Children's Memorial Research Center™

InTouch
WITH RESEARCH
at Children's Memorial Research Center

Winter 2009
Volume 5: Issue 4

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View from the Bench:

The Essential Elements

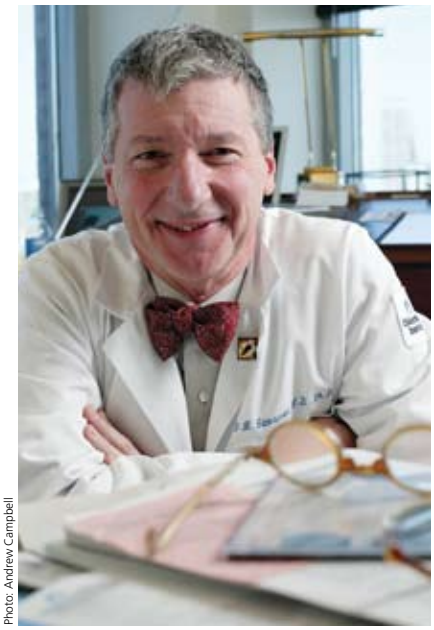

Photo: Andrew Campbell

Philip M. Iannaccone, MD, PhD, Senior Vice-President and Deputy Director for Research — Basic Sciences

Einstein famously said, "The eternal wonder of the world is that it is comprehensible." This is to me one of the most succinct statements of the motivation for our principal mission, to generate new knowledge.

We have the great privilege to work on this mission in a beautiful modern facility that constantly adapts to the changing needs of our investigators and helps us to be competitive. A recent letter from Dr. Hendrix outlining Children's Memorial Research Center's accomplishments led me to speculate about the essential elements of a successful scientific enterprise, and to reminisce about the research center's origins. I remember first seeing the structure that had been built through the efforts of so many and thinking "Here is a rare opportunity, to help build an organization in the way we want, with the highest level of scholarship that we can achieve as our goal." It was odd and fun to explore the mostly empty spaces and imagine what might happen with the right people and equipment, and the freedom to pursue questions presented to us by our curiosity and passion for understanding. So, what are those essential elements? I suppose them to be autonomy, focus, personal responsibility and, importantly, leadership.

Looking back, it is hard not to be struck by how much more there is to scientific inquiry than western blots, microscopes and the other trappings of modern labs. Although technique reigns in science, much more is needed to pursue the work we have chosen. We must not, as Michael Pollan wrote in "The Omnivore's Dilemma", "mistake what we can know for all there is to know." As we learn other skills and an expanded philosophy of science, we acquire leadership abilities. Each of us in our own way displays leadership, and without it our enterprise could not succeed. In our labs, seminars, committees and many

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In This Issue

View from the Bench:

The Essential Elements (continued)

other venues, each of us contributes crucial threads to the tapestry that makes our center viable.

That is why I believe that on the eve of the 14th anniversary of the center's opening, it is no longer a raw unproven place with an uncertain future but rather a stable, robust, mature scientific enterprise that fits well into a broader structure designed to understand better, improve on what has been done, inspire more, and renew ourselves by passing on what we have learned.

I am always struck by the quality of effort and creativity that arises from a collective dynamic of people working for common purpose. That is what we all provide to the need for leadership. However, as we reflect on what we have achieved and look forward to what we have left to do, remember the simple acceptance of a very prestigious senior position by my most important scientific mentor, "Of course, the experiments will continue to come first."

View from the Bench is a new invited commentary forum. Comments, discussions about the inaugural essay? Write to: pmjones@childrensmemorial.org

Director's Message:

A Year of Accomplishments

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

It is my privilege to report the basic and translational research milestones of 2008 to advance the mission of Children's Memorial Research Center—providing the best health care for children. Our research investigators have been awarded a record-breaking $31.5 million in extramural funding, including a 21 percent increase in funding from the National Institutes of Health (NIH) through grants and subcontracts. It is noteworthy that the total amount of extramural support represents an 11 percent increase compared with last year's portfolio, and demonstrates the competitive and vibrant nature of the research enterprise.

Our ongoing commitment to enhance the research infrastructure remains strong. We have made a major investment in licensing a powerful translational research tool called XenoBase. This bioinformatics system allows the integration and analyses of data retrieved from basic and clinical research—to identify viable strategies for accurate diagnoses and treatments, and to expedite drug target and biomarker discovery. For the first year of testing, three pilot projects evaluate XenoBase's potential:

- A pediatric brain tumor project, led by Drs. Marcelo Bento Soares and Stewart Goldman;
- A food allergy project, led by Drs. Xiaobin Wang and Jackie Pongracic; and
- A pediatric critical care project, led by Dr. Mark Wainwright.

