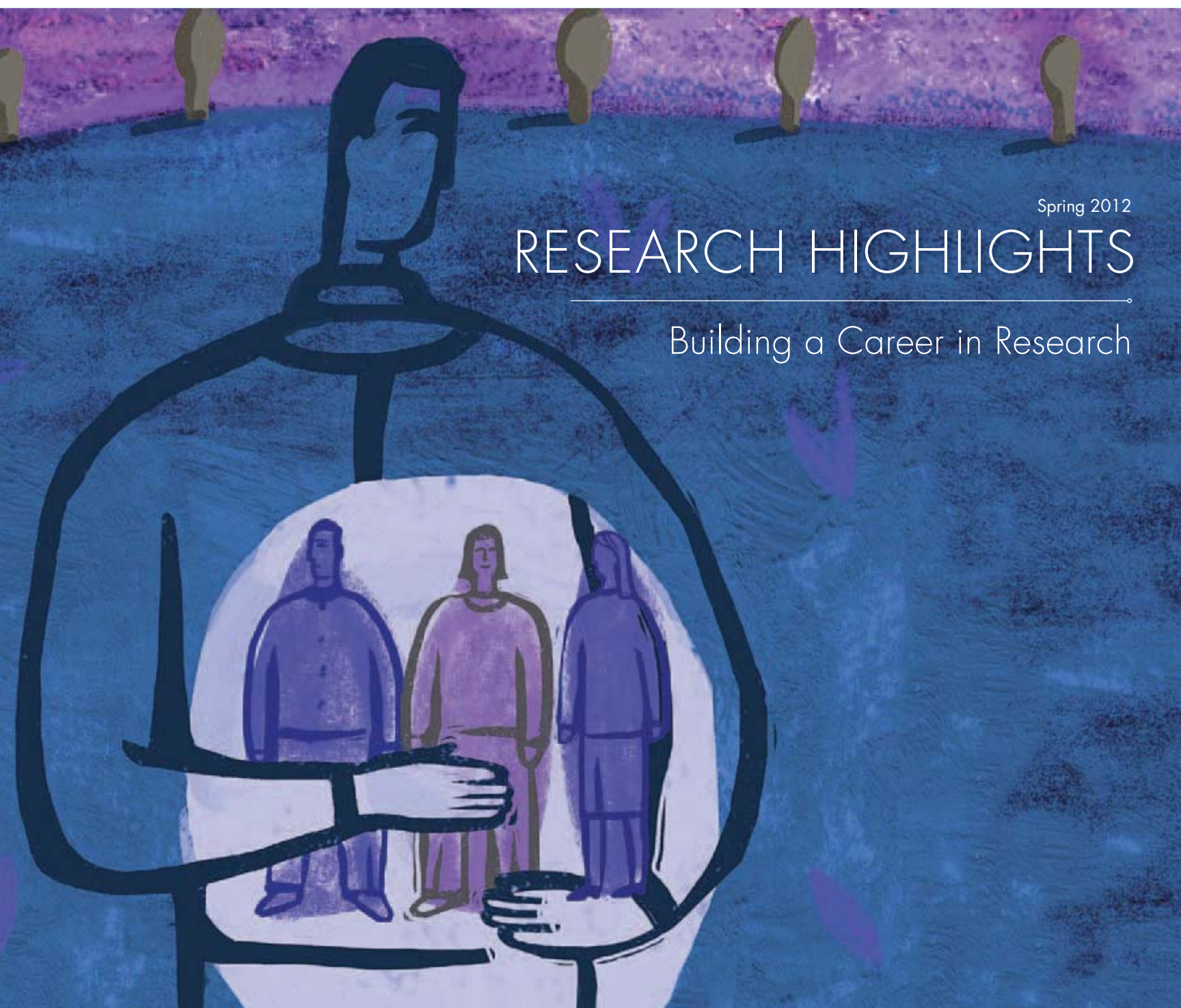


MENTOR • EDUCATE • COLLABORATE

Spring 2012

RESEARCH HIGHLIGHTS

Building a Career in Research



Children's
Hospital
LOS ANGELES™

THE SABAN RESEARCH
INSTITUTE

The Saban Research Institute of Children's Hospital Los Angeles

The Saban Research Institute is one of the few freestanding research centers in the U.S. where scientific inquiry is combined with clinical care and is devoted exclusively to children. Our goal is to improve the health and wellness of children through a combination of basic, clinical and translational studies. Research is performed at the lab bench, in the clinic and in the community.

Our research program is built into seven thematic areas:

- Developmental biology and regenerative medicine
- Developmental neuroscience
- Diabetes and obesity
- Community and behavioral health, health promotion and disease prevention
- Cancer
- Human physiology and imaging
- Immunology, infectious disease and pathogens

Originally established in 1992, The Children's Hospital Los Angeles Research Institute became The Saban Research Institute in 2003 following a \$40 million gift in support of pediatric research made by Cheryl Saban, PhD, Haim Saban and The Saban Family Foundation.

In Fiscal Year 2011, The Saban Research Institute received \$25.5 million in National Institutes of Health (NIH) funding and \$43.8 million in total funding.

The Saban Research Institute maintains strong scientific and strategic affiliations with the University of Southern California (USC) and, in particular, the Keck School of Medicine of USC. All of the Institute's principal investigators (clinical investigators, physician-scientists and PhD-scientists) are USC faculty, and many have collaborative projects with scientists at the Keck School of Medicine and other departments at USC. The Institute's researchers also are involved in collaborative projects with academic institutions throughout the U.S. and abroad.



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Listening is a Virtue

The best advice I've ever been given is to spend more time listening.

Listening is a virtue. Not everyone does it well, but good listeners have the ability to provide insights into other people and to develop problem-solving skills from which others can learn. Winston Churchill once said, "Courage is what it takes to stand up and speak; courage is also what it takes to sit down and listen."



At The Saban Research Institute of Children's Hospital Los Angeles, we continue in our quest to listen more with the intent of better understanding the developmental origins of health and disease. We are studying the developmental implications—either in utero or after birth—that promote health or increase the likelihood of disease in children. These factors can be related, or not, and can include a combination of genetics and epigenetics, environmental exposures, nutritional issues or even social and economic influences.

In this issue of *Research Highlights*, we emphasize the importance of listening as the foundation for solid mentoring, education and collaboration. These are equally important attributes as we build a pipeline of future pediatricians, pediatric subspecialists, physician-scientists and researchers—ensuring that we have the workforce of the future to address important questions of child health and well-being.

Having a good mentor is invaluable. Personally, I have benefited from influential individuals at every stage of my career development, and I continue to benefit to this day. In particular, a physiologist and adult gastroenterologist introduced me to the idea of gastrointestinal biology as an area ripe for investigation. As a result, today we have a much better understanding of the role of the gastrointestinal tract in influencing everything from



Researcher Mark Frey, PhD, with his mentor, D. Brent Polk, MD

obesity to drug metabolism. Stanley Cohen, MD, Nobel Prize winner in Physiology or Medicine, had tremendous influence on my scientific career by introducing me to the very strong principles of scientific rigor, the joy of asking questions relevant to human health and the importance of continually pushing a field forward. And my very own grandmother, who passed away this year at the age of 97, emphasized the need to give back and mentor others.

Mentoring and collaboration continue at The Saban Research Institute through the Gut Club, a novel concept for bringing together faculty from the departments of Pediatrics, Surgery, Microbiology and Immunology, among others, to create a platform and environment for asking important questions about the role of the gastrointestinal tract in child health and disease.

