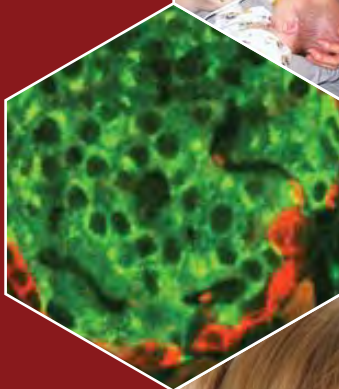
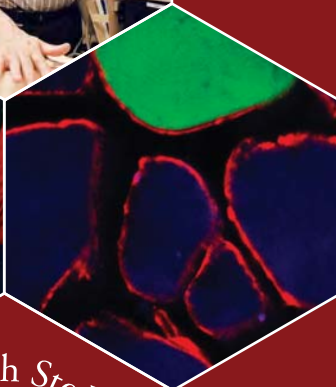


Research Annual Report

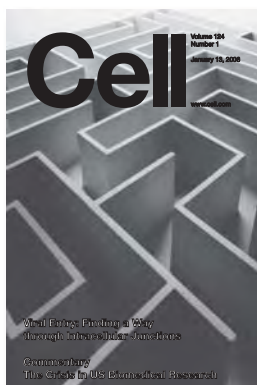
Scientific
Discovery to
Medical
Innovation



2006

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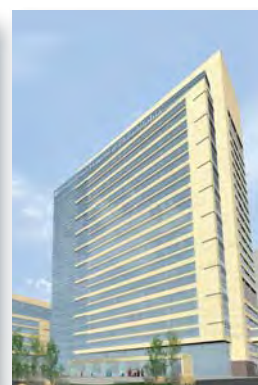
BERGELSON



OFFIT



STANLEY



COLKET

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I have been associated with Children's Hospital as a Board member for more than 30 years. Over those three decades, I have witnessed a real transformation in pediatric medicine. Today, our physicians are curing diseases that were incurable a generation ago.

Just as importantly, we can now prevent many serious childhood illnesses before they ever get started. For example, the rotavirus vaccine developed by scientists at Children's Hospital will ultimately save millions of lives throughout the world. Nevertheless, many debilitating and deadly diseases of childhood are still with us. And some, like obesity, are reaching epidemic proportions that threaten the future health of our children and our nation.

Thus, now more than ever, we must rededicate ourselves to the goal of eradicating serious illnesses in children. I believe this lofty goal can only be achieved through cutting-edge research and the new medicines and vaccines that will emerge from our laboratories and clinics. Children's Hospital and its Joseph Stokes Jr. Research Institute are uniquely poised for this challenge as we move full steam ahead into the twenty-first century. The new research building on our South Campus is but one tangible example of our long-term commitment to our patients and their families.

It is important to recognize that our past and current successes leave us with the responsibility to lead the way in pediatric healthcare. And this is a responsibility we do not take lightly. My sincere hope is that over the next 30 years, we achieve our goal of a world where children flourish untainted by the diseases of today.

Tristram C. Colket Jr.

Chair, Joseph Stokes Jr. Research Institute Board Committee

Stokes Chair

CEO & CSO



SCIENTIFIC DISCOVERY TO MEDICAL INNOVATION

At the Joseph Stokes Jr. Research Institute, our mission is clear and lasting: we advance the health of children by turning scientific discovery into medical innovation. Unfortunately, this compelling raison d'être is "easier said than done." We face enormous and diverse challenges in our quest to improve the lives of children. The dwindling NIH budget, a raging war for talent and a constant barrage of disruptive technologies are just a few of the difficult issues we face every day.

These challenges notwithstanding, our progress is unrelenting. Through unique and ambitious programs like the new Center for Applied Genomics, we will soon be able to predict a patient's predisposition to certain diseases of childhood. Armed with this information, individualized treatment approaches can be designed — so-called "personalized medicine." And as we gather this genetic information on behalf of our patients, their families will also benefit, especially when we can offer tailored treatments for diseases like asthma and obesity that can affect entire families. Other programs launched during the year were aimed at providing greater protections for patients taking part in clinical trials, enhancing services and resources available to investigators and expanding our physical facilities to meet the needs of the Stokes Institute's growing research program.

These are exciting times at the Stokes Institute and Children's Hospital. Never before has the promise of research been so palpable. The pages of this report represent only a small fraction of the wonderful work that goes on everyday in the laboratories and clinics on our campus. But the stories, captured in pictures and words, can never convey the real impact of what we do. Because this year and for years to come, thousands and thousands of lives will be saved because of research done at Children's Hospital.



Steven M. Altschuler, M.D.
President and Chief Executive Officer



Philip R. Johnson Jr., M.D.
Chief Scientific Officer and Senior Vice President
Director, Joseph Stokes Jr. Research Institute

PURSuing RESEARCH PREEMINENCE

AMBITIOUS PROGRAM LAYS THE FOUNDATION FOR PERSONALIZED MEDICINE

Therapies for many pediatric illnesses today are largely focused on treating the symptoms or consequences of the disease process. What if there were a way to manage a given disease over a lifetime, or prevent it from occurring altogether based on a person's genetic predisposition?



Children's Hospital plans to turn that concept into a reality with the creation of the Center for Applied Genomics, which is leading the search for the genes underlying pediatric diseases. The Center's ultimate aim is to discover important disease-causing genetic variants that will lead to new strategies for prevention and intervention. Some have called this the first step toward "personalized medicine."

Such an individualized approach will focus on treating the *cause* of the disease and not just the *symptoms* or *consequences*, thereby potentially improving children's health and enhancing quality of life.

A critical element in the Hospital's goal of pediatric research preeminence, the Center for Applied Genomics uses state-of-the-art technology to house one of the world's largest programs for detecting gene variations and linking them to particular illnesses, a process called genotyping.

3

The program will focus on some of the most prevalent diseases of childhood — asthma, obesity and diabetes, among others — as well as pediatric cancer, all of which are thought to involve the contributions of multiple, interacting genes. The Center's researchers will then work to translate genetic knowledge into precisely targeted treatments for the diseases in question, customizing treatments to a child's genetic profile.

The Center's genotyping effort makes use of the BeadLab, a highly automated laboratory produced by the biotechnology company Illumina Inc., which can process 264 patient samples per day and simultaneously analyze more than 550,000 genetic variants for each sample. The equipment can produce approximately 150 million genotypes per day, all extracted from blood samples. Children's Hospital will be the only pediatric hospital to have this technology entirely at its disposal.

Hakon Hakonarson, M.D., Ph.D., leads the ambitious program, which early on attracted nationwide attention from the *Wall Street Journal* and *Science*, among other publications.



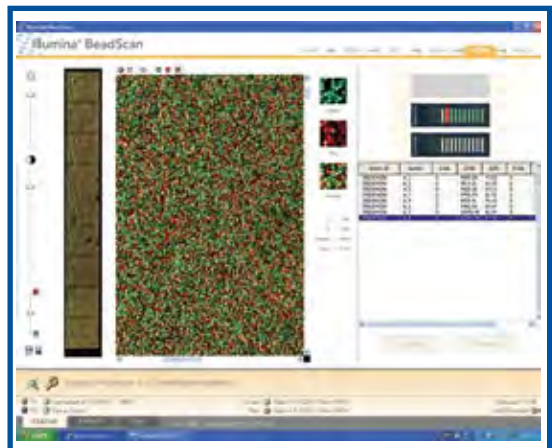
Hakon Hakonarson, M.D., Ph.D., works with Joseph Glessner, bioinformatics analyst, and other staff members in the Center's BeadLab.

Over the next three years, the Center — one of several planned “Centers of Emphasis” aimed at bolstering the Hospital’s translational research program — will analyze blood samples from more than 100,000 children, and employ a sophisticated information-management system to track the samples and store medical records information in an encrypted form to preserve patient confidentiality.

“As one of the world’s largest and most comprehensive pediatric networks, we have a sizable base of patients and families from which to collect data,” says Philip R. Johnson Jr., M.D., the Hospital’s chief scientific officer. “This focused effort in genomics reaffirms that we are absolutely committed to finding cures for childhood diseases.”



Christine Onyiah, research technician, and Cecilia Kim, lab manager, prepare DNA chips for analysis.



BeadScan 3.0 software translates data from raw intensity to a digitized format for export into the BeadStudio analysis software.



Andrew Eckert, lab manager, and Rohan Shroff, research technician, load cartridges of DNA chips into the automated slide reader.



PROGRESS NOTES



INNOVATIVE PROGRAMS, HIGH-IMPACT PUBLICATIONS CHANGING THE FUTURE

As a global innovator in pediatric medicine, the Hospital provides a direct link from the bench to the bedside that allows patients to benefit from and contribute to the vibrant research community. The bench-to-bedside nature of research at the Hospital, in combination with innovative research questions, unique and cutting-edge programs, and interdisciplinary collaborations, enable Children's Hospital to grow despite a significant stagnation in National Institutes of Health (NIH) funding.



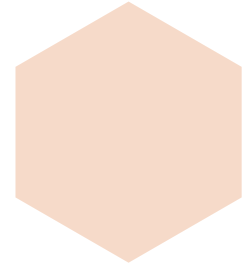
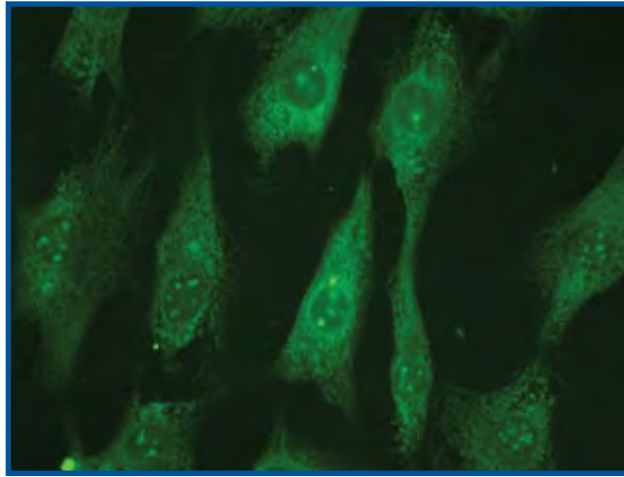
Children's Hospital ranks as the third-largest recipient of NIH funding among pediatric hospitals, receiving 210 awards during fiscal year 2006. The awards featured here represent a small sample of the wide array of research and demonstrate the potential impact of Hospital research on children's health.

The numerous grants awarded to Hospital researchers yielded more than 450 publications during the year, including many in high-impact journals such as *Science*, the *New England Journal of Medicine*, *Nature*, *Cell*, the *Journal of the American Medical Association* and the *Proceedings of the National Academies of Science*. While the publications listed here are only a portion of the total for the fiscal year, they demonstrate the significant efforts by Stokes investigators to affect the health of children worldwide.



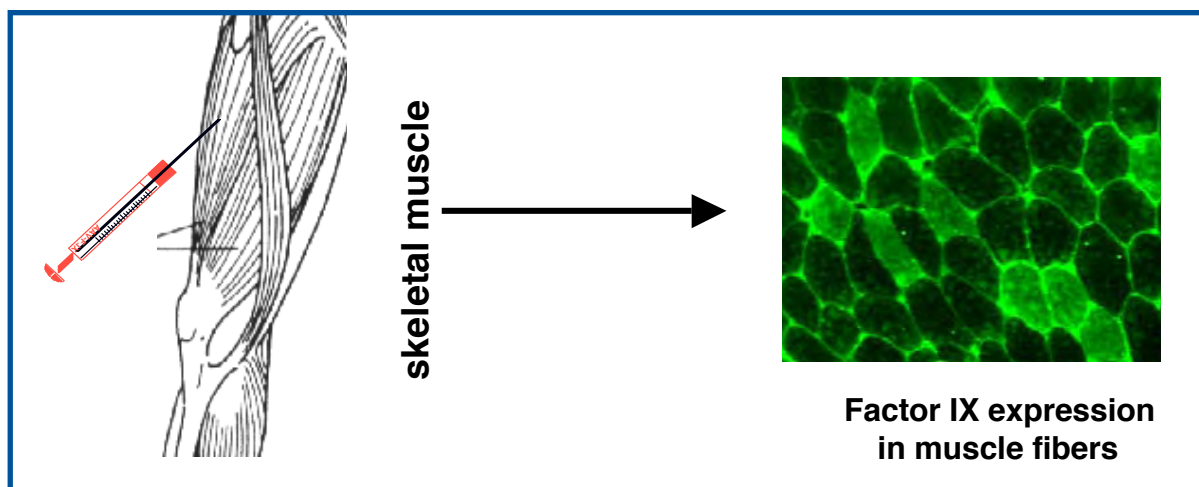
National Children's Study

Children's Hospital, in conjunction with Drexel University School of Public Health, was chosen as one of six "Vanguard Centers" for the NIH National Children's Study, planned as the largest study ever undertaken to assess the effects of the environment on child and adult health. Study researchers are seeking information to prevent and treat such health problems as autism, birth defects, diabetes, heart disease and obesity by examining environmental influences on human health — and their relationship to genetic constitution. **Donald Schwarz, M.D., M.P.H.**, chief, Craig-Dalsimer Division of Adolescent Medicine, serves as the principal investigator of the Children's Hospital-Drexel Vanguard Center.



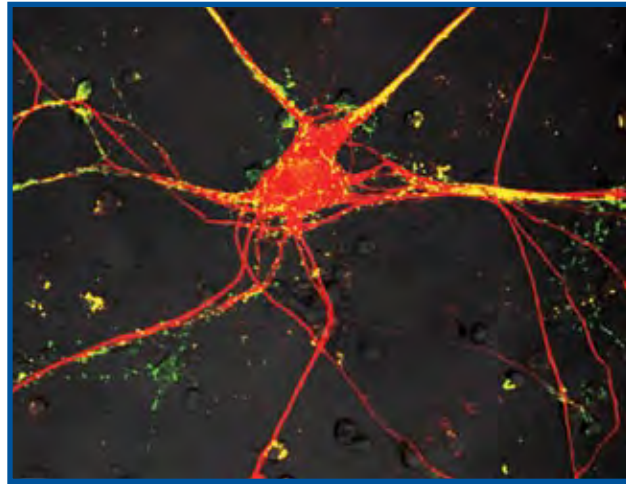
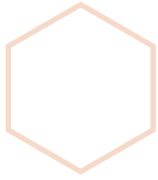
Vaccines

By understanding the mechanisms underlying vaccine responses, investigators may be able to improve vaccinations for immunocompromised patients vulnerable to the risks of influenza and provide new approaches to preventing influenza infection. The National Institute of Allergy and Infectious Diseases awarded Children's Hospital a five-year, \$10.7 million contract as part of its Biodefense program. Led by **Kathleen Sullivan, M.D., Ph.D.**, chief, Division of Allergy and Immunology, the project evaluates influenza vaccine responses in six immunocompromised populations with different specific immunologic deficits to provide insights into the immunologic mechanisms involved in vaccine response.



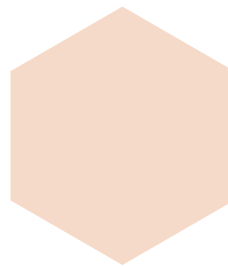
Gene Therapy

The current treatment options for hemophilia have a number of limitations that make it difficult for physicians to provide comprehensive, accessible treatment to all hemophilia patients. NIH recognizes the need for improved treatment strategies and recently awarded Children's Hospital a five-year, \$9.7 million program project grant to continue working toward developing gene therapy treatments for hemophilia. The program, led by Howard Hughes Medical Institute investigator **Katherine High, M.D., Valder Arruda, M.D., Ph.D., and Mortimer Poncz, M.D.**, aims to develop gene-transfer techniques to provide continuous therapy to prevent bleeds, rather than treat them after injury. Dr. High and her colleagues expect to continue making progress toward successful treatment of hemophilia B and to begin clinical trials for hemophilia treatment in the next few years.



