they can act as signal modulators, influence actin dynamics, regulate cell architecture and control gene transcription. Recent work in the laboratory of Hans-Georg Simon has revealed that the protein family member Pdim7 has important activities at the cellular level, mediating signals between the



Ann Harris (left) and graduate student Christopher Ott at his thesis defense.

nucleus and the cytoskeleton, with significant impact on organ development. In *BioEssays*, the group reviewed and integrated current knowledge about the PDZ-LIM protein family and proposed a new role: sequestering nuclear factors in the cytoplasm. The cover photograph for the issue showing a developing coronary vessel and the surrounding myocardium was the work of the Simon laboratory. First author Jennifer Krcmery is an IGP student.

The mammalian intestine harbors complex societies of beneficial bacteria that are maintained in the lumen with minimal penetration of mucosal surfaces. Intestinal luminal contents contain large amounts of peptidoglycan (PGN), a potent immune adjuvant derived from bacterial cell walls. It influences immunity at the intestinal mucosa and remote sites. How PGN interacts with intestinal epithelial cells and is transported across the intestinal lining remain unknown. The findings of the laboratory of Xiao-Di Tan, MD, published in the *Journal of Cellular Physiology*, suggest that crypt-based immature intestinal epithelial cells play an important role in transport of luminal PGN. The absorbed PGN and its derivatives may facilitate maintenance of intestinal immune homeostasis, the breakdown of which can lead to inflammatory bowel disease or cancer. First authors Heng-Fu Bu, PhD and Xiao Wang, MD, PhD are postdoctoral fellows. Tan is a member of the Clinical and Translational Research Program.

# Core Facilities

Director of Research Technologies: Jhumku Kohtz, PhD

Children's Memorial Research Center members enjoy use of core facilities and regulatory research oversight committees, assistance with intellectual property development, assistance with grant applications and notification of funding opportunities, access to workshops, research seminars, scientific mentoring and collaborations, funding for basic and clinical research, pilot projects and bridge support, expansion of the clinical research infrastructure, and access to XenoBase.

## BIostatistics RESEARCH CORE (BRC)

Director: Deli Wang, MD, PhD

BRC strengthens the area of statistical consultation and develops collaborations with faculty investigators. Services include consulting on projects, providing guidance on grants, collaborating, critically reviewing research, supervising study design, and writing sections related to statistical analysis. Zhenling Huang and Ying Zhou are the statisticians, and Kate Hickey is administrative assistant. In 2010, the Medical Research Junior Board Foundation granted BRC an award.

## CHILDREN'S VIRAL VECTOR TRANSLATIONAL RESOURCE CENTER (VVF)

Director: Martha C. Bohn, PhD

The VVF develops high titer, high quality, helper-free viral vectors for laboratory research. We provide consultation on viral vector design, virus type, promoter, expression cassette design, virus use in vitro and in vivo, biosafety requirements and letters of support for grant applications.

## DNA SEQUENCING CORE

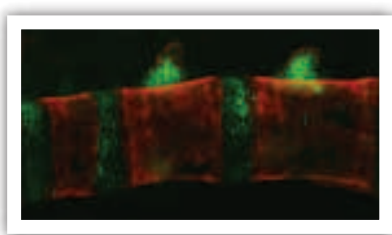
Manager: Christina Smith

The DNA Sequencing Core provides research center investigators access to high-quality automated DNA sequencing technology. Turnaround time is very short: results are made available within 48-72 hours of sample submission. The core accepts DNA samples (pure plasmids, mini-prep plasmids, M13 clones, PCR products, gel isolated fragments) and processes them according to protocols for Applied Biosystems DNA Sequencers (Model 3730).