In this magazine you will be introduced to one of the best examples of mentoring and educating young minds that I have ever been exposed to—the Latino & African-American High School Internship Program (LA-HIP). It's a rare program where minority and underserved teenagers are introduced to meaningful careers in research, with a particular focus on

child health. Graduates of the program have gone on to matriculate at America's top schools, often selecting careers in science or medicine as their areas of focus.

Among others, you'll also read about Rima Jubran, MD, MPH, director of our pediatric subspecialty fellowships, who is asking questions on how best to teach pediatric and subspecialty medicine to the current generation of fellows, and about Roger De Filippo, MD, who is leading a research collaborative aimed at prolonging lives through kidney regeneration.

Elizabeth Sowell, PhD, is helping to advance our understanding of how to improve brain function and capacity, while Yves DeClerck, MD, and colleagues are piecing together the puzzle of drug resistance as it relates to improving outcomes for children afflicted with cancer.

Listening is part of the research process. Good science starts with a good research question, and investigators spend their entire careers "listening" for answers through data, surveys and patient outcomes. Each of our investigators' stories is different, yet each shares a common goal—to improve the lives of children afflicted with disease.

Please enjoy this issue of *Research Highlights*, and I hope you agree that listening is powerful medicine.

Sincerely,

D. Brent Polk, MD
Chair, Department of Pediatrics
Director, The Saban Research Institute
Children's Hospital Los Angeles

In the News



Vicente Gilsanz, MD, PhD

Vicente Gilsanz, MD, PhD, delivered the opening address at the Global Pediatric Network Meeting held in Beijing, China. The conference addressed the need for global standards in pediatric imaging that will unify research data and more accurately inform preventive medical treatments.

Clinical imaging equipment, such as CT, MR and PET scanners, is manufactured for adults. These scanners need to be optimized for the clinical diagnosis of pediatric diseases. The lack of universal standards creates inconsistencies in the imaging data that are reported by different researchers. Therefore, the need for unifying consensus on how to interpret clinical and research imaging studies remains a critical issue for both physicians and patients.

Steven Mittelman, MD, PhD, and Pisit "Duke" Pitukcheewanont, MD, were interviewed by the media regarding premature puberty, an increasingly common occurrence that is being observed worldwide. As pediatric endocrinologists, they are diagnosing and treating greater numbers of young girls, some entering puberty as young as age 5.

Research into the causes of this phenomenon is ongoing, but some of the potential influences include obesity, genetics, prematurity, environmental toxins and stress. In addition to a truncated childhood and the emotional effects of girls achieving physical maturity prior to adolescence, premature puberty creates a heightened risk of certain cancers associated with a longer lifetime exposure to estrogen.



Steven Mittelman, MD, PhD



David Warburton, DSc, MD

The Saban Research Institute co-sponsored the 2011 World Stem Cell Summit, held this year in Pasadena, Calif. The meeting brought together global leaders from government and the medical and business communities. Leading discussions and participating on a number of panels were David Warburton, DSc, MD, and D. Brent Polk, MD, who spoke about the challenges in advancing the mission of regenerative medicine.

Other presenters at the Summit included Tracy Grikscheit, MD, on successfully growing tissue-engineered small intestine, and Laura Perin, PhD, and Roger De Filippo, MD, on repairing kidneys using amniotic fluid-derived stem cells. Warburton also spoke on stem cells and lung disease.

Major Grants Awarded

Shahab Asgharzadeh, MD, was awarded \$1.6 million from the Department of Defense for studies on the tumor microenvironment in pathogenesis of neuroblastoma.



Shahab Asgharzadeh, MD



Yves A. DeClerck, MD

Yves A. DeClerck, MD, received a cooperative specialized research center grant of \$2.5 million from the National Cancer Institute to create the Center for Environment-Mediated Drug Resistance in Pediatric Cancer, a consortium he will be establishing with City of Hope.

Markus Müschen, MD, PhD, was awarded \$3.6 million by the California Institute for Regenerative Medicine to further investigate the dual targeting of tyrosine kinase and BCL6 signaling for leukemia stem cell eradication. Müschen also received an award in the amount of \$1.7 million from the National Cancer Institute to study the infectious origin of childhood leukemia.



Markus Müschen, MD, PhD



D. Brent Polk, MD

D. Brent Polk, MD, received \$2.1 million from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. This award is in support of increased mentoring, research training and career development to facilitate the transition of junior faculty pediatricians into productive and independent scientists.

Marvin Belzer, MD, received \$3.6 million from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. This grant will fund a continuing collaboration that is researching interventions for youth living with HIV as well as research to reduce the infection rates for youth in the U.S.



Marvin Belzer, MD



Fatih Uckun, MD, PhD

Fatih Uckun, MD, PhD, was awarded \$1.7 million by the National Cancer Institute to investigate the effects of targeting SYK tyrosine kinase to overcome radiation resistance in children with relapsed acute lymphoblastic leukemia.

Prasadarao Nemani, PhD, received \$2.3 million from the National Institute of Allergy and Infectious Diseases for his research on brain endothelial cell receptors for E. coli.



Prasadarao Nemani, PhD



ACCESS TO OPPORTUNITY

LA-HIP exposes students to the rigors of science and research.

At a meeting of The Saban Research Institute Committee of the Board of Trustees in 2005, Emil Bogenmann, PhD, EdD, was wrapping up his report on the Institute's successful intern program with Marlborough School, an area private girls' school, when the Swiss-born molecular scientist took a detour from his presentation.



Bogenmann noted that there was little ethnic diversity among the interns, and what was really needed was a program that would recruit minority interns from public schools in underserved areas.

Three days later, Bogenmann, director of Research Education at the Institute, got an unexpected gift: a \$60,000 pledge from Children's Hospital Trustee Ted Samuels, a portfolio manager at Capital Guardian Trust Company, and his wife, Lori. "Dr. B," Samuels said, "go and do your vision."

With that, the Latino & African-American High School Internship Program (LA-HIP) was born. The student science research program, which enters its seventh year in 2012, has trained 77 underserved students in the rigors of science and research and guided them into such top universities as Harvard, Yale, Princeton, Columbia, the University of Southern California and the University of California, Berkeley.

"I thought I might be a pharmacist, but now I want to be a doctor," says Daniel Artiga, 19, LA-HIP's first Harvard student. Artiga studied drug resistance in tuberculosis while in the program and confides: "I'd be clueless in my Harvard labs without LA-HIP. I'm so thankful; Dr. B. changed my life."

This spring, Bogenmann and his admissions committee will cull 16 ambitious science students from more than 100 applicants, juniors from 20 Los Angeles Unified School District high schools. Many of these schools have double-digit dropout rates. The mission of Children's Hospital Los Angeles is reflected in this program, says Samuels. "It provides underserved students exposure to research and science. It's life-altering."

Last year, the first LA-HIP group—the pioneering eight-student class of 2006—graduated from college. Six earned degrees from the likes of Princeton University, Johns Hopkins University and the University of California, San Diego, while two others will finish up this spring.

"Jessica Sanchez's family of seven lived in a one-bedroom apartment, and she's graduating from UCLA," Bogenmann says with pride.

"Brandon Bell arrived here never having heard of Princeton," he adds. "He graduated from there and now works in our lab."

Lizet Gallardo, 22, of East Los Angeles, wasn't sure she could afford college and was set on being a shoe saleswoman until LA-HIP intervened. "I wanted a way out, but people around me didn't see the potential in me that Dr. B. did," says Gallardo, who graduates from West Point this spring. "He took a chance on me; that's what LA-HIP is all about."

