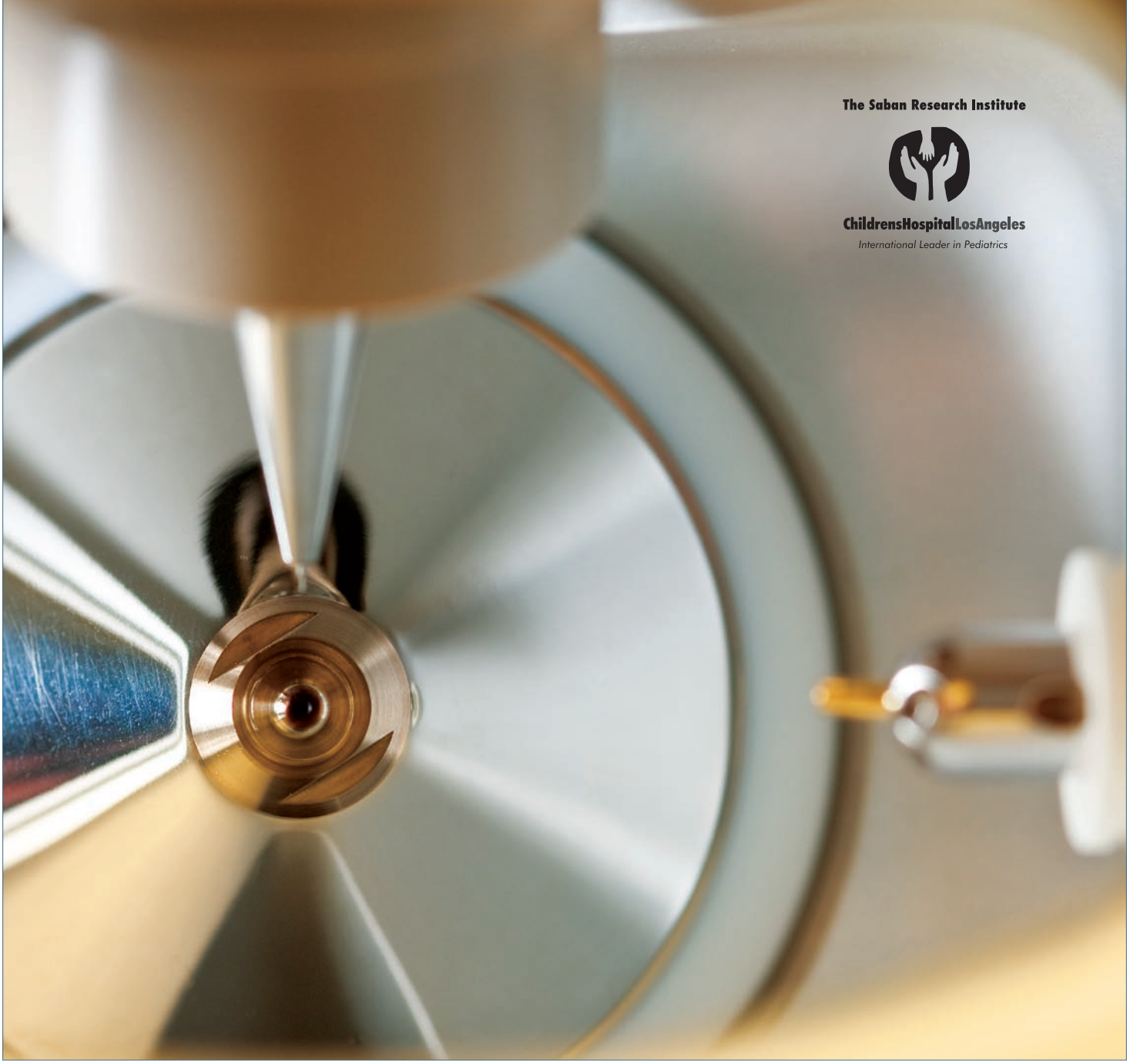


SCIENCE & SYNERGY

The Saban Research Institute of Childrens Hospital Los Angeles

RESEARCH HIGHLIGHTS 2009

The Saban Research Institute

ChildrensHospitalLosAngeles
International Leader in Pediatrics

KECK
SCHOOL OF MEDICINE OF USC

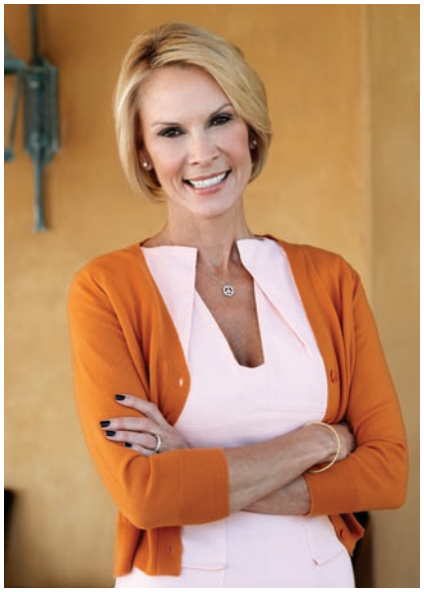
The Saban Research Institute

The Saban Research Institute of Childrens Hospital Los Angeles is among the largest, most productive pediatric research facilities in the United States. It ranks among the top 10 standalone pediatric institutions and 11th among 101 academic pediatric centers in funding from the National Institutes of Health. The Childrens Hospital Los Angeles Research Institute was established in 1992. It was designated The Saban Research Institute in 2003, following a transformational gift in support of pediatric medical research from Cheryl Saban, PhD, and Haim Saban and the Saban Family Foundation. The Sabans are the largest individual donors in Childrens Hospital's history.

On the cover: The LTQ Orbitrap Hybrid Mass Spectrometer, which measures peptides at minute levels, is a key component of the new USC/CHLA Proteomics Core Facility established in 2009.

The scientific images in *Research Highlights* were created during investigations at The Saban Research Institute of Childrens Hospital Los Angeles.

WELCOME



It is my pleasure to welcome you to The Saban Research Institute of Childrens Hospital Los Angeles. I'm proud to note that we are one of the country's pre-eminent pediatric research centers.

My husband, Haim Saban, and I have long been dedicated supporters of pediatric research because we truly believe that research makes a lasting difference in the lives of children. Discoveries taking place here at The Saban Research Institute are changing children's futures not only in our community, but in every corner of the globe. Many of these dramatic advances will benefit adults as well.