Motor Neuron Diseases

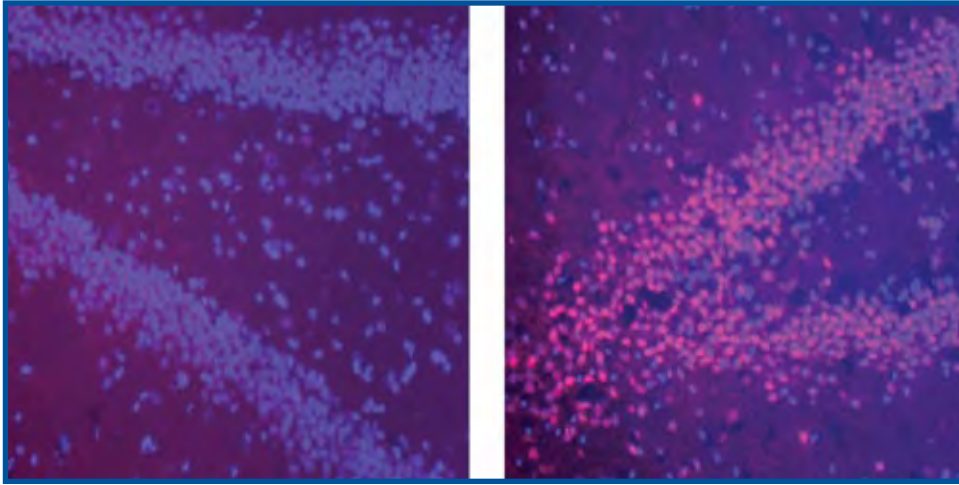
Scientists believe that certain pathophysiological events are common to all forms of motor neuron diseases, which are characterized by progressive weakening and wasting of muscles. NIH granted Children's Hospital a \$1.5 million, five-year award to study the pathogenesis of motor neuron disease. Led by **Robert Kalb, M.D.**, Division of Neurology, the grant supports research focused on small proteins called trophic factors. Specifically, Dr. Kalb's group will focus on cell surface receptors for a trophic factor called brain-derived neurotrophic factor (BDNF). Motor neurons become vulnerable to insult when BDNF binds to and activates a cell surface receptor called TrkB. Blocking TrkB activation can stop many of the insults thought to play a prominent role in motor neuron disease.





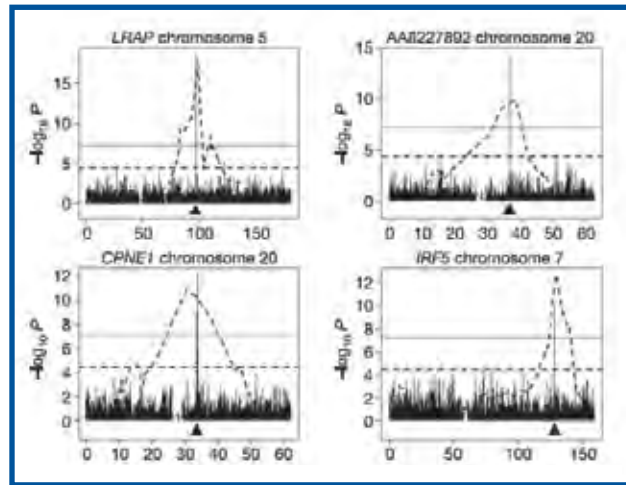
Cornelia de Lange Syndrome

Multiple structural birth defects, slow growth, cardiac abnormalities and mental retardation are some of the hallmarks of Cornelia de Lange syndrome (CdLS), a rare and little-known genetic disorder. Although investigators have shown that mutations in the *Nipped-B-like* (*NIPBL*) gene cause CdLS, the role of the gene in cells is unknown and it remains unclear how the mutations result in the multisystem problems seen in patients with CdLS. A multicenter team led by **Ian Krantz, M.D.**, Division of Human Genetics and Molecular Biology, hopes to characterize *NIPBL*'s function, identify its target genes, and evaluate their roles in causing the birth defects often seen in CdLS with the aid of a five-year, \$5 million program project grant from the National Institute of Child Health and Human Development.



Epilepsy

Growing evidence suggests that abnormalities in inhibitory neurotransmission play a critical role in epilepsy. Research has demonstrated that long-term changes in the expression of certain receptor subunits that mediate the action of neurotransmitters, such as GABRA1, occur after prolonged seizures and are associated with marked changes in receptor pharmacology and function. NIH granted an award to **Amy Brooks-Kayal, M.D.**, Division of Neurology, to build upon her previous research that suggested regulation of GABRA1 expression could be an important target for developing new therapies to prevent or treat epilepsy. Specifically, she will examine how two signaling pathways regulate *GABRA1* after prolonged seizures and determine if the constellation of transcription factors that interact with the *GABRA1* promoter in the signaling pathways changes after prolonged seizures.



Genetics

Association analysis may be a tool to overcome some of the challenges of finding genes that contribute to complex diseases. This technique allows investigators to identify co-occurrence of a genetic variant and a disease (or phenotypic trait). **Vivian Cheung, M.D.**, Division of Neurology, led the first genome-wide association study to identify regulators that influence the expression level of human genes. The results confirm some of the regulators previously mapped by this group using a genetic linkage approach. The study results, published in *Nature*, suggest that with advances in genomic technologies and analysis methods, large-scale association studies will become a practical means to identify genes for complex traits and diseases.

Cheung VG, Spielman RS, Ewens KG, Weber TM, Morley M, Burdick JT. Mapping determinants of human gene expression by regional and genome-wide association. *Nature*. 2005 Oct 27;437(7063):1365-9.



Infection

Group B coxsackieviruses (CVBs) — well-known etiologic agents of meningitis and heart inflammation — must cross the epithelium of the gastrointestinal tract to cause infection. **Carolyn Coyne, Ph.D.**, a postdoctoral fellow working with **Jeffrey Bergelson, M.D.**, Division of Infectious Diseases, found that CVBs trigger two distinct intracellular signals to enter epithelial cells by exploiting decay-accelerating factor (DAF)-mediated signaling pathways. The results, published in *Cell*, show that activation of the tyrosine kinase Abl permits a virus to move to the cell's tight junction and interact with the major CVB receptor, coxsackievirus and adenovirus receptor (CAR), which is not accessible on the cell surface. Once in the junction, interaction with CAR promotes conformational changes in the virus needed for the virus to enter cells. The investigators also found a second signaling pathway that leads to virus entry in specific vesicles called caveolae.

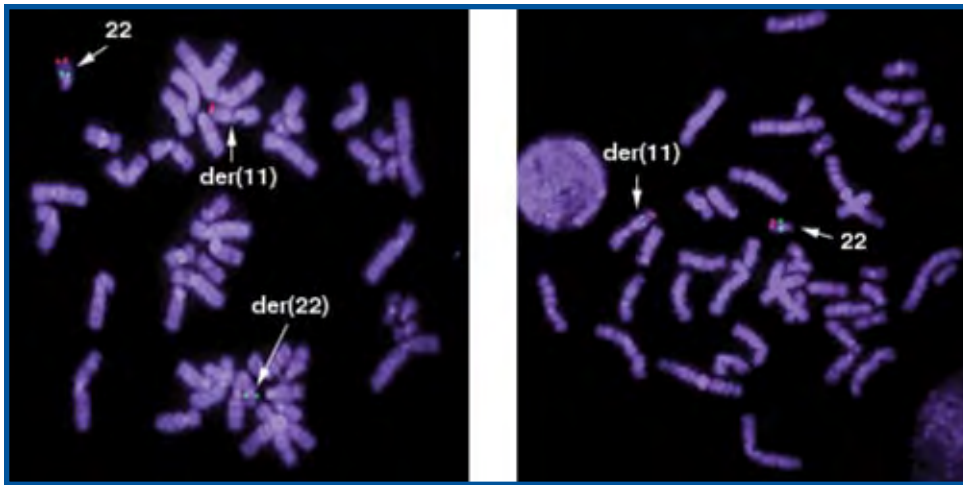
Coyne CB, Bergelson JM. Virus-induced Abl and Fyn kinase signals permit coxsackievirus entry through epithelial tight junctions. *Cell*. 2006 Jan 13;124(1):119-31.



Influenza

Ron Keren, M.D., M.P.H., Division of General Pediatrics, found that patients with neurological and neuromuscular disease are at high risk for respiratory failure caused by influenza. In a retrospective study of 745 patients hospitalized for influenza, respiratory failure requiring mechanical ventilation occurred in 32 patients, and children with neurological and neuromuscular disease were at highest risk for respiratory failure. The study results, published in the *Journal of the American Medical Association*, were new but not surprising, because children with neurological and neuromuscular disease have diminished pulmonary function and ability to handle secretions at baseline. These findings supported the decision of the Advisory Committee on Immunization Practices to add these patients to the list of groups that should have an annual influenza vaccine and highlight the importance of influenza vaccination in these groups.

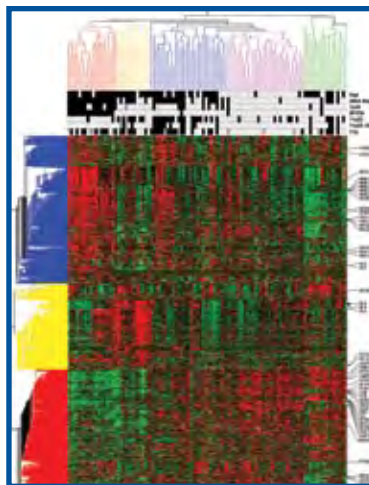
Keren R, Zaoutis TE, Bridges CB, Herrera G, Watson BM, Wheeler AB, Licht DJ, Luan XQ, Coffin SE. Neurological and neuromuscular disease as a risk factor for respiratory failure in children hospitalized with influenza infection. *JAMA*. 2005 Nov 2;294(17):2188-94.



Emanuel Syndrome

A “carrier” of the translocation that causes Emanuel syndrome, while generally healthy, has a balanced rearrangement derived by a swapping of genetic material between chromosomes 11 and 22. All of the “carrier’s” cells have the right number of chromosomes but carry the constitutional $t(11;22)$ translocation and his or her offspring may have Emanuel syndrome. **Beverly Emanuel, Ph.D.**, chief of the Division of Human Genetics and Molecular Biology, found that the genetic rearrangements that create new “carriers” of this translocation are less random than previously thought and are likely to occur more frequently in some people. In healthy men with DNA containing longer palindromic sequences — repetitive stretches of DNA bases that are unstable and rich in the bases adenine and thymine — newly arising $t(11;22)$ translocations occurred in one in 100,000 sperm cells, a higher frequency than in men with shorter sequences. These findings, which show the importance of genome sequence and configuration on human chromosomal rearrangements, were published in *Science*.

Kato T, Inagaki H, Yamada K, Kogo H, Ohye T, Kowa H, Nagaoka K, Taniguchi M, Emanuel BS, Kurahashi H. Genetic variation affects de novo translocation frequency. *Science*. 2006 Feb 17;311(5763):971.



Neuroblastoma

Genomic changes in neuroblastoma tumors can be used to distinguish patients with aggressive disease from those with a high likelihood of cure, an important step in customizing treatments for individual patients. Oncologist **John Maris, M.D.**, led an investigation to analyze the gene defects within tumor samples. The study found that loss of heterozygosity (LOH) — the loss of one copy of a gene due to damage or mutation — on chromosome bands 1p36 and 11q23 were independent markers of worse outcomes for patients, regardless of other prognostic clues. Based on these findings, the Children's Oncology Group now uses chromosome arm 1p and 11q LOH assays to stratify therapy for children for whom prognosis is difficult to determine. The study was published in the *New England Journal of Medicine*.

Attiyeh EF, London WB, Mosse YP, Wang Q, Winter C, Khazi D, McGrady PW, Seeger RC, Look AT, Shimada H, Brodeur GM, Cohn SL, Matthay KK, Maris JM; Children's Oncology Group. Chromosome 1p and 11q deletions and outcome in neuroblastoma. *N Engl J Med*. 2005 Nov 24;353(21):2243-53.



Gene Delivery

Metallic stents that expand blocked arteries can cause complications if the polymer coating used to deliver drugs to the artery causes an inflammatory response and reobstructs the artery. Cardiologist **Robert Levy, M.D.**, the William J. Rashkind Endowed Chair in Pediatric Cardiology, discovered a method to attach therapeutic gene vectors — small pieces of DNA used for treatment — to the metallic stent without using the polymer associated with inflammation. Published in the *Proceedings of the National Academy of Sciences*, these results are the first to show that vector delivery can be achieved using polyallylamine bisphosphonate, a unique water-soluble compound that binds gene therapy vectors to the stent's metallic surface. These results may lead to the use of implantable medical devices to deliver gene therapy for other disease treatments.

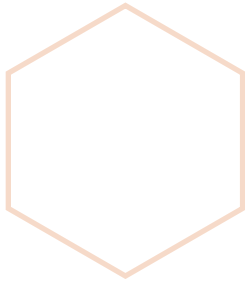
Fishbein I, Alferiev IS, Nyanguile O, Gaster R, Vohs JM, Wong GS, Felderman H, Chen IW, Choi H, Wilensky RL, Levy RJ. Bisphosphonate-mediated gene vector delivery from the metal surfaces of stents. *Proc Natl Acad Sci U S A*. 2006 Jan 3;103(1):159-64.



Injury

Dennis Durbin, M.D., M.S.C.E., and Kristy Arbogast, Ph.D., Division of Emergency Medicine, found that sport utility vehicles (SUVs) do not provide superior protection for child occupants and that age- and size-appropriate restraints and rear seating are critically important to minimize the risk of injury. SUVs and passenger cars have similar injury risks, due to SUVs' increased risk for rollovers. Rollover occurred more than twice as frequently in SUVs, partially offsetting the potential safety benefits associated with the larger, heavier-weight vehicles. Children involved in rollover crashes were three times as likely to be injured as children in non-rollover accidents. The study results, published in *Pediatrics*, also show that nearly half the unrestrained children in SUV rollovers suffered serious injury, versus only 3 percent of appropriately restrained children, a nearly 25-fold difference in the odds of injury. The overall risk of injury for appropriately restrained children in passenger cars is less than 2 percent.

Daly L, Kallan MJ, Arbogast KB, Durbin DR. Risk of injury to child passengers in sport utility vehicles. *Pediatrics*. 2006 Jan;117(1):9-14.

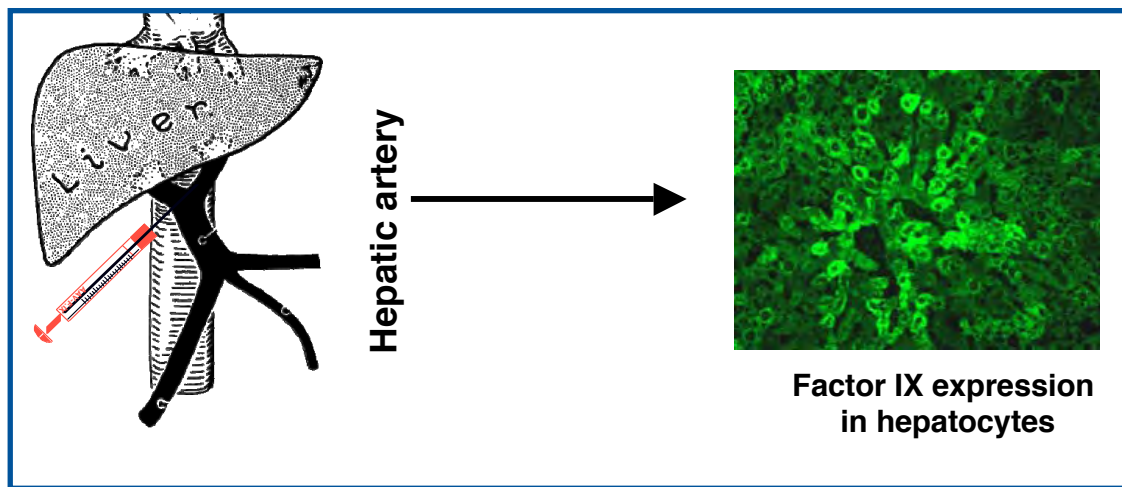


Cardiac Arrest and Resuscitation

Vinay Nadkarni, M.D., and colleagues including Peter Meaney, M.D., M.P.H., Department of Anesthesiology and Critical Care Medicine, led the largest-ever study of cardiac arrests and found that about one quarter of children who have in-hospital cardiac arrests have abnormal heart rhythms that require electric shock — an occurrence that physicians often assume is extremely rare. Two studies analyzing the American Heart Association's National Registry of CPR, published in the *Journal of the American Medical Association* and the *New England Journal of Medicine*, revealed that a significant number of children with cardiac arrest have arrhythmias that may respond to cardiac, not respiratory, interventions. With the appropriate treatment, more than 27 percent of children and 18 percent of adults with pulseless cardiac arrests survived to hospital discharge, mostly with good neurological outcomes.