In its early incarnation, LA-HIP mirrored its students in one respect: both were works in progress. Skeptical faculty had to be convinced the kids could carry out the research tasks, while students had to overcome the jitters. "It's intimidating," says LA-HIP alumna Noemi Rivera, a recent Belmont High School grad now attending Smith College. "But I learned to take risks."



Emil Bogenmann, PhD, EdD

"When opportunities are equal, when kids are taught and shown how to do the work, there's no difference between them."

Emil Bogenmann, PhD, EdD

May Ramos, LA-HIP class of 2011, is a senior at John Marshall High School.



Bogenmann is helping introduce minority students to the field of science.

On weekdays during the summer program, students arrive in an LA-HIP-funded van at 8:15 a.m. They spend the first week learning lab fundamentals and protocol before they are paired with scientists to conduct research on such weighty subjects as HIV, meningitis, diabetes and cancer. After six weeks, each intern completes an LA-HIP rite of passage: a presentation of his or her work to an auditorium filled with Saban faculty and staff. Interns also meet board members and Richard D. Cordova, FACHE, president and chief executive officer of the hospital, who often shares his own brand of inspiration.

"One intern began a sentence, 'If I go to college ...'," Samuels recalls, "and Richard stopped him and said, 'Not if, but when.'"

As the program developed, Bogenmann adjusted on the fly, too. "I was naïve," he says. "I discovered they had no means to apply to college! SATs, applications, financial aid—they were unsure about everything." The scientist, who was educated in Switzerland and boasts a doctorate in education from USC, hired an SAT prep counselor to work with the teens. Their individual scores soared by as many as 300 points.

Charlene Liebau, a retired admissions officer who worked at Occidental College and California Institute of Technology, came aboard pro bono to help arrange college tours and counsel students and their families, enlightening them on the generous financial aid offered by private universities. "From the science to college, the LA-HIP message is 'don't give up,'" Liebau says. "Emil means business, but by the end, you see the love and admiration the students have for him, and the stars in their eyes; the confidence to go beyond what they know."

Bogenmann keeps the teens on track by paying them a \$1,000 stipend in increments as they complete each phase of the program, which starts with the six-week internship and ends with the annual farewell dinner before the group leaves for college. He and LA-HIP Program Coordinator Mercedes Gonzalez stay in touch with all 77 alumni and their families via Facebook.

"He won't hesitate to ask about my classes, my grades or my plans," chuckles Gallardo, who has set her sights on a research career after the military. Building research careers is what Bogenmann had in mind when he secured new funding from the NIH to set up a satellite program to LA-HIP that offers research training to undergraduates. "It's one thing getting into a great college," Bogenmann observes. "It's another to succeed."

Nowadays, Bogenmann says his research colleagues lobby him constantly to have LA-HIP students assigned to their teams. With these elements in place and secure—the Doris Duke Foundation recently awarded a three-year, \$195,000 grant for LA-HIP—Bogenmann would love his program to become a template for medical research institutes nationwide. In the meantime, he keeps fine-tuning LA-HIP.

"We still have the program for Marlborough students," he says. "They come in with more access to learning opportunities than our LA-HIP kids, but when opportunities are equal, when kids are taught and shown how to do the work, there's no difference between them." ○



The LA-HIP class of 2010

In His Own Words: Brandon Bell's LA-HIP Experience

Brandon Bell participated in LA-HIP while he attended the King/Drew Magnet High School of Medicine and Science. He applied to the program after hearing Emil Bogenmann's presentation at school during his junior year. He was accepted and paired with Henri Ford, MD, MHA, surgeon-in-chief at Children's Hospital Los Angeles. The experience was a revelation.

"I would say one of the greatest blessings in my life was meeting Dr. Ford when I was in high school," Bell says. "I couldn't thank the program enough for pairing me with a mentor who is more devoted to mentorship and teaching than anyone I have ever met."



Bell graduated from high school and then attended Ford's alma mater, Princeton University. He graduated this past spring with a Bachelor of Science in molecular biology. He is currently working with Ford as a research assistant, studying the role of bacteria in the development of necrotizing enterocolitis, a serious intestinal disease affecting newborns. Bell will be applying to medical school in the next year to achieve his life-long dream of becoming a pediatric surgeon. The experience continues to inspire Bell and has changed his own perception about mentorship.

"The example that Dr. Ford has set for me has made me passionate about mentorship myself," he says. "I have spoken at my former high school and schools in the Pasadena Unified School District, and I continue to share my story and inspiration with underprivileged and underrepresented youth. Ultimately I hope to form a bridge between education, medicine and urban outreach by creating an organization whose mission is to inspire, motivate and heal the youth in struggling black communities."

Brandon Bell joins Henri Ford, MD, MHA, in the operating room to get an up-close look at his mentor's work. LA-HIP empowers students to actively pursue their interests in medicine and research.

Maximizing Our Brightest Minds

How do you create better outcomes for patients? It's a collaborative effort.

Physicians and scientists are trained to ask questions. Specifically, how do you help a patient suffering from a disease? But the demand for sustained excellence when delivering patient care leaves little time and resources to study diseases and outcomes in the clinical setting. At the end of the day, the patients come first, and clinicians need to find ways to carve time out of their demanding schedules to explore their research interests.

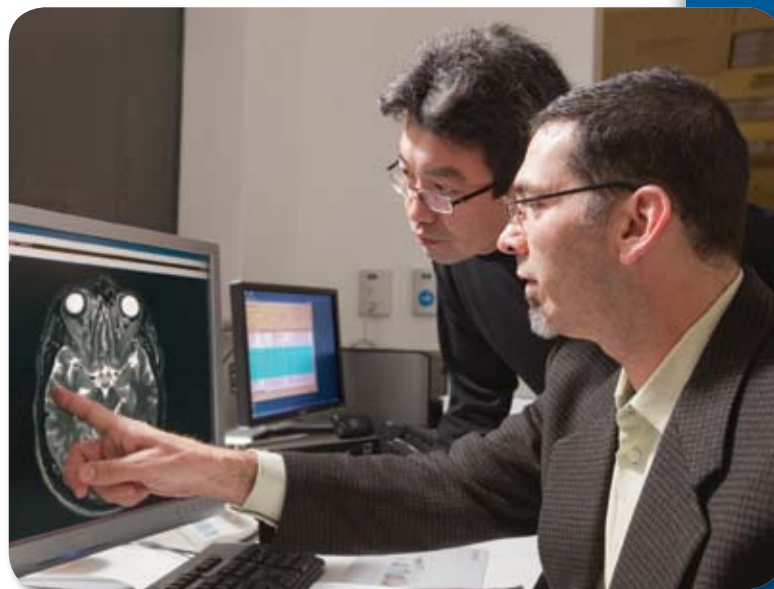


At Children's Hospital Los Angeles, the Children's Outcomes, Research and Evaluation (C.O.R.E.) program is a unique structure that supports a clinician's research interests. Based in the Department of Anesthesiology Critical Care Medicine (ACCM), C.O.R.E. is a program that directly supports and provides mentorship for physicians and scientists who want to investigate how specific medical practices might inform patient care.