## FISH FACILITY

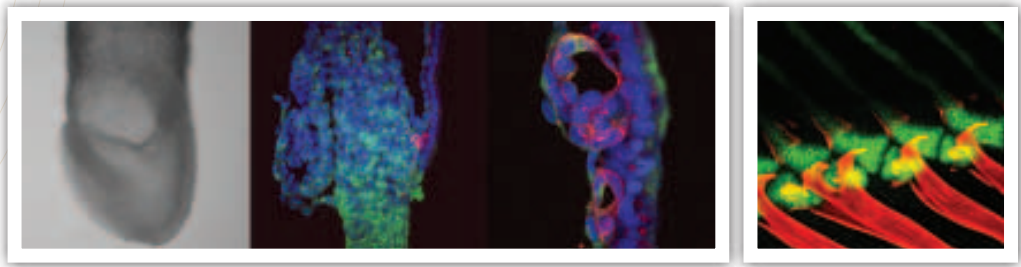
Director: Jacek Topczewski, PhD

The research center supports a shared facility for the rearing and maintenance of zebrafish. In the past few years the fish facility was dramatically expanded to accommodate the growing needs of investigators studying problems of development and cancer biology, neurobiology and regeneration. The facility supports research projects from six research center laboratories. In addition, investigators from Northwestern University, DePaul University and the University of Illinois at Chicago have also used its resources.



Formation of vertebrae (red) around zebrafish notochord (green), neural arches visible. (Rodney Dale)

*The research center and the clinical departments of Children's Memorial partnered to underwrite full tuition for up to four candidates for a Master of Science in Clinical Investigation (MSCI) degree at the Feinberg School.*



*Left: Blood and vessel development at mouse headfold stages. (Jerry Rhee) Right: Details of zebrafish anal fin skeleton with bone (red) and cartilages (green). (Rodney Dale)*

### **FLOW CYTOMETRY FACILITY**

Manager: Jhumku Kohtz, PhD

The Flow Cytometry Facility is equipped with a user-friendly FACSCalibur flow cytometer that provides a convenient way to perform live cell immunophenotyping, viability study and DNA analysis. A FACSARIA cell sorter is also available in the High-Speed Cell Sorting Facility.

### **iPS AND HUMAN STEM CELL CORE FACILITY**

Director: Vasil Galat, PhD

Co-director: Philip Iannaccone, MD, PhD

The iPS and Human Stem Cell Core Facility isolates and studies the biology of stem cells. The focus is genetic regulation of lineage, utilization for therapy and the study of human disease. We are establishing partnerships with IVF clinics nationwide and developing tools for induced pluripotent stem cells (iPS).

### **MICROSCOPY AND IMAGING FACILITY**

Manager: William Goossens

The Microscopy and Imaging Facility is a shared resource with full access to the Children's Memorial research community. Our researchers have unlimited access to the latest and best technological tools. The facility also provides technical support and training on our instruments, including light and fluorescent microscopes, confocal laser scanning microscopes, digital image processing and analysis and darkroom facilities.

### **PRITZKER RESEARCH LIBRARY**

Manager: Peggy Murphy, MILS

The Pritzker Research Library provides services and collections for the Children's Memorial research community. Literature searches, funding opportunity searches, current awareness, interlibrary loans and training are offered. A collection of journal articles published by members is maintained, and recent articles are made available on publication. The library's website lists numerous resources, including databases and protocols.

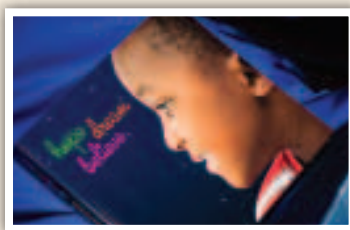
### **RESEARCH HISTOLOGY FACILITY**

Manager: Samantha Gadd, PhD

The Research Histology Facility at Children's Memorial Hospital assists investigators by providing high quality research histology services. We produce sections from frozen and paraffin-embedded tissues, and routine hematoxylin and eosin stained slides; and perform special stains and immunohistochemistry. With these tools, investigators are able to evaluate the pathologic consequences of disease processes in a quick, cost-effective and reproducible manner.

# THE MEDICAL RESEARCH INSTITUTE COUNCIL

## 60 Years of Extraordinary Philanthropy for Medical Research



The 2009 Children's Ball theme was "Magical Moments: Hope, Dream, Believe".