We anticipate the launching of new projects in 2009. This is truly a transformational research initiative for Children's Memorial investigators.

I end on a note of gratitude for our special partnerships, especially our long-standing relationship with the Medical Research Institute Council, which has helped us to survive and thrive. The generosity of philanthropists David and Denise Bunning continues to support the Children's Memorial Food Allergy Study. Lastly, I congratulate our academic partner, Northwestern University, for its success in garnering a prestigious Clinical and Translational Sciences Institute (NUCATS) Award from the NIH. The award supports NUCATS' ongoing efforts and funds five centers, two of which will be led by Children's Memorial attending physicians.

Appointments and Promotions

Photo: Children's Memorial Audio-Visual Department

Carl L. Backer, MD

Carl L. Backer, MD was recently appointed the division head of Cardiovascular-Thoracic Surgery. Backer received his medical degree from the Mayo Medical School in 1980 and finished residency programs in general surgery and cardio-thoracic surgery at Northwestern University Medical School. He completed his fellowship in pediatric cardiovascular-thoracic surgery at Children's Memorial Hospital under the supervision of the late **Farouk Idriss, MD**. Backer and Idriss performed the first heart transplant at Children's Memorial Hospital on May 13, 1988.

Backer is a member of the American Association for Thoracic Surgery, European Association for Cardio-Thoracic Surgery, the Congenital Heart Surgeons' Society, and the International Society for Heart & Lung Transplantation. He is also the chair of the Medical Advisory Board of the Children's Heart Foundation. For the past five years, Backer has served as the surgical director of the Heart Transplant Program at Children's Memorial.

In addition to heart transplantation, his expertise includes neonatal heart surgery, arrhythmia surgery and tracheal surgery. During his career, he has authored 179 peer-reviewed articles and 70 book chapters. Backer served as co-editor of the second and third editions of the comprehensive textbook, "Pediatric Cardiac Surgery". Backer is on the editorial boards of the *Journal of Thoracic and Cardiovascular Surgery* and the *Journal of Cardiac Surgery*. He is editor of the congenital section of CTSNet, an internet-based resource for education and scientific information. Since 2001 he has been Professor of surgery at Northwestern University's Feinberg School of Medicine and the A.C. Buehler Professor of Surgery.

Marleta Reynolds, MD has been appointed as the interim surgery department head and surgeon-in-chief, effective September 1, 2008. She is replacing Constantine Mavroudis, MD, who has accepted the position as head of the Congenital Heart Surgery Program at the Cleveland Clinic.

Photo: Children's Memorial Audio-Visual Department

Marleta Reynolds, MD

Reynolds has been at Children's Memorial since 1985. Currently she is the division head of Pediatric Surgery, director of the ECMO Program (extracorporeal membrane oxygenation or heart/lung bypass support), and a co-director of the Institute for Fetal Health. She holds the Lydia J. Fredrickson Professorship in Pediatric Surgery and is a Professor of surgery at the Feinberg School.

Reynolds received her BS degree from Stanford University and her MD degree from the Tulane University School of Medicine. She completed her residency at Tulane Affiliated Hospitals, Children's Memorial and Northwestern University Medical Center. She is board certified in four specialties, including general surgery, pediatric surgery, cardio-thoracic surgery and surgical critical care.

InTouch WITH RESEARCH at Children's Memorial Research Center

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Children's Memorial Research Center is the research arm of Children's Memorial Hospital, and a virtual center for pediatric research at Northwestern University's Feinberg School of Medicine. Founded in 1989, the research enterprise has grown to include more than 200 investigators and more than $31 million in external funding for research, two-thirds from the NIH and other federal agencies.

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Research Team Helps Get Female Athletes Back on the Field

Photo: Children's Memorial Audio-Visual Department

Cynthia R. LaBella, MD

Sports-related knee pain is a common complaint among female adolescent athletes and frequently limits sports participation. A research team led by Cynthia R. LaBella, MD tested the hypothesis that preseason neuromuscular training would reduce sports-related knee pain and improve self-rated athletic performance. The results suggest that this is the case, and support the development of curricula to train coaches in incorporating neuromuscular exercises into their preseason routines. The study is published in *Clinical Pediatrics*. LaBella is medical director of the Children's Memorial Institute for Sports Medicine and Assistant professor of Pediatrics at the Feinberg School. Co-authors are **Michael R. Huxford, MEd, Tracie L. Smith, MPH** and **Jenifer Cartland, PhD**. Smith and Cartland are members of the Mary Ann and J. Milburn Smith Child Health Research Program of the research center.

