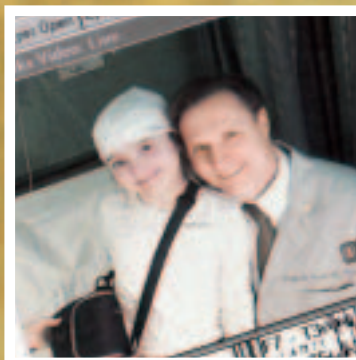
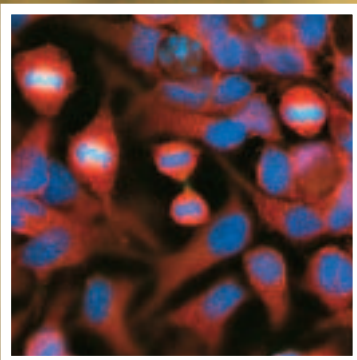


Carousel

THE MAGAZINE OF CHILDREN'S MEMORIAL HOSPITAL • SPRING 2004

Pediatric research today: sophisticated tools for complex problems

- *The role of genes in birth defects*
- *Can fevers cause epilepsy?*
- *Repairing problems through tissue engineering*




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On the cover:
Thumbnail-sized synthetic scaffolding allows bladder tissue to grow in the laboratory for surgical augmentation (see page 5).

ABOUT THIS ISSUE

The progress of biomedical research in the 20th century led to improved infant survival, the conquest of polio and smallpox, and cures for many childhood cancers. As we move into the 21st century, investigators at Children's Memorial and around the world are employing sophisticated new tools and methods to find answers to the increasingly complex health problems—ranging from obesity to hereditary illnesses to cancer—that affect children and their families today.

Powerful imaging technologies allow scientists to view

the biochemical activity

inside living cells. The map-

ping of the human genome

and related technologies,

such as computerized gene analysis, allow scientists to examine the

molecular changes that lead to birth defects and disease.

Collaborations, made easier by the Internet, bring new information

and new methods to research. Partnerships exist not only across insti-

tutions, but across scientific disciplines, bringing multiple perspectives

to bear on difficult problems.

This issue of *Carousel* focuses on just a few of the hundreds of research

projects under way at the Children's Memorial Institute for Education

and Research, the research arm of Children's Memorial Medical Center.



Q&A with Mary Hendrix

In January, cancer biologist Mary J. C. Hendrix, PhD, began her tenure as president and scientific director of Children's Memorial Institute for Education and Research (see page 10). She recently met with the *Carousel* editors to share her thoughts on the state of biomedical research and her plans for the research institute.

Q. What are the most exciting developments in biomedical research?

Functional genomics—which means understanding the functions of genes—is very important, especially all the new genes that have been discovered. Although gene therapy had a rocky start with some of the trials that needed to be shut down, there's still tremendous promise in this field. Stem cell biology and regenerative medicine are exciting areas. How to use stem cells to correct a heart attack, or to correct a gene defect in a child are just a couple of examples of today's research and the hope for tomorrow's cures.

The field of molecular diagnostics is going to explode, because it can feed off all the wonderful new discoveries from the human genome project. As genes are associated with certain diseases, they can be used by pathologists to predict disease outcome. Pharmacogenomics will be a great new field that will allow us to tailor-make drug therapies for a patient's particular disease. That's important because your body may react differently to a certain set of drugs than my body. Pharmacogenomics would allow us to predict which therapy would work best in an individual.

Finally, imaging is an area that has so many new technological advances. For example, in an experimental model we can now trace the migration of one cancer cell over time, as it gives rise to a tumor, and as



Mary J. C. Hendrix, PhD, pictured in the Molecular and Human Genetics Laboratory of the Children's Research Center.

it metastasizes. The information that we generate using imaging technology can be adapted for humans.

Q. What do you think are the biggest challenges facing biomedical scientists in the 21st century?

The five-year congressional mandate to double the NIH budget, which led to annual increases of about 15 percent, has ended. The future budget looks very bleak for the NIH. Nationally, the biggest challenge will be focused on what to do with all the new scientists who were recruited into the "pipeline" in the past five years. Are they going to be discouraged because the funding and the budget are so tight?

The second challenge is adequate time to do research. We are so distracted by our myriad responsibilities and various duties, whether it's teaching, training, fundraising, research, grant preparation, manuscript writing or interviewing. If you think about everything together, it's more than a nine-to-10-hour day can support.

Third, as technology advances, the challenge for many of us will be to learn how to use the new technologies to make new discoveries. How do we train our students about the ethics of conducting research, as regulatory and compliance

guidelines come into play?

Q. How does the fierce competition for funding affect the scientist?

To obtain federal funding, you have to propose a research project that has a low risk of failure, because reviewers of scientific applications at the federal level are looking for a "sure thing." That means you've already done a portion of the project, you've proven you can do it.

But to do their best work, scientists need the freedom and courage to be creative. Philanthropy ends up being one of the major sources that will fund new and creative ideas that may or may not work out or develop into a very large NIH-supported grant. That is the critical nature of philanthropy—it can fund those out-of-the-box ideas.

Q. What role does biomedical research play in the health of our society?

I have said when I testified before Congress that the investment in research is truly an investment in the quality of our lives. The more time, energy and financing put into biomedical research, the better the outcome in discoveries that can be trans-

continued on page 4

lated to improve quality care and health.

As a biomedical researcher, my role right now is to provide a first-class research infrastructure at Children's Memorial Institute for Education and Research that will allow our very talented investigators to make these discoveries, and to ensure that we align all the research activities with the clinical mission of the hospital.

Q. What is your vision for Children's Memorial Institute for Education and Research?

The vision that I've adopted is: discovery, development, delivery. It's a simple message, but the implications are great. That is, discovery in our laboratories will give way to the development of new therapies and products that can be delivered in clinical care. We're going to achieve this goal only through partnerships. Right now there is a special focus at the national level on building unique interdisciplinary research teams. Our laboratory building is geared for that, with core facilities and investigators who share equipment and ideas with one another.

Our goal is to also interact with people outside the research institute. Researchers with different backgrounds have a unique way of looking at a problem. I'm very excited about this potential to build interdisciplinary teams, from epidemiologists to molecular biologists to clinical practitioners and statisticians. The funding for these unique teams is critical for their success, and for the success of the enterprise.