The year 2011 will mark the 60th anniversary of the founding of the Medical Research Institute Council (MRIC), which has raised over \$105 million to further scientific discovery at two of Chicago's revered institutions, Michael Reese Hospital and Children's Memorial Hospital.

In the early years, the MRIC funded research on dialysis, hypertension and the causes of coronary arteriosclerosis. Later investigations focused on the causes of infertility, Rh disease and heart rhythm irregularities. In the following years, scientists examined new and unusual chemotherapeutic agents in patients with advanced cancer and ways to minimize drug toxicity. In order to finance these important studies, the MRIC organized an annual gala ball each year, attracting hundreds of formally clad guests who generously donated funds earmarked for medical research.

In 1991, the MRIC began its affiliation with Children's Memorial Hospital, refocusing its mission on raising funds for pediatric research and renaming its signature gala, The Children's Ball. Children's Memorial Hospital had made a commitment to construct a free-standing research institute dedicated to pediatrics, and had recruited Bernard Mirkin, PhD, MD, a visionary scientist, to design and direct the new facility, then called CMIER — Children's Memorial Institute for Education and Research — and now named Children's Memorial Research Center. In 1992 the president of Children's Memorial, Earl Frederick, stated: "The realization of CMIER is the most important undertaking of the Medical Center at this time, and we are most fortunate to include [the] MRIC as a major participant in this initiative."

In 1995, the research building opened its doors on Halsted Street to great acclaim and with great celebration. The event was covered prominently in the *Chicago Tribune*, and Mayor Daley was one of the keynote speakers at the inauguration of the building. It was a proud moment for the city of Chicago, as the institute was one of only five free-standing pediatric research centers in the nation at that time.

The MRIC initially enhanced the mission of the Institute by funding a \$2 million endowment for genetic research; a \$1.5 million

professorship in neurobiology; the purchase of the INTRABEAM system for the delivery of intraoperative radiotherapy; and by investing \$1 million in the MRIC Education Center. Next, the MRIC created the \$1 million Young Investigator Chair and inaugurated an international research and resident exchange program with Schneider Children's Medical Center of Israel.

In 2002, the MRIC generously pledged \$5 million to support an addition to the main research building to add 52,000 feet of much needed laboratory space. A groundbreaking ceremony was held with Senator Richard Durbin and other notable dignitaries in attendance, and construction on the new space began.

With the arrival of Mary J.C. Hendrix, PhD as the President and Scientific Director of the research center in 2004, the MRIC was inspired to increase its philanthropy of basic, clinical and translational research. In the years 2005–2009, the MRIC donated \$3 million for the President and Scientific Director's endowed Professorship; \$3 million for recruitment in the Human Molecular Genetics Program; \$2 million for the Rachele and Mark Gordon Endowed Research Professorship in Cancer Biology and Epigenomics for a Chair held by Marcelo Bento Soares, PhD; \$1 million to advance the Experimental Therapeutics Program led by Ram Yogeve, MD; \$1 million for kidney disease research led by Craig Langman, MD; \$250,000 toward implementation of the XenoBase project; and \$450,000 from the Links ProAm Golf Tournament to advance Earl Cheng, MD's studies in urology.

The nineteen years that the MRIC has been affiliated with Children's Memorial have been fruitful. During this time, the MRIC has significantly raised awareness in the community of the benefits of innovative biomedical research. In addition, the MRIC has generated two successful Junior Boards comprised of energetic young donors who raise funds for research projects each year. The MRIC's festive Children's Ball has consistently attracted over 1,000 attendees who are introduced each year to the important work occurring at the research center and the hospital. In 2008, the MRIC Ball Co-Chairs, Meredith Bluhm-Wolf and Emily Emmerman, set a breath-taking fund raising record — \$5.3 million — a milestone.

The MRIC looks forward to its 60th anniversary with great optimism as it continues its remarkable mission to improve the lives of children and their families through scientific investigation.