Jeffrey I. Gold, PhD, pediatric psychologist at Children's Hospital and associate professor of Anesthesiology and Pediatrics at the Keck School of Medicine of the University of Southern California (USC), is the founder and director of C.O.R.E. In this recently created position, he helps physicians navigate the sometimes daunting process of initiating and running a research study. This process includes writing the protocol, achieving regulatory approval for the study and collecting and analyzing patient data—all while ensuring patient safety and providing the best possible clinical care. It can be a daunting task. That's where Gold comes in. He uses his own experience to guide and support clinicians in pursuing their research.

"I arrived at Children's Hospital Los Angeles as the co-director of the Pain Clinic," says Gold. "My first two years at the hospital were devoted entirely to clinical practice. It was from my own interest in research that I began studying pain in children. Alongside my own work, new brain imaging and virtual reality technologies emerged, and I incorporated these new components into my own research. The whole process was very much an organic initiative that ultimately helped me to secure intra- and extramural funding."

Investigator-initiated studies aim to answer important clinical or basic scientific questions, with the hope of compiling preliminary or pilot data. Ultimately, the pilot data can assist in securing longer-term funding from the government, philanthropic organizations or pharmaceutical sponsors. Once a study receives funding, an investigator can collaborate with other scientists and have access to specialized equipment. With the higher level of access, hypothesis-driven




Vincent Chen, PhD, (left) with Jeffrey Gold, PhD

research projects can be efficiently studied and, ultimately, result in better diagnostics, treatments and outcomes for patients and their families.

The C.O.R.E. program is specifically focused on the medical and functional outcomes for child and adolescent patients and their families. The goal is to move beyond clinical pathology and disease and study how to increase healthy, functional outcomes that can positively affect overall health.

"Mentoring younger physicians and scientists in their own interests is a central value at Children's Hospital, and C.O.R.E. is a part of that tradition," says Gold. It is presumed that each generation benefits from both the knowledge and guidance of their mentors—and in turn will offer the same support to the next generation. C.O.R.E. supports current research interests within the department and aims to collaborate with other clinicians and scientists at Children's Hospital, The Saban Research Institute and colleagues at USC. The ultimate goal is to affect health care policy.

"We have created a structure that maximizes the potential of our brightest minds through collaboration," Gold says. "That is really the underpinning that drives research in academic medicine." 

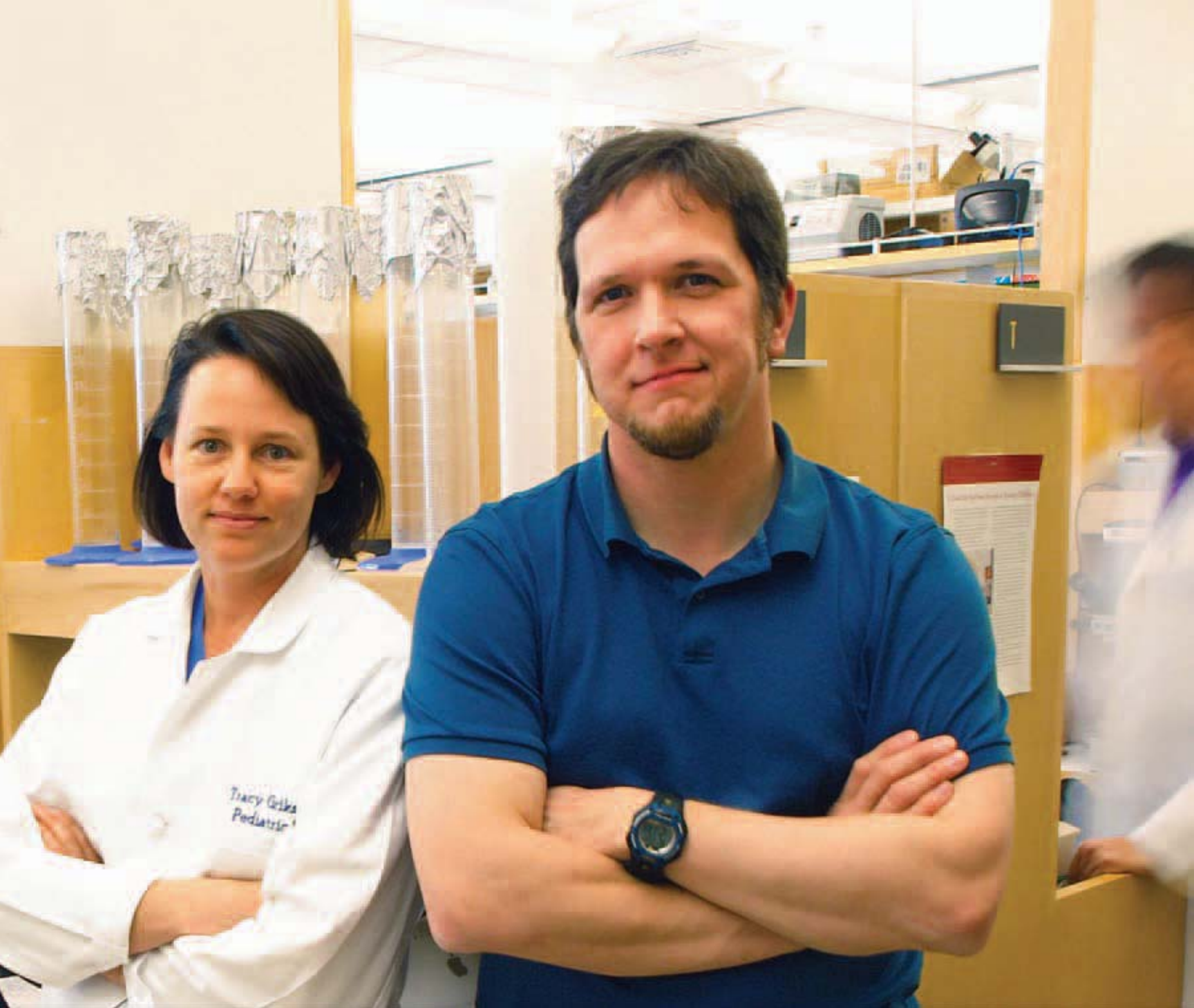
"Mentoring younger physicians and scientists in their own interests is a central value at Children's Hospital, and C.O.R.E. is a part of that tradition."

Jeffrey I. Gold, PhD



GUT CHECK

Mentorship and collaboration are key in advancing research to save the lives of children. At The Saban Research Institute of Children's Hospital Los Angeles, a new club fosters those relationships.



Coffee cups in hand, a group of investigators gather around a conference table on a late Monday afternoon. The most senior faculty at The Saban Research Institute of Children's Hospital Los Angeles sit next to their junior counterparts, mixed between clinicians, post-doctoral fellows and graduate students.

At Gut Club meetings, it's all about being vertically integrated. For Mark Frey, PhD, club organizer, the sessions

also provide a coveted opportunity to collaborate and focus on research at every stage.

"At some point we reached a critical mass of intestine-focused researchers," Frey says. "Not long after I arrived, I looked around and noticed a number of people all working on different aspects of intestinal health. Getting everyone together once a month to discuss the ways we can help each other seemed the smart thing to do."