One of the ways we're going to maximize our communication capabilities is by using technology, such as our new videoconferencing equipment, to interact with investigators throughout the world, such as at Scripps Institute in San Diego or at the Karolinska Institute in Sweden. If that is how we assemble the best possible team, then we will not be limited by our geography. ●



Left: U.S. Rep. Rahm Emanuel, JoAnn Eisenberg, of the Medical Research Institute Council, and Mary Hendrix, PhD, celebrate the partnerships that made the research institute expansion (above) possible.

Research building expands

Illinois' First Lady Patti Blagojevich, Sen. Dick Durbin, U.S. Rep. Rahm Emanuel, U.S. Rep. Jesse Jackson, Jr. and state Rep. John Fritchey, joined Children's Memorial Board members, community leaders and other supporters on January 26, for a ribbon-cutting and celebration of the completed addition to the Children's Research Center, the main laboratory and headquarters of Children's Memorial Institute for Education and Research. The expansion to 122,000 square feet nearly doubles the space for laboratory research and will accommodate more than 325 scientists and other staff.

"What you are doing here, in terms of research, will not only bring satisfaction and hope to so many parents and children, but to others all around the country who really look to the leadership of this institution," said Durbin in his address to the group gathered in the building's lobby.

"With Mary Hendrix's leadership, our state-of-the-art facility and the continued support of government leaders and donors, such as the Medical Research Institute Council (MRIC) and so many others, we know the institute will continue to thrive and make meaningful contributions to a healthier future for children," said Kirk Johnson, chairman of the board of the institute. The MRIC has raised more

"What you are doing here, in terms of research, will not only bring satisfaction and hope to so many parents and children, but to others all around the country..."

—Sen. Dick Durbin

than \$25 million for medical research at Children's Memorial including the five-year, \$5 million pledge for the research center expansion. Cancer biologist Mary Hendrix, PhD, began her tenure as president and scientific director of the research institute January 1 (see page 10).

Searching for better solutions

Tissue engineering lends hope for transformation in care

After an uneventful pregnancy, Ricky and Amy Michelon were shocked to learn that their son, Myles, had a rare urological disorder known as bladder exstrophy. He was born with the front of his bladder and the abdominal wall open. The

This technique achieves in one surgery on a newborn what used to take several operations during the first three-to-five years of the child's life.

inside of the bladder was exposed, like a balloon with the top half missing.

Within 48 hours of Myles' birth, he became the second child at Children's Memorial to benefit from a recently developed surgical technique. During a single operation, urological surgeons William Kaplan, MD, and Earl Y. Cheng, MD, closed the bladder, made repairs to the genital structures and repositioned the bladder beneath the pelvic bone where it normally resides. This technique achieves in one surgery on a newborn what used to take several operations during the first

three-to-five years of the child's life.

For reasons medical science does not understand, in some children with bladder exstrophy, the bladder does not grow or function normally. For these patients, surgeons augment the bladder by placing a piece of the child's own intestine on the top of the bladder. While bladder augmentation is quite successful in increasing bladder capacity, the intestinal patch does not grow and function like normal bladder tissue. Consequently, many bladder augmentation patients are at risk of developing infections, bladder stones and other problems. Myles' doctors will need to carefully monitor his progress to see if he will require bladder augmentation in the future.

Earl Y. Cheng, MD, gets up close and personal with patient Myles Michelon during a recent check-up at Children's Memorial.

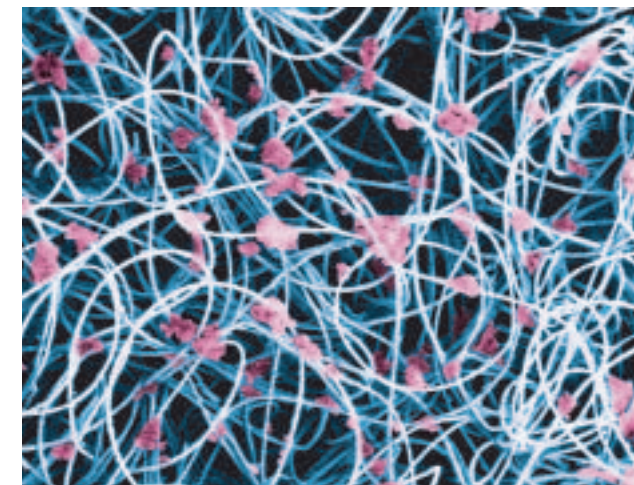


Cheng hopes that through laboratory research, within the next decade he will find a better solution than bladder augmentation for his patients. An associate professor of urology at Northwestern University's Feinberg School of Medicine, he is a surgeon-scientist in urology research at Children's Memorial.

Surgeon-scientists offer a unique and important bridge between basic science research and patient care. "Surgeons see problems in the operating room that we know we can't fix and wonder if there is a better way to treat the patient," says Cheng. "I'm able to take the questions that arise in surgery and see if we can find an answer in the lab."

Researchers at Children's Memorial and other institutions have had success in isolating animal bladder cells, growing the cells in the lab on specialized membranes until they form a sheet of tissue, and then

Microscopic view shows bladder cells (pink) growing on scaffolding material (blue) in the laboratory.



continued on page 6

reimplanting the composite tissue back into the animal's bladder. The body is then able to further integrate the composite with existing bladder tissue. If this technology can be successfully developed for humans, it could help children with

“As a surgeon-scientist, I’m able to take the questions that arise in surgery and see if we can find an answer in the lab.”

—Earl Y. Cheng, MD

bladder exstrophy and other bladder disorders achieve more normal bladder function than current surgical reconstruction offers. Cheng hopes that the research will also lead to new treatment options for other types of congenital disorders that involve the bladder, such as spina bifida.

“Our work shows great promise for the future, but I caution parents that it is still in its early stages,” Cheng says. “It may be a decade before we can safely transplant a laboratory-engineered bladder into a child.”

To foster these kinds of research efforts, Children’s Memorial hopes to establish 10 endowed surgeon-scientist positions through philanthropy of approximately \$1.5 million for each endowed chair.

The Michelin family supports this vision. “A year ago, we didn’t even know bladder exstrophy existed,” says Amy Michelin. “We need to raise funds and awareness now, so that it can help Myles and other children like him—soon.” ●

Seed grant nurtures neuroscience research

Nerve cells inside our brains enable us to think, feel, move and communicate. Until recently, these cells were thought to be irreplaceable if damaged by disease or injury. Then, in the mid-1990s, neuroscientists discovered that parts of the brain produce stem cells throughout life. Stem cells give birth to new nerve cells that could, potentially, restore functions lost to brain damage.