# Summary of Award Activity

During the current fiscal year, external sponsors have funded awards to Children’s Memorial and the Northwestern University Department of Pediatrics in the amount of \$40,860,633. Compared to Fiscal Year 2009, this represents an 11.9 percent increase in total funding. Overall, the research portfolio was balanced with funding coming equally for both fundamental laboratory research and from clinic and community based research projects.

Additionally, an award of \$7,000,000 was received from the Illinois Department of Commerce and Economic Development for the construction of the Neonatal Intensive Care Unit of the new Ann & Robert H. Lurie Children’s Hospital of Chicago. This construction award was not included in the annual award totals above.

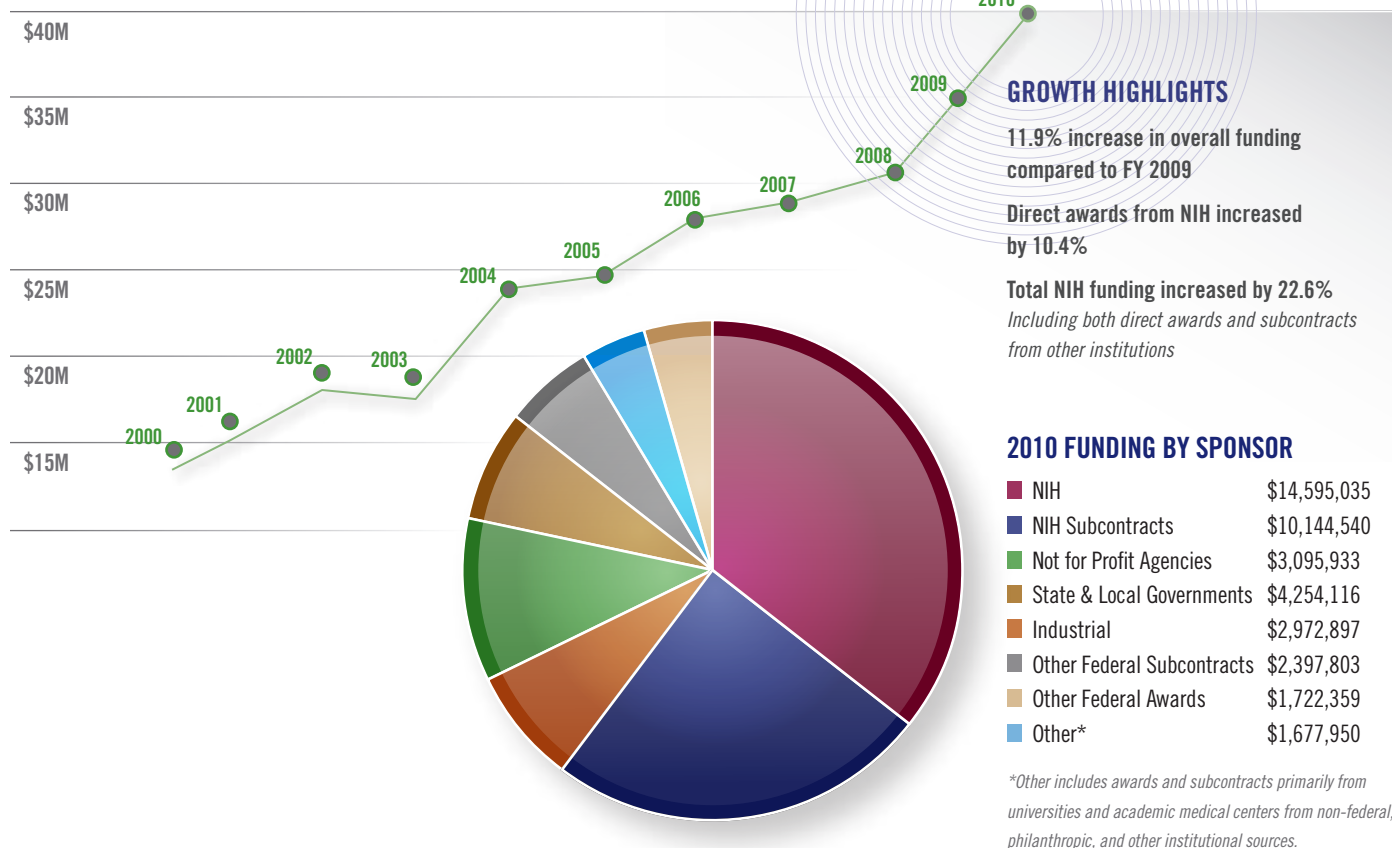
To date this fiscal year, Children’s Memorial Medical Center has received a total of 35 American Recovery and Reinvestment Act of 2009 (ARRA) awards with total funding of