Awards

Yong-Chao Ma, PhD

Yong-Chao Ma, PhD, Assistant professor of Pediatrics at the Feinberg School and a member of the Neurobiology Program of the research center, is the recipient of a 2009 Searle Scholar Award from the Searle Leadership Fund in the Life Sciences through Northwestern University. The Searle Award is a prestigious career development award from the Chicago Community Trust. Highly qualified nominees from across the university compete for this honor; selections are made by a committee of distinguished faculty representing a range of disciplines.

Photo: Children's Memorial Audio-Visual Department

Isabelle De Plaen, MD

Isabelle De Plaen, MD, was awarded a 2008 American Gastroenterological Association Foundation for Digestive Health and Nutrition Bridging Grant. Her long-term goals are to elucidate the molecular mechanisms that lead to neonatal enterocolitis (NEC), a deadly disease affecting the bowel of the premature infant, and to develop new therapeutic approaches. De Plaen's laboratory has developed and characterized a neonatal mouse model of NEC. Using this model, she is studying the cell-specific role of the transcription factor nuclear factor-kB, a major regulator of inflammation, on bowel injury and NEC. She expects that the results will have an important impact on the understanding of NEC pathogenesis and promote specific cell-targeted therapies to change the outcome of this devastating disease. De Plaen is Associate professor of Pediatrics at the Feinberg School, a member of the Center for Digestive Diseases and Immunobiology of the research center and a neonatologist at Children's Memorial Hospital.

Presentations

Martha C. Bohn, PhD, director of the Neurobiology Program of the research center and Medical Research Institute Council Professor of Neurobiology at the Feinberg School, presented a talk entitled "Viruses offer cures! Gene therapy for Parkinson's disease and other brain diseases" on January 27, 2009 at the Copper Mountain Resort in Colorado. Bohn's talk, a "town meeting" for all residents of Summit County, was sponsored by the Winter Conference for Brain Research. Other outreach activities included visits to local schools

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Correction

The title of **Michael L. Miller, MD**, was incorrectly listed in the Fall 2008 issue of *InTouch*. Miller is director of clinical services, Division of Immunology/ Rheumatology at Children's Memorial Hospital and Associate professor of Pediatrics at Northwestern University's Feinberg School of Medicine.

by neuroscientists to introduce children to a variety of aspects of nervous system function.

Laura Herzing, PhD will present at the Keystone Symposia meeting, Epigenetic Basis of Neurodevelopmental Disorders, in Keystone, Colorado, March 6-10, 2009. Her talk is entitled "Epigenetic consequences of fetal alcohol exposure". Herzing is Assistant professor of Pediatrics at the Feinberg School and a member of the Human Molecular Genetics Program of the research center.

Research in the News

December 8, 2008 —
New York Times Health Section

In a feature about the Children's Memorial Food Allergy Study, Xiaobin Wang, MD, MPH, ScD, director of the Smith Child Health Research Program, explained that the research uncovered large variations in food allergy between a rural population in China and urban populations in the United States. "What can explain the U.S. and China difference?" she asked. "Is it urban versus rural exposure? Diet and lifestyle? Or genetic susceptibility? These are all questions we are trying to find some clear answers for." Jacqueline Pongracic, MD, head of the Division of Allergy and Immunology at Children's Memorial and co-author on the study, said even trace amounts of allergens can cause life-threatening reactions. "Ultimately, we hope that our research will lead to the discovery of ways to predict which child is likely to outgrow food allergy," she wrote, adding that doctors hope to develop therapies "that can lessen the severity of an allergic reaction, and even protect against the reaction in the first place."

Photo: Children's Memorial Audio-Visual Department

Rajesh Kumar, MD

November 21, 2008 —
Reuters Health

A "distressingly high" proportion of inner-city children with asthma are exposed to cigarette smoke at levels that could be harming their health. More than two-thirds of the 8- to 14-year-olds in a study conducted by Rajesh Kumar, MD, Assistant professor of Pediatrics at the Feinberg School and attending physician in the Division of Allergy and Immunology at Children's Memorial and colleagues, had levels of the nicotine byproduct cotinine in their saliva, demonstrating that they were breathing enough second-hand smoke to affect their asthma. Identifying caregivers of asthmatic children who are smokers and providing intense intervention to help them quit could help reduce harm from asthma in poor inner city children, the researchers conclude. The study was published in the October 2008 issue of the *Journal of Allergy and Clinical Immunology*.