In this annual report, you will have the opportunity to see some of the questions our investigators and physician-scientists are exploring right now—and how their answers will be the miracles of tomorrow. We must do all we can to support them. Please join me in this important cause.

Cheryl Saban, PhD

Member, The Saban Research Institute Committee
Member, Board of Trustees, Childrens Hospital Los Angeles

WHERE SCIENCE IS SYNERGISTIC AND GLOBAL

Yves A. DeClerck, MD*
Director, The Saban Research Institute of Childrens Hospital Los Angeles
Vice President of Research, Childrens Hospital Los Angeles

At The Saban Research Institute of Childrens Hospital Los Angeles, synergy is a fundamental operating principle. Here, the conduct of science is increasingly global—global in its approach, as we now can examine all the genes and soon all the proteins in a disease—and global in its impact, as discoveries made at Childrens Hospital begin to affect the health of children everywhere.

Our investigators are engaged in research projects that cross boundaries between the laboratory, the clinic and the community as they bring together scientists from various disciplines and locations.

No subject is too tough to take on. In this 2009 *Research Highlights*, you will read about a few of our current investigations, including how:

- amniotic fluid stem cells may be used to grow new tissue and organs;
- some leukemia cells escape efforts to eradicate them—so far;
- neuroscientists, physiologists and engineers are collaborating to tackle autism;
- a fundamental finding about the spread of HIV by an investigator at Childrens Hospital will improve the health of Zambian children; and
- hematologists, cardiologists and engineers work together to develop non-invasive diagnostic techniques to guide the application of better treatments for children with inherited blood disorders at home and around the globe.

Supporting this adventure are rapidly developing technologies and scientific infrastructures in which The Saban Research Institute continues to invest.

The caliber of these investigations is evidenced by the quality of the publications of our faculty and the competitive funding they have earned from the National Institutes of Health (NIH) and other organizations.

However vital, such funding does not always provide the seed money for junior investigators just starting their careers or for promising, yet unproven and more risky experiments. That support must come from visionary donors who share our passion for science that makes a difference. Thank you for being part of this important journey.

* Faculty member, the Keck School of Medicine of the University of Southern California

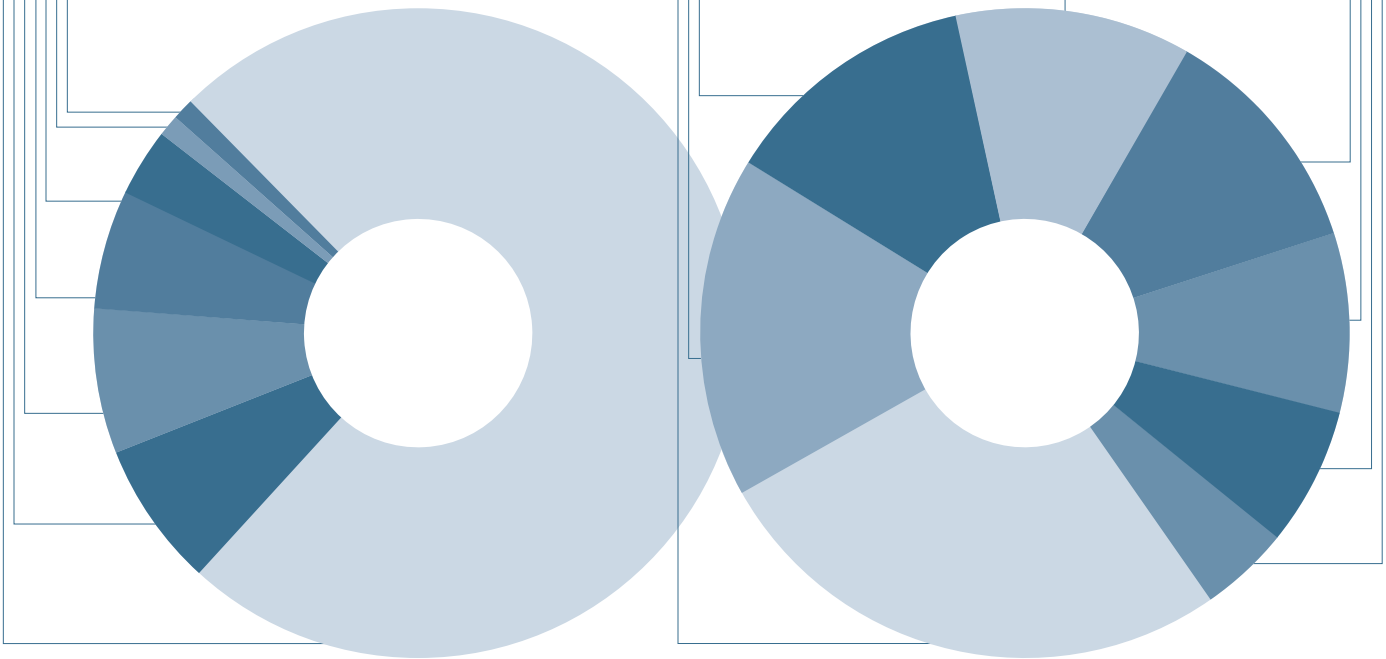
In the one-year period ending June 30, 2009, Childrens Hospital received $30.5 million in extramural funding for biomedical research. Funding came from a variety of government agencies, industry and philanthropic sources.

Sources of Funding

National Institutes of Health	$ 23,893,975	**78%**
Foundations	1,730,687	**6**
Other Federal Agencies	1,712,063	**6**
California Institute for Regenerative Medicine	1,499,044	**5**
Industry	973,792	**3**
Societies	401,000	**1**
USC	266,301	**1**
Total	$30,476,862	

Areas of Reseach

Cancer	$ 9,062,400	**29%**
Regenerative Medicine	5,489,041	**18**
Outcome & Prevention	3,823,939	**13**
Immunology & Pathogens	3,478,958	**11**
Human Physiology & Imaging	3,370,854	**11**
Others	2,423,682	**8**
Diabetes/Obesity	1,690,026	**6**
Neuroscience	1,137,962	**4**
Total	$30,476,862	



Markus Müschen, MD; Nora Heisterkamp, PhD; John Groffen, PhD; and Steven D. Mittelman, MD, PhD

TARGETING CHILDHOOD LEUKEMIA

More than 80 percent of children diagnosed with acute lymphoblastic leukemia (ALL), the most common pediatric cancer, are cured. The bad news: many eventually relapse, and their second round of disease is much harder to defeat. Indeed, the battle is won only half the time.