\$3,503,705. We expect \$635,675 for non competing continuation awards in FY2011. We estimate total ARRA funding received from 2009 through 2011 will be \$6,277,595.

In the highly competitive environment for grant-seeking, the researchers and staff are to be highly commended for their efforts in submitting proposals and their successes in obtaining external funding.

## TOTAL ANNUAL AWARDS 2000–2010

(Fiscal years, dollars in millions)



# Research Center Offices and Support

## OFFICE OF RESEARCH INTEGRITY AND COMPLIANCE (ORIC)

ORIC is dedicated to building an environment that fosters the responsible conduct of research by promoting the principles of scientific and administrative excellence, and compliance with both the letter and spirit of governing regulations. ORIC oversees the research compliance committees, including:

- Institutional Review Board (IRB)
- Institutional Animal Care and Use Committee (IACUC) and
- Institutional Biosafety Committee (IBC).

Annie Muñana, BSN, MJ, *Director*

Angela Carrico, *Assistant director, IRB*

Nancy Danielov, *Associate director, ORIC*

Tricia Hermanek, *Research compliance coordinator, IRB*

Mandy Kozlowski, *Research compliance coordinator, IACUC*

Sharon Modelski, *Administrative assistant, ORIC*

Andrea Slay, *Senior administrative assistant, IRB*

Elizabeth Smith, *Research compliance coordinator, IRB*

## OFFICE OF SPONSORED PROGRAMS (OSP)

OSP expedites funding for sponsored programs and assures excellent stewardship of financial resources. OSP is responsible for the administration of sponsored programs, which includes management of proposals, grants and contracts, and assists physician-scientists in seeking and managing external funding.

Harmony Maple, MPA, *Director*

Roberta Gerard, BSN, *Assistant director, Post-award*

Colleen Grogan, *Associate director, Grants & Contracts*

Krista Harnish, *Assistant director, Grants & Contracts*

Kristine Martens, JD, *Assistant director, Industry Sponsored Clinical Trials*

Tara Massimino, MA, *Assistant director, Grants & Contracts*

Rochanna Thomas, *Senior administrative assistant*

Greg Wendling, *Assistant director, Post-award*

## INFORMATION TECHNOLOGY (IT)

The IT department provides services supporting desktop management and server services for end users. It aids in the acquisition and/or development of software and hardware systems as well as implementation.

Jason Ruprecht, MBA, *Director*

James Crandall, *Network analyst*

Chris De Espinosa, *Network analyst*

Jefferey Shaw, *Senior network analyst*

Timothy Skimina, MS, *Manager of research computing*

## OFFICE OF THE PRESIDENT AND SCIENTIFIC DIRECTOR

Francine Blazowski, MSW, *Special assistant to the President*

## OFFICE OF THE SENIOR VICE PRESIDENT AND CHIEF OPERATING OFFICER

Peg Rainey, *Executive assistant*

## ENGINEERING

Thomas Morlock

John Van Valkenberg

## FACILITY OPERATIONS

Tony Rankin

## HUMAN RESOURCES

Javette Simmons

## PURCHASING

Gail Wright

## RECEIVING

Steven Simmons

## RESEARCH SUPPORT

Jose Hernandez, DVM, *Director*

Irina Davtyan

Lisa Forman, MS, DVM (*consultant*)