Karen Sheehan, MD, MPH

November 28, 2008 —
***Washington Post* (HealthDay News)**

In response to the annual toy safety report, Trouble in Toyland, issued by the nonprofit U.S. Public Interest Research Group (PIRG), Karen Sheehan, MD, MPH, medical director of the Injury Prevention and Research Center at Children's Memorial, and medical director of the Injury Free Coalition for Kids, thinks more must be done to protect children from dangerous toys. "For decades, the Consumer Product Safety Commission has been under-funded and lacked the resources to be proactive in screening for hazards. Parents need to carefully choose toys — especially for young children," Sheehan said.

A study conducted by Jill Morris, PhD during her tenure as a postdoctoral fellow at the NIH, was featured in the November 2008 issue of *The Scientist*. The 1997 study, published in *Science*, was the first to describe the NPC1 gene, which is responsible for a rare neurodegenerative disorder called Niemann-Pick Type C. As a result of this discovery, the NIH is currently conducting drug screens for the treatment of NPC and Alzheimer's disease. Morris is Assistant professor of Pediatrics at the Feinberg School and a member of the Human Molecular Genetics Program of the research center.

Profile:

Debra E. Weese-Mayer, MD

photo: Children's Memorial Audio-visual Department

Debra E. Weese-Mayer, MD

Debra E. Weese-Mayer, MD, director of the Center for Autonomic Medicine in Pediatrics (CAMP) at Children's Memorial Hospital, leads an interdisciplinary program for children who suffer from dysregulation of the autonomic nervous system (ANS; the system that regulates control of automatic functions including breathing, heart rate, temperature regulation and more). A newly established Center and the first of its kind in the world, the CAMP team utilizes comprehensive physiologic assessment in a state-of-the-art laboratory coupled with genetic tools to diagnose and effectively manage complicated patients internationally.

In 2001, Weese-Mayer described the constellation of symptoms characteristic of congenital central hypoventilation syndrome (CCHS), demonstrating involvement of virtually all organ systems affected by the ANS. This was a critical advance for a disorder previously thought to reflect primarily a control of breathing deficit. This advance led to focused candidate gene inquiry. In 2003, Weese-Mayer and colleagues demonstrated that the Paired Like Homeobox gene (*PHOX2B*), occurring early in the embryology of the ANS, is the CCHS disease-defining gene. With colleague Elizabeth Berry-Kravis, MD, PhD, she developed and patented the assay that has evolved into the *PHOX2B* Screening Test; the patent is donated to fund research. Between the *PHOX2B* Screening and Sequencing Tests, Weese-Mayer and colleagues have demonstrated that all individuals with the CCHS phenotype will have a *PHOX2B* mutation; genetic testing has simplified confirmation of the diagnosis of CCHS considerably. Most children with CCHS are heterozygous for a polyalanine repeat expansion mutation (PARM), while the minority have a missense, nonsense, or frameshift non-PARM (NPARM) mutation.

With the genetic testing came a more comprehensive understanding of the genotype-phenotype relationship. Why were some children completely ventilator-dependent and others needing ventilatory support during sleep only? Why did some have near total gut Hirschsprung disease and others only suffered from severe constipation? And why did some children have prolonged cardiac pauses and others none at all? Weese-Mayer and colleagues demonstrated that the clinical phenotype varied with the nature of the *PHOX2B* mutation. Among the PARM cases, the clinical picture corresponds with the number of alanine repeats on the affected allele. The normal allele has 20 alanines and the affected allele has 24 to 33 alanines; more alanines correlate with a more severe phenotype among the most common *PHOX2B* genotypes (20/25, 20/26, 20/27). Children with the NPARMs typically have the most severe CCHS phenotype.

Weese-Mayer uses the *PHOX2B* test results to provide anticipatory guidance for parents and referring physicians. She described mosaicism in a subset of parents and presentation of CCHS in adulthood in a subset of cases, both situations demonstrating that CCHS is inherited in an autosomal dominant manner with a stable mutation. Weese-Mayer is working with a colleague in Italy to better understand how each mutation affects cellular expression of *PHOX2B*, with the aim to modify the phenotype with pharmacologic intervention. She and Vasil Galat, PhD, director of the Stem Cell Core Facility of the research center, hope to develop pluripotent stem cells for implementation of translational research inquiry into CCHS.