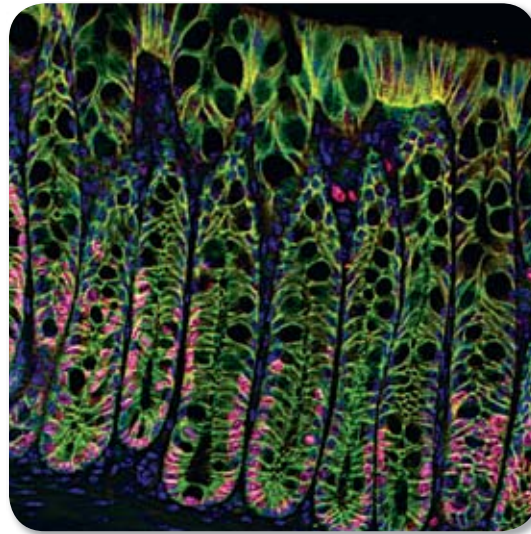
Tracy Grikscheit, MD, (left) and Mark Frey, PhD, founders of the Gut Club at The Saban Research Institute

Frey, an assistant professor in the departments of Pediatrics and Biochemistry and Molecular Biology at the Keck School of Medicine of the University of Southern California (USC), was recruited a year ago from Vanderbilt University by his mentor, D. Brent Polk, MD, chair of the Department of Pediatrics and director of The Saban Research Institute. Given the depth of research into gastrointestinal health and disease at the hospital, Frey felt that a regular informal meeting would serve to continue and advance the history of scientific excellence, collaboration and mentoring that Children's Hospital Los Angeles promotes.

Since March 2011, the monthly sessions have been uniting gastrointestinal researchers at the Institute one meeting at a time—providing opportunities to discuss the latest publications in their field of focus, as well as a venue for first-run discussion of homegrown ideas. The meetings also include clinicians, along with anyone else who has shared interests.

"It brings all the labs here at the hospital together, including groups from Saban, Smith Tower and USC," says Tracy Grikscheit, MD, an investigator at the Institute also specializing in the digestive system. An assistant professor of Surgery at the Keck School of Medicine of USC, Grikscheit helped start the Gut Club with Frey.

"That's a broad swath that comes together in one place for helpful discussion," Grikscheit says. "It's also good for the PIs (principal investigators) and trainees."



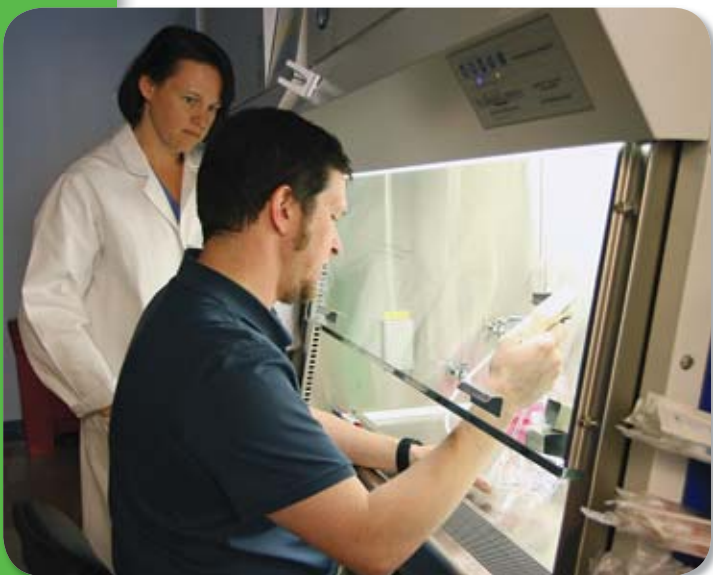
Colon epithelium

A typical meeting goes something like this: different labs are responsible for either choosing papers to read or preparing data from a study-in-progress to workshop. The first half of the gathering is spent discussing the article, and the second half is devoted to an informal presentation. Throughout, questions are asked and answers discussed.

A combined journal club and workshop of sorts, the sessions also provide an outlet to harness collective expertise. For example, a cooperative research effort between Grikscheit and Frey arose from the club.

Together, their respective labs are investigating repair-promoting factors released by subepithelial myofibroblasts, a layer of cells located immediately beneath the intestine's thin lining of epithelial cells, and ways that the cells stimulate intestinal epithelial wound healing.

Their research has found that myofibroblasts exposed to inflammatory molecules such as interleukin-1 β have enhanced capacity to stimulate epithelial wound healing. Working with Susan Lee, PhD, in the Children's Hospital Los Angeles Proteomics Core Laboratory, researchers have identified candidate pro-healing molecules released by myofibroblasts. That means the possibility of new therapies for people who suffer intestinal damage from conditions such as necrotizing enterocolitis, Crohn's disease and ulcerative colitis.



Grikscheit and Frey



A meeting of the Gut Club

An even bigger result of these newfound partnerships is the creation of a synergistic forum of research collaboration and mentorship for all involved.

For Vivien Nguyen, a clinical fellow at Children's Hospital, the no-barriers approach to exploring her interests in pediatric gastroenterology has been an interdisciplinary and supportive experience.

"It's great that relationships are being built between all these groups in a meaningful way," Nguyen said. "And it opens up the doors for collaboration between clinicians and researchers."

Nguyen works with Will DePaolo, PhD, an assistant professor of Molecular Biology and Immunology at USC, who was introduced to her through his relationship with Frey and Polk.

"It bridges the two campuses," DePaolo says of the Gut Club. "It's hard to do but we're trying. Getting over here a few times a month makes a difference."

What's more, the kind of collaboration sparked by the club provides invigorating stimulation for researchers—a change from the usual work in the lab.

"You come up with ideas you never would have come up with on your own," Frey says. "And that's invaluable." ○

"Not long after I arrived, I looked around and noticed a number of people all working on different aspects of intestinal health. Getting everyone together once a month to discuss the ways we can help each other seemed the smart thing to do."

Mark Frey, PhD



Chronic kidney disease (CKD) afflicts roughly 26 million Americans, causing their organs to lose the ability to filter waste and toxins from the bloodstream—and leading to life-impacting complications like anemia, weak bones, nerve damage and cardiovascular disease.

In time, these complications compound, and the kidneys of CKD patients may fail. More than 88,000 Americans die each year from causes related to kidney failure. It's a number that experts say is growing.

PARTNERS IN PROGRESS

Researchers use collaboration and combined experience to further regenerative biomedicine.



Roger De Filippo, MD

Procedures like dialysis and kidney transplantation make a difference, but they're invasive, costly and typically viewed as acts of last resort. A better alternative would be to help damaged kidneys self-heal, and perhaps even regenerate healthy and whole.

Medical science isn't there yet, but a glimpse of the future can be seen in the GOFARR Laboratory for Organ Regenerative Research and Cell Therapeutics in Urology—part of The Saban Research Institute of Children's Hospital Los Angeles.

There, Roger De Filippo, MD, and Laura Perin, PhD, co-directors of the GOFARR Lab, are experimenting with stem cells harvested from amniotic fluid to treat kidney failure. They've already reported substantial success in treating

kidney dysfunction in mouse models. Within five years, they hope to be ready with a phase 1 clinical trial for patients.

"We're a long way from actually generating new organs, but we think amniotic fluid stem cells can be a form of treating chronic kidney disease in such a way that instead of succumbing to CKD in 10 or 15 years, patients might add five to 20 years to their lives," says De Filippo, an associate professor of Urology at the Keck School of Medicine of the University of Southern California (USC). "It may even stave off organ failure entirely."

Amniotic fluid stem cells (AFSC) offer nearly all of the advantages of their better-known and more controversial cousins, embryonic stem cells (ESC). They are shed as a fetus develops, accumulating in the surrounding amniotic fluid, where they can be readily and harmlessly retrieved via needle aspiration. AFSCs are easily cultured and almost as pluripotent as ESCs: researchers can induce them to become many different kinds of cells. But unlike ESCs, amniotic fluid stem cells do not form teratomas or tumors—a distinct advantage when the goal is to engineer new tissue or therapies.