Neurobiologist Francis Szele, PhD, and his colleagues at Children’s Memorial Institute for Education and Research are among those mapping the movements of neural stem cells and their offspring to understand how they might be directed to replace damaged nerve cells. In a study recently published in the journal *Brain Research*, Szele showed that neural stem cells increase production of nerve cells in response to brain injury. Monitoring this activity in laboratory models, Szele noted the new cells migrated toward the injured area in what may be a rudimentary attempt at brain repair.

With the support of a \$34,000 seed grant awarded by the institute, Szele and collaborator Philip Hockberger, PhD, associate professor of physiology at Northwestern University’s Feinberg School of Medicine, are developing techniques that will allow scientists to visualize cell migration inside the brains of living animals using multiphoton time-lapse microscopy, a powerful technology that produces three-dimensional digital images of living cells. Using resources provided by the seed grant, Szele has already employed multiphoton microscopes to create detailed ‘movies’ of cell migration in laboratory models.

“The seed grant provided us with the resources we needed to take advantage of this rare technology and begin applying it to cell migration studies,” says Szele, assistant professor of pediatrics at Northwestern University. “The ability to visualize the behavior of cells in living animals will be of paramount importance in understanding how these cells are regulated and how they can be induced to repair brain damage.”

Migrating brain stem cells labelled with fluorescent protein.

The institute’s seed grant program nurtures promising avenues of research as they develop and begin to attract outside funding. Since 2001, grants totaling more than \$778,000 have been awarded to 24 investigators. The grants are made possible through the generous support of the Medical Research Institute Council (MRIC), the Children’s Memorial Hospital Faculty Practice Plan and the State of Illinois Excellence in Academic Medicine program.

“The seed grant program connects MRIC members in a personal way with the challenges and opportunities investigators encounter in the early stages of their work,” adds Ruth Geller, MRIC chairman. “We want to provide resources to sustain their studies and fuel their success.” ●



Francis Szele, PhD

A future of healthy babies

Developmental biologists explore errors leading to defects, cancers

A human zygote, made from one egg cell and one sperm cell, grows in 40 weeks to become the trillions of cells that make a healthy baby. But first the zygote develops into a blastocyst, a cluster of cells that implants in the uterus and develops into a fetus. This process is controlled by



Philip M. Iannaccone, MD, DPhil

the coordinated effort of many genes. Developmental biologists at Children’s Memorial Institute for Education and Research are studying errors that can occur in certain genes, called Gli genes, during the embryonic period. These errors can cause birth defects and cancer.

“After implantation, the cells divide very, rapidly. At the same time, they are differentiating into particular cells that will become muscles, skin, the brain, the heart and the bones,” says Philip M. Iannaccone, MD, DPhil, director of the Developmental Systems Biology program and deputy director for Basic Research at the institute.

While each cell in our bodies carries all the genes we need, scientists have discovered that what makes the cells differentiate is gene activity. “Depending on which genes are active, or turned on, in a particular cell, the cell will have one set of proteins, and another cell will have a different set,” says Iannaccone, who is also the George Eisenberg Professor of Pediatrics at Northwestern University’s Feinberg School of Medicine.

With funding from a Program Project Grant from the National Institute of Environmental Health Sciences, Iannaccone and colleagues, including pediatric oncologist David Walterhouse, MD, are studying the activity of the Gli1, Gli2 and Gli3 genes, which regulate other genes involved in the formation of muscle, skeletal and other structures.

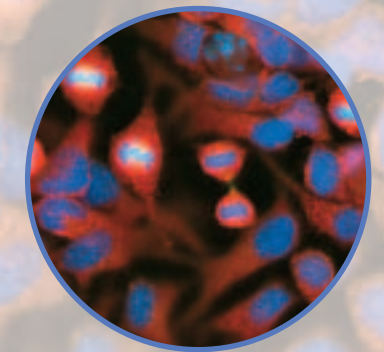
“Problems due to the dysregulation of these genes range from very severe birth defects to lethal childhood cancers,” says Iannaccone. “Many of these babies die shortly after birth, but those who survive suffer serious defects in the shape of the brain and head accompanied by severe mental retardation.”

Malfunctions in the Gli genes are also associated with medulloblastoma, a common and aggressive brain tumor in children, and a variety of childhood soft tissue cancers called sarcomas, including rhabdomyosarcoma, which affects the skeletal muscles.

“In the last five or six years there has been a tremendous amount of work done to show the connections between Gli and these problems, and by what mechanisms the problems occur. Several of these mechanisms have been described in our laboratory,” says Iannaccone.

“We now strongly suspect that the Gli1 gene is much more important in controlling proliferation of cells than it is to differentiation. If this can be proven, it would explain why Gli1 plays a role in cancers, but Gli2 and Gli3 seem not to.

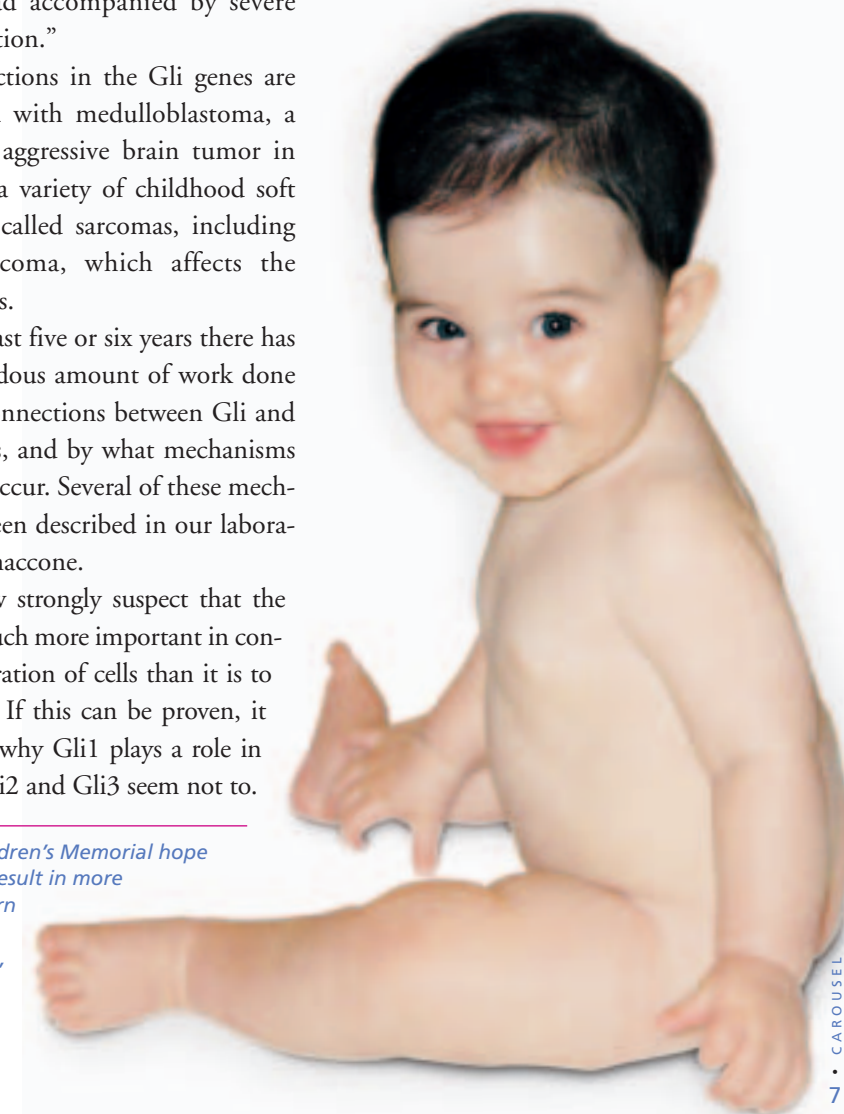
Scientists at Children’s Memorial hope their work will result in more babies being born healthy, like Claire Silverstein, pictured here.