Weese-Mayer envisions an enormous mosaic or puzzle of disorders including ANS dysregulation. She anticipates experts in all pediatric disciplines involving organ systems affected by the ANS working in concert to implement intervention. Says Weese-Mayer: "Our passion has grown to understanding the expanded constellation of autonomic disorders we study in CAMP. This entirely new discipline for Pediatrics has captured the interest of many in our efforts to help special children and adults with these rare but extraordinary diseases. Comprehending the nature of these disorders will ultimately improve our understanding of basic systems in health as well as disease."

Debra E. Weese-Mayer, MD, is medical director of CAMP and Professor of Pediatrics at the Feinberg School.

Student News

Photo: Children's Memorial Audio-Visual Department

Troy Camarata

Troy Camarata, graduate student in the laboratory of Hans-Georg Simon, PhD, Developmental Biology Program, defended his thesis on Nov 19, 2008 and received his diploma from Northwestern University in December. The title of his thesis was "Pdlim7 regulates nuclear/cytoplasmic localization and activity of Tbx5 during cardiac development". Camarata will begin a postdoctoral fellowship at Harvard University, focusing on progenitor cells in the adult kidney for therapeutic approaches in acute and chronic kidney disease.

Photo: Children's Memorial Audio-Visual Department

Katharine M. Hardy, PhD

Katharine M. Hardy, PhD, has joined Dr. Mary Hendrix's laboratory as a postdoctoral fellow. She will be examining how the reactivation of embryonic pathways influences the plasticity of aggressive melanoma, with particular emphasis on nodal signaling. Hardy obtained her MS in Gerontology and her doctorate in Cell Biology and Anatomy from the University of Arizona, Tucson in 2003 and 2008, respectively. Her master's research concentrated on the cellular trafficking pathway of the protein product of the glaucoma gene known as Myocilin, in the trabecular meshwork of the eye. Her doctoral thesis focused on the regulation of cell behavior by multiple signaling pathways during the early developmental process of avian gastrulation.

Tyler Schwend, graduate student in the laboratory of Sara Ahlgren, PhD, Developmental Biology Program, has been awarded a Ruth L. Kirschstein National Research Service Award for Individual Predoctoral Fellows from the National Institute of Dental and Craniofacial Research. His award is entitled "Sonic hedgehog signaling in zebrafish branchial arch development". The research will seek to delineate the signaling mechanism whereby the Sonic hedgehog (Shh) pathway promotes zebrafish skeletal development in the branchial arches (jaw and gills) of the fish. Human craniofacial diseases arise from the misregulation of the Shh signaling pathway during early development; a better understanding of its temporal and spatial regulation will be fundamental in helping to explain phenotypic variation in the human disease state.

Photo: Children's Memorial Audio-Visual Department

Tyler Schwend

Photo: Children's Memorial Audio-Visual Department

Jorge Cantu

Jorge Cantu, graduate student in the laboratory of Jacek Topczewski, PhD, Developmental Biology Program, and **Jenny Kerschner**, graduate student in the laboratory of Ann Harris, PhD, Human Molecular Genetic Program, have been selected as trainees for the Cellular and Molecular Basis of Disease Training Program at Northwestern University. The CMBD, funded through the NIH, Institute of General Medical Sciences, is an interdisciplinary and cross-campus program that provides state-of-the-art training in the cellular and molecular sciences for highly qualified predoctoral candidates.

Photo: Children's Memorial Audio-Visual Department

Jenny Kerschner

by Tyler Schwend

Fundraising:

MRIC Matters

The Medical Research Institute Council (MRIC) was established in 1951 as a private, independent initiative to raise funds for innovative biomedical research. In 1991, the MRIC began its affiliation with Children's Memorial Hospital. Since that time, the MRIC has raised $45 million, including support of Children's Memorial Research Center construction and expansion. MRIC funding has led to advanced investigation in cancer, heart disease, genetics, microbiology and neonatology.

2008 Children's Ball Caps off Record-breaking $5.3 Million Campaign for MRIC

More than 1,200 guests packed the ballroom at the Hilton Chicago last December for the 50th annual Children's Ball, the MRIC's signature fundraising event. Seasons: A Year of Discovery was the theme for the ball that capped off a record-breaking 2008 fundraising campaign, which raised $5.3 million for pediatric medical research.

Co-chairs Emily Emmerman and Meredith Bluhm-Wolf chose the theme of Seasons: A Year of Discovery in celebration of the beauty of the seasons and the hope and promise of each new day.