Nadkarni VM, Larkin GL, Peberdy MA, Carey SM, Kaye W, Mancini ME, Nichol G, Lane-Truitt T, Potts J, Ornato JP, Berg RA; National Registry of Cardiopulmonary Resuscitation Investigators. First documented rhythm and clinical outcome from in-hospital cardiac arrest among children and adults. *JAMA*. 2006 Jan 4;295(1):50-7.

Samson RA, Nadkarni VM, Meaney PA, Carey SA, Berg MD, Berg RA, for the AHA National Registry of CPR investigators. Outcomes of In-hospital Ventricular Fibrillation in Children. *N Engl J Med*. 2006;354:2328-39.



Hemophilia

Hemophilia B is a bleeding disorder caused by mutations in the gene for a blood plasma protein called factor IX. **Catherine Manno, M.D., Valder Arruda, M.D., Ph.D.,** and HHMI investigator **Katherine High, M.D.,** led a clinical study using recombinant adeno-associated viral-2 (rAAV-2) vectors expressing factor IX for hemophilia B. The results, published in *Nature Medicine*, show that rAAV-2 vectors can directly transduce human liver cells *in vivo* to result in therapeutic levels of factor IX. The doses studied were not associated with acute or long-lasting toxicity, and the study successfully identified a dose to achieve a therapeutic level of factor IX for approximately six to eight weeks. The investigators plan to conduct future studies to achieve long-lasting, sustained expression in humans through a modified protocol that will alter the immune response to the transduced cells.

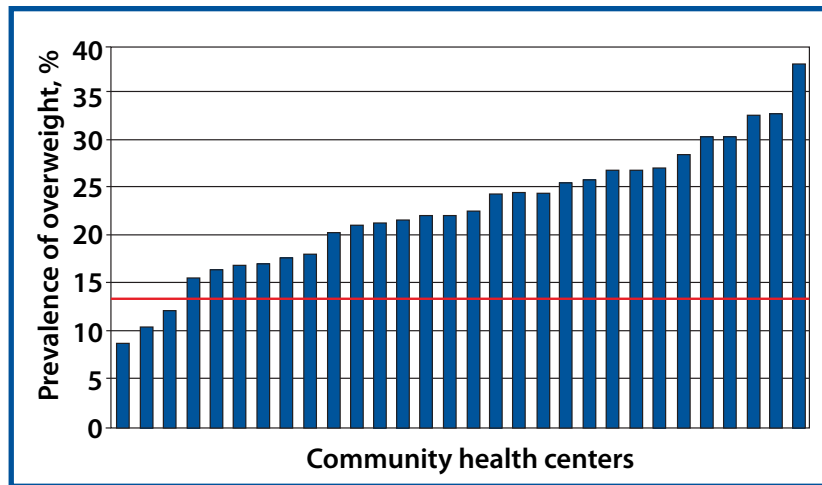
Manno CS, Arruda VR, Pierce GF, Glader B, Ragni M, Rasko J, Ozelo MC, Hoots K, Blatt P, Konkle B, Dake M, Kaye R, Razavi M, Zajko A, Zehnder J, Nakai H, Chew A, Leonard D, Wright JF, Lessard RR, Sommer JM, Tigges M, Sabatino D, Luk A, Jiang H, Mingozi F, Couto L, Ertl HC, High KA, Kay MA. Successful transduction of liver in hemophilia by AAV-Factor IX and limitations imposed by the host immune response. *Nat Med*. 2006 Mar;12(3):342-7.



Vaccine Practices

During the early 1950s, polio was the cause of widespread panic. A polio vaccine developed by Jonas Salk promised an end to the devastating epidemic. However, a number of polio cases occurred in infants and children who received the vaccine produced by Cutter Laboratories, one the vaccine's five American producers. **Paul Offit, M.D.**, chief of the Division of Infectious Diseases, authored a critically acclaimed book titled *The Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis*. Dr. Offit provides a comprehensive account of the events surrounding the polio vaccine and the Cutter incident, the lasting consequences of these events, and powerful social commentary that calls for reevaluation of vaccine practices in the United States.

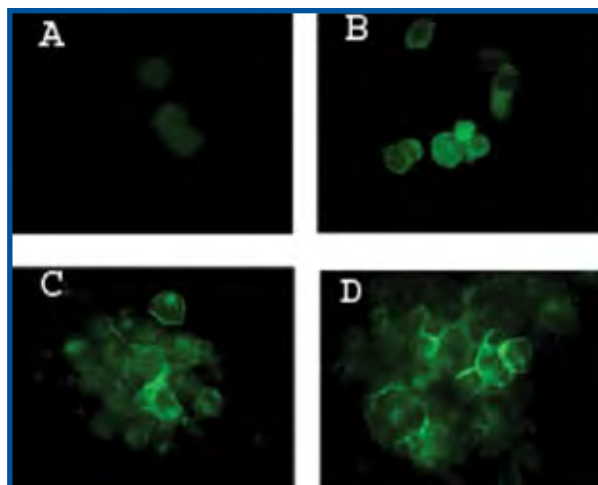
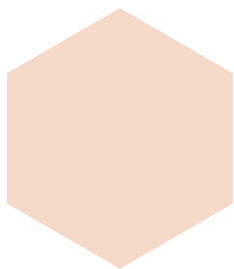
Offit PA. *The Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis*. New Haven:Yale University Press, 2005.



Obesity

Nicolas Stettler, M.D., M.S.C.E., Division of Gastroenterology, Hepatology and Nutrition, found a higher prevalence of overweight children in 27 community health centers, compared with children in the general population. The greater prevalence was particularly prominent in younger children but present regardless of race, gender, ethnicity or geographic characteristics. These findings suggest that children who use community health centers may be at particularly high risk for obesity and that the condition has an earlier onset in the more than 4.7 million children served by such centers. Identifying this high-risk population may be useful for optimally directing services, training and research resources for pediatric obesity prevention. This study was published in *Pediatrics*.

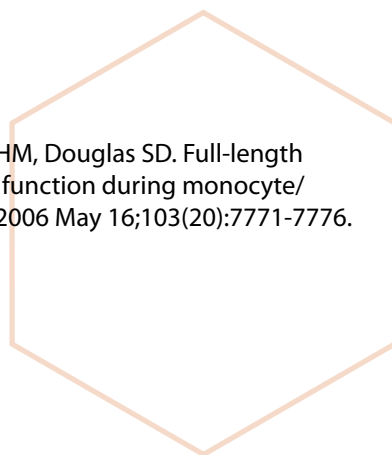
Stettler N, Elliott MR, Kallan MJ, Auerbach SB, Kumanyika SK. High prevalence of overweight among pediatric users of community health centers. *Pediatrics*. 2005 Sep;116(3):e381-8.



Cellular Signaling

The neurokinin-1 receptors (NK-1R) are docking sites for substance P, a neurotransmitter that plays important roles in the immune and nervous systems. **Steven D. Douglas, M.D.**, chief of the Section of Immunology, led a study that investigated two forms of NK-1R and found that they both responded to substance P with an increase in calcium ions but used distinct signaling pathways. Aprepitant, a drug that binds to NK-1R to block its activity, inhibited signaling from both forms. The observed differences between the forms of NK-1R offer insights into the differences in signaling pathways and the mechanisms by which they interact with other molecules. These findings, published in the *Proceedings of the National Academy of Sciences*, also advance the scientific foundation for a potential HIV treatment that may block the virus that causes AIDS.

Lai JP, Ho WZ, Kilpatrick LE, Wang X, Tuluc F, Korchak HM, Douglas SD. Full-length and truncated neurokinin-1 receptor expression and function during monocyte/macrophage differentiation. *Proc Natl Acad Sci U S A*. 2006 May 16;103(20):7771-7776.



ENDOWED CHAIRS

PROVIDING CRITICAL SUPPORT FOR RESEARCH, PROGRAMS

Endowed chairs are among the most influential forms of philanthropy at Children's Hospital. Funds from these generous gifts support investigators who seek to break new ground and forge paths critical to understanding and treating disease and providing optimal care to children on a variety of fronts.



Endowed chairs also help support the institution's longstanding mission to provide training and education to the next generation of pediatric investigators, whose vision and determination are essential elements of the Hospital's evolution toward pediatric research preeminence.

Since its inception in the mid-1980s, the Hospital's endowed chair program has flourished and now includes 63 chairs. The program's support for research is a particular asset to the Hospital's drive to recruit the best and brightest investigators.

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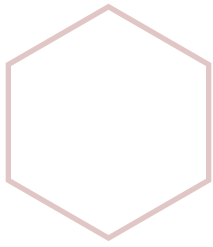
Endowed chairs support research across all pediatric subspecialties, including neonatology, oncology, neurology, cardiology and infectious diseases. The program also supports specialized research in pediatric diabetes, liver disease, rehabilitation medicine, child abuse, nursing and genomics, among other areas.

Children's Hospital Board of Trustees ratified the establishment of two new endowed chairs in fiscal year 2006 to support the Hospital's growing research program: the John W. Duckett Jr. Endowed Chair in Pediatric Urology and the Oberkircher Family Chair in Pediatric Radiology.

The Duckett Chair honors the memory of John Duckett, M.D., who joined the Hospital's Division of Urology in 1970 and served as its director from 1972 until his death in 1997. Dr. Duckett was a world-renowned urologist acclaimed for his innovations in pediatric surgical techniques that became the treatments of choice around the world. He operated on more than 13,500 children during his 27 years of service to Children's Hospital. The Duckett Endowed Chair was established through a fund from former colleagues, students and patients, as well as Children's Surgical Associates Inc. and the Division of Urology.



John Duckett, M.D.



The Oberkircher Family Chair in Pediatric Radiology is made possible through a generous contribution by David and Kathy Oberkircher. It is named for David's father, Paul E. Oberkircher, M.D., who was passionately committed to the field of radiology and served for a time as a clinical professor of Radiology at the Hospital of the University of Pennsylvania. The chair honors his legacy by supporting Children's Hospital's clinical, research and teaching efforts in radiology as a tool to diagnose and treat children.

Timothy Roberts, Ph.D., the vice-chair of research for the Department of Radiology at Children's Hospital, holds the Oberkircher chair. His work focuses on developing novel radiologic imaging technologies.



Paul Oberkircher, M.D., at the dedication of the Oberkircher Family Endowed Chair in Pediatric Radiology.



Timothy Roberts, Ph.D., chair holder (seated), with members of the Oberkircher family and Hospital staff.



Timothy Roberts, Ph.D., and Richard I. Markowitz, M.D., former president of the medical staff.

NURSING RESEARCH

FOCUSING ON THE ART AND SCIENCE OF NURSING RESEARCH

The word “nurse” often conjures images of compassionate caregivers, supporting and comforting patients and attending to their every need — the art of the discipline that complements the science of the field.

The science of nursing is coming into greater view at Children’s Hospital as nurses emerge as scholars and an integral component of the Hospital’s research enterprise. In this role, Children’s Hospital nurses are helping to shape the future of pediatric healthcare.



In addition to their clinical responsibilities, nurses may take on roles as coordinators on research teams or undertake their own areas of investigation based on a need or problem they perceive in the clinical setting.

“Children’s Hospital nurses provide cutting-edge care in the clinical setting, and questions naturally arise about the evidence supporting what nurses do and ways to improve patient care,” says Leslie Clarke, R.N., M.S., M.B.A., senior vice president and chief nursing officer at Children’s Hospital. “Nursing research is there to answer those questions specific to nursing clinical practice, education and leadership.”

There are approximately 85 research projects involving nurses at Children’s Hospital, spanning multiple subspecialties and issues, including diabetes, HIV, patient safety, CPR, breastfeeding and end-of-life care.

The prospect for contribution to research and patient care innovation from

Children's Hospital nurses is enhanced by the recent recruitment of doctorally prepared nurses to lead and support the development of the Hospital's pediatric nursing research program.

These doctorally prepared nurses will serve as leaders, mentors and consultants to current and future bedside nurse scholars, helping them develop research questions and guiding them through the process of inquiry. The nurse researchers also will evaluate the applicability of nursing research to effective and efficient patient care and outcomes, while maintaining their own active research programs and engaging in multidisciplinary collaborative research.

"It is through the nurse at the point of care and rigorous scientific inquiry that we can advance pediatric nursing research at Children's Hospital," Clarke says. "This work will further support and enable Children's Hospital nurses as they advance their expertise in clinical care, education and leadership — and help create a new era in pediatric health."



Barbara Medoff-Cooper, Ph.D., F.A.A.N., helps a mother use an infant feeding monitoring system that enables researchers to discern patterns in feeding behaviors.

Nursing research at Children's Hospital was given a significant boost by the appointment of Barbara Medoff-Cooper, Ph.D., F.A.A.N., as the Ruth M. Colket Endowed Chair in Pediatric Nursing.

The Colket Chair in nursing, one of 63 endowed chairs at Children's Hospital, recognizes and supports nurses with doctoral degrees who conduct cutting-edge research. The chair embodies the Hospital's philosophy of collegueship, offering nurses the opportunity to conduct research alongside physicians and play a significant role in shaping a new era of pediatric health.



The first University of Pennsylvania School of Nursing faculty member to be appointed to a Children's Hospital endowed chair, Dr. Medoff-Cooper investigates infant development, feeding behaviors in high-risk infants and infant temperament. She serves as principal investigator and co-investigator of several grants in collaboration with Children's Hospital researchers and has received numerous research awards, including five from the NIH to study neurodevelopmental outcomes of high-risk infants. She is also the director of the Center for Biobehavioral Research at the University of Pennsylvania School of Nursing and has received the university's Helen M. Shearer Professorship in Nutrition.

"What is exciting about being the recipient of this endowed chair is the recognition that nursing research matters and makes a contribution to the overall health and well-being of our nation's children," says Dr. Medoff-Cooper.

Nursing Chair

INNOVATION FUELING PROGRESS

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INNOVATIVE RESEARCH COULD LEAD TO NEXT GENERATION OF HEART VALVES



Surgery remains the most effective therapeutic strategy for treating heart valve disease, a congenital condition diagnosed in as many as 5 million children and adults in the U.S. each year. Because of the invasive nature of most surgical procedures and the potential for serious side effects, investigators are looking into ways to focus therapy on a precise target by using regional, or site-specific, approaches instead of traditional systemic therapy.



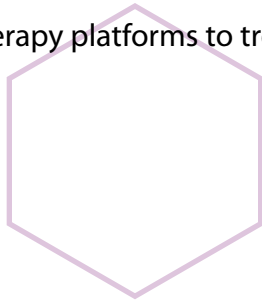
Site-specific therapy for heart valve disease is one of the main research interests of Robert J. Levy, M.D., the William J. Rashkind Chair in Pediatric Cardiology and director of the Division of Cardiology's research laboratories. Such a therapeutic approach allows physicians to use unconventional but promising agents that could not be given to patients by other methods, and may allow for more potent treatment to a specific area while reducing side effects.

Dr. Levy's investigations have spanned the entire aspect of heart valve disease, from the developmental biology of the valve to the progression of the disease to the formulation and fabrication of prosthetic heart valves, many of which are in clinical use throughout the world.

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Dr. Levy's investigations have resulted in 25 U.S. patent awards, most of which are for site-specific therapeutic approaches for treating heart valve disease, gene delivery stents for vascular disorders, biomaterials for therapeutic implants and nanotechnology.

His laboratory was the first to report the successful delivery of gene therapy vectors from polymer-coated intravascular stents used to expand blocked arteries. This finding opened the possibility that stents could be used as gene therapy platforms to treat heart valve disease.