Microscopic view of cancer (rhabdomyosarcoma) cells dividing. Bright red shows Gli genes turned on during cell division.

And why Gli3 is associated with birth defects, but Gli1 is not. We didn’t know any of this when we started,” he says.

“Once we know where in the normal mechanism of action the problems are occurring, then we can look for ways to halt the problems, and ultimately find potential cures,” he says. ●



Pursuing the link between fevers and epilepsy

Multicenter study seeks answers

Despite the latest diagnostic technology such as video electroencephalogram (EEG), positron emission tomography (PET) scans and more than 50 medications at physicians' disposal, the number of children who develop intractable epilepsy—the kind that doesn't respond to treatment—hasn't changed in

be to cure it once it develops, and the third would be to treat it more effectively.”

In a new National Institutes of Health funded, multicenter clinical study, Nordli and colleagues are pursuing one of epilepsy's many causes. Neurologists have long debated whether prolonged febrile seizures lead to epilepsy. Febrile or “fever”

seizures are very common among children under 5 years old. They occur in approximately 100,000 U.S. children annually when body temperatures rapidly rise above 101 degrees Fahrenheit. Studies on animals have shown an association between a rapid rise in body temperature and seizure activity. In most children these seizures have no lasting consequences. But the study will focus on the 3 percent of children who have a febrile seizure lasting

more than 30 minutes and develop scar tissue in the brain.

“This is a landmark study,” says Nordli, the central EEG reader for the study. “It will show if this population develops epilepsy as a result of scarring, and if so, what the risk factors are. Principal investigator Shlomo Shinnar, MD, at Einstein Medical School in New York, has assembled a first-class team.”

Previous studies have attempted to find a link between febrile seizures and epilepsy, but have lacked the funding, methodology and patient population large

enough to answer the question. With six medical centers participating in the current study, investigators hope to enroll 200

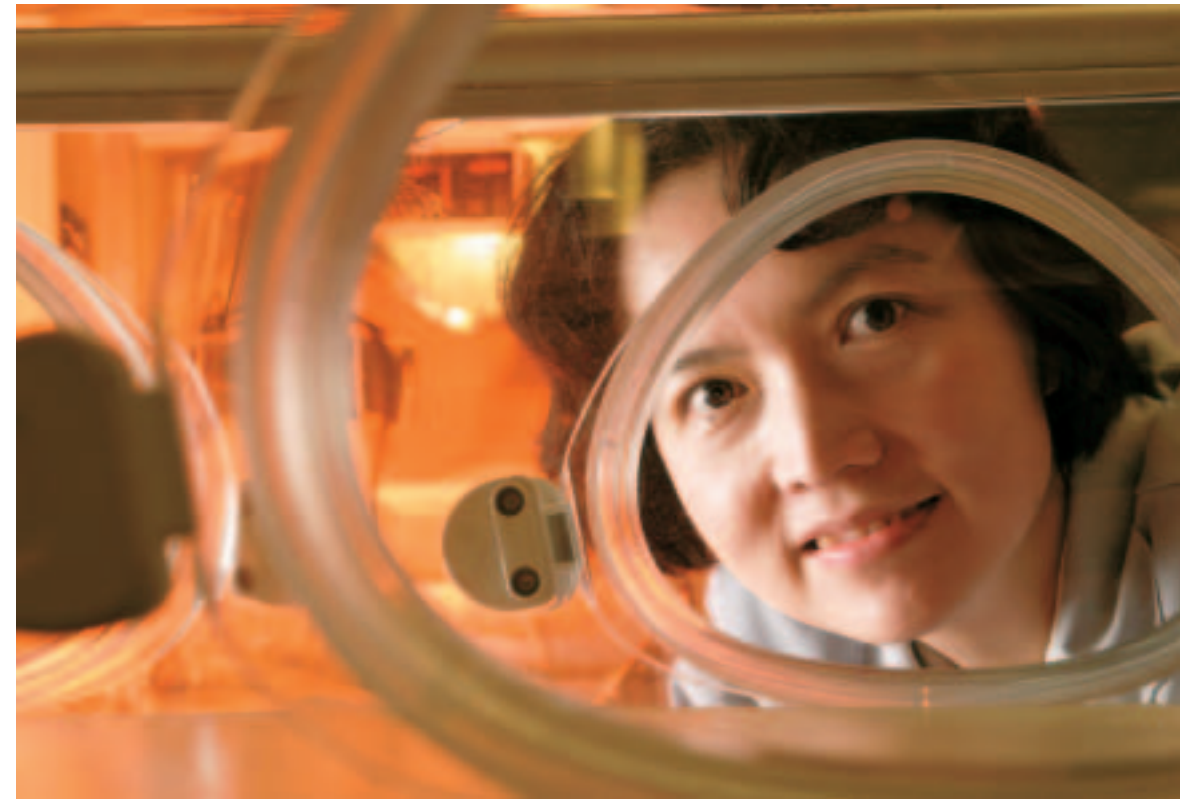
“This is a landmark study. It will show if this population develops epilepsy as the result of scarring, and if so, what the risk factors are.”