The elegant, season-filled evening consisted of exciting entertainment, fabulous food, dramatic decor and most importantly, fundraising for pediatric medical research. Young violinists from the Suzuki Orff School of Music greeted guests at the bottom of the Grand Staircase. Spring was in full bloom as guests enjoyed the cocktail reception, which consisted of a "butterfly" dancer under an elaborate tree. Upon entering the ballroom for dinner, guests were transported to a winter wonderland. The ballroom looked like a sparkling crystal ice palace with all white décor, an all white dance floor with large crystal chandeliers overhead and centerpieces made up of white hydrangea blossoms with crystals and rock candy creating a beautiful icicle effect.

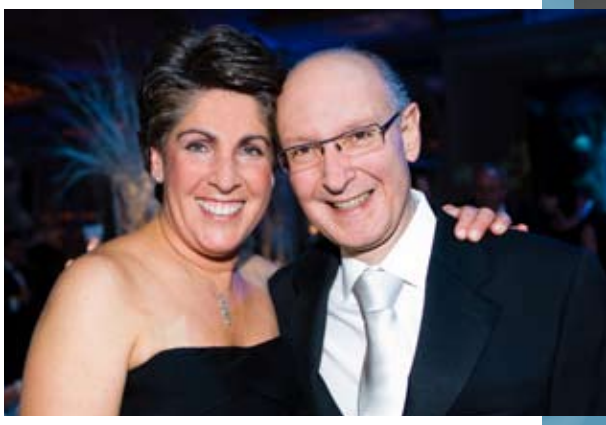


Photo: Garbo Productions

MRIC Vice-chair Nancy Berberian and Marcelo Bento Soares, PhD

Michael Lerich's orchestra provided the soundtrack for the evening while 15 professional dancers from Stage Factor, Inc. boogied on stage as the crowd kept the dance floor packed at all times.

At the ball, the co-chairs for the 2009 campaign and ball were announced: They are Donna Drescher and Debbie Marcus.

Both co-chairs are thrilled about their new roles and look forward to an exciting and busy year of fundraising and events culminating with the Children's Ball on December 12 at the Hilton Chicago. While Drescher is new to the MRIC this year, she is not new to Children's Memorial. She and her family first became involved with the hospital when her son, Jake, was successfully treated for leukemia when he was a teenager. Her family, along with the Schaffer family, began the Children's Memorial Car Raffle in 1996 as a way of giving back to the hospital.

To date, the car raffle has raised more than $3.2 million for the hospital over the last 12 years.

Marcus is also new to the MRIC this year, but she is well aware of the group's impressive history and fundraising success. She is honored to have been selected as a co-chair and eager to get started on fulfilling the mission of the MRIC.

The co-chairs are already hard at work on theme development for the 2009 ball and developing their fundraising strategy for the year, which

[continued]

Photo: Garbo Productions

2008 MRIC Campaign and Ball co-chairs Emily Emmerman (left) and Meredith Bluhm-Wolf with professional dancers from Stage Factor, Inc.

Fundraising:

MRIC Matters (continued)

Photo: Garbo Productions

2009 Campaign and Ball co-chairs Debbie Marcus (left) and Donna Drescher

includes broadening the MRIC's reach within the community. The co-chairs are also eager to begin working towards completing the MRIC's $7.5 million pledge to support four critical areas of research including human molecular genetics, clinical and translational research, cancer biology and epigenomics, and kidney disease research.

Next up for the co-chairs and the MRIC is the 2009 campaign kick-off event coming up in the spring at which the theme for the ball will be unveiled.

by Arla Silverstein

MRIC Web Site

To get the latest information on MRIC events and fundraising campaigns, please visit the group's web site at www.mricchildrens.org.

Noteworthy:

Cracking the Code with the Bear Research Symposium 2008

(From left) Kathleen Casey, Laura Soucek, PhD, and Marcelo Bento Soares, PhD

Photo: Children's Memorial Audio-Visual Department

The 3rd annual "Cracking the Code with the Bear" Research Symposium was held on November 21, 2008 at the research center. Eight postdoctoral scientists and two graduate students were nominated by distinguished colleagues and came from across the country to present their seminal achievements in cancer research.