De Filippo and Perin, an assistant professor of Urology at the Keck School of Medicine of USC, have been working together on AFSCs since they first met at the Children's Hospital, Boston, Harvard Medical School. De Filippo, who specialized in tissue engineering, was a research fellow. Perin was a PhD student focusing on stem cells. In 2003, De Filippo joined the Urology faculty at Children's Hospital and the Keck School of Medicine, launching the tissue engineering and organ regenerative lab in the hospital's division of Urology. He recruited Perin to join him a year later.

"We decided to combine our expertise and see what we could do together," says Perin. The pair also collaborate with Kevin Lemley, MD, PhD, and Carl Grushkin, MD, in nephrology at Children's Hospital and David Warburton, DSc, MD, who heads the Developmental Biology and Regenerative Medicine Program at The Saban Research Institute.

"The primary focus of the GOFARR Lab is to use amniotic stem cells to treat diseases that affect the kidney," Perin adds.

In mouse models, the scientists have shown that injected kidney cells derived from amniotic fluid appear to slow the progression of disease, helping maintain and extend the organ's functions and structure.

"We don't think the cells are regenerating a new organ per se," says De Filippo. "They seem to be temporizing kidney failure for a period of time."

One of the goals of the scientists is to further tease out cell types in the kidney, grow them on matrices or scaffolds, then insert the new material into ailing organs where it can be assimilated as new tissue. De Filippo says one application would be in cases of an extensive partial nephrectomy. "We would remove portions of the dysfunctional kidney and replace it with new tissue that would augment the original cells and help restore lost kidney function or prevent further loss."

Conceivably, he says, the approach could also be used for children with hypoplastic kidneys, which appear normal in structure but lack sufficient numbers of nephrons, or kidney cells.

The stem cell work of De Filippo and Perin isn't limited to kidneys. The researchers say their work also has generated promising data indicating that AFSCs might be successfully used to grow replacement tissues for other organs, notably the heart, lungs and pancreas.

"We've had some encouraging results, which we're also pursuing," says Perin.

Ultimate success will take time, of course, but De Filippo and Perin are optimistic. With sufficient resources, hard work and maybe a bit of luck, De Filippo says AFSC research could be translated into clinical therapies within the decade. Building a kidney will take much longer, if at all.

"It's a very complicated organ," says Perin. "Maybe we'll get there, but in the meantime, I think we can learn how to use stem cells to slow CKD progression and improve kidney function. If we can do that, perhaps we can make life easier and longer for a lot of people." ◉



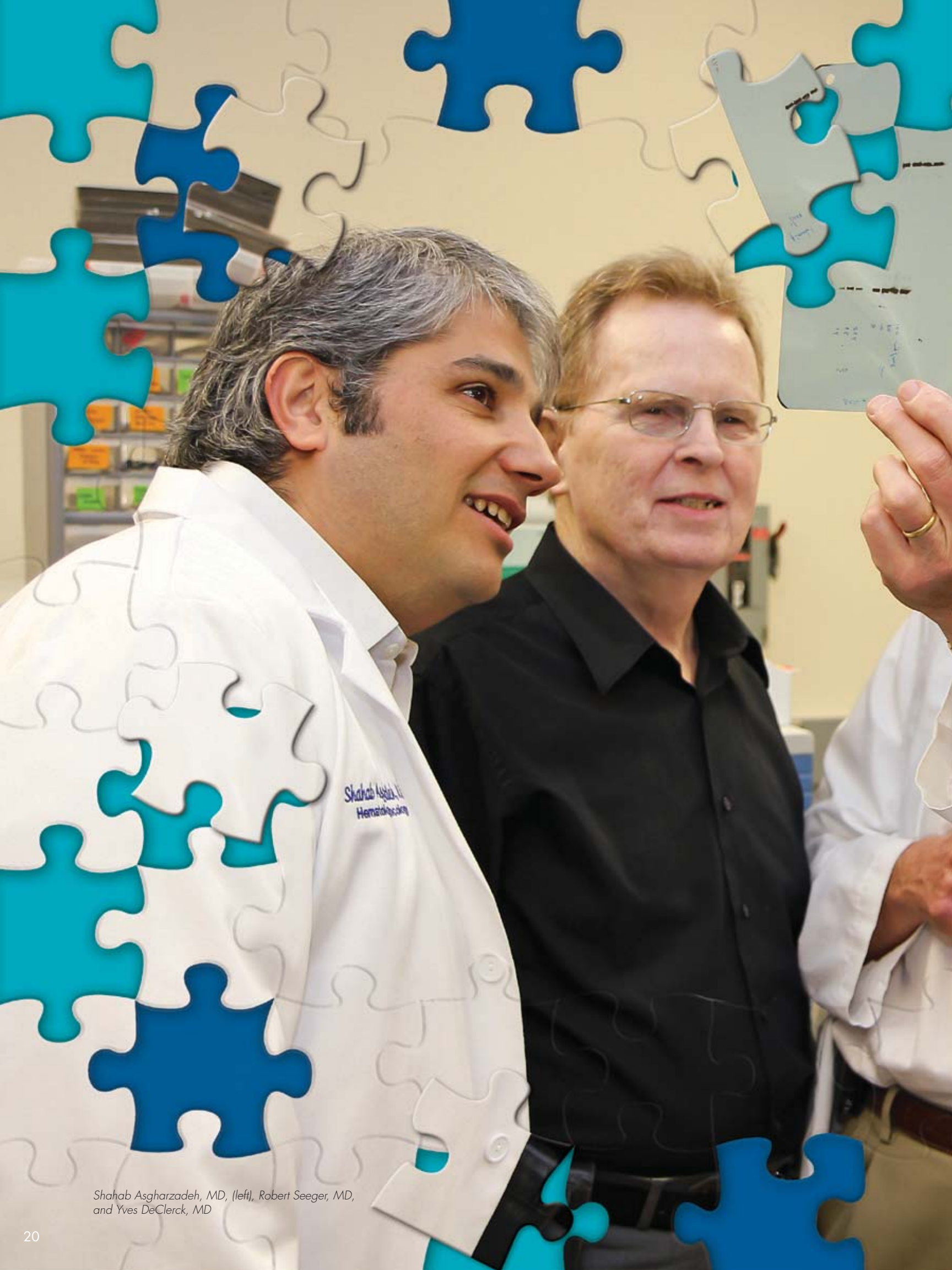
Laura Perin, PhD



De Filippo and Perin are working with amniotic fluid stem cells to treat kidney failure.

"We're a long way from actually regenerating organs, but we think amniotic fluid stem cells can be a form of treating chronic kidney disease in such a way that instead of succumbing to CKD in 10 or 15 years, patients might add five to 20 years to their lives."

Roger De Filippo, MD



Shahab Asgharzadeh, MD, (left), Robert Seeger, MD,
and Yves DeClerck, MD



PIECING TOGETHER THE PUZZLE, One Expert at a Time

A new center sheds light on the inner workings of tumor development in pediatric cancer.

Resistance to drug treatment is the major reason why we sometimes fail to cure children with cancer. Fifty years ago, cancer was essentially a death sentence for children. Today, although more than 70 percent of patients can be considered cured, more than 25 percent will experience disease relapse in a form that is very often resistant to treatment.