— Douglas R. Nordli, Jr., MD

children and track them for five years. In addition to collecting traditional data such as a medical history, magnetic resonance images (MRIs), and EEG analysis, two new vital pieces of information will be gathered from each of the patients—evidence of previous viral infection and genetic markers. Leon G. Epstein, MD, head of the division of neurology, is leading the viral component of the study.

“With this information,” says Nordli, “we'll be able to determine who's at risk by recognizing if it's a particular set of clinical characteristics, infection with a particular virus, or a genetic pre-disposition. Then we can do something about it.” Nordli points to his basic science research colleagues at Children's Memorial and throughout the country who are investigating “neuroprotective strategies” such as diet and medications that might prevent the development of epilepsy in patients identified as high-risk.

Though it is still in the very preliminary stages, Nordli says he is encouraged by the design of the febrile seizure study. “We've learned that it is practical to do collaborative studies in the field of epilepsy,” he says. “Even in one very large institution you won't have enough patients to answer a question. It's critical for this kind of research to be conducted multi-institutionally.” ●



Xiaobin Wang, MD, MPH, ScD, the Mary Ann and J. Milburn Smith Research Professor, looks to genes and the environment for answers to preterm and low birthweight babies.

smoking and infant birth weight. She recently published her results in the *Journal of the American Medical Association*. While the dangers of smoking during pregnancy are fairly common knowledge, Wang points out that there are vast differences in a person's

capacity to avoid the negative effects. “This capacity is largely determined by genes.” Her study found that women who smoked and had two gene variants (CYP1A1 and GSTT1) had a markedly increased risk of

“More than one in 10 U.S. babies comes into the world either too early or too small. Both preterm and low-weight births are associated with high death rate in infants and a high risk for illness in children.”

—Xiaobin Wang, MD, MPH, ScD

having a baby with low birth weight versus those women who smoked and did not have these genetic variants.

Wang says the smoking-gene interaction study is just the beginning. “With a multidisciplinary team of investigators and our expertise in clinical medicine, epidemiology, molecular genetics, biostatistics and bioinformatics, we have a great potential to better understand the causes of preterm births and low birth weight, and to improve clinical practice and public health interventions.” ●

Confronting complex childhood problems

Searching for clues

Fifty years ago, the diseases that threatened children and challenged scientists typically had isolated causes such as viral or bacterial infections. According to Xiaobin Wang, MD, MPH, ScD, today's health challenges such as preterm birth, asthma, obesity, diabetes, cancer and emotional and behavioral disabilities have broader and more complex origins.

“Unlike tetanus, polio and measles, which we now can control,” she says, “today we confront disorders that have multiple causes, including environmental and genetic factors.” These problems require a new model for treatment and prevention. As the new director of the Mary Ann and J. Milburn Smith Child Health Research Program at Children's Memorial Institute for Education and Research, Wang is excited about the opportunity to

work with investigators from multiple disciplines to address the most challenging child health problems.

Wang's own research focuses on the interactions between genes and environment, and their effects on reproductive outcomes. “More than one in 10 U.S. babies comes into the world either too early or too small,” says Wang. “Both preterm and low-weight births are associated with high death rate in infants and a high risk for illness in children.” In 1988, with funding from the March of Dimes and the National Institutes of Health (NIH), Wang and her team at Boston Medical Center began recruiting mothers and their newborns for a comprehensive study of the genetic and social-environmental factors that contribute to preterm births and low birth weight. With more than 2,500 mother-infant pairs already enrolled, it is one of the largest studies of its kind in the country. At Children's Memorial, Wang will continue to recruit research subjects.

Wang, a molecular epidemiologist, has also extensively examined the link between genetic factors, maternal cigarette

Six-year-old Bartolina Faugno, a patient in Children's Memorial's Nordstrom Epilepsy Observation Unit, talks with Douglas R. Nordli, Jr., MD, director of the hospital's Epilepsy Center.

half a century, says Douglas R. Nordli, Jr., MD, who holds the Lorna S. and James P. Langdon Chair in Pediatric Epilepsy.

“Seizures are very disabling,” says Nordli, who is also associate professor of pediatrics at Northwestern University's Feinberg School of Medicine. “They interfere with getting an education, driving a car, maintaining a job and social relationships.” But Nordli also believes in the potential of research to some day eliminate the threat of epilepsy to children. “Ideally, we'd prevent the development of epilepsy in the first place. The second best thing would

Medical Research Institute Council

Fostering the potential of medical research

The mapping of the human genome, and the inherent promise it holds to understanding human health and disease, has revolutionized biomedical research. Scientists at Children's Memorial Institute for Education and Research are hoping to harness knowledge from the Human Genome Project to make important contributions to pediatric medicine. And organizations like the Medical Research Institute Council (MRIC) are needed, now more than ever, to support their work.

The MRIC is a fundraising organization with a 53-year history committed to supporting medical research. Since 1991, when the MRIC affiliated with Children's Memorial, it has dedicated its resources to the hospital's research efforts,

raising more than \$25 million, including \$5 million toward the recently completed addition to the Children's Research Center. Other support includes endowments for research scholars and professorships, seed grant funding for young scientists and the purchase of an interoperative radiation therapy system — new technology showing promise for the treatment of brain tumors.

“Research has never been more important for the future of the hospital. Who knows what scientists will discover next or what they'll do with their discoveries?”

— Ruth Geller, chairman, MRIC

“Philanthropic gifts are viewed as important partnerships by external funding agencies like the National Institutes of Health and are critical for our competitiveness in securing external funding,” says Mary J.C. Hendrix, PhD, president and



Ruth Geller, MRIC Chairman

scientific director of Children's Memorial Institute for Education and Research. “To keep up with pressing needs and save precious lives, we need the best researchers, the best technology, the best facilities,” says Ruth Geller, MRIC chairman. “To be able to do this, you need to raise money. The amount of money we've raised has far outpaced our expectations.”

The MRIC recently announced a new commitment to research at Children's Memorial — a pledge to raise \$3 million to fund an endowed chair for Hendrix, who arrived in January.