Bear Necessities Pediatric Cancer Foundation was pleased to award a $40,000 grant to **Laura Soucek, PhD**, Associate research molecular biologist from the University of California, San Francisco for her work in inhibiting MYC as a cancer therapy. **Alysson Muotri, PhD**, Assistant professor from the University of California, San Diego, and a 2007 presenter, was the keynote speaker. This symposium is a joint effort of Marcelo Bento Soares, PhD, Stewart Goldman, MD and **Kathleen Casey**, president and founder of Bear Necessities.

National Children's Study Update

Photo: Andrew Campbell

Jane Holl, MD, MPH

"The National Children's Study will examine the effects of environmental influences on the health and development of 100,000 children across the United States, following them from before birth until age 21. The goal of the Study is to improve the health and well-being of children."

— NCS web site

Jane Holl, MD, MPH is leading the study center responsible for the Chicago region. In September 2008, the National Institute of Child Health and Human Development awarded Northwestern University a five-year, $14.5 million contract to extend the study to DuPage and Will Counties; Cook County is already part of the study. Data collection in the field for the "vanguard centers" — the first seven centers to be established — will begin in 2009; Holl says that her team will be going into the field in 2010.

Holl is an attending physician in the Division of General Academic Pediatrics and medical director for Patient Safety at Children's Memorial; and director of the Institute for Healthcare Studies and Associate professor of Pediatrics and Preventive Medicine at the Feinberg School.

Ann Harris, PhD, Professor of Pediatrics at the Feinberg School, director of the Human Molecular Genetics Program and the Valerie and George D. Kennedy Research Professor in Human and Molecular Genetics of the research center, and colleagues, have published two papers on elements that interact with the cystic fibrosis transmembrane conductance regulator (CFTR). The first, entitled "An insulator element 3' to the CFTR gene binds CTCF and reveals an active chromatin hub in primary cells" was published in *Nucleic Acids Research* in January 2009. The first author is Neil Blackledge, PhD, a former graduate student and postdoctoral fellow in the Harris laboratory. The data suggest that the CFTR locus exists in a looped conformation, characteristic of an active chromatin hub. A second paper, entitled "A complex intronic enhancer regulates expression of the CFTR gene by direct interaction with the promoter" will be published in the *Journal of Cellular and Molecular Medicine*. The first author is Christopher Ott, a current graduate student in the laboratory. The data provide the first insight into the 3D structure of the CFTR locus and confirm the contribution of intronic cis-acting elements to the regulation of CFTR gene expression.

Photo: Children's Memorial Audio-Visual Department

Neil Blackledge, PhD

Photo: Children's Memorial Audio-Visual Department

Christopher Ott

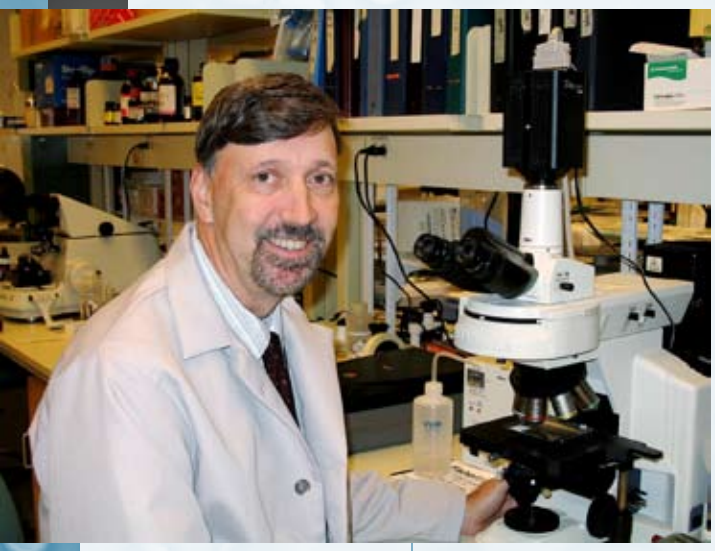
Web Extras

Read Dr. Aleksandra Glavaski's interview about her visit with Martha C. Bohn, PhD, to the laboratory of Mari Dezawa in Sendai, Japan.

Recent Awards
Research Center Publications

Interview:

Barry Wershil, MD



Barry Wershil, MD

Barry Wershil, MD is the head of the Division of Gastroenterology, Hepatology and Nutrition at Children's Memorial and Professor of Pediatrics at the Feinberg School. *InTouch* met with Wershil recently to discuss his research.

Tell us about your research interests, past and present.