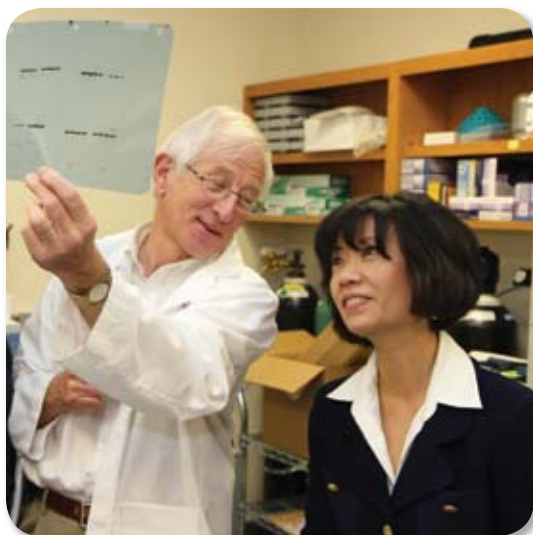
The emergence of recurrent and drug-resistant cancer cells is both a significant medical challenge and a reminder of the need to find new ways to treat this deadly disease.

With the newly funded Center for Investigation of Environment-Mediated Drug Resistance in Pediatric Cancer, scientists at The Saban Research Institute hope to shed new light on the inner workings of drug resistance and develop more effective treatments for patients.

Cancer is the second leading cause of death in children in the U.S., and neuroblastoma, which is one focus of the new research center, is the second leading type of solid tumor in children afflicted with cancer. These cancer cells originate in the peripheral nervous system, fail to mature and then uncontrollably proliferate. Recent treatments combining intensive high-dose chemotherapy, bone marrow transplantation and immunotherapy have improved the overall survival of patients with high-risk neuroblastoma to 45 percent. However, for the patients who fail to respond to initial treatment, there are few options for long-term survival.

Yves DeClerck, MD, pediatric hematologist-oncologist at Children's Hospital Los Angeles, an investigator at The Saban Research Institute and professor of Pediatrics and Biochemistry and Molecular Biology at the Keck School of Medicine of the University of Southern California (USC), was recently awarded, along with his co-investigators, a five-year, \$2.5 million grant by the National Cancer Institute (NCI). He and his colleagues will investigate bone marrow and its role in protecting cancer cells from the effects of therapy.

Also included in the award were Robert Seeger, MD, professor of Pediatrics, and Shahab Asgharzadeh, MD, assistant professor of Pediatrics and Pathology, both of USC and researchers at The Saban Research Institute, and Hua Yu, PhD, co-leader of the Cancer Immunotherapeutics Program, and Richard Jove, PhD, professor and chair of Molecular Medicine, both of the Beckman Research Institute at City of Hope. Each investigator will contribute to the task of identifying specific reasons for why and how neuroblastoma cells survive drug treatment.



DeClerck and Hua Yu, PhD

Currently, scientists believe that drug resistance is a major reason for cancer treatment failure, including for neuroblastoma. "Our thoughts are shifting away from a somewhat reductionist view of cancer cells developing independently of their surroundings," DeClerck says. "Instead we see the cancer cell as a seed that requires favorable soil to grow, and that soil includes normal cells. We are focusing on how the cancer cells communicate with the normal cells in the body and turn them to their advantage."

Studies at the Center will be based on the hypothesis that bone marrow, which is a common site of metastasis in neuroblastoma, provides a unique microenvironment within the body that serves as a protective sanctuary for cancer cells. Researchers believe that normal cells in bone marrow activate specific signaling pathways in tumor cells that give them the ability to survive chemotherapy treatment and then allow them to replicate into drug-resistant offspring. One recently identified pathway, called STAT3, is activated by inflammation.

The growth of drug-resistant cancer cells in bone marrow contributes to cancer progression and significantly lowers the rate of long-term disease-free survival for the patient. The ultimate goal of the Center is to test novel agents in pediatric clinical trials that will interfere with these pathways and prevent the development of drug-resistant cancer cells.

"We are focusing our efforts on first identifying the pathways that cancer cells use to communicate with the body," continues DeClerck. "Once we learn how the disease communicates with the healthy cells, we can identify drugs that will shut down the signal and test them in preclinical models. If they work, then we will test them in clinical studies for patients with the help of the New Approaches to Neuroblastoma Therapy (NANT) consortium, headquartered at Children's Hospital Los Angeles."

The immediate goal of the Center is to create more effective treatments for neuroblastoma patients. Ultimately, investigators anticipate applying some of the discoveries to other cancers. One main characteristic of the Center is that each scientist's expertise contributes to a more complete picture of the disease.

DeClerck's work focuses on the biology of the bone marrow microenvironment. Seeger contributes his extensive knowledge on the biology and immunotherapy of neuroblastoma. Asgharzadeh developed a pre-clinical model that mimics the inflammatory reaction that is thought to contribute to drug-resistance in neuroblastoma. Yu has extensive experience studying how the STAT3 pathway activates cancer cell genes that promote their survival. Jove brings his knowledge of molecular inhibition of the pathways that promote drug resistance.

The sum of their knowledge makes them uniquely equipped to investigate the tumor microenvironment. "This is truly team science at work," says Seeger.




The project team for the Center for Investigation of Environment-Mediated Drug Resistance in Pediatric Cancer includes Jianping Sun, MD, (left), Hung Tran, MD, Tasnim Ara, MD, PhD, Shahab Asgharzadeh, MD, Yves DeClerck, MD, Hua Yu, PhD, Robert Seeger, MD, Fan Yang, PhD, and Yibing Xu, PhD.

The Center will be one of 11 national centers focusing on the role of the microenvironment in different types of cancer, and the only program solely devoted to pediatric cancer. All research will be supported by the \$2.5 million grant from the NCI.

Previous initiatives from each researcher contributed to securing the larger federal funding. A program project grant from the National Institutes of Health (NIH), directed by Seeger since 2000, and seed grants from the ThinkCure! Foundation and The T.J. Martell Foundation, helped The Saban Research Institute scientists and their colleagues at City of Hope to obtain the preliminary data that led to the successful submission of this grant to the NIH. DeClerck further credits the Richard Call Family Endowed Chair in Pediatric Research Innovation, a position that he holds, with helping him dedicate the time required to write the grant proposal.

The Center offers the promise of advancing cancer treatments for both pediatric and adult patients. But in these times of economic cutbacks, philanthropy from private donors remains essential to keeping programs productive.

"We spent about two years brainstorming and conceptualizing the projects for the Tumor Microenvironment Center prior to writing the grant," DeClerck says. "Each of us has a specific interest and is devoted to working together to yield better treatments for patients. The NCI award bridges our interests with actual work and results. But much of the work is dictated by our budgets, and we will continue to seek philanthropic support to further treatments and educate the community about neuroblastoma."

Despite challenges, each physician and scientist remains driven by a desire to learn from and heal those suffering from cancer. In this light, the diversity of interests drives and unfolds the mystery one piece at a time. In the race to cure cancer, brilliant minds do not necessarily think alike—and that is a good thing for the rest of us. 

"Our thoughts are shifting away from a somewhat reductionist view of cancer cells developing independently of their surroundings. Instead, we see the cancer cell as a seed that requires favorable soil to grow, and that soil includes normal cells. We are focusing on how the cancer cells communicate with the normal cells in the body and turn them to their advantage."