“Research has never been more important for the future of the hospital,” says Geller. “Who knows what scientists will discover next or what they'll do with their discoveries?” ●

Leader in biomedical science heads research institute

Cancer biologist Mary J. C. Hendrix, PhD, arrived at Children's Memorial in January as president and scientific director of Children's Memorial Institute for Education and Research, and professor of pediatrics at Northwestern University's Feinberg School of Medicine. The institute, the research arm of Children's Memorial Medical Center and the center for pediatric research at Northwestern University, conducts basic science, clinical and translational research on diseases and other problems that affect children and their families.

Hendrix came to Chicago from the University of Iowa in Iowa City, where she was head of the Department of Anatomy and Cell Biology as well as the deputy director of the Holden Comprehensive Cancer Center in the university's Carver



College of Medicine. “Dr. Hendrix brings scientific excellence and visionary leadership to research at Children's Memorial and Northwestern University,” says Patrick Magoon, president and CEO of Children's Memorial Medical Center.

“Dr. Hendrix is a gifted researcher whose laboratory has uncovered key findings that increase our understanding of how cancer metastasizes,” says Lewis Landsberg, MD, dean of the Feinberg School.

Hendrix, who holds a doctorate in anatomy and cell biology from George Washington University, and received post-doctoral training at Harvard Medical

School, has published more than 150 scientific papers, numerous books and book chapters. Her work is funded by the National Institutes of Health (NIH), including a prestigious MERIT (Method to Extend Research in Time) award from the National Cancer Institute.

Hendrix holds leadership roles in many national professional and scientific societies. She is past president of the Federation of American Societies for Experimental Biology, the largest coalition of biomedical researchers in the U.S. In May 2003, she was appointed to the National Advisory Council for Human Genome Research, which establishes program priorities for the National Human Genome Research Institute and sets goals for U.S. efforts in the International Human Genome Project. ●

Improving outcomes for respiratory distress

A multicenter nursing study

Children in intensive care units with severe infections, organ failure or serious injuries often also suffer a lung problem called acute respiratory distress syndrome (ARDS). Kids with this condition build up fluid in their damaged lungs and ventilator support is required to supply oxygen to the child. Approximately 45 percent of these children die from ARDS and 15 percent of surviving kids have permanently impaired lung function.

Children's Memorial advanced practice critical care nurse Lauren Sorce, RN, MSN, and colleagues at 14 other pediatric hospitals are trying to improve these statistics. Funded by the National Institute of Nursing Research at the National Institutes



Lauren Sorce, RN, MSN, with pediatric intensive care unit patient, is site investigator for respiratory distress study.

of Health, they are conducting one of the first multicenter pediatric intensive care nursing studies in the country. “We want to find out if positioning children with respiratory distress on their bellies makes a dif-

ference in their long-term outcomes,” says Sorce. She says that while studies of adults and newborns with ARDS have shown that belly (or prone) positioning improves oxygen levels in the blood, no studies have yet

Sorce and colleagues are conducting one of the first multicenter pediatric intensive care nursing studies in the country.

been conducted on a pediatric population ages 10 months to 18 years. In the current study, Sorce and her colleagues hope to determine if prone positioning improves lung function in children and whether this leads to less time spent on a ventilator. Fewer days on a ventilator can mean fewer long-term complications for kids.

“The outcome of the study will forever impact the clinical care of these kids,” explains Sorce. “Because the criteria for inclusion in the study is so strict, we'll really know if it's the positioning that makes a difference.” ●

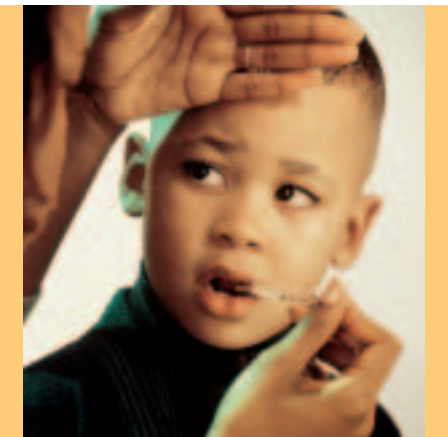
Institutional Review Board protects the public

1972 was a turning point for the ethical treatment of human subjects involved in research projects. That year the Tuskegee syphilis study came into public light through a front-page article in the *New York Times*. Researchers in the study had denied medical treatment to African American men with syphilis to understand the progression of untreated disease. In response to this and other abuses, the National Institutes of Health (NIH) developed a process requiring each institution receiving federal research funds to establish an Institutional Review Board (IRB) responsible for protecting the rights and safety of participants in research projects.

According to Vita Land, MD, MBA, chair of Children's Memorial's IRB, the

hospital's committee evaluated more than 725 proposals for research projects in 2003—a 27 percent increase in activity in the last five years. “Our IRB is a 24-person committee. Four have no hospital affiliation—a philosophy professor, a bible scholar, a parent, and a health care attorney,” says Land. “The other 20 members are healthcare professionals including physicians, nurses, pharmacists, psychiatrists, scientists, statisticians.” The committee reviews all research proposals for scientific merit, patient safety and to ensure that consent documents are easy for research subjects to understand and present the risks as well as the benefits of the research.

Today, as breaches in research safety still make headlines, vigilant protection



of research subjects remains critically important. “We're concerned in every way, shape and form that research subjects are protected, especially children,” says Leon Epstein, MD, associate director of the General Clinical Research Center at Children's Memorial and deputy director for clinical research at Children's Memorial Institute for Education and

Grants and awards

Jacqueline Pongracic, MD, newly appointed head of the Division of Allergy, is site investigator for a \$55.8 million multicenter study funded by the National Institute of Allergy and Infectious Diseases.



The study will evaluate whether using a new noninvasive technology to measure levels of exhaled nitric oxide as a biomarker of airway inflammation will lead to improved control of the disease in urban children with asthma.

A researcher in Children's Memorial's Diabetes Program is site investigator for a multicenter study to improve family management of Type I diabetes in children and adolescents. With funding from the National Institute of Child Health and Development at the National



Institutes of Health, pediatric psychologist in the Division of Child and Adolescent Psychiatry and diabetes educator **Jill Weissberg-Benchell, PhD**, and colleagues at three other sites around the country will conduct a year-long pilot study to develop interventions that will be tested and refined during the remaining four

years of the family-focused study. The researchers hope new interventions will lead to improvements in blood sugar levels and in quality of life for adolescents.