Many experts theorize the relapse is the handiwork of a few leukemia stem cells that survive chemotherapy and act on their capacity for self-renewal. That's why the Leukemia Research Program in The Saban Research Institute focuses on how stem cells escape treatment. "We're seeking their Achilles' heel," says Markus Müschen, MD *, program director. "Once we find it, we'll know better how to strike back."

All 18 researchers in the program—a synergy of clinicians, basic scientists and structural chemists—are individually funded by the National Institutes of Health (NIH). Each takes a unique approach to solving the leukemia riddle.

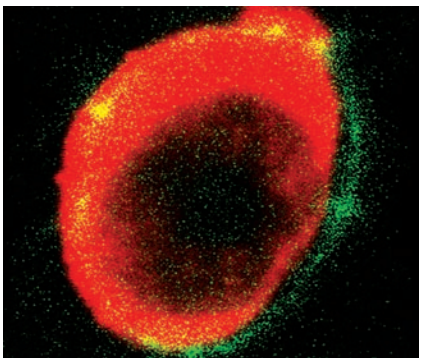
Dr. Müschen, for example, studies how genes contribute to a leukemia cell's drug resistance. He currently works on BCL6, a gene stimulated by chemotherapy. When BCL6 is over-expressed in leukemia cells, they are all but impervious to treatment. Eliminating the gene results in virtual immunity to the disease. He hopes to expand testing of an amino acid to neutralize the gene. His work recently appeared in the prestigious journals, *Cancer Cell* and *The Journal of Experimental Medicine*.

Meanwhile, Yong-Mi Kim, MD *, is working with a molecule that makes stem cells grow old and feeble. In combination with chemotherapy, it prevents relapse leukemia in mice. Nora C. Heisterkamp, PhD*, and John H. Groffen, PhD*, speculate that the leukemia stem cells are essentially "invited in" by receptors in the connective tissue of bone marrow, then allowed to cling to that scaffolding. They've identified a molecule that inhibits one such receptor, leaving cells more vulnerable to chemotherapy.

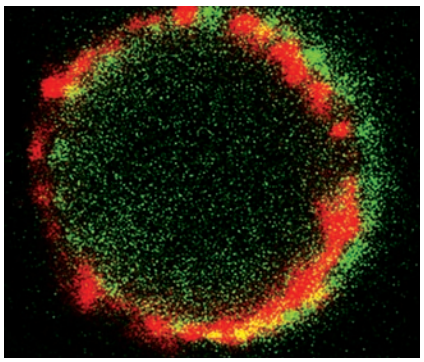
Steven D. Mittelman, MD, PhD*, is a physician-scientist in the Center for Endocrinology, Diabetes and Metabolism at Childrens Hospital Los Angeles. He became fascinated by an observation made by Anna Butturini, MD*, and her colleagues in the Childrens Center for Cancer and Blood Diseases that children who are obese when diagnosed with ALL have a greater chance of relapse. Dr. Mittelman now hypothesizes that increased risk may occur because fat cells protect cancer. His findings recently were published in *Cancer Research*.

The Leukemia Research Program collaborates on questions about the inception of ALL with colleagues at the USC/Norris Comprehensive Cancer Center, where Dr. Müschen heads the Leukemia and Lymphoma Program, including Michael R. Lieber, MD, PhD; Jae U. Jung, MD, PhD; and Michael Kahn, PhD.

Phase I clinical trials on agents developed by the Leukemia Research Program will start later this year, coordinated by its clinical partner, the Therapeutic Advances in Childhood Leukemia Consortium, led by Paul S. Gaynon, MD*. "Our goal is to make that first treatment as definitive as possible and to lower the relapse rate," says Dr. Müschen. With ALL likely to claim nearly 700 children this year, success can't come too soon.



Before experimental treatment: Oncogenic signaling (red) in a leukemia cell is excessively strong and diffusely active in the leukemia cell in the absence of treatment.



After experimental treatment: The red signal is weaker and localized to the outer cell membrane, which reflects normal function of the red-labeled signaling molecules.

Funding for this research has come from:

- The Saban Research Institute
- Childrens Center for Cancer and Blood Diseases; Center for Endocrinology, Diabetes and Metabolism; Department of Pediatrics, Childrens Hospital Los Angeles
- USC-CHLA Institute for Pediatric Clinical Research
- USC Center for Translational Research Institute
- USC Transdisciplinary Research on Energetics and Cancer Centers
- Bogart Pediatric Cancer Research Program
- The Leukemia and Lymphoma Society
- Nautica Malibu Triathlon
- T.J. Martell Foundation
- The V Foundation for Cancer Research
- National Cancer Institute and National Institutes of Health

* Faculty member, the Keck School of Medicine of the University of Southern California

Left to right: Laura Perin, PhD; David Warburton, DSc, MD; and Sargis Sedrakyan, PhD, in The Saban Research Building

REGENERATIVE MEDICINE

Stem cells from human amniotic fluid (hAFSC) may be equally or even more powerful and flexible in their therapeutic benefits as embryonic stem cells (hESC). As a bonus, hAFSC come free of controversy.

Amniotic fluid stem cells are derived from the liquid surrounding growing fetuses, but not from embryos. These pluripotent hAFSC can transform into fully differentiated cells representing each of the three major kinds of tissue found in the body. They also are chromosomally stable and less likely to form tumors than hESC.

"We're very excited about their potential," says Roger E. De Filippo, MD*, head of the Laboratory for Organ Regenerative Research and Tissue Engineering in the Developmental Biology and

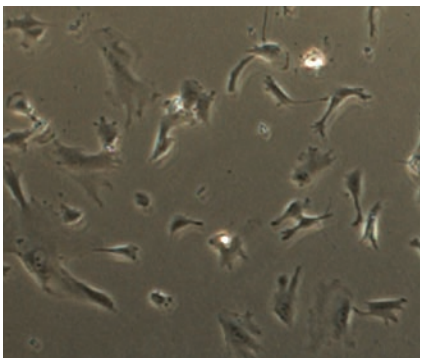
Regenerative Medicine Program at The Saban Research Institute of Childrens Hospital Los Angeles.