Raul Gonzalez

Alyssa Hoekstra

Brooke Palmer

Jennifer Stierman

Adam Suarez

John (J.C.) Williams

## SAFETY / RADIATION SAFETY

Glenn Sullivan, MBA

## SECURITY

Peter Gorham

## Children's Memorial Research Center Board of Directors 2010

Peter B. Bensinger, Jr.  
Jill Brennan  
Mrs. Charles F. Clarke, Jr. (Eleanor)  
James Donaldson, MD  
James R. Donnelley  
Andrew R. Gelman  
Thomas P. Green, MD  
Mary J.C. Hendrix, PhD  
J. Larry Jameson, MD, PhD  
Kirk B. Johnson  
Malcolm S. Kamin  
Anthony K. Kesman  
Patrick M. Magoon  
James E. Malackowski  
John F. Manley  
Marleta Reynolds, MD  
Hilary Sallerson  
Alan Schriesheim, PhD  
H. Scott Silverman, DPhil  
Jeffrey A. Wolfson  
*Board Advisor:* Arthur L. Holden

## Medical Research Institute Council Officers

*Chairman:* Seth Prostic  
*Vice Chairmen:* JoAnn Eisenberg\*+, Lesli Falk, Corey R. Harris, Alison M. Mitchell  
*Vice Chairmen 2010 Medical Research Campaign and Co-Chairmen 2010 Children's Ball:* Elizabeth S. Appelbaum, Tina Wolf  
*Secretary:* Richard Tannenbaum+  
*Treasurer:* David P. McHugh  
*Legal Advisor:* Sally Venverloh

## Board Committee Chairmen

*Advisory:* Lisa Lewis  
*Annual Giving:* Lisa Florence-Ray, Emilio S. Salvi  
*Corporate:* Gail H. Gassner, Mimi Sherman  
*Data Integrity:* Debra Jarett, Beth Gross, Robin Weissman  
*Golf Event:* Hilary Sallerson  
*Major Gifts:* Ruth Geller, Ned S. Robertson, Sandra Kamin  
*Marketing:* Rebecca Erlich, David Sherman  
*Membership:* Lori Gersten  
David McHugh  
*MRJBF Liaison:* David McHugh, Judy Weitzman  
*Nominating:* Ruth Geller  
*NSMRJB Liason:* Gail Gassner  
*Planned Giving:* Lori Hess

## FACILITIES

### Children's Memorial Research Center

2430 North Halsted Street  
Chicago, Illinois 60614  
773.755.6528  
www.childrensmrc.org

*Publicity:* Marti Zelikoff  
*Research/Education:* Gail Gassner, Danny Zoeller, Mimi Sherman  
*Special Events:* Jenny Patinkin  
*Tribute:* Lori Gersten, Ned Robertson  
*Web Site:* Jennifer Crane

## Board of Directors

Nancy Berberian\*  
Meredith Bluhm-Wolf\*  
Alice Cannon  
Jennifer Crane  
Ashley Dougherty  
Donna G. Drescher\*  
Emily Emmerman\*  
Rebecca Katz Erlich  
Lisa M. Florence-Ray  
Alan Freeman  
Marilyn Freund  
Jacqueline Friedman  
Gail Gassner\*  
Ruth Geller\*\*+  
Andrew R. Gellman+  
Lori Gersten\*  
Lynda Sax Gordon  
Beth M. Gross  
David Heller  
Lori Hess-Pleiss  
Stephen J. Jacobsen  
Debra H. Jarett  
Deborah Jarol  
Malcom S. Kamin+  
Sandra Kamin\*  
Rebecca K. Kempton, MD  
Lisa Lewis\*  
Debra K. Marcus\*  
Bradley Martin  
Steven Mogul  
Virginia Mullin, PsyD  
Jamie Pasquale, PsyD  
Jenny Patinkin\*  
Julie A. Reeder  
Ned Robertson+  
Roger 'Biff' Ruttenberg  
Emilio Salvi  
Ellen Saslow  
David A. Sherman  
Mimi Sherman\*  
H. Scott Silverman, DPhil  
Scott Strusiner  
Robin B. Weissman  
Judy Weitzman  
Gary M. Wolfson+  
Marti Zelikoff  
Debra Ziegelman  
Stephen Zimmer  
Danny Zoller