In 2006, Dr. Levy's team went on to show that gene vectors could be delivered from the bare metal surfaces of stents without a polymer coating, a finding that could prove useful for virtually any metallic prosthesis and decrease the chances of an inflammatory response.

In ongoing work, Dr. Levy's laboratory has focused increased attention on biomaterials for cardiovascular devices and nanotechnology. In particular, the laboratory is interested in a technique that uses magnetic targeting of nanoparticles to modulate both pharmaceutical and gene therapy approaches to cardiac diseases and disorders.



Robert J. Levy, M.D.

Dr. Levy's innovations in the laboratory have resulted in therapeutic devices used today in patient care. In conjunction with the Minneapolis-based St. Jude Medical, he developed three new bioprosthetic heart valves that are in clinical use. His research team has also synthesized a new protein crosslinker called triglyciudylamine, or TGA, that has been the subject of two patents. This compound could be used for preparing prosthetic heart valve devices or other prostheses, such as artificial cartilage for knee surgery.

Future research will examine the connection between heart valve disease and the neurotransmitter serotonin. This work is part of the Specialized Center of Clinically Oriented Research (SCCOR) on the genetic mechanism in pediatric heart disease. Dr. Levy directs the SCCOR, one of four NIH-supported centers designed to foster multidisciplinary collaborations so that basic research advances are rapidly translated to clinical care.

"This program has been the farthest reaching thus far in terms of laying the groundwork for identifying the genetic basis of congenital heart disease," says Dr. Levy.

"Plans are underway now so that in five to 10 years we will be able to screen all children with heart defects to hopefully identify the genetic basis for virtually all pediatric heart disease and develop therapeutic targets."

Rotavirus

Rotavirus accounts for approximately 70,000 hospitalizations, 500,000 visits to primary care offices, and 20 to 70 deaths annually in the U.S. Throughout the world, the disease is far more lethal, responsible for nearly half a million deaths every year in children under the age of 5.

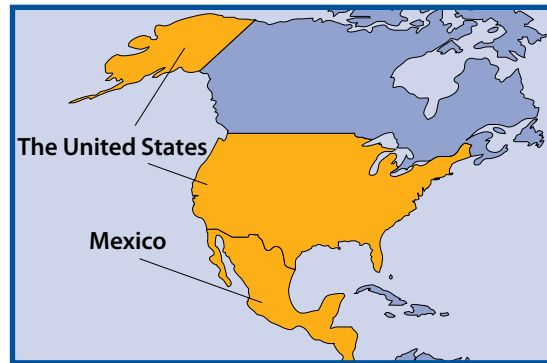
As part of its distinguished legacy of developing vaccines to improve the lives of children, Children's Hospital investigators Paul Offit, M.D., chief, Division of Infectious Diseases; H Fred Clark, D.V.M., Ph.D.; Stanley Plotkin, M.D.; and The Wistar Institute developed RotaTeq®, the oral rotavirus vaccine that was licensed and further developed by Merck & Co. Inc.

After extensive clinical trials involving more than 70,000 subjects, the Food and Drug Administration approved the vaccine for use in the U.S. in February 2006. Shortly thereafter, the government's Advisory Committee on Immunization Practices recommended the vaccine become part of the routine infant immunization schedule. As a result, the demand for the potentially lifesaving vaccine has been great and Merck anticipates 3 million doses will be administered to children in the U.S. by the end of 2006.



The FDA's approval of the vaccine moved the technology developed at Children's Hospital and Wistar ever closer to saving the lives of hundreds of thousands of children around the world. Merck has applied for licensure of RotaTeq® in 70 countries, and the vaccine is nearing approval in Mexico and the European Union.

RotaTeq® will reach developing countries in the near future with the assistance of Merck and the Gates Foundation, which is creating an infrastructure to get the vaccine distributed in the developing world. Small clinical trials are underway in Indonesia and Kenya to ensure the vaccine works and is safe in those and other developing countries before distribution.



Rotavirus

Patent Awards

As Stokes investigators continue their quest to better understand and treat pediatric disease, some discoveries lead to patentable inventions. These patented technologies illustrate the translational relevance of research conducted within the Stokes Institute and may ultimately affect the development of new therapies and products to improve the health and quality of life of children throughout the world.

Seven patents were issued by the U.S. and other countries during fiscal year 2006 for technologies developed by Children's Hospital investigators:

Vivian Cheung, M.D., Division of Neurology, and **Richard Spielman, Ph.D.**, a University of Pennsylvania researcher, received a patent in December for methods used for identifying heterozygous carriers of autosomal recessive diseases. This invention provides a reliable method for rapidly and accurately identifying carriers of recessive genetic disorders.

US Patent 6,979,542

Kevin Franck, Ph.D., Division of Otolaryngology, discovered an improved method of programming and fitting neural prostheses such as hearing prostheses, vision prostheses, tactile sensation prostheses, olfactory prostheses and others. This method ultimately results in enhanced performance of these devices. *US Patent 6,925,332*

Beth Goldberg, R.N., Division of Gastroenterology, Hepatology and Nutrition, invented a low-profile combination device optimized for delivering food or medication to pediatric patients who are unable to chew or swallow properly. The device received a patent in February.

US Patent 6,997,909

Stephen Grupp, M.D., Ph.D., and **Valerie Brown, M.D., Ph.D.**, both of the Division of Oncology, received a patent in April for methods of treating acute lymphocytic leukemia. This invention provides methods for using an immunosuppressive agent in the treatment of early B cell-derived leukemia.

US Patent 7,026,330

Robert Levy, M.D., Peter L. Jones, Ph.D., and **Quanyi Li, Ph.D.,** all of the Division of Cardiology, discovered methods and compositions for enhancing the delivery of a nucleic acid to a cell. The methods and compositions of this invention are of great value in overcoming barriers to successful therapeutic and prophylactic applications of gene therapy.

US Patent 6,919,208

George Rothblat, Ph.D., Division of Gastroenterology, Hepatology and Nutrition, invented a cell culture system for determining the cholesterol efflux potential for serum.

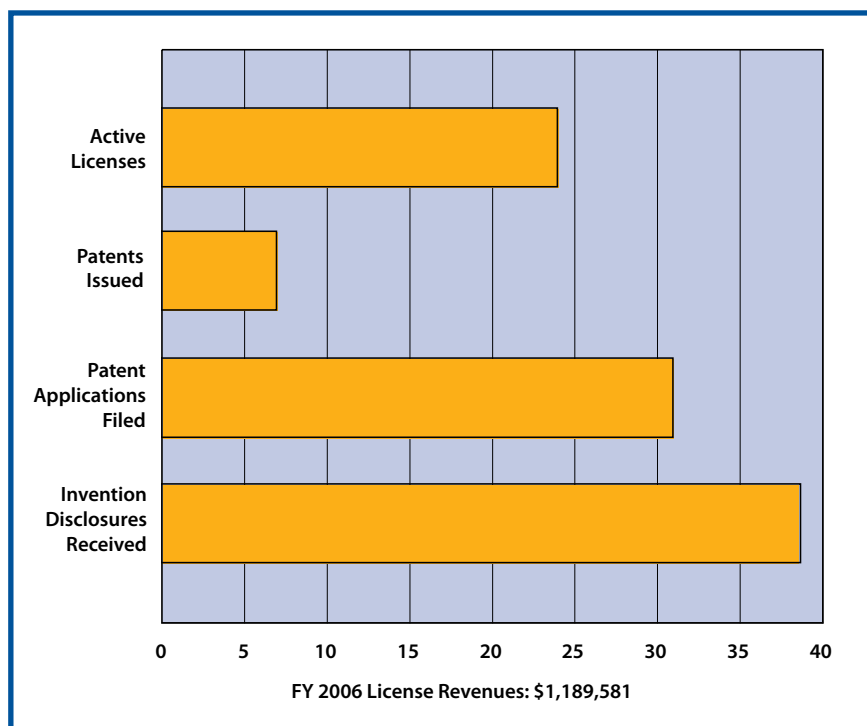
The system, issued a patent in April, provides a tool for assessing the potential of a patient's serum for preventing the accumulation of cholesterol in arteries that leads to atherosclerosis.

US Patent 7,029,863

Former Children's Hospital investigator **Jeffrey Weiser, M.D.,** discovered a method to enhance production of pneumococcal capsular polysaccharide, the encapsulation matrix of streptococcus pneumoniae that is useful as the basis for developing a vaccine against this pathogenic organism.

New Zealand Patent 521343,

Australian Patent 20011245795



THE WAR FOR TALENT

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NEW INVESTIGATORS



To turn scientific discovery into medical innovation, Children's Hospital continuously adds to the cadre of talented investigators working to advance research and children's health. The Stokes Institute actively pursues investigators with proven expertise or fresh approaches to research in their areas of specialty.





New investigators at the Institute strengthen the research program and breathe new life into both laboratory and clinical research at Stokes.

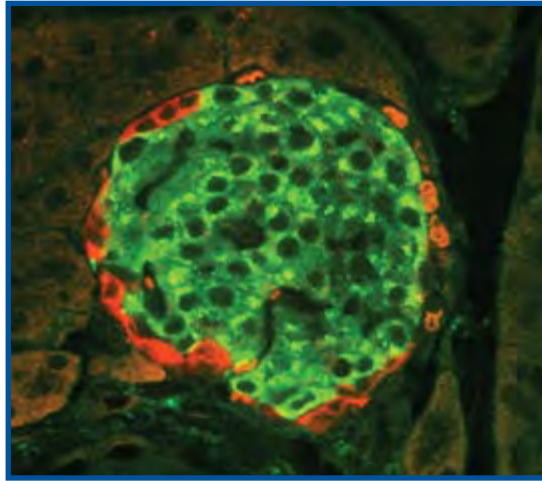
The following investigators are just a few of the approximately 40 who joined Children's Hospital or received a faculty appointment during the fiscal year.

The wide array of their research specialties are representative of the diversity of the research focus and investigative techniques that new investigators bring to Stokes.



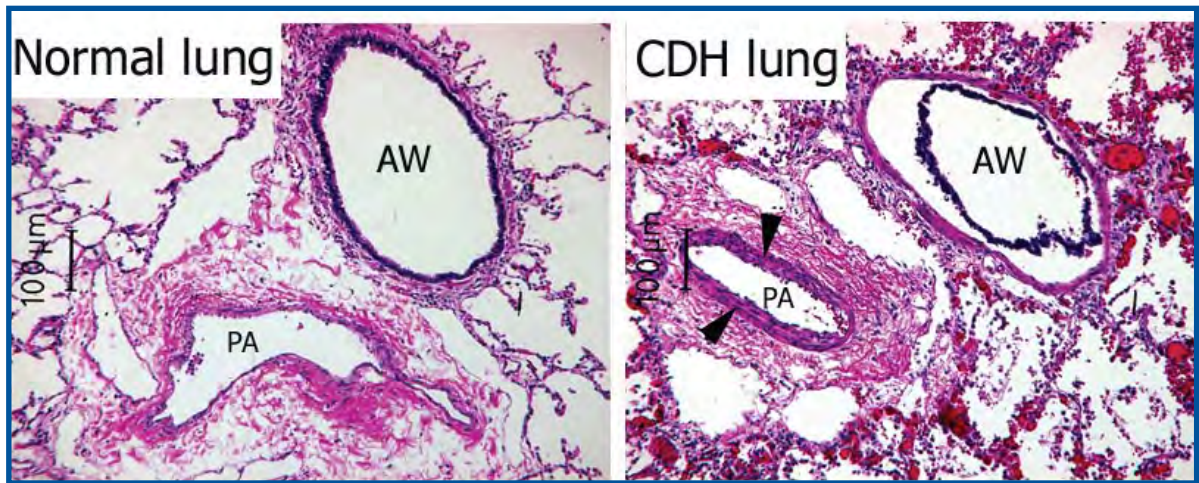
Regenerative Medicine

Tim Brazelton, Ph.D., Division of General, Fetal and Thoracic Surgery, performs research in regenerative medicine, specifically on the role of physiologically circulating stem cells (CSCs), “adult” stem cells that arise from the bone marrow compartment throughout life. Dr. Brazelton focuses on the pathway by which CSCs contribute to skeletal muscle regeneration, which normally occurs at a low frequency but can be increased substantially by unknown regulatory signals. The long-term objective of his research is to identify the receptors and damage-induced factors that allow specific and robust recruitment of CSC to sites where they are needed. A better understanding of the prerequisites for this transition is not only of fundamental interest but could potentially result in novel therapies for acquired and inherited muscle-wasting diseases.



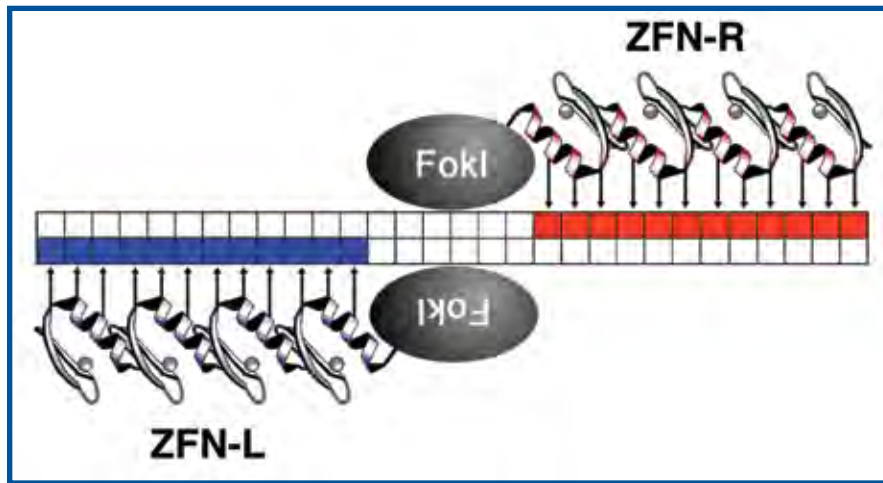
Diabetes

Catherine Lee May, Ph.D., Department of Pathology and Laboratory Medicine, aims to understand type 1 and type 2 diabetes by examining β -cell development and the maintenance of proper pancreas function. Using genetic approaches to understand how the pancreas is formed, Dr. May investigates the roles of transcriptional regulation in both pancreatic development and in maintaining β -cell function and growth in the adult pancreas by the gene, *Islet-1* (*Isl-1*). *Isl-1* may be involved in β -cell differentiation as well as in maintaining pancreatic β -cell function and/or growth in adults. Dr. May's laboratory has generated knockout models of *Isl-1* with the goal of identifying the roles of *Isl-1* during pancreas development, function and growth.



Fetal Surgery

Marcus Davey, Ph.D., Department of Surgery, focuses his research on congenital diaphragmatic hernia (CDH), a condition that occurs when the fetal diaphragm fails to develop normally, allowing abdominal organs to invade the thoracic cavity and compress the developing heart and lungs. Research in Dr. Davey's laboratory centers on reversing underdevelopment of the lungs seen in CDH by fetal tracheal occlusion. As part of his research, Dr. Davey investigates adjunct therapies to fetal tracheal occlusion, including exogenous surfactant therapy and prenatal exposure to glucocorticoids, which have been found to dramatically enhance postnatal gas exchange. His research is also focused on investigating novel vasodilator drugs and lung-specific delivery strategies for pulmonary hypertension, a condition secondary to underdevelopment of the lungs and a major determinant of neonatal survival in CDH.