This past year has seen a number of successes for Dr. De Filippo's lab, which may bring the promise of cell-based therapies and organ regeneration that much closer. Led by Gianni Carraro, PhD, and lab co-director Laura Perin, PhD*, a 14-member team published its findings about the impact of hAFSC on acute lung injury in the prestigious journal, *Stem Cells*. Their study showed that hAFSC can integrate and differentiate into specific lineages of upper airway cells in an embryonic mouse lung. The hAFSC expressed genes important in both early lung development and adult lung damage. Investigators now are evaluating whether hAFSC can alter the course of such chronic lung diseases as bronchopulmonary dysplasia or cystic fibrosis.

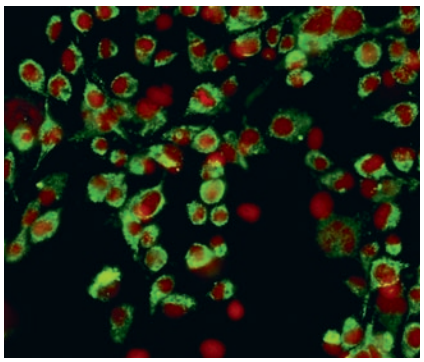
In 2008, the lab received a two-year, $300,000 grant from the Iacocca Family Foundation for studies into regenerating the pancreas with hAFSC. In another significant development, researcher Stefano Da Sacco, PhD, successfully isolated from amniotic fluid the progenitor cells for the heart, pancreas, lung, liver and kidney. (Progenitor cells don't replicate themselves but give rise to more specialized cells.) This technique is now protected by a pending U.S. patent.

The next step: Sargis Sedrakyan, PhD, will place these cells on a scaffold and nourish them to reconstruct a kidney, step by step. Dr. De Filippo hopes to someday soon test the ability of these cells to regenerate a kidney in patients. As a surgeon in the Division of Pediatric Urology at Childrens Hospital, he brings a patient-focused point of view to the work, something Dr. Perin finds invaluable. "We gain a greater understanding of the ultimate meaning of our experiments," she says.

"Our program is based on the simple idea that children are developing human beings," adds director David Warburton, DSc, MD*, "and, therefore, it's important to understand the molecular and genetic foundations of human organ development. Knowing these facts will be key to the translation of cell-based therapies for tissue protection and regeneration."



These kidney precursor cells show the potential for differentation into kidney cells. The goal: to someday regenerate a kidney in human patients.



This lab experiment in The Saban Research Institute demonstates the expression of type-IV collagen (highlighted in green) in amniotic fluid stem cells, a reflection of their renal characteristics.

Funding for this initiative has come from:

- The Saban Research Institute
- Department of Surgery, Childrens Hospital Los Angeles
- American Heart Association
- Anonymous donor funding
- The Iacocca Family Foundation
- National Kidney Foundation
- Pasadena Guild
- California Institute of Regenerative Medicine
- National Institute of Diabetes and Digestive and Kidney Diseases and the National Heart, Lung and Blood Institute, National Institutes of Health

* Faculty member, the Keck School of Medicine of the University of Southern California

Grace M. Aldrovandi, MD, CM

FROM LOS ANGELES TO ZAMBIA

Every day, at least 1,000 more children become infected with HIV—one third to one half through breast milk. Ninety percent live in sub-Saharan Africa, where alternatives to breastfeeding are unsafe, unaffordable and culturally unacceptable. In response to this crisis, maternal and child health experts, faith-based and government leaders and private funders have lent support to an international community of researchers, all looking to understand and arrest the disease.

Grace M. Aldrovandi, MD, CM*, has devoted her career to this conundrum. A recipient of the Elizabeth Glaser Scientist Award for pediatric AIDS research, she is a physician-scientist in the

Division of Infectious Diseases at Childrens Hospital Los Angeles and a member of The Saban Research Institute's Microbial Pathogens Initiative.

One of her most recent projects tested the validity of a popular theory that infant formula would save lives by preventing HIV transmission through breastfeeding. There's logic to the idea. However, breast milk also protects babies from infection—important in a world where children are exposed to many pathogens, often lack immunizations and go without adequate care.

Trying to balance benefits against risks, the World Health Organization (WHO) recommended that HIV-positive mothers nurse for four months, the minimal time thought to offer protection. "That theory, too, was untested," says Dr. Aldrovandi. She designed the Zambia Exclusive Breastfeeding Project, a five-year clinical trial, to see how many children born to HIV-infected Zambian women would be alive and free of HIV infection at age two years. All participants exclusively breastfed for four months. Then they were randomized to continue nursing or switch to a local, nutritionally replete weaning blend.

Dr. Aldrovandi's 2008 findings are changing public health policy. Among uninfected four-month-olds, there was no difference in two-year, HIV-free survival between those who breastfed and those who didn't. Survival actually was lower for infected four-month-olds on formula. This data has prompted WHO to extend the recommended breastfeeding period to six months.

However, her study also showed that mothers whose disease progressed to AIDS had babies five times more likely to die than did HIV-infected mothers. In these cases, formula is equal to breast milk in keeping babies alive, but neither food has the immune factors that prevent HIV transmission. Far better than focusing on diet, Dr. Aldrovandi argues, would be new drugs that make mothers healthier.

Her proposal has generated support from the federal government; Pfizer, Inc.; and the Stephen Lewis Foundation to provide antiretroviral drugs and fund a microloan program that assists Zambian women in achieving economic self-sufficiency. And so the collaboration continues.

A Zambian woman carries her water basket to the river.

This clinic building was constructed in Lusaka District, Zambia, for Dr. Aldrovandi's study into the relationship of breastfeeding and HIV transmission. Photos by Grace Aldrovandi, MD.

Funding for this research has come from:

- The Saban Research Institute
- Division of Infectious Diseases, Childrens Hospital Los Angeles
- Elizabeth Glaser Pediatric AIDS Foundation
- The Stephen Lewis Foundation
- Centers for Disease Control and Prevention, U.S. Department of Health and Human Services
- National Institute of Child Health and Human Development, National Institutes of Health

* Faculty member, the Keck School of Medicine of the University of Southern California

Michele Kipke, PhD, and Richard Simerly, PhD, confer in The Saban Research Building.