I have been studying the in vivo function of mast cells—granulated cells that are critical in host defense—in the gastrointestinal tract. I was involved in developing a model in the laboratory of Dr. Stephen Galli at Beth Israel Hospital in Boston. Using a naturally occurring mutant strain of mouse that was deficient in mast cells, we developed a technique to culture mast cells in vitro and transplant them into the deficient mice. We then investigated how mast cells participated in reactions using normal mice, mice that were mast cell deficient, and mast cell deficient mice that had their deficiency repaired. It allowed us to exquisitely dissect the function of mast cells in any reaction. We were concurrently involved in the identification and characterization of a major cytokine called stem cell factor that influences mast cell initiation, maturation, survival and function.

I've become interested in a number of disease processes known collectively as eosinophilic diseases of the gastrointestinal tract*. These include eosinophilic esophagitis (EoE)† and eosinophilic gastroenteritis‡. Formerly rare, these conditions are becoming more prevalent, perhaps due to food allergies that are site-specific within the GI tract. Because this is an emerging disease process, companies are interested in new therapies. We have the opportunity to lead both basic and translational research in these eosinophilic diseases.

I am on the steering committee for The International Gastrointestinal Eosinophilic Researchers (TIGERs), a group of clinical and basic researchers who investigate eosinophilic diseases of the GI tract. We have organized several national meetings focused on these problems. In 2007, we published a consensus guideline for the diagnosis and treatment of EoE. I was recently elected to chair the Scientific Advisory Council for TIGERs, which will review and allocate funding support for collaborative research within the organization.

At Northwestern, a core of people interested in EoE has the opportunity to expand our place on the national stage with a program that will provide novel diagnostic approaches and therapies. We have one clinical trial running and three in stages of planning or submission.

What are your research plans for the Division?

The Division consists of several component subsets. Hepatology, which encompasses liver transplantation, has a long history of outstanding clinical care and ground breaking innovation led by Drs. Peter Whitington and Estella Alonso. GI and Nutrition is composed of young, talented physicians who are actively building their careers. This presents an opportunity to mentor them while we establish various programs within the Division. Today, research is about translational studies, and we want to strengthen translational research efforts as much as possible. Those kinds of studies are already under way in the Liver Transplant Program, and I hope to recruit a leader for our Inflammatory

[continued]

* A heterogeneous group of diseases that are characterized by symptoms such as abdominal pain, nausea, vomiting and diarrhea, and by increased eosinophils – granular leukocytes – in the intestinal mucosa.

† A severe disease of the esophagus characterized by a marked accumulation of eosinophils, which are normally absent in the esophagus.

‡ Eosinophilic inflammation limited to the stomach and small intestine.

Interview:

Barry Wershil, MD (continued)

Bowel Disease program who's going to help make that happen with EoE.

We have a vibrant clinical program in motility disorders in children. Opportunities exist for basic research agendas to materialize in cores that either don't have the critical mass or the personnel at present. Over the next few years, the Division will be pushing a research agenda forward within the motility program, the inflammatory bowel disease program and the EoE program, among others.

I've discussed a pancreatobiliary center with several faculty members at the Feinberg School. For diseases of the pancreas or biliary tract, I'm interested in creating a program that can conduct the kinds of specialized studies and procedures that are required to evaluate these children. If we build that center, we will be able to develop a cohort of patients, then jump-start studies and other kinds of investigations.

Langman Featured on ABC 7 Chicago

Craig B. Langman, MD

The Vitamin D research of Craig B. Langman, MD, head, Division of Kidney Diseases at Children's Memorial, the Isaac A. Abt, MD, Professor of Kidney Diseases, Northwestern University's Feinberg School of Medicine, and a member of the Developmental Biology Program at the research center, was featured on ABC7 Chicago's *HEALTHBEAT* section on January 15, 2009. Langman says his soon to be published research from the 1990s and 2006 shows that between 50 to 70 percent of the thousands of children screened were Vitamin D deficient. "So I think it's going to be very important to change the paradigm of care and start seeing much more supplementation," says Langman.

AAALAC Accreditation

Children's Memorial Research Center has received full accreditation status from the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). The AAALAC accreditation program evaluates organizations that use animals in research, teaching or testing. Those that meet or exceed AAALAC standards are awarded accreditation.

The accreditation process includes an extensive internal review conducted by the institution applying for accreditation. Next, AAALAC evaluators conduct an on-site assessment. Accreditation benefits an institution and the animals in its care in many ways. In addition, each time a new organization becomes accredited, the global benchmark for animal well-being in science is raised.

The Office for Research Integrity and Compliance, the Research Support Facility and the Institutional Animal Care and Use Committee at the research center are to be congratulated for this achievement.