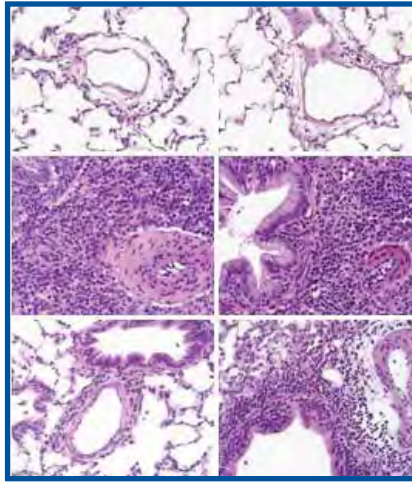
Immunology

Pediatric immunologist **Elena Perez, M.D., Ph.D.**, Division of Allergy and Immunology, has been involved in translational research for therapy for HIV-1 and plans to move to translational research in gene therapies for primary immunodeficiency diseases. In collaboration with Sangamo Biosciences, Dr. Perez is working on a novel approach for gene disruption using zinc finger protein nucleases to knockout the CCR5 co-receptor for HIV in T cells, a primary target of HIV. Generating HIV-resistant cell populations may be a therapeutic intervention in the treatment of HIV/AIDS. Dr. Perez also investigates the potential use of these techniques for the development of adoptive immunotherapies of primary immunodeficiencies.



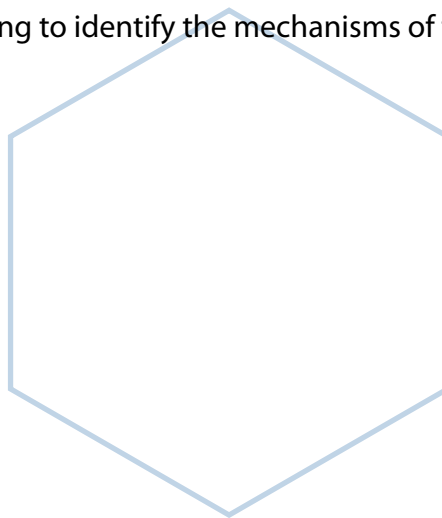
Anesthesia

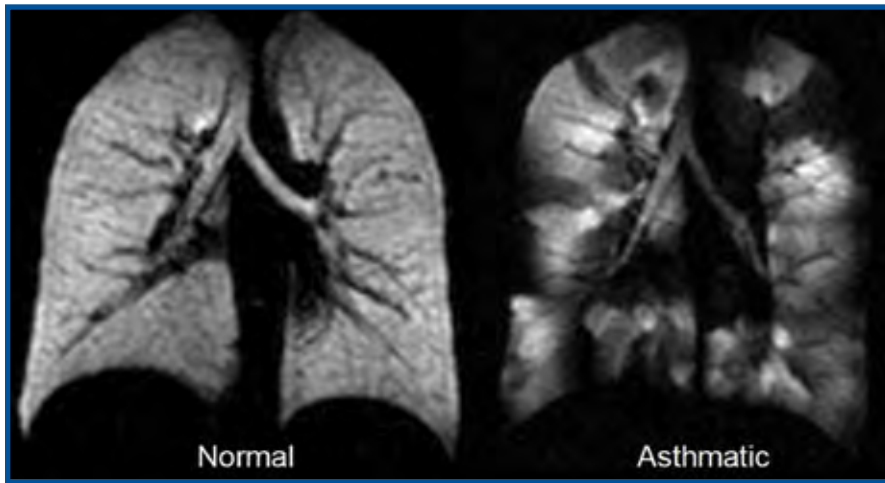
Some pediatric diseases can be deadly to a developing fetus, and sometimes surgical intervention on the fetus *in utero* allows the fetus to grow and survive to birth — and hopefully into childhood and adulthood. **Kha Tran, M.D.**, joined the Department of Anesthesiology and Critical Care Medicine to investigate the use of anesthesia during fetal surgery, especially with respect to twin-twin transfusion syndrome. This syndrome occurs when a woman is carrying twins and one receives too much blood flow while the other does not get enough. Surgery can be performed to correct the situation, but because this area of surgery is relatively new, anesthesia techniques are still evolving. Dr. Tran's research is centered on examining historical records to determine if the type of anesthesia provided for this surgery is associated with improved survival for one or both twins.



Transplantation

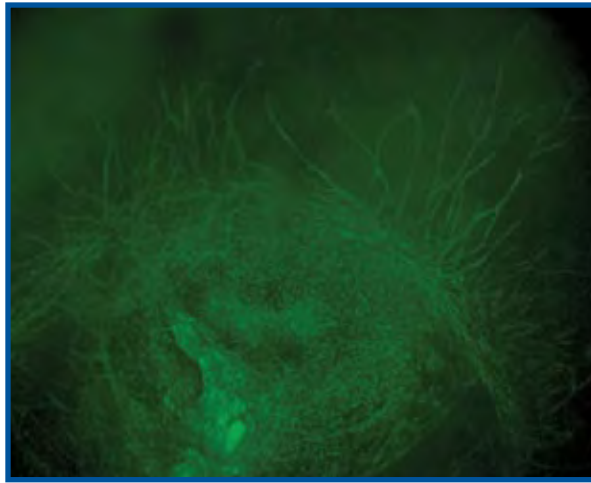
Lung transplantation often carries poor long-term survival as a result of a variety of transplant-related complications. **Gary Visner, D.O.**, joined the Division of Pulmonary Medicine to investigate graft survival genes and evaluate the delivery of these genes and their potential role in providing long-term lung graft survival. Specifically, Dr. Visner's laboratory is using a model of lung transplantation to identify the role of indoleamine 2,3-dioxygenase — found to result in remarkable protection against lung transplant rejection and injury — in long-term protection. His lab is also working to identify the mechanisms of the gene's protective actions.





Imaging

Talissa Altes, M.D., Department of Radiology, performs translational research with new imaging modalities. Her primary research focus is on hyperpolarized gas magnetic resonance imaging (MRI). Hyperpolarized gases are a new type of inhaled contrast agent for MRI that provides detailed images of the ventilated airspaces of the lung. Hyperpolarized gas ventilation images may be useful in understanding the pathophysiology of obstructive lung diseases such as asthma, cystic fibrosis and chronic obstructive pulmonary disease. In addition to providing ventilation images, hyperpolarized gases can help image the size of lung structures at the alveolar level. This appears to be a promising area of research in adults with emphysema and children with chronic lung disease of prematurity.



Hypoxia

Preeclampsia and intrauterine growth restriction are the leading causes of fetal, neonatal and maternal morbidity and mortality. In both conditions, improper responses to reduced oxygen levels — known as hypoxia — may play an important role in the progression of the disorders. **Diana Ramirez-Bergeron, Ph.D.**, Department of Pathology and Laboratory Medicine, is interested in understanding how responses to changes in oxygen tension are important for the growth of the embryo. Her lab is also involved in defining the role of hypoxia in the maintenance of cardiovascular progenitor cells. She is focusing on the Hypoxia Inducible Factor protein complex and its involvement in the development of the yolk sac, placenta, heart, vessels and blood. Dr. Ramirez-Bergeron anticipates gaining insight into the regulatory effects of hypoxic responses important in various diseases including preeclampsia and intrauterine growth restriction.

New Division Chief

Leading immunology researcher **Kathleen Sullivan, M.D., Ph.D.**, has assumed the role of chief of the Division of Allergy and Immunology. **Steven Douglas, M.D.**, served as interim chief of the division prior to Dr. Sullivan's appointment.

Dr. Sullivan has been involved with research at the Stokes Institute since joining Children's Hospital in 1993. Her research interests center on the genetics, molecular pathogenesis and immunopathogenesis of autoimmune diseases.

As part of her research, Dr. Sullivan is conducting an evaluation of influenza vaccine response in six immunocompromised populations sponsored by the Biodefense program of the National Institute of Allergy and Infectious Diseases.

Dr. Sullivan was also named the recipient of the University of Pennsylvania's Lady Barbara Colyton Prize for Autoimmune Research. She received the award for her continued research into the inflammatory disorder systemic lupus erythematosus.



Steven Douglas, M.D., and Kathleen Sullivan, M.D., Ph.D.

Jean A. Cortner, M.D., who served as the Hospital's physician-in-chief from 1974 to 1986, passed away May 31 at the age of 74.

During his career with Children's Hospital, Dr. Cortner also served as the William Bennett Professor and chairman of the Department of Pediatrics at the University of Pennsylvania School of Medicine, and was a professor of Genetics.

After stepping down as physician-in-chief, Dr. Cortner spent the next 13 years working in his laboratory and serving as chief of Genetics, director of Children's Hospital's Nutrition Center and director of the Lipid-Heart Research Center until his retirement.

In his honor, the Department of Pediatrics established the Jean Cortner Endowed Chair in Pediatric Gastroenterology.



Jean Cortner, M.D., as the new physician-in-chief and chair of the Department of Pediatrics.



Dr. Cortner working in the lab with his long-standing scientific collaborator, Paul Coates, Ph.D.



Former U.S. Surgeon General C. Everett Koop, M.D., Sci.D., who served as surgeon-in-chief and physician-in-chief at Children's Hospital, with Dr. Cortner.

Tribute

Awards / Recognition

Virginia A. Stallings, M.D., Division of Gastroenterology, Hepatology and Nutrition, has been elected as a member of the Institute of Medicine (IOM). Dr. Stallings was among the 64 members selected from a slate of nominees for professional achievements as a leading researcher in the nutritional needs of children. She is now one of six Children's Hospital investigators bestowed with the honor.

Established by the National Academy of Sciences, IOM serves as a national resource for science-based advice on matters of biomedical science, medicine and health.

The IOM provides a vital service by working outside the framework of government to ensure scientifically informed analysis and independent guidance. The IOM's mission is to serve as advisor to the nation to improve health. An honorific membership organization, IOM members are selected in recognition of major contributions to the advancement of medical sciences, healthcare and public health.



Dr. Stallings's research has focused on nutrition-related growth failure in children and adolescents with chronic medical conditions. Her work has examined conditions such as cerebral palsy, cystic fibrosis, obesity, sickle cell disease and osteoporosis and has helped establish national standards for nutritional care for children with these diseases.



Virginia Stallings, M.D., with Jean Cortner, M.D., in whose honor the Department of Pediatrics established the Jean Cortner Endowed Chair in Pediatric Gastroenterology.

In addition, Dr. Stallings has lectured extensively on pediatric nutrition and bone health. Her contributions to nutritional research and to the Hospital were recognized in 2005 when she was named the holder of the Jean Cortner Endowed Chair in Pediatric Gastroenterology and Nutrition.

Cancer is often associated with chromosomal translocations, which happen when a segment of DNA moves to a new location and changes the regulation of gene expression, creating an oncogene. These chromosomal translocations are likely related to errors in the process of repairing double strand breaks (DSBs) that occur in the DNA.

The National Advisory Committee of the Pew Scholars Program in the Biomedical Sciences has recognized the importance of research into this area and has selected **Craig Bassing, Ph.D.**, Division of Cell Pathology, as a Pew Scholar for 2005, supporting his groundbreaking work on DNA DSB repair.

Dr. Bassing received the prestigious Pew award for his specific research on the role of a histone variant, known as H2AX, in the repair of DNA DSBs. Histones are a group of small proteins around which the DNA is wrapped to make chromatin, which condenses to form the chromosomes.

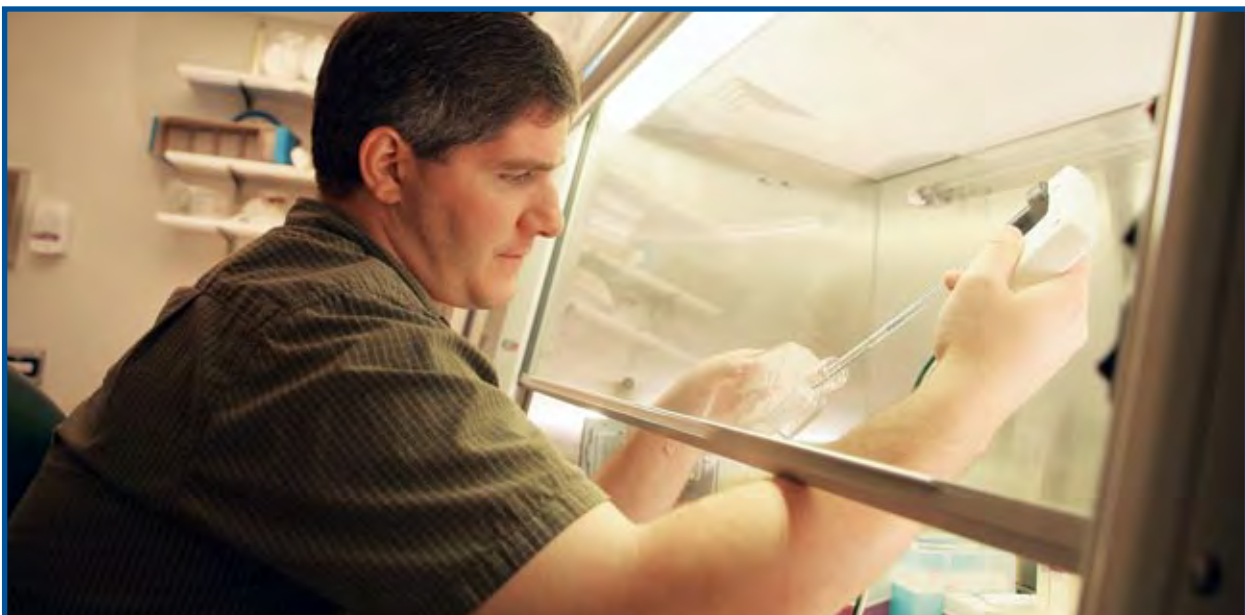
Dr. Bassing's previous findings show that H2AX functions to hold broken ends of DNA in proximity to each other, so that the DNA repair machinery can correctly reattach them, preventing translocations.

With support from the Pew Charitable Trusts, Dr. Bassing is creating a new experimental system that exploits the DSB-induced recombination of the variable (V), diversity (D) and joining (J) gene segments of T cell receptor loci, known as V(D)J recombination. The system allows investigators to induce a specific, pinpoint break in DNA and monitor the mechanisms of repair genetically, molecularly, biochemically and visually.

The support that the Pew Charitable Trusts granted for Dr. Bassing's research has already yielded benefits. Through this powerful experimental system, Dr. Bassing and his colleagues at Washington University in St. Louis have found that ataxia telangiectasia mutated (ATM) protein, known to modify H2AX after DSBs, maintains DNA ends in repair complexes after DSBs occur. The results of their collaborative study were published in the June 2006 issue of the journal *Nature*.

This is the first validation of the function of ATM in DNA repair and a significant finding. In addition, the novel and innovative experimental system that led to these results will continue to yield critical mechanistic insights into the role of chromatin modifications in DSB repair for many years.

By gaining better insights into the molecular events surrounding DSB repair, Dr. Bassing hopes to understand the mechanisms through which H2AX suppresses translocations and cancer, ultimately leading to the development of therapeutic, diagnostic or preventive applications.



Pew Award

One indication of the impact that Stokes researchers have on the scientific community is the recognition investigators receive from that community. The awards listed here are a sampling of those that Children's Hospital investigators received during the year.

A study by Charles Stanley, M.D., chief, Division of Endocrinology, and his colleagues confirming that mutations in an enzyme called glutamate dehydrogenase can cause congenital hyperinsulinism was featured as the "Paper of the Week" in the *Journal of Biological Chemistry*, a journal of the American Society for Biochemistry and Molecular Biology.

The results of the study on congenital hyperinsulinism, which can cause hypoglycemia in infants and children, have potential for many therapeutic and diagnostic applications. Specifically, the results may provide targets for developing new drugs that inhibit the glutamate dehydrogenase enzyme. The findings support the use of genetic mutation analysis of glutamate dehydrogenase to diagnose children with hypoglycemia, and the findings suggest the enzymes could ultimately serve as targets for drugs to treat diabetes.