AUTISM RESEARCH

One in 150 children in America may be living with autism spectrum disorder (ASD), a complex developmental disability that causes problems with social interaction and communication. Estimates are that as many as one in five suffer from some kind of neurodevelopmental disorder, ranging from hyperactivity to retardation.

These dramatic numbers are inspiring a multi-faceted research effort that links investigators at The Saban Research Institute with colleagues at USC. "We're seeing the payoff of investments in the 1960s and 1970s into cancer research, with higher survival rates for childhood cancer," notes Richard Simerly, PhD*, director of the Neuroscience Program in The Saban Research

Institute. "If we're going to make a difference in autism, we must ramp up our investment in this research now."

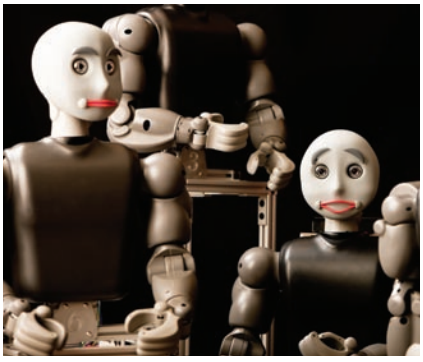
Understanding early development of brain circuitry and behavior holds the key, he says. "The problem lies in the formation of neural connections, but we don't yet know which specific processes lead to autism. However, promising new insights are emerging."

This year, the Neuroscience Program recruited investigator Aaron McGee, PhD, who is exploring how anatomical changes influence functional changes in the brain. His goal is to understand how the brain retains greater flexibility, or plasticity, during childhood. Armed with a specialized laser scanning microscope, he can peer inside the living brain to study the formation of anatomical connections. "If we can understand how the brain's flexibility is regulated, and acutely enhance it," says Dr. McGee, "this would both augment current therapies for autism and potentially create new ones."

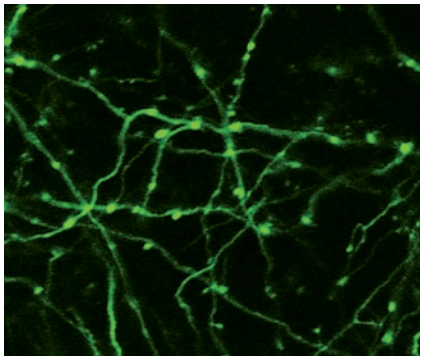
At the same time, Michele D. Kipke, PhD*, director of the Community, Health Outcomes and Intervention Research Program in The Saban Research Institute, is testing new tools to intervene in autism. She is collaborating with robotics experts, including Maja J. Mataric, PhD, director of the Center for Robotics and Embedded Systems in the USC Viterbi School of Engineering. Their quest: to find out if the use of robots can encourage social interaction in children with ASD.

Dr. Kipke also has joined forces with Pat Levitt, PhD, director, and Barbara Thompson, PhD, investigator, in the Zilkha Neurogenetic Institute at the USC Keck School of Medicine in behavioral intervention research that asks whether a child's reluctance to engage socially is triggered by a lack of reward or aversion. Such studies will take place in the Boone Fetter Clinic, the comprehensive clinical component of the CHLA-USC Institute for the Developing Mind.

Dr. Kipke is planning to recruit additional faculty to the project to encourage more research. "The earlier we can intervene in diagnosing ASD," she says, "the more opportunities we have to change a child's life for the better."



Robots from the USC Viterbi School of Engineering are being used to encourage social interaction in children with autism spectrum disorder.



Studies of the growth of axons (core nerve fibers shown here in green) may help reveal how the brain retains its plasticity during childhood.

Funding for this research has come from:

- The Saban Research Institute
- USC Provost's Office
- The Associates Endowment for Neuroscience
- Dr. and Mrs. George N. Boone
- Lynda and Blaine Fetter
- Las Madrinas Endowment for Autism Research, Interventions and Outcomes
- Cheryl Saban, PhD, and Haim Saban
- Saban Family Foundation

* Faculty member, the Keck School of Medicine of the University of Southern California

Thomas Coates, MD, left, and John Wood, MD, PhD, are co-recipients of the H. Russell Smith Award for Innovation in Pediatric Biomedical Research. The award is named for H. Russell Smith, longtime donor and former chair of Childrens Hospital's Board of Directors.

ERASING BOUNDARIES

In The Saban Research Institute, investigations that merge molecular biology and engineering, physiology and physics are erasing any artificial lines that once separated clinicians, scientists and engineers.

Hematologist Thomas D. Coates, MD*, and cardiologist John C. Wood, MD, PhD*, embody this meeting of the minds. When they met a decade ago, they clicked over "a shared way of looking at problems," says Dr. Wood, who earned his undergraduate degree in electrical engineering and holds a PhD in biomedical engineering. Today, he directs the Cardiovascular MRI program at Childrens Hospital Los Angeles.

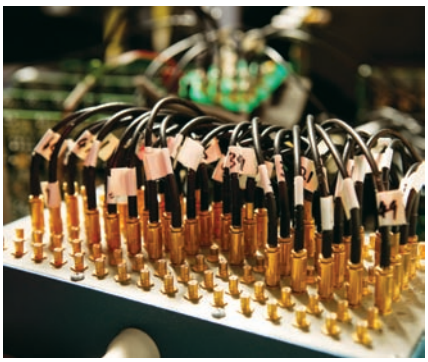
Dr. Coates, whose undergraduate degree is in physics, is head of Hematology at Childrens Hospital and director of one of 12 federally funded Basic and Translational Research programs studying sickle cell disease and one of six Thalassemia Centers.

This year, they became co-recipients of the 13th H. Russell Smith Award for Innovation in Pediatric Biomedical Research. They were recognized for their translational research into the physiologic and cellular consequences of iron overload in patients with hemoglobinopathies, a group of disorders affecting red blood cells. "Their work demonstrates how teamwork and the synergy of different disciplines can advance science and impact clinical treatment," says Yves A. DeClerck, MD, director of The Saban Research Institute.