Karan Emerick, MD, attending physician in the Division of Gastroenterology,

Hepatology and Nutrition, and **Robert Garofalo, MD, MPH**, medical director of the Adolescent HIV Program at Children's Memorial's Uptown

Teen Health Center, are among the first pediatricians to receive NIH-funded Mentored Clinical Scientist Development Program Awards through the Feinberg School of Medicine at Northwestern University. The program is designed to support clinicians so that they can conduct research.

Board approves new facilities planning process

In February, the Children's Memorial Medical Center Board of Directors unanimously approved a resolution directing the hospital's management to begin planning for a potential replacement of the hospital's facilities. The decision came after an analysis of the hospital's financial and operational

Appointments

Philip M. Iannaccone, MD, DPhil, was appointed deputy director for basic research



at the Children's Memorial Institute for Education and Research. Iannaccone is the George M. Eisenberg Professor of Pediatrics at Northwestern University's Feinberg School of Medicine. He is also director of the Developmental Systems Biology Program at the institute.

Neuroscience symposium on brain injury

A symposium, "New Perspectives on Pediatric Brain Injury," sponsored by **Children's Research on Injury to the Brain**, an initiative of Children's Memorial Institute for Education and Research, was held April 29 and 30 at Chicago's Field Museum. Neuroscientists from around the country presented their current research on genetic and environmental factors in brain development and on new therapeutic approaches to treating brain damage caused by disease, birth defects or trauma. The symposium was supported in part by the Davee Foundation.

performance and projections concerning future growth. The planning will encompass issues of size, location, cost and funding for the new construction. The initiative was prompted by a growing demand for specialty services and overcrowding that has forced the hospital to turn away increasing numbers of



Joel Charrow, MD, acting head of the Division of Genetics at Children's

Memorial, and professor of pediatrics at the Feinberg School of Medicine, was named interim director of the Human and Molecular Genetics Program at the institute.

Amy Paller, MD, head of the hospital's Dermatology Division, was recently appointed chair of the Department of Dermatology at Feinberg School of Medicine, where she is a professor of pediatrics.

Bile diversion

Study to measure outcomes

Partial external biliary diversion, a procedure in which half of the liver's bile is siphoned off to a tiny bag outside the body, has benefited many children with genetic liver diseases. Thirteen-year-old Alaina Hahn, an Alagille syndrome patient from Tigard, Oregon, was the first

"We hope that after the study we'll be able to say honestly to a family, 'We have found that patients like your child will respond excellently to this procedure.'"

—Karan Emerick, MD

patient in a new study of biliary diversion. Hepatologist Karan Emerick, MD, is conducting the study to determine which patients are most likely to benefit from the procedure, pioneered by Peter Whittington, MD, head of the division of Gastroenterology at Children's Memorial.

The diversion is used for patients with either progressive familial interhepatic cholestasis (PFIC), or Alagille syndrome. In both diseases the liver has a defect in its ability to excrete bile, which causes incessant itching, bone weakness, and can lead to liver failure. Although the procedure appears to actually cure PFIC, and has allowed children with either of the diseases to lead near-normal lives, no studies have been conducted on it.

"Physicians have done biliary diversion on a case-by-case basis, but no one really understands the mechanism by which it helps," says Emerick, assistant professor of pediatrics at Northwestern University's Feinberg School of Medicine. "Also, there are patients for whom the procedure only works marginally, and we don't want to subject them to an unnecessary invasive procedure."

All children in the study will undergo liver biopsies and other tests, and will be monitored for a year after undergoing biliary diversion to measure bone density and cholesterol levels. Quality-of-life factors such as itching, sleep quality and



Alaina Hahn had an excellent outcome with complete resolution of itching after receiving biliary diversion.

school performance will also be evaluated. "We hope that after the study we'll be able to say honestly to a family, 'We have found that patients like your child will respond excellently to this procedure,' or 'Your child would benefit most from medication therapy,'" says Emerick. To support her research, Emerick has received a grant from National Institute of Health's Mentored Clinical Scientists Development Program through the department of Preventative Medicine at the Feinberg School of Medicine. ●

Clinical research center grows

The biliary diversion study is one of several studies under way at Children's Memorial in which the investigator is using the services of the NIH-sponsored General Clinical Research Center (GCRC) of Northwestern University. Children's Memorial is the pediatric satellite of the center.

"At Children's Memorial, GCRC funding supports a clinical trials coordinator, a research nurse and research pharmacists who help investigators conduct clinical research," says Leon Epstein, MD, head of the division of Neurology at Children's Memorial, associate director for pediatric research of the GCRC and deputy director for

clinical research at the Children's Memorial Institute for Education and Research.

In 1959, Congress authorized the GCRC program at NIH to provide essential support for clinical research at major medical institutions throughout the nation. The centers provide the infrastructure that allows investigators to conduct safe, state-of-the-art, patient-oriented research. In addition to approval from Children's Memorial's IRB (see page 11), each clinical research project must be approved by the scientific advisory committee of the GCRC.

"Every medication, every therapy designed has to be tested and proved

to be both safe and efficacious in human beings," says Epstein. "Besides ensuring the safety of research subjects in the studies, it's important that the trials are done with the greatest amount of scientific rigor so that the results are reliable."

In 2003, outpatient visits for clinical research at Children's Memorial grew from 20 to 250, with more growth expected in 2004. To support this growth, an additional research nurse will be recruited and dedicated clinical research space will be constructed within the hospital. ●

Round up



Woman's Board events brighten up the holidays

Two December events sponsored by the Woman's Board raised more than \$425,000 in support of its \$6.5 million pledge to the Division of Neonatology. More than 400 guests attended the 26th annual ArtisTrees held at the Winter Garden of the Harold Washington Library. Guests enjoyed a reception, dinner buffet and bid on more than 150 silent and live auction items including 25 uniquely decorated trees. **Jennifer Bianchi** (left) and **Ro Thompson** served as co-chairs for the event.



Ann Ryan (left) and **Joan Angulo** served as co-chairs for the 15th annual "Children Celebrate Children" event held at Navy Pier. Students from Prescott School joined 1,500 other Chicago elementary school children and individuals representing corporate sponsors to decorate holiday trees with handmade ornaments for patients at Children's Memorial. Of the 35 trees decorated, five remained on display at Navy Pier's Winter WonderFest and the remainder were used to decorate the hallways and rooms of patients unable to spend the holidays at home.

Corporate co-chairs for both events were **Lorna Langdon** and **Leslie Newman**.