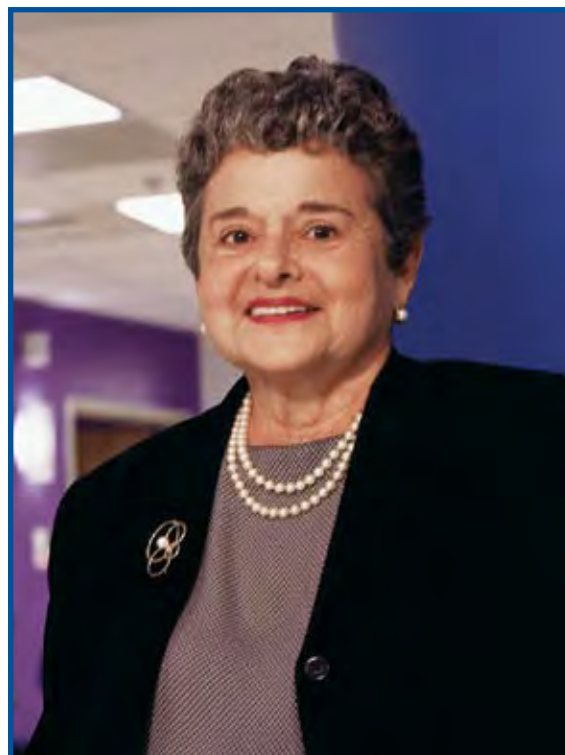


The American Society of Clinical Oncology awarded **Anna T. Meadows, M.D.**, with its 2006 Pediatric Oncology Award, which is made to those who have contributed outstanding scientific work to the future of pediatric oncology.

An internationally recognized expert in the after-effects of children's cancer, Dr. Meadows and her colleagues were the first to investigate the late effects of childhood cancer. Their studies, which began in the 1970s, showed that radiation then used to treat leukemia damaged the children's cognitive development and increased the risk of later brain cancer.

The findings prompted a change in medical practice, with physicians eliminating or reducing the doses of radiation to the head.

Since 1993, Dr. Meadows has served as a prominent investigator in the Childhood Cancer Survivor Study, a National Cancer Institute-sponsored, long-term national study of 15,000 cancer survivors. She also directs the Hospital's Cancer Survivorship Program and leads both the Cancer Survivorship Research Program and the Lance Armstrong Foundation Living Well After Cancer Program at the University of Pennsylvania.



Anna T. Meadows, M.D.

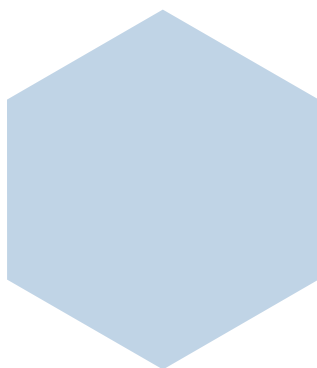
The journal *Circulation* awarded Nicolas Stettler, M.D., M.S.C.E., Division of Gastroenterology, Hepatology and Nutrition, the 2005 Best Paper Award in the category of "Population Science." *Circulation* is a renowned publication, ranking as the top journal in the Cardiac and Cardiovascular Systems, Hematology and Peripheral Vascular Disease categories.



Dr. Stettler's paper, entitled "First Week of Life and Overweight in Adulthood: A Cohort Study of European American Subjects Fed Infant Formula," reports that weight gain in formula-fed infants during the first week of life may be a critical determinant for the development of obesity several decades later. His results contribute to the understanding of chronic disease programming and suggest new approaches to obesity prevention.

A leader among the nation's nursing associations, the Association of Women's Health, Obstetrics and Neonatal Nursing (AWHONN) selected **Barbara Medoff-Cooper, Ph.D., F.A.A.N.**, to receive the Award of Excellence in Research. The award honors an AWHONN member recognized by his or her peers as exemplifying the highest standards of nursing research

Dr. Medoff-Cooper, who holds the Ruth M. Colket Endowed Chair in Pediatric Nursing, investigates infant development, feeding behaviors and temperament.



University of Pennsylvania Awards

Jon (Sandy) Burnham, M.D., Division of Rheumatology, and **Scott Lorch, M.D., M.S.C.E.**, Division of Neonatology, were chosen for the Thomas B. and Jeannette E. Laws McCabe Fund Award, which provides seed money grants to junior faculty who plan to bridge clinical and basic science through innovative biomedical and surgical research projects. Dr. Burnham also received both the Harold Frost/ASBMR Young Investigator Award and ASBMR Young Investigator Award from the American Society for Bone and Mineral Research.

Hallam Hurt, M.D., Division of Neonatology, received the Scott Mackler Award for Teaching Excellence in Substance Abuse Teaching and was named one of the "Top Docs" in 2006 by *Philadelphia* magazine.

Steven Ludwig, M.D., Division of General Pediatrics, received the I.S. Ravdin Master Clinical Award in recognition of his contribution toward clinical integration of the University's Health System and his demonstrated commitment to the improvement of quality patient care.

Other Awards/Honors

Elizabeth R. Alpern, M.D., M.S.C.E., Division of Emergency Medicine, was voted onto the Department of Pediatrics Faculty Teaching Honor Roll.

Kristy Arbogast, Ph.D., Division of Emergency Medicine, received the Elaine Wodzin Young Achiever Award from the Association for the Advancement of Automotive Medicine and the Excellent Technical Paper Presentation Award at the 2005 Japanese Society of Automotive Engineers Annual Congress.

Jaclyn Biegel, Ph.D., Division of Human Genetics and Molecular Biology, was the Adam Balinsky Lecturer at the Hospital for Sick Kids in Toronto, Canada, where she gave a lecture on hSNF5/INI1 and the development of rhabdoid tumors.

Cindy Christian, M.D., Division of General Pediatrics, was elected to the Committee on Child Abuse and Neglect for the American Academy of Pediatrics.

Dennis Durbin, M.D., M.S.C.E., Division of Emergency Medicine, has been elected a member of the scientific review group on Unintentional Injury Prevention for the Centers for Disease Control and Prevention.

Ricardo Eiraldi, Ph.D., Division of Child Development, was appointed to the Professional Advisory Board of Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD). CHADD is the largest and most influential support and advocacy group for individuals with ADHD in this country.

Carolyn Felix, M.D., Division of Oncology, was elected to the Association of American Physicians. She also received the Eagles Fly for Leukemia Award for Excellence in Treatment of Pediatric Cancer Patients and was named one of the "Top Docs" by *Philadelphia* magazine.

Susan Guttentag, M.D., and **Mary Cay Harris, M.D.**, both of the Division of Neonatology, were elected to the American Pediatric Society.

Amy Brooks-Kayal, M.D., Division of Neurology, was elected to the American Neurological Association.

Several faculty members were elected to the Society for Pediatric Research in FY06: Cherie Foster, M.D., Division of Neonatology; James Guevara, M.D., M.P.H., Division of General Pediatrics; Jonathan Spergel, M.D., Ph.D., Division of Allergy and Immunology; Jake Kushner, M.D., Division of Endocrinology; and Joseph Zorc, M.D., Division of Emergency Medicine.

Faculty Honors

John Maris, M.D., Division of Oncology, was appointed chair of the Neuroblastoma Disease Committee in the Children's Oncology Group. He was also elected to the Board of Trustees for the American Society of Pediatric Hematology/Oncology.

Vinay Nadkarni, M.D., Department of Anesthesiology and Critical Care Medicine, received the Presidential Citation from the Society of Critical Care Medicine. He was elected to the board of directors for the World Federation of Pediatric Intensive and Critical Care Societies and elected president of the American Heart Association Pennsylvania/Delaware Regional Board of Directors.

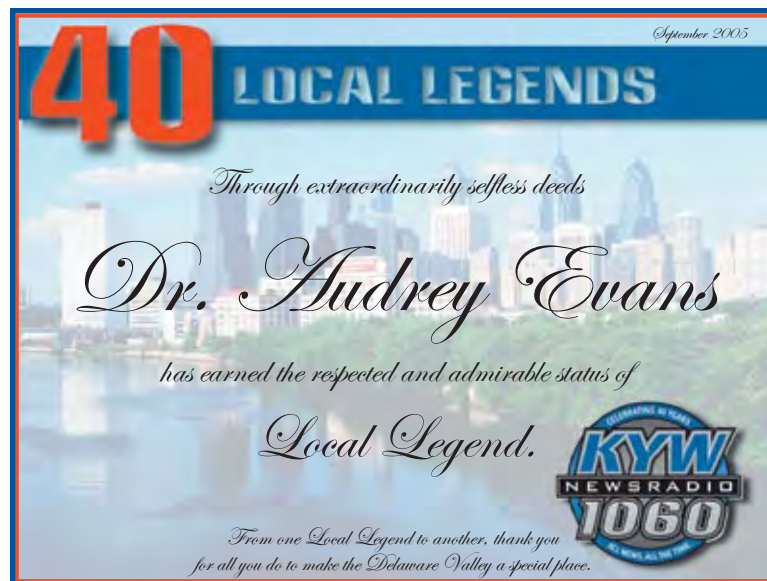
Thomas Spray, M.D., chief, Division of Cardiothoracic Surgery, was named president-elect of the American Association for Thoracic Surgery for 2009.

Virginia Stallings, M.D., Division of Gastroenterology, Hepatology and Nutrition, and director of the Office of Faculty Development, received the 2006 E.V. McCollum Award from the American Society of Nutrition. The award is given to a clinical investigator perceived as a major creative force who is actively generating new concepts in nutrition, and personally seeing to the execution of studies testing the validity of these concepts.

Flaura Koplin Winston, M.D., Ph.D., director of the Hospital's Center for Injury Research and Prevention, received the Outstanding Research Project Award from the Emergency Medical Services for Children, a nationwide initiative aimed at reducing child and youth disability and death due to severe illness and injury.

The concept for the world's first Ronald McDonald House was based on the observations of a Stokes investigator, **Audrey Evans, M.D.**, Division of Oncology. Dr. Evans' belief that to treat a child with cancer, it is necessary to treat the whole family, was underscored by the fact that many families had no place to stay locally while their children underwent treatment. Dr. Evans worked to fill the need for temporary lodging for children undergoing medical treatment and their families.

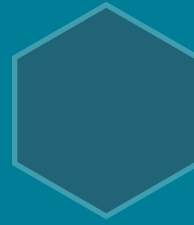
As part its 40th anniversary, KYW Newsradio honored Dr. Evans by naming her one of 40 "Local Legends" who have made significant contributions to the Philadelphia region. In its tribute, the station noted Dr. Evans' achievement in creating the world's first Ronald McDonald House, now one of hundreds worldwide, which provides a home away from home for families whose children receive treatment at hospitals in Philadelphia.



Ronald McDonald Houses provide temporary homes for families whose children receive treatment at area hospitals and create places where families can help each other.

Local Legend

REENGINEERING STOKES



NEW SERVICES AND RESOURCES STRENGTHEN AND SUPPORT RESEARCH

The Stokes Institute made several changes during the fiscal year aimed at offering additional services and resources to investigators and research staff, providing the highest possible protections to those participating in research studies, and enhancing its visibility as the preeminent institution in pediatric research.





The research mission at the Stokes Institute centers on ensuring that scientific discoveries in the laboratory or clinic are moved rapidly and efficiently to a patient's bedside in a scientifically rigorous, child-centered manner — the essence of translational research.

Recognizing that innovative and high-quality translational and clinical research is critical to the continued success of its mission, the Stokes Institute launched the **Office of Clinical and Translational Research (OCTR)** to focus its efforts and resources while providing a high level of services to faculty.

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Directed by Peter C. Adamson, M.D., chief, Division of Clinical Pharmacology and Therapeutics, the office works with clinical and translational investigators, administrators, division chiefs, department chairs and others across the organization to identify important scientific opportunities and foster productive research collaborations throughout academic communities at Children's Hospital and the University of Pennsylvania School of Medicine.

"By helping to identify and nurture scientific collaborations, and by providing a supportive infrastructure, the OCTR aims to fill an important role at the Stokes Institute," says Dr. Adamson. "We look forward to working with investigators and support personnel to continually improve upon our infrastructure and enhance the Institute's clinical and translational research programs."

The OCTR works to facilitate patient-oriented research at Stokes, a task that is of particular importance given the increasing complexities of conducting clinical and translational research. To that end, the OCTR develops and implements improvements in the clinical and administrative research infrastructure, including working with the leaders of the Committee for the Protection of Human Subjects, the General Clinical Research Center, the Clinical Trials Office and the Biostatistics and Data Management Core to support investigators throughout the institution.



The Stokes Institute enhanced its visibility as the preeminent institution in pediatric research through its redesigned Web site.

Located at <http://stokes.chop.edu>, the site uses the latest Web standards with the aim of fostering greater collaboration with colleagues and industry and aiding in the recruitment of talented investigators and research staff.

The redesigned site is the product of a yearlong collaboration among members of the Stokes Institute, the Hospital's Web team and the Web site designer Pixelworthy. The site features substantial information about the Stokes Institute, including its history, leadership, facilities and administration; detailed information on programs like the Research Affinity Groups and centers; and investigator profiles and research resources.

In addition, the new Stokes Web site provides information on careers and training, including current openings; information for industry interested in research collaborations and licensing opportunities; and news and publications, including research press releases, back issues of the research newsletter, Bench to Bedside and the Research Annual Report.

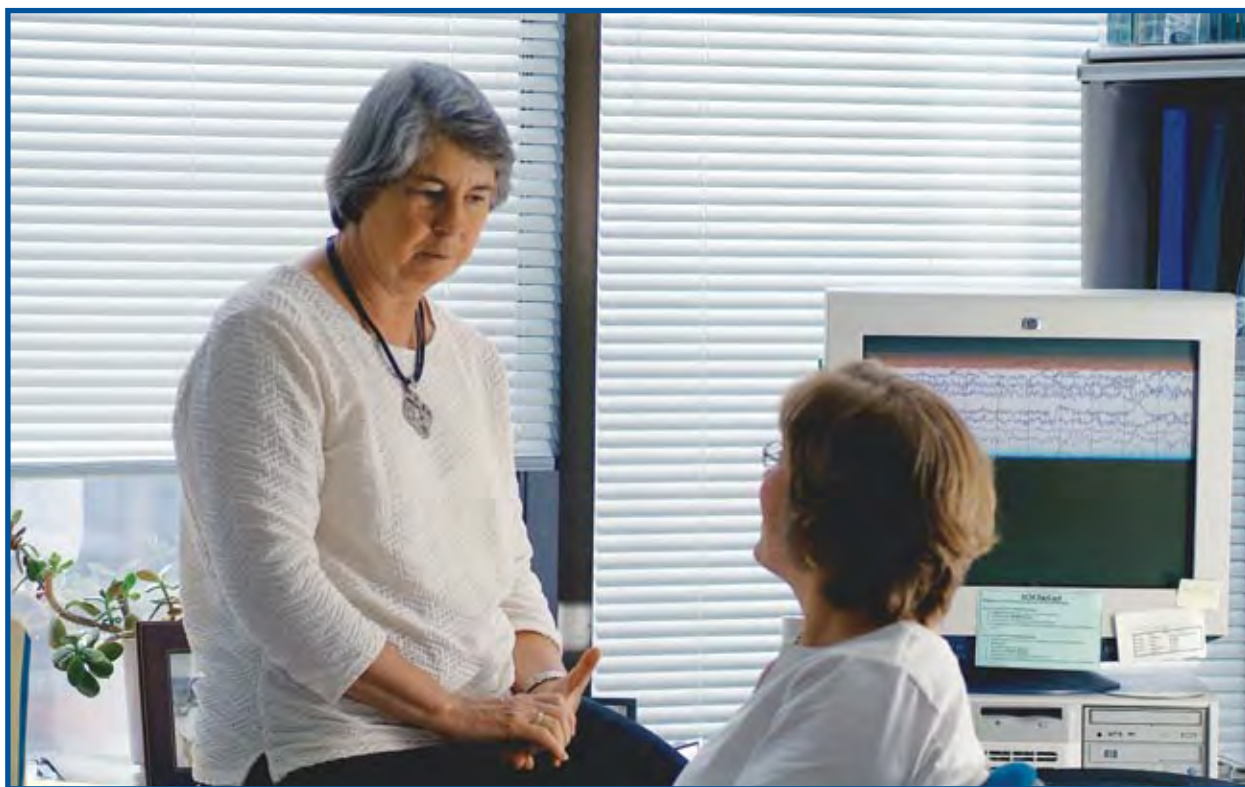


Faculty Development

Research preeminence is also a driving force behind the **Office of Faculty Development, (OFD)** established by the Stokes Institute to create an environment to ensure the success of faculty members, especially those in the early stages of their research careers.