### The Mary Ann & J. Milburn Smith Child Health Research Program

1840 North Clybourn Avenue  
Chicago, Illinois 60614  
www.childrensmrc.org/  
childhealthresearch

## Sustaining Members

Joan B. Brodsky  
Andrea Kott  
Jan Bergman Weinstein

## MRJBF Co-Chairmen

Ryan Friedman  
Alys Hanzlik

## NSMRJB Co-Chairmen

Courtney Fahn  
Melanie Goodman

## Honorary Life Members

Eva Cohon  
Marilyn Fields\*  
Ellyn K. Katz  
Herbert A. Loeb, III+  
Cindy F. Wile+

## Ex-Officio Directors

Mary J.C. Hendrix, PhD  
Patrick M. Magoon  
Bernard L. Mirkin, PhD, MD\*\*

The MRIC is fortunate to have two thriving junior boards, which also support pediatric biomedical research at Children's Memorial Hospital — the Medical Research Junior Board Foundation (MRJBF) and the North Suburban Medical Research Junior Board (NSMRJB).

## Distinguished Lecturer Seminar Series Committee

*Chair:* Marilyn Lamm, PhD  
Monica Cintron  
Isabelle De Plaen, MD  
Laura Herzing, PhD  
Sookyong Koh, MD, PhD  
Jhumku Kohtz, PhD  
Jennifer Krcmery  
Nikia Laurie, PhD  
Denise Lilly, *Seminar Series Coordinator*  
Yong-Chao Ma, PhD  
Christopher Payne, PhD  
Marcelo Bento Soares, PhD

### Children's Memorial Hospital

2300 Children's Plaza  
Chicago, Illinois 60614  
www.childrensmemorial.org

## News Committee

*Chair:* Peggy Murphy, MILS  
Francine Blazowski, MSW  
William Goossens  
Marianne Reed  
Jason Ruprecht, MBA  
Paul Schumacker, PhD  
Erin Shields  
Cheryl Sroka  
Ellen Szalinski  
Jolanta Topczewski, PhD  
Greg Wendling

## Pritzker Research Library Committee

*Chair:* Philip Iannaccone, MD, PhD  
Sara Ahlgren, PhD  
Jenifer Cartland, PhD  
Jim Crandall  
Laura Herzing, PhD  
Peggy Murphy, MILS, *Librarian*  
Jhumku Kohtz, PhD  
Tara Massimino, MA  
H.J. Przybylo, MD  
Xiao-Di Tan, MD  
Alexis Thompson, MD, MPH

## Radiation Safety Committee

*Chair:* Eugene Anandappa, MD  
Sandra Clark  
Isabelle De Plaen, MD  
Barbara Fleming  
Ken Gray  
Joel Charrow, MD  
Erik King, MD  
Annie Muñana, BSN, MJ  
Michael Mutolo, MS  
Frederick Smith, MD  
Abbey Studer  
*Radiation Safety Officer:*  
Glenn Sullivan, MBA  
Ralphella Washington  
David Wax, MD

## Institutional Animal Care and Use Committee

## Institutional Biosafety Committee

## Institutional Review Board

### Northwestern University Feinberg School of Medicine

303 East Chicago Avenue  
Chicago, Illinois 60611  
www.feinberg.northwestern.edu

\*Advisory Board Member

+Past MRIC Chairman

\*\*Deceased



Children's Memorial  
Research Center  
2430 North Halsted Street  
Chicago, Illinois 60614  
773.755.6528  
[www.childrensmrc.org](http://www.childrensmrc.org)

The Mary Ann & J. Milburn Smith  
Child Health Research Program  
1840 North Clybourn Avenue  
Chicago, Illinois 60614

Children's Memorial Hospital  
2300 Children's Plaza  
Chicago, Illinois 60614

Northwestern University  
Feinberg School of Medicine  
303 East Chicago Avenue  
Chicago, Illinois 60611-3008

To view the 2010 Annual Report online go to [www.childrensresearchreport.com](http://www.childrensresearchreport.com)