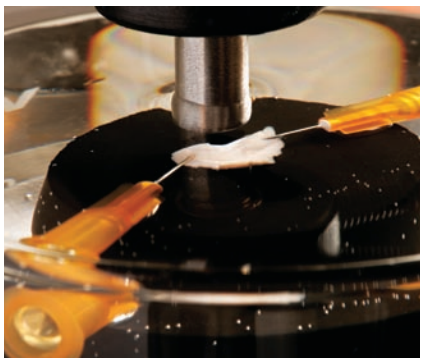
Dr. Coates and Dr. Wood both have active collaborations with colleagues at the USC Viterbi School of Engineering and the USC Keck School of Medicine's Department of Physiology and Biophysics. "Having great colleagues allows me to bridge the gap between physiology and engineering," notes Dr. Coates, "and do what I enjoy most—providing care to sick kids."

Other investigators who collaborate with faculty at the USC Viterbi School include:

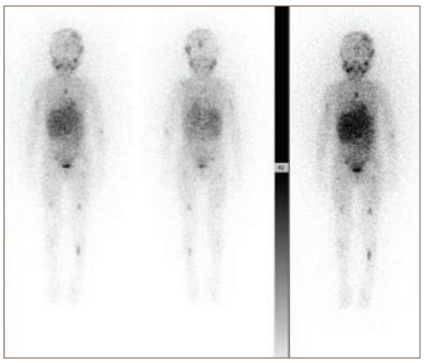
- Shahab Asgharzadeh, MD*, an oncologist in the Division of Hematology/ Oncology at Childrens Hospital and a member of the Cancer Program in The Saban Research Institute, who is using sophisticated bioinformatics to identify "molecular signatures" of tumors and devise targeted strategies against cancer;
- Stephan G. Erberich, PhD*, director of Functional Imaging and Biomedical Informatics at Childrens Hospital and co-director of the Medical Information Systems division of the Viterbi School's Information Sciences Institute, who has developed breakthrough networking technology to exchange medical images and data;
- Thomas G. Keens, MD*, and Sally L. Davidson Ward, MD*, of the Division of Pulmonology at Childrens Hospital, who are employing tools devised in the Viterbi School's Department of Biomedical Engineering (BME) to further knowledge of respiratory and sleep disorders; and
- Ching-Ling (Ellen) Lien, PhD*, of the Cardiovascular Research Program in The Saban Research Institute, who is exploring the zebrafish's regenerative ability to regrow heart cells after injury. Her collaborations with the BME already have produced two scientific papers, including one in the *Annals of Biomedical Engineering, 2009*.



This connection box is part of a high-frequency ultrasonic imaging system developed by K. Kirk Shung, PhD, at the Viterbi School, which provides improved spatial resolution in dermatological, ophthalmological, intravascular and small animal imaging.



A high-frequency ultraosund probe from Dr. Shung's lab, used to scan small tissue samples, is aiding studies at The Saban Research Institute of the heart-regenerative qualities of zebrafish.



An image shared through Grid computing technology developed at Childrens Hospital and the Viterbi School; dark areas indicate the presence of neuroblastoma cells.

* Faculty member, the Keck School of Medicine of the University of Southern California

EMERGING TOOLS

"Gene chips"—microchips imprinted with millions of spots representing genes—are enabling scientists to devise molecular signatures of tumors, composed of bits of genetic material. These 21st-century tools may lead to more personalized therapies.

Science is increasingly dependent on rapidly developing technologies. To stay ahead of the curve, The Saban Research Institute continues to make significant investments in a scientific infrastructure where these emerging tools—and the expertise to use them—are available to its scientists.

In this new era of biomedicine, "we can't say 'one-size-fits-all' when it comes to designing effective therapies," notes Timothy J. Triche, MD, PhD*, who will head the new Center for Personalized Medicine (CPM) at Childrens Hospital Los Angeles. The CPM will support and expand basic and translational research in genomics, proteomics, bioinformatics, molecular genetics, molecular microbiology and cytogenetics (cell structure and function). "As we move forward, we'll begin to be able to characterize each patient's disease and possible interventions," adds Dr. Triche, chair of the Department of Pathology and Laboratory Medicine and pathologist-in-chief.

In 2009, The Saban Research Institute's investments in scientific infrastructure include:

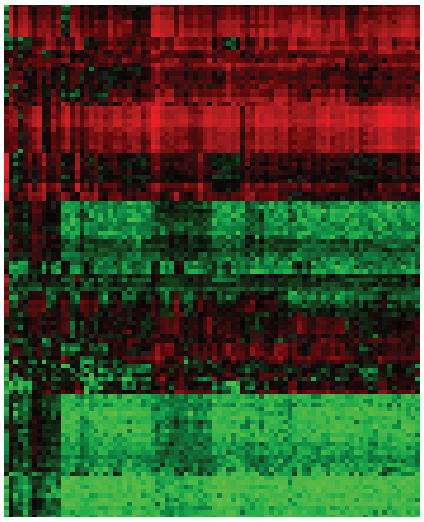
Proteomics Core

Early evidence of disease is hidden in the proteins that our genes produce. Even more intriguing for physician-scientists, when protein components are present in certain repetitive patterns, they become biomarkers of developing trouble.

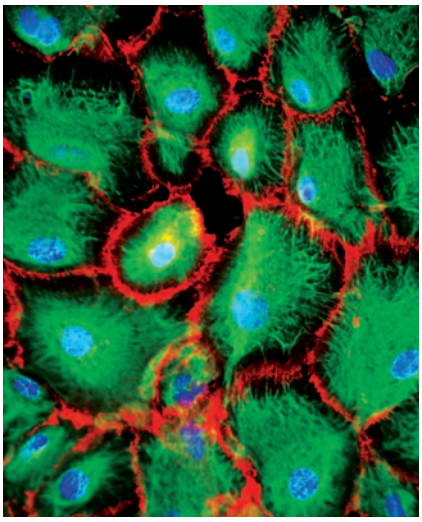
"The quest for biomarkers impacts every research field," says A. Linn Murphree, MD*, director of the Retinoblastoma Program in The Vision Center at Childrens Hospital Los Angeles. "Find the biomarker and you know the battle has begun, long before disease is otherwise detectable." For example, children affected in both eyes with retinoblastoma, a malignant eye cancer, are permanently at increased risk for various other cancers. "Yet all we can do today is watch for symptoms," adds Dr. Murphree.