With the goal of recruiting and retaining the best and brightest investigators — considered one of the Institute's most important resources — the OFD mentors, supports and monitors faculty, with a focus on those with the rank of instructor or assistant professor who spend significant time and effort in research.

Virginia Stallings, M.D., directs the office, which facilitates the successful transition from fellow to faculty investigator, encourages and supports activities that lead to promotion, engenders the spirit of mentorship for the future and provides tools for achieving work-life balance.



The OFD is working with the University of Pennsylvania Faculty Affairs and Professional Development Office to provide skills-building sessions for faculty in areas such as teaching effectiveness and scientific writing. The office will also work with Stokes administrative groups like Research Education and Sponsored Projects to fortify the resources and information available to faculty.



“The Office of Faculty Development aims to be a place Stokes investigators will turn to for whatever information they need to help them succeed in research and their personal lives,” says Dr. Stallings.

“That information can span from strategies to enhance the recognition of their efforts through grants and publications to personal issues like retirement planning.”

AAHRPP Accreditation

Clinical research is a vital component of the overall research program at Children's Hospital, which aims to protect those participating in research studies while moving discoveries from the bench to the bedside.

Stokes anticipates continued growth in clinical research and recognizes the importance of providing the greatest protection to patients and their families.

The Institute is among the leaders in the emerging national trend toward establishing standards to ensure the protection of the rights and welfare of research subjects.

The Hospital is therefore pursuing voluntary accreditation of its human research protection program through the Association for the Accreditation of Human Research Protection Programs (AAHRPP). AAHRPP accreditation demonstrates the most comprehensive protections for research participants and overall research excellence.



*Clinical investigator, Barbara A. Haber, M.D.,
and a research study participant.*

Accreditation will require an institution-wide effort that largely mirrors the accreditation process required by the Joint Council on Accreditation of Healthcare Organizations, which evaluates and accredits nearly 17,000 hospitals in the country.

“Gaining accreditation through AAHRPP — currently granted to only 35 U.S. organizations — harmonizes with the Hospital’s clinical research vision and mission and its commitment to attaining the highest standards in human research protection,” says Mark Schreiner, M.D., chair of the Hospital’s Institutional Review Board.

Leading the Way:



**Excellence in Research
Participant Protection**

Conducting research with human subjects, and particularly with children, is a serious responsibility that requires a delicate balance between protecting the rights of study participants while promoting scientific innovation. Children's Hospital has a long tradition of pursuing research of the highest quality that is conducted with great integrity and in compliance with ethical mandates and regulatory requirements.

Mark Schreiner, M.D., Department of Anesthesiology and Critical Care Medicine, assumed the role of overall chair of the Hospital's Committees for the Protection of Human Subjects, which are essential components of the multifaceted infrastructure that supports clinical research at Children's Hospital.

In his role as chair, Dr. Schreiner is responsible for fostering a culture of respect for the Institutional Review Board and Children's Hospital research policies and procedures, and for helping to maintain a culture that respects the ethical conduct of clinical research.



Mark Schreiner, M.D.

By ensuring the protection of the rights and welfare of participants in clinical research, the members and staff of the Institutional Review Boards play a vital role in maintaining the public trust in Children's Hospital.

Dr. Schreiner previously was the medical director of Children's Clinical Research Institute, an academic clinical research organization at the Hospital. In this role, he became a nationally recognized advocate for well-designed pediatric trials for testing therapeutics in children as well as an expert on the ethics of pediatric research.



IRB Chair Mark Schreiner, M.D., and Lynn Bevan, director of Research Regulatory Affairs.



IRB subcommittee members (left to right) Janet Kwiatkowski, M.D., Mark Schreiner, M.D., Babette Zemel, Ph.D., and Janine Beal Larr.

BUILDING THE FUTURE OF RESEARCH



HOSPITAL'S SOUTH CAMPUS TO HOUSE ADVANCED RESEARCH FACILITY, HONOR VISIONARY BENEFACTORS



The tremendous growth of the Hospital's clinical and research programs has not only required changes in the way research is organized and administered but has also propelled the dramatic expansion of the institution's physical facilities.



The latest expansion plans supporting the Hospital's flourishing research enterprise were publicly revealed in June, with the ceremonial groundbreaking for an eight-story research building dedicated to translational research.

Sitting upon an eight-acre parcel of land that was formerly the Philadelphia Civic Center site, the building represents the first phase of development for the Children's Hospital's South Campus Research Complex.

The ceremonial groundbreaking honored long-time board trustees Ruth M. and Tristram C. Colket Jr., in appreciation of their substantial gift that will allow the Hospital to move toward its goal of doubling the size of its existing research space. In recognition of the Colkets' longstanding generosity and leadership, which has spanned more than three decades, the Hospital will name the new research building in their honor.

“Ruth and Tristram Colket’s recent gift of \$25 million has given an enormous boost to the advancement of research at Children’s Hospital by helping to fund our new research building on our South Campus,” says Steven M. Altschuler, M.D., the Hospital’s president and chief executive officer. “With more than 30 years of support, Ruth and Tristram Colket have given more than \$35 million to help ensure that Children’s Hospital remains the preeminent pediatric institution in this country and the world.”

The philanthropy of the Colkets is evident in the Hospital’s light-filled atrium and the lobby of the Leonard and Madlyn Abramson Pediatric Research Center, both of which bear their name. In addition, the Colkets’ generosity has fostered continued research through endowed chairs in pediatric surgery and pediatric nursing.

“The Children’s Hospital of Philadelphia provides us the greatest opportunity to make a difference in the lives of children,” say Ruth and Tristram Colket. “This new research building will help ensure a healthier future for the children of tomorrow.”



The ceremonial groundbreaking of the new translational research building attended by (left to right): Stephen B. Burke, Hospital trustee and president, Comcast Cable; State Representative Dwight Evans; Philip R. Johnson Jr., M.D., chief scientific officer of the Stokes Institute; Tristram C. Colket Jr., Hospital trustee; Emma Cullen, granddaughter of Ruth and Tristram Colket Jr.; Ruth M. Colket, Hospital trustee; Steven M. Altschuler, M.D., Children’s Hospital president and chief executive officer; Edward G. Rendell, Governor of the Commonwealth of Pennsylvania; and State Representative James Roebuck.

This \$400 million, 558,000-square-foot research building will have eight stories — four new laboratory floors, administration and conference space, and a two-story ground floor housing a lobby and cafeteria. An additional four stories below grade consist of infrastructure and laboratory support space. To accommodate future growth, there is potential to expand the building to 22 stories.

The new research building is part of the overall South Campus Research Complex directly across from the Hospital's current clinical and research facilities. Once complete, the South Campus will house not only a translational research facility but also a central utility plant to support the entire Children's Hospital campus, underground parking and garage, and an ambulatory building with outpatient care, day medicine, day surgery and imaging, as well as enhanced amenities for patients, families and employees.

The total facility development is estimated at \$845 million and could total more than 1 million square feet.



An artist's rendering of the planned translational research building.

“This state-of-the-art facility enables Children’s Hospital to recruit top-level researchers by providing the space, equipment and technology required to advance pediatric medicine,” says Chief Scientific Officer Philip R. Johnson Jr., M.D. “The Hospital is poised to be the preeminent institution conducting translational research for the benefit of children.”

FINANCIAL/AWARD INFORMATION

GRANTS, GIFTS AND AWARDS TO STOKES FOR FISCAL YEAR 06

Research funding to Stokes Institute investigators grew during fiscal year 2006, despite across-the-board funding cuts from the National Institutes of Health, which provides approximately 85 percent of Stokes' external funding.

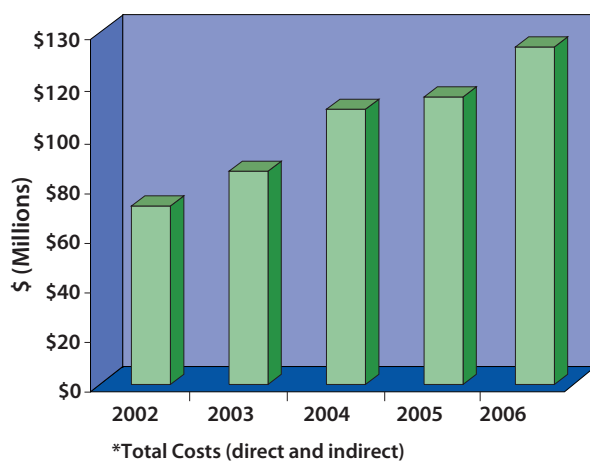




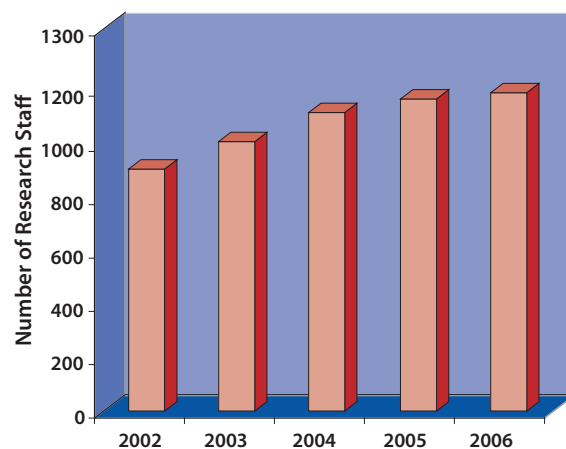
This sustained, peer-reviewed support awarded to Children's Hospital underscores the significance of research conducted by Stokes investigators and reflects the Institute's past successes and dedication to remain a world leader in pediatric research.

Support from endowments and donations also contribute to the strength of the Institute's research program. This generosity provides funds for new investigators, enables established investigators to explore new areas of research and helps establish innovative research approaches.

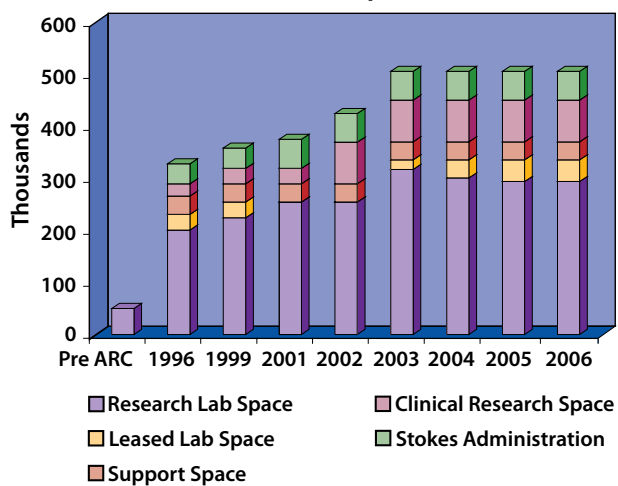
External Grant and Contract Expenditures*

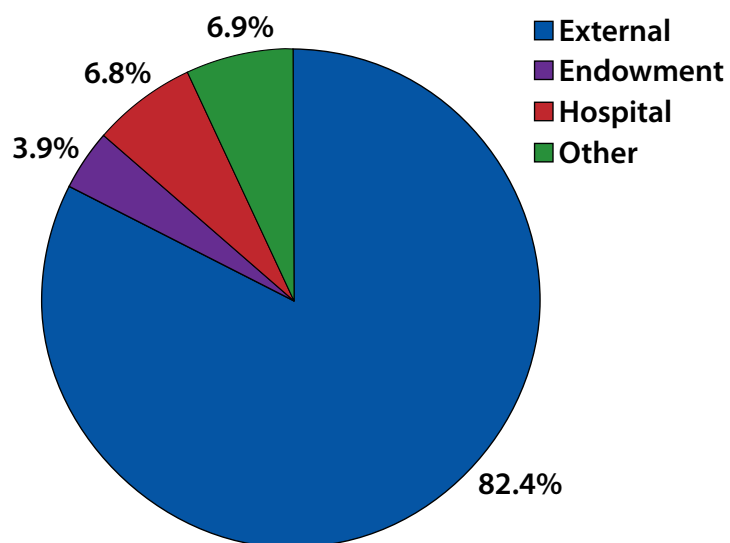
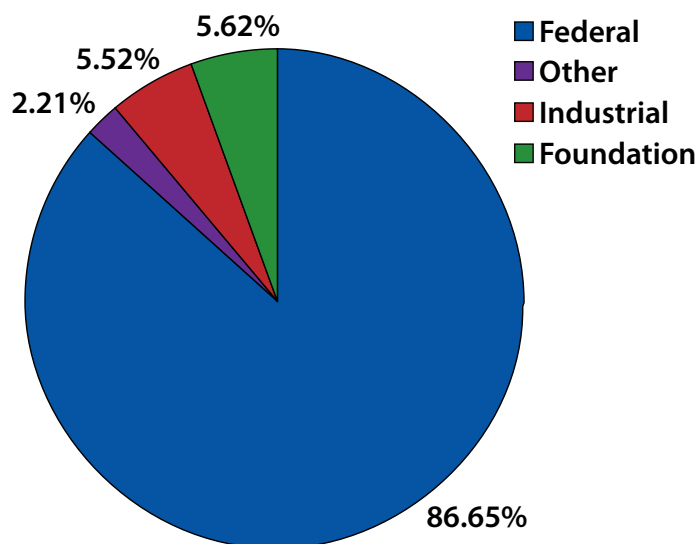


Number of Research Staff



Dedicated Research Space (net sq. ft.)



FY06: All Sources of Funding**FY06: Sources of External Funding**

Private Sources

\$1,000,000 or more

Anonymous (1)
Fred and Suzanne Biesecker/
Biesecker Foundation
Children's Health Care Associates Inc.
Radiology Associates of Children's
Hospital Inc.
State Farm Insurance Companies

\$100,000 - \$999,999

Anonymous (2)
Alex's Lemonade Stand Foundation
The Allerton Foundation
American Academy of Allergy, Asthma
and Immunology
American Cancer Society Inc.
American Heart Association
American Society of Clinical Oncology
Bayer Healthcare
Estate of Evelyn Eyre Bromley
Children's Anesthesiology Associates Ltd.
Children's Surgical Associates Ltd.
Mr. and Mrs. Robert J. Edmunds
Mr. and Mrs. Mark Fishman
Mr. and Mrs. John K. Hillman
Juvenile Diabetes Research Foundation
Mr. and Mrs. John A. London
Karen Lubert
Memorial Sloan-Kettering Cancer Center
The Merck Company Foundation
Muscular Dystrophy Association Inc.
National Multiple Sclerosis Society
Mr. and Mrs. David Oberkircher
Otto Haas Charitable Trust #2
The Pediatric Endocrine Society
The Pew Charitable Trusts
The Philadelphia Foundation
Phoebe W. Haas Charitable Trust B
Respiroics Sleep & Respiratory
Research Foundation
Drs. John and Josephine Templeton

\$25,000 to \$99,000

Madelyn Bucksbaum Adamson and
Allen Adamson
Dr. and Mrs. Steven M. Altschuler
American Association of Cancer Research
American College of Surgeons
American Diabetes Association
American Epilepsy Society
American Foundation for Urologic
Diseases Inc.
American Hearing Research Foundation
American Liver Foundation
American Society of Transplantation
AOPpine North America
Mr. and Mrs. Stephen D. Arnold
Arthritis Foundation
Dr. and Mrs. Toshio Asakura
Raymond J. Battaglia Sr.
Mr. and Mrs. Frederick B. Berman
Bryce's Bridge of Hope
Children's Neuroblastoma Cancer Foundation
Citizens United for Research in Epilepsy
CureSearch National Childhood Cancer
Foundation
Cystic Fibrosis Foundation
Foundation for Anesthesia
Friends of Brian
Friends of Trisomy 21 Center
GlaxoSmithKline
Hope Street Kids
Dolores E. Howell
Jeffrey Modell Foundation
Mr. and Mrs. Steven H. Kapp
Mrs. Philip Kind Jr.
Kohl's Department Stores
Louis Callmann Goldschmidt Family
Foundation Inc.
Lupus Research Institute
March of Dimes Philadelphia Chapter
National Alliance for Autism Research
National Alliance for Research on
Schizophrenia & Depression

National Neurofibromatosis Foundation Inc.
 Mr. and Mrs. Stephen Olitsky
 Robert J. Kahn Foundation
 Mr. and Mrs. John C. Shute
 Southwest Leadership Foundation
 Honorable Richard A. Sprague
 Patrick Sullivan
 Jacqueline E. Swartz
 Nancy and Richard Wolfson
 W. W. Smith Charitable Trust

\$10,000 to \$24,999

Sandrea Goerlich Alexander
 Amanda Kanowitz Foundation
 American Academy of Pediatrics
 Ballyshannon Partners, LP
 Mr. and Mrs. Wilson J.C. Braun Jr.
 Catherine D. Brown
 Mr. and Mrs. Louis P. Canuso
 Capita Foundation
 Connell Anastasi Memorial Fund
 Cooley's Anemia Foundation
 Cornelia de Lange Syndrome Foundation Inc.
 Deafness Research Foundation
 Mr. and Mrs. A. Aboud Dweck
 Lenny Feinberg
 Mr. and Mrs. John Giordano
 Thomas A. Giovine
 Mr. and Mrs. Peter Hearn
 Mr. and Mrs. Edward M. Jacobs
 Michael Kim and Sara Lee
 David Kipper
 Laerdal Foundation for Acute Medicine
 Don LaRossa, M.D.
 Leonard Davis Institute
 James Lemon
 Lester and Liesel Baker Foundation
 McCabe Pilot Award
 Mr. and Mrs. Norman L. Miller
 Estate of Harold J. Minton
 Mr. and Mrs. Michael Mulligan
 Ruth L. Nathanson
 Pennsylvania Lions Hearing Research
 Foundation Inc.