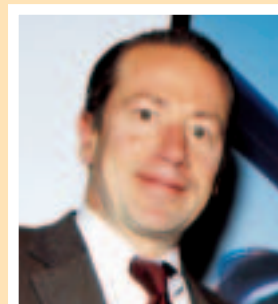
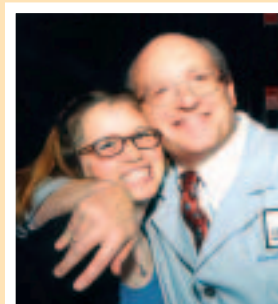
Kohl's associates spread good cheer

In December, 125 employees from 16 Chicago-area Kohl's department stores, including **Jackie Chopin** (left) and **Kathy Olecowski**, took time out from their busiest season of the year to help make the holidays merrier for the patients and families at Children's Memorial. Volunteers decorated Kohl's House, a home away from home for transplant patients and their families, and prepared goody bags for the hospital's annual holiday party for patients with cancer. The projects were in celebration of Kohl's gift of \$617,000 to the hospital last year. The donation is part of the company's "Kohl's Cares for Kids" program.



Two honored with Kennedy Award

Stephanie Flood, 16, a patient at Children's Memorial (below, left with her physician Stewart Goldman, MD), and **Kirk Johnson**, chairman of the board of Children's Memorial Institute for Education and Research, were each honored with the George D. Kennedy Distinguished Leadership Award during the 2003 Children's Memorial annual meeting held in December.



The Children's Memorial Medical Center's Board of Directors presents the award annually to individuals who have demonstrated outstanding leadership in supporting the mission of Children's Memorial.

During Johnson's 10-year tenure as chairman, Children's Memorial's research program has reached tremendous milestones, including the construction and recent expansion of the Children's Research Center. In addition, external funding for

research at Children's Memorial has almost tripled and many new investigators have been recruited to the institute.

Stephanie Flood was diagnosed with a recurring, malignant brain tumor at age nine. Nearly two years ago, she underwent surgery using the Intrabeam intraoperative radiation therapy system to treat the tumor. She agreed to be part of the clinical trials for this treatment because it showed tremendous promise and because it represented an opportunity to advance research that may help other children facing similar diagnoses. She has become a friend and mentor to other patients and an outspoken advocate for cancer research.

Parents ask top physicians, "What's Up, Doc?"

The second installment of the "What's Up, Doc?" series was held in November at the Michigan Shores Club in Wilmette. Nearly 200 guests had the opportunity to talk with 43 leading pediatric experts from Children's Memorial. **B U.K. Li, MD**, (left, photo above) participated in the event, co-chaired by **Maryann** and **Mike Atkinson**. Attendees met with physicians in small groups to learn more about a variety of children's health topics including allergies, sleep,



2003 Children's Ball creates good vibrations

More than 1,000 guests felt the rhythm of philanthropy at the 2003 Children's Ball sponsored by the Medical Research Institute Council (MRIC). With a theme of Música Para Los Niños, the ball, held at the Hilton Chicago in December, had a Latin flair with authentic Latin food and music and a miniature palm tree at every table. The ball celebrates the culmination of a year-long fundraising campaign that resulted in more than \$3.35 million for research at Children's Memorial.



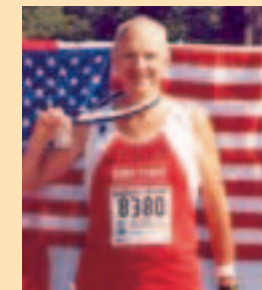
Carol Streicker (left) and **Lori Gersten** served as campaign and ball co-chairs. **Gail Gassner** and **Cheryl Cook** will serve as co-chairs for the 2004 Medical Research Campaign and Children's Ball.



sports medicine and peer pressure. **Katherine** and **James Hickey** enjoyed dinner with **Edward Ogata, MD**, (right, photo below) as they learned about the business of running a children's hospital. Presenting sponsors for the event were Nuveen Investments and Wintrust Financial Corporation; contributing sponsors were CPRI, a national staff augmentation and outsourcing firm, and DHR International, an executive search firm.

Marathon runners go the extra mile for kids

Gerald Heller (pictured) was one of 175 runners representing the Kids First Marathon Team who laced up his shoes and hit the pavement in The 2003 LaSalle Bank Chicago Marathon last October. This dedicated group of athletes raised \$185,000 for the patients and families of Children's Memorial. They trained together and raised funds through a variety of activities, including fundraising parties and letter-writing campaigns. The 2004 Kids First team is now forming. For more information, please call 773-868-8045.



Luxury car raffle picks up speed

A 2004 Chrysler Crossfire, a 2004 Mercedes C230 Sports Sedan, a 2004 Land Rover Freedlander, a 2004 BMW Z4 and a pair of 2004 Mini Coopers are the luxury cars featured in the 8th annual car raffle for Children's Memorial organized by members of Chicago's financial services community. Tickets are \$100 and a maximum of 5,000 tickets will be sold. Each winner will have the choice of a car

or \$40,000. All proceeds benefit the patients at Children's Memorial Hospital. The

drawing will take place on July 16.

To purchase tickets or for more information, call 773.868.8045

or visit www.childrensmemorial.org/carraffle.



Fashion show has high style, big heart

The 48th Annual Gold Coast Fashion Awards Show sponsored by The Children's Service Board brought together 1,200 guests in September for an afternoon of high fashion and fundraising for cardiology programs at Children's Memorial Hospital. **Clare Morrison** (left) and **Andrea Hosbein** (right)

served as co-chairs for the event, which raised \$310,000 for pediatric cardiology. Designer **Pamella DeVos** (center), who describes her Pamella Roland collection as encompassing "timeless beauty for active, sophisticated women," took home the prize for best designs as voted by fashion show guests.





Extra, Extra! *Chicago Sun-Times* Kids' Day needs volunteers

On June 10, a special morning edition of the *Chicago Sun-Times* will be sold for \$1, with net proceeds benefiting Children's Memorial Hospital. It's all part of *Chicago Sun-Times* Kids' Day, which is sponsored this year by Kohl's department stores and TCF Bank. Hundreds of volunteers are needed to sell the paper on street corners, at train stations and in corporate lobbies throughout Chicago and the suburbs from 6 a.m. until 9 a.m. Organizations and businesses can also purchase newspapers in advance.

To get the scoop on volunteering and other opportunities related to *Sun-Times* Kids' Day, call 773.880.8106 or visit www.childrensmemorial.org/kidsday.



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