Eager for better diagnostic tools, The Saban Research Institute and the USC Keck School of Medicine established the USC/CHLA Proteomics Core Facility in 2009. It will provide high-sensitivity and

A patient inside a Magnetic Resonance Imaging machine at Childrens Hospital



Molecular portrait of gene activity in a neuroblastoma tumor (red = high gene level; green = low)



Human stem cells that have differentiated or changed in the lab to become lung cells

ultrahigh-resolution mass spectrometry for the analysis of proteins and their peptide fragments. Researchers from both institutions will be able to use the primary core facility at USC and a satellite location at The Saban Research Institute, which is equipped with an LTQ Orbitrap Hybrid Mass Spectrometer, capable of measuring peptides at unimaginably minute levels.

"Every project is collaborative," says Susan Lee, PhD*, who manages the satellite facility. "We work together to generate useful data." Some studies examine whether a particular protein is present in blood or culture. Others quantitate protein amounts, monitoring the extent to which disease has infiltrated.

The Rory Anne Proteomics Fund has provided support for two years of research at The Saban Research Institute. Funding from the state of California for the USC/CHLA Proteomics Core was spearheaded by Representative Adam Schiff (D-CA).

Imaging Technology

Instead of simply observing the symptoms of disease and deducing their cause, physicians now can see and measure what's inside the body—thanks to amazing advances in imaging technology.

"That only scratches the surface of what imaging experts can accomplish," says Vicente Gilsanz, MD, PhD*, director of The Saban Research Institute's Childrens Imaging Research Program.

Today, researchers can collaborate with clinicians of every stripe, looking at adult survivors of childhood diseases to see if deficiencies result from the therapies that once saved their lives. Or they can study large populations of children, seeking the earliest visual markers of adult disorders like diabetes or osteoporosis.

The newest technological marvel in Childrens Hospital's program will be the 3.0 Tesla MRI (magnetic resonance imaging) device, which not only gathers still-life images but also displays vital organs as they function, in real time, as they respond to illnesses and therapies intended to treat them. In addition, the 3.0 Tesla MRI avoids the radiation risks associated with other imaging technology.

* Faculty member, the Keck School of Medicine of the University of Southern California

The 3.0 Tesla MRI will be housed in a 2,000-square-foot, state-of-the-art area of the hospital dedicated to an expanding clinical research program. "It didn't come out of its box ready to use on children, however," explains Marvin B. Nelson, Jr., MD*, chair of the Department of Radiology at Childrens Hospital Los Angeles. "The equipment is made for adults, so we collaborated with bioengineering scientists and fully optimized it for kids."

Central Biorepository

Medical breakthroughs can't happen in a vacuum. They require significant resources—including the biomedical specimens and data with which to conduct the studies that may transform our understanding of human disease.

This fall, The Saban Research Institute will launch a Research Biospecimen and Data Repository, overseen by the Childrens Clinical Investigation Center (CLIC). This centralized resource will facilitate biospecimen collection, acquisition and storage services for all investigators at Childrens Hospital Los Angeles.

Such biospecimens—including normal and diseased human tissue, bone marrow, blood and other bodily fluids—are key to the new and emerging technologies that promise to allow individualized diagnosis and treatment. "As the fields of genomics and proteomics are advancing, they are providing new ways to obtain valuable information for pediatric research," notes Karen Miller-Graham, CLS, MT(ASCP), manager of the biorepository in the CLIC. "Informatics also supports the collection and analysis of clinical data on a large scale."

She is teaming with Hiro Shimada, MD, PhD*, in the Department of Pathology and Laboratory Medicine at Childrens Hospital to develop a virtual link to its longstanding Anatomic Pathology Biorepository. The CLIC will invite individual investigators to house their collections in the central repository or to link to it, expanding the potential usefulness.

"Many patients come to Childrens Hospital with rare diseases and offer a rich diversity in ethnicities," notes Edward D. Gomperts, MD*, director of CLIC and of clinical research at Childrens Hospital. "This repository represents a tremendous resource to optimize and grow biomedical research to find answers to very challenging diseases of childhood."

Stem Cell Laboratories

A well-designed laboratory space can encourage interaction, exchange and the birth of new ideas. This proven hypothesis inspired the California Institute for Regenerative Medicine (CIRM) to award Shared Research Laboratory grants—one of which went to Childrens Hospital Los Angeles in 2007.

In 2009, The Saban Research Institute completed construction of 3,000 square feet of dedicated laboratory space in its H. Russell and Jeanne R. Smith Research Tower. Included are four tissue-culture suites for up to 11 scientists culturing stem cells, in addition to rooms and equipment for stem cell evaluation and analysis.

"Having a shared laboratory space will increase interaction among scientists doing this kind of research—which is what CIRM intends—getting a community working together on common problems," notes Carolyn Lutzko, PhD*, who led the renovation project and chairs a committee in The Saban Research Institute that will allocate use of the space based on scientific merit.

Dr. Lutzko credits The Saban Research Institute's longstanding support for enabling the stem cell program to achieve CIRM backing. "That vision allowed us to develop a track record before we even applied for funding," she says.

The focus of the new laboratories is on pluripotent stem cells, which can develop into almost any kind of cell in the body, but are not capable of creating an entire organism. (Human embryonic stem cells, which can divide indefinitely, are pluripotent cells.) The questions researchers are asking remain fundamental. Dr. Lutzko's own lab is examining what signals tell a stem cell to stay a stem cell. "These cells have the potential to give rise to every cell in the body, but we have no idea how to control that." Now, such inquiries will have more room to grow.

Funding for these initiatives has come from:

- The Saban Research Institute
- Childrens Clinical Investigation Center; Department of Pathology and Laboratory Medicine; Department of Radiology, Childrens Hospital Los Angeles
- The Associates Endowment for Clinical Imaging Research and Technology
- Family of Suzan K. Smigel
- The Rory Anne Proteomics Fund
- Cheryl Saban, PhD, and Haim Saban
- Saban Family Foundation
- California Institute for Regenerative Medicine

RESEARCH EDUCATION

Sebastien Bouret, PhD, left, with LA-HIP interns Alexaundrea Smith, center, a senior at King Drew Medical Magnet High School, and Karen Medina, right, currently attending Occidental College.

Osvaldo Rodriguez, a senior at King Drew, tends the fish tanks holding zebrafish, studied for their ability to regenerate heart tissue.

African-American and Latino students combined earn only 4.7 percent of doctorate degrees across all of the sciences in the United States—an alarming statistic that spotlights the under-representation by minorities in biomedical careers. "Increasing the number of minority science professionals is a national emergency," says Emil Bogenmann, PhD, EdD*, director of research education at The Saban Research Institute.