Philadelphia Chapter of Credit Unions
 PhRMA Foundation
 The Proctor and Gamble Company
 Mr. and Mrs. Robert A. Shoemaker
 Ms. Mason Smith and Mr. Gordon Green
 Mr. and Mrs. Richard Smith
 Mr. and Mrs. Thomas Sprague
 Cheryl Toffler
 Hal and Beth Tunick
 United Way of Delaware
 Wawa Inc.
 Mr. and Mrs. Steven M. Weinstein
 Bryan A. Wolf, M.D., Ph.D. and Britt Amlie

\$5,000 to \$9,999

American Foundation for Suicide
 Prevention
 Mr. and Mrs. David F. Arena
 Dr. and Mrs. Allen M. Barnett
 Mr. and Mrs. Dominic J. Caruso
 Children's Health Associates
 Mrs. Bertie R. Cohen
 Mr. and Mrs. Caesar Crognale
 Epilepsy Foundation
 Mr. and Mrs. David A. Gansky
 Lorraine Hilleman
 Mr. and Mrs. Peter Korneffel
 Charles Lafkas
 Mrs. Julius A. Mackie Jr.
 Mark Massry
 Mr. and Mrs. John S. Price
 Society of Pediatric Radiology
 Talecris Biotherapeutics
 Teammates for Kids Foundation
 Mr. and Mrs. Joseph Goldblum
 Feldman Family Foundation
 Catherine G. Mozino
 Society of Pediatric Radiology
 The Virgil Kauffman Foundation
 Mr. and Mrs. Douglas A. Warner III
 Mr. and Mrs. Aaron L. Wadell
 William and Sakurako Fisher Fund
 Karen and Allan Zarembski Family

Private Sources

\$1,000 - \$4,999

Frank E. Accardi
 Louise A. Angelucci
 Mr. and Mrs. Mark D. Arian
 Madeline and Louis Bell
 Dr. and Mrs. Douglas A. Canning
 Cheltenham Township Police Department
 Jack R. Cortner
 Daughters of Penelope
 Drug Plastics Charity Fund
 George Drach and Peggy Duckett
 Fidelity Charitable Gift Fund
 Folsom Tool & Mold Corporation
 Mr. and Mrs. William C. Fox
 Duncan A. Haas
 Mr. and Mrs. Patrick T. Hackett
 Christopher Hall and Mary A. Boyer
 Ellen Nalle Hass
 Mr. and Mrs. Francis R. Hinchman
 Holicong Middle School
 Mr. and Mrs. Peter Ippolito
 Mr. and Mrs. J.J. Jagodinski
 Mr. and Mrs. John Scarpa
 Kansas City Chiefs
 Mr. and Mrs. Thomas J. Kennedy Jr.
 Brian, Phyllis, Sarah and Carolyn Kushner
 Sheila E. Kushner
 Lanco York Inc.
 Dr. and Mrs. Robert J. Levy
 James G. Logue
 Mr. and Mrs. William D. London
 Jean Ann Longacre
 Lupus Foundation of American
 Mr. and Mrs. Thomas Mahoney
 Una D. McDaid
 McNeil Consumer Healthcare
 Mr. and Mrs. John P. McNiff
 Michael's Miracle Foundation
 Dorothy and Charles Minter
 National Hemophilia Foundation
 NFL Films
 Mr. and Mrs. Robert W. O'Donnell
 Olympic Tool & Machine Corporation
 Mr. and Mrs. Thomas F. O'Neil III

Ratner Companies
 Arnold S. Rothstein
 Dr. and Mrs. Anthony W. Salem
 Mr. and Mrs. Eric Schwartz
 Mr. and Mrs. James Solano
 Dr. Virginia Stallings and Dr. Jacqueline Pastis
 Mr. and Mrs. Thomas P. Reynolds
 The Simon & Lyna P. Levin Charitable
 Foundation Philanthropic Fund
 United Way of Tri-State Inc.
 Mr. and Mrs. Daniel F. Wainfan
 Lois A. Wainfan
 Christopher D. Walters
 Mr. and Mrs. Harvey A. Weiner
 Stuart Weitzman
 WGD Holdings LLC
 Mr. and Mrs. Alexander B. Wheeler Jr.
 Mrs. Alexander B. Wheeler
 Mr. and Mrs. Warwick S. Wheeler
 The William J. & Dorothy K. O'Neill
 Foundation
 The William Penn Foundation
 Xerox Corporation U.S.A.
 Mr. and Mrs. Graham F. Zug

Who's Who at Stokes in 2006 Joseph Stokes Jr. Research Institute Leadership

Philip R. Johnson Jr., M.D.
*Chief Scientific Officer and
Senior Vice President, Director of
The Joseph Stokes Jr. Research Institute*

Judith Argon
Vice President, Research Administration

Mary Tomlinson
*Vice President, Research Finance
and Sponsored Projects*

Joseph Stokes Jr. Research Institute Board Committee

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Steven M. Altschuler, M.D.
Richard M. Armstrong Jr.
Robert I. Berkowitz, M.D.
Aminta Hawkins Breaux, Ph.D.
Richard R. Carr
Alan R. Cohen, M.D.
James Digan
William J. Greeley, M.D., M.B.A.
Philip R. Johnson Jr., M.D.
Richard I. Markowitz, M.D.
R. Anderson Pew
Phillip S. Schein, M.D.
Salem D. Shuchman
James M. Steven, M.D.
Frank E. Weise III

Research Operations

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N. Scott Adzick, M.D.
Steven M. Altschuler, M.D.
Robert I. Berkowitz, M.D.
Thomas J. Todorow, C.P.A., M.B.A.
Alan R. Cohen, M.D.
Charles Enicks

William J. Greeley, M.D., M.B.A.
Diego Jaramillo, M.D., M.P.H.
Meg Jones
Philip R. Johnson Jr., M.D.
Gavin Kerr
Virginia A. Stallings, M.D.
James M. Steven, M.D.
Mary Tomlinson
Bryan A. Wolf, M.D., Ph.D.

Institutional Review Board

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Committee A

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Brian Hanna, M.D., *Vice Chair*
Janine Beal, CIP
Lynn Bevan, CIP
Betsy Bickert, Pharm.D.
Tyra Bryant-Stephens, M.D.
Nancy Bunin, M.D.
Scott Cook-Sather, M.D.
Richard Davidson, M.D.
James Guevara, M.D., M.P.H.
Richard Hodinka, Ph.D.
Thomas Innes, J.D.
Laureen Kotzer, Pharm.D.
Jennifer Long, M.S., M.J.
Roger Marsh, Ph.D.
Oscar Mayer, M.D.
Ann O'Sullivan, Ph.D., F.A.A.N., C.R.N.P.
George Reath Jr., Esq.
Linda Rosenthal, R.Ph.
Charles Scott, Ph.D.
Jennifer Smith, M.D.
Babette Zemel, Ph.D.

Committee B

Mark Schreiner, M.D., *Chair*
Erin Simon, M.D., *Vice Chair*
Julian Allen, M.D.
Janine Beal, CIP
Lynn Bevan, CIP
Betsy Bickert, Pharm.D.

Who's Who

Shirley Bonnem
Leonard Buchoff, Ph.D.
Avital Cnaan, Ph.D.
Jacquelyn Evans, M.D.
Michael Fisher, M.D.
Mark Fogel, M.D.
Janice Glisson, R.N.
Adda Grimberg, M.D.
Jean Hassler, R.N.
Jennifer Long, M.S., M.J.
Anna Meadows, M.D.
Pierre Russo, M.D.
Elaine Skypala
Joseph Zorc, M.D.

Committee C

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Richard Lin, M.D., *Vice Chair*
Roberto Accorsi, Ph.D.
Richard Aplenc, M.D.
Janine Beal, CIP
Arthur Benedict
Lynn Bevan, CIP
Avital Cnaan, Ph.D.
Kim Davis, M.A.
Kevin Franck, Ph.D.
Judith Goodman, M.D.
Marta Guttenberg, M.D.
Thomas Kolon, M.D.
Laureen Kotzer, Pharm.D.
Janet Kwiatkowski, M.D.
Jennifer Long, M.S., M.J.
Jeanne Manson, Ph.D.
Elizabeth Rand, M.D.
John L. Rodgers, D.Min.
Rabbi Murray Silberman
Baird M. Standish
Donna Sylvester, R.N., B.S.N

Institutional Biological Safety Committee

Katherine High, M.D., *Chair*
Jeffrey Bergelson, M.D.
H Fred Clark, D.V.M., Ph.D.
Raymond Colliton

Crawford Hill III
Ian D. Krantz, M.D.
Mortimer Poncz, M.D.
Sue Souder
Jacqueline Wagner

Research Compliance and Oversight Committee

Judith Argon, *Chair*
Douglas Coulter, Ph.D.
Michael Robinson, Ph.D.
Sara Dubberly
Jacqueline Wagner
Jeffrey Kahn
Mark Schreiner, M.D.
Mary Tomlinson
John Matthews
Peter Adamson, M.D.
Philip R. Johnson Jr., M.D.
Richard Dashefsky
Carol Sazama
Virginia Stallings, M.D.
Shifra Vega, Ph.D.
Wendy Williams, Ph.D.

Postdoctoral Affairs Committee

Brant Burkhardt, Ph.D.
Chunxia Chen, Ph.D.
Carolyn Felix, M.D.
Jane Kim
Ian Krantz, M.D.
Sriram Krishnaswamy, Ph.D.
Jeanne Manson, Ph.D., M.S.C.E.
Denise Outlaw
Jerilyn Radcliffe, Ph.D.
Michael Robinson, Ph.D.
Wendy Williams, Ph.D.
Babette Zemel, Ph.D.
Lisa Paravecchia

Research Affinity Groups

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Group Leader: Mortimer Poncz, M.D.

Cell and Gene Therapy

Group Leader: Katherine High, M.D.

Child Health Services

Group Leaders: Louis Bell, M.D., and
Jeffrey H. Silber, M.D., Ph.D.

Defective Proteins and Disease

Group Leader: Yair Argon, Ph.D.

Developmental Biology and Pediatric Disorders

Group Leader: Jeffrey Golden, M.D.

Fetal Research

Group Leader: Alan Flake, M.D.

Genes, Genomics and Pediatric Disease

Group Leaders: Nancy Spinner, Ph.D., and
John Maris, M.D.

Metabolism, Nutrition and Physical Development

Group Leaders: Babette Zemel, Ph.D., and
Rebecca Simmons, M.D.

Mind Brain Research Center

Group Leader: Michael Robinson, Ph.D.

Normal and Malignant Hematopoiesis

Group Leader: Carolyn Felix, M.D.

Pediatric Injury Research

Group Leader: Flaura Winston, M.D., Ph.D.

Pharmacologic Basis of Pediatric Therapeutics

Group Leader: Jeffrey Barrett, Ph.D.

Vaccines and Immunotherapies

Group Leader: Terri Finkel, M.D., Ph.D.;
Co-leaders: Steven Douglas, M.D., and
Paul Offit, M.D.

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Chief, Division of Urology

Leonard and Madlyn Abramson

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Physician-in-chief

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Psychiatrist-in-chief; Chair, Department of
Child and Adolescent Psychiatry

Gisela and Dennis Alter

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Director, Neonatology Research

*David Lawrence Altschuler Endowed Chair
in Genomics and Computational Biology*

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*Mary D. Ames Endowed Chair
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Deputy Physician-in-chief; Chief, Division of
Adolescent Medicine

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Chief, Division of Endocrinology

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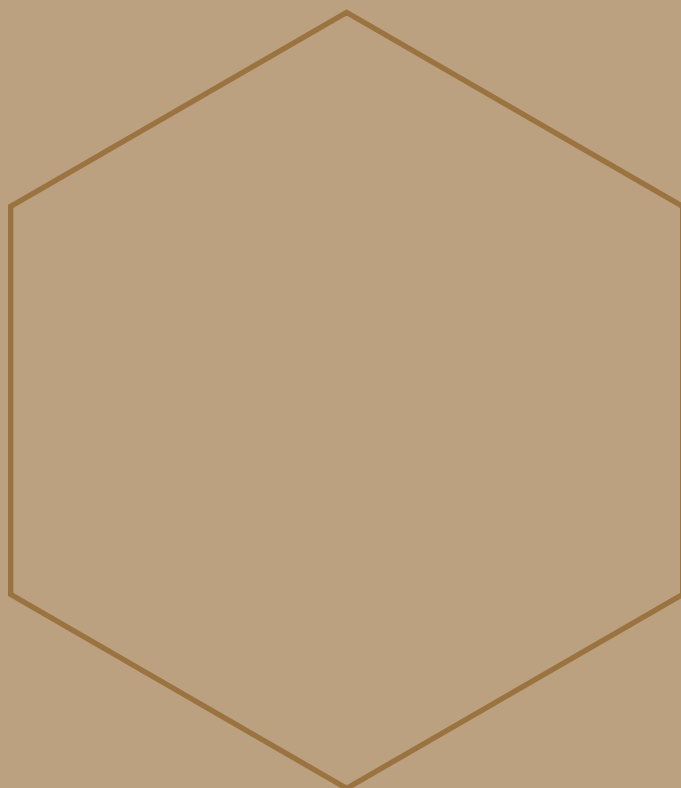
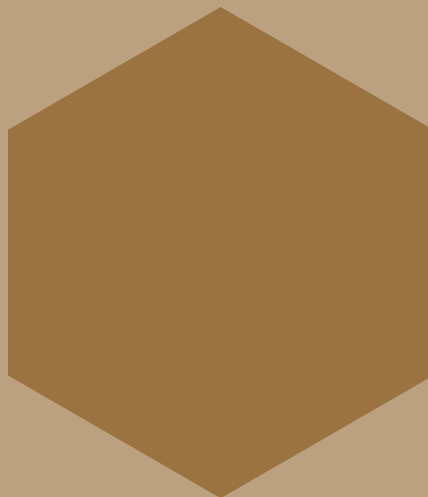
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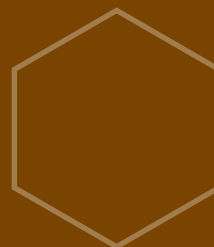
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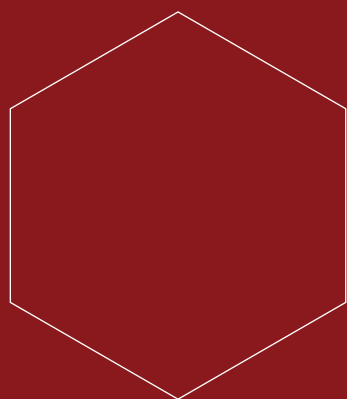
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