The Saban Research Institute is helping to transform that reality with multi-level research education for minority students from high school to post-graduate levels. Its Latino and African-American High School Internship Program (LA-HIP), now in its fourth year, draws applicants from South Los Angeles-area public high schools for a six-week summer research internship. LA-HIP receives support from Lori and Ted Samuels; he is a former chair of The Saban Research Institute committee and vice chair of the Childrens Hospital Board of Trustees. The program also receives support from the National Institutes of Health, the Leonetti/O'Connell Family Foundation, the Kayne Foundation and Union Bank of California.

This summer, Dr. Bogenmann also coordinated the mentoring of 28 undergraduates in the Short-Term Education Program for Underrepresented Persons (STEP-UP) supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). These students conducted research at sites throughout the U.S. in diabetes, obesity, heart disease, sickle cell anemia or related health problems.

Now, Dr. Bogenmann has obtained funding from the NIDDK to develop a program to provide translational research training and career development to minority post-doctoral fellows (PhD, MD, and/or MD/PhD). Trainees will direct a research project relevant to minority health based in the laboratory, a clinical setting or the community. The three-year program will culminate with a master's degree in clinical and biomedical investigations. "To enact real change," he notes, "we need to develop a pipeline of role models who help more minorities enter a career in science and medicine."

* Faculty member, the Keck School of Medicine of the University of Southern California

2009 INTRAMURAL RESEARCH AWARDS

Through these intramural research awards, The Saban Research Institute and the Department of Pediatrics at Childrens Hospital Los Angeles nurture the development of new science and new scientific careers. The awards are reviewed by outside experts and are highly competitive.

Graduate Student Award

Hua Fang
Division of Hematology/Oncology
The Saban Research Institute Program: Cancer–Solid Tumors
*Mentor: Yves A. DeClerck, MD**
"Plasminogen Activator Inhibitor-1 in Angiogenesis and Tumor Dormancy"

Raul Nahar
Division of Hematology/Oncology
The Saban Research Institute Program: Cancer–Leukemia
*Mentor: Markus Müschen, MD**
"Pre-B Cell Receptor Signaling in Acute Lymphoblastic Leukemia"

Jingying Xu
Division of Hematology/Oncology
The Saban Research Institute Program: Cancer–Solid Tumors
*Mentor: Anat Erdreich-Epstein, MD, PhD**
"Abl Mediates Endothelial Apoptosis Induced by Integrin Inhibition and Actin Disruption"

Career Development Fellowship Award

Sabine M. Schmidhuber, PhD
Division of Hematology/Oncology
The Saban Research Institute Program: Cancer–Leukemia
*Mentor: Nora C. Heisterkamp, PhD**
"Role of CD2 in the Neonatal Pulmonary Immune System"

Min Yu, MD
Division of Hematology/Oncology
The Saban Research Institute Program: Cancer–Leukemia
*Mentor: John H. Groffen, PhD**
"Roles of Abr/Bcr in Pulmonary Hypertension"

Research Career Development Award

Aaron McGee, PhD
Department of Pediatrics
The Saban Research Institute Program: Neuroscience
*Mentor: Richard B. Simerly, PhD**
"Deciphering the Role of Nogo-66 receptor 1 (NgR1) in Limiting Experience-Dependent Plasticity in the Developing Visual System"

Laura Perin, PhD*
Department of Surgery
The Saban Research Institute Program: Developmental Biology & Regenerative Medicine
*Mentor: Roger E. De Filippo, MD**
"Multipotent Stem Cells and Renal Progenitors Derived from Amniotic Fluid as Potential Tools for Chronic Kidney Disease Therapies"

Clinical Research Academic Career Development Award

Awards are funded by The Saban Research Institute, the Department of Pediatrics at Childrens Hospital and the associated divisions of Hematology/Oncology, Endocrinology, Infectious Diseases and General Pediatrics.

Girish Dhall, MD*
Mentors: Jonathan Finlay, MB, ChB, and Robert C. Seeger, MD**
"Phase I Trial of Dasatinib, Lenalidomide, and Temozolomide in Patients with Relapsed or Refractory Central Nervous System (CNS) Tumors"

Mimi Kim, MD
Mentors: Mitchell E. Geffner, MD, and Deborah Merke, MD, MS*
"Cardiovascular Disease Risk Factors in Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency"

Pia S. Pannaraj, MD, MPH*
Mentor: Laurene Mascola, MD, MPH, FAAP
"Impact of School-Based Influenza Vaccination on School Populations"

Douglas L. Vanderbilt, MD*
*Mentor: Istvan Seri, MD, PhD**
"Assessing Factors in the Neurodevelopmental Outcomes in Infants with Twin-Twin Transfusion Syndrome"

* Faculty member, the Keck School of Medicine of the University of Southern California

HONOR ROLL OF DONORS

from July 1, 2008 to June 30, 2009

We are proud to recognize the following donors who made gifts of $1,000 and above during the last fiscal year to advance research at Childrens Hospital Los Angeles. The dedicated investigators at The Saban Research Institute of Childrens Hospital Los Angeles would like to extend our deepest gratitude for the support of all of our donors, especially Cheryl Saban, PhD, and Haim Saban, the hospital's largest individual donors, without whom our dream of a world without pediatric disease would not be possible. We also offer our special thanks to the hospital's many Associate and Affiliate groups for their exceptional and longstanding philanthropic support of research. In spite of our best efforts in compiling this Honor Roll, errors and omissions may occur. Please inform us of any inaccuracies by contacting Michele Phillips, assistant director of Donor Relations, at 323-361-1788, or mphillips@chla.usc.edu. For more information on how you can provide philanthropic support, please contact Melany Duval, vice president of Major and Planned Gifts, at 323-361-1705 or mduval@chla.usc.edu.

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In Memoriam

Childrens Hospital Los Angeles lost Jeanne Smith, a dear friend and supporter, this year. We would like to recognize Mrs. Smith's dedication and commitment to the health of children everywhere, particularly at Childrens Hospital. Together with her husband, Honorary Trustee H. Russell Smith, she was actively involved in the growth and development of Childrens Hospital for many years and was a strong advocate of research. When The H. Russell and Jeanne R. Smith Research Tower opened in 1988, it symbolized Childrens Hospital's commitment to being an international leader in pediatric research and medicine.

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