Yves DeClerck, MD

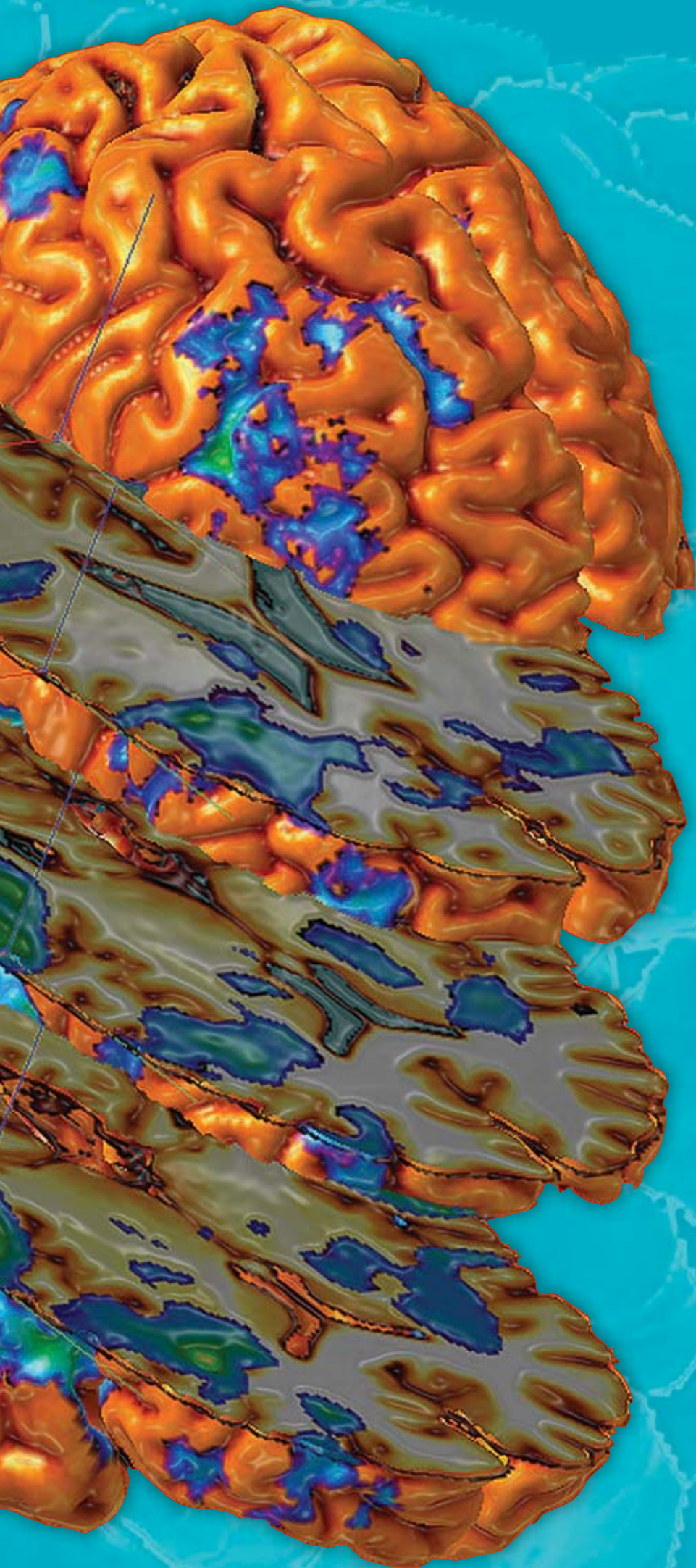
REWIRING THE BRAIN

Changing the environment to promote more productive neurological connections.

Want to know what your kids are thinking? So does Elizabeth Sowell, PhD, an expert in neuroimaging and neurocognitive development at The Saban Research Institute. Using specialized noninvasive equipment, she can look into a child's brain and study the process of how he or she thinks.

"If I scanned your child's brain, I would get a set of images," says Sowell, a professor of Pediatrics at the Keck School of Medicine of the University of Southern California (USC). "If I then asked him or her to learn how to juggle, and I scanned the brain a second time, the images would be different. Based on the difference in these images, we know that 'something' is happening: a change is taking place. My goal is to use this knowledge to help children with neurodevelopmental or other cognitive differences."





Currently, there is a tremendous focus on the “First 5” federal programs that attempt to address neurodevelopmental and cognitive deficits during the first five years of a child’s life. The common wisdom is that after age 5, the window of opportunity is lost. But it is now known that neural plasticity continues a lot longer than had been previously thought.

“We know that the brain changes dynamically during development,” Sowell says. “Once it stops growing, tremendous changes continue to take place at the cellular level. What drives this growth isn’t just genetics but also context: the environment where the child is living and growing.”



Elizabeth Sowell, PhD

Sowell continues, “The questions that I’m working toward answering are: What happens when we change that environment? Is it possible to promote more productive neurological connections? Can we rewire the brain?”

Using specialized equipment, Sowell plans to find out.



Suzanne Houston, MA, (left), and Sowell

Conventional magnetic resonance imaging (MRI) is a noninvasive tool that uses a powerful magnet and radio waves to produce detailed images of the organs and tissues in the body. Functional magnetic resonance imaging, or fMRI, employs similar equipment to detect alterations in blood oxygenation levels as a way of measuring neural activity. When a specific area of the brain is active, it consumes more oxygen, causing an increase in blood flow to that area. Using fMRI, researchers can now visualize which specific areas of the brain are activated during any given mental process.

Based on her extensive experience studying children with fetal alcohol syndrome, Sowell believes this will be a powerful technique for studying children with neurological differences like autism or attention deficit hyperactivity disorder (ADHD).

"I think the possible applications for neuroimaging are extensive," says Sowell. "Consider children who may have been exposed to powerful medications that we know can affect cognition—in utero exposure to HIV prophylaxis to prevent mother-child transmission of the disease, or early childhood treatment of pediatric cancer. Is there something that we can do to help these kids toward more typical neurodevelopment? I think the answer is 'yes.'"

Consider children with dyslexia. In addition to their neurological differences compared with children without dyslexia, these children also have a profoundly different relationship with the written word. Reading is likely confusing for them, so they may avoid reading to minimize their frustration. If there was a way to encourage children with dyslexia to spend time with written language, it might be possible to alter their experience so that they could more comfortably live in a world where they are constantly bombarded with the written word.

Sowell continues, "Imagine if we could send these children home with a tablet computer with a special game for them to 'play.' On the tablet, we'd load a computer game that involves text, encouraging a sensory/motor response. So here you have a child who never spends time with books, spending a lot of time interacting with written language.

"Even if they aren't reading the words, I would be very interested in studying the wiring in this child's brain to determine the effect of 'playing' with words," Sowell says. "Would the images of their brain change, even in a small way, to be more like the brains of kids without dyslexia?"

Sowell and her staff are actively recruiting healthy, normally developing children whose parents agree to have them undergo fMRI. “For this kind of research, we need to establish baselines—what does the brain of a normally developing 6-year old look like?” she says. “How is it different at 7 years of age? Ultimately, we will compare these baseline scans to those from kids with neurodevelopmental or cognitive effects and see how the pictures are different.”



Scanner for performing functional magnetic resonance imaging (fMRI)

Once she identifies the differences, Sowell will determine what to do about them. “We’ll select an intervention to help make the brain of the kid with ADHD more like the brain of the typically developing kid,” she says. “Rewiring sounds complicated, and it is. But not for the children—all they will see is a new game to play.”

The only difference is this game has the potential to positively affect children’s lives—today and in the future. That’s a game that would make every parent happy. ○

“The questions that I’m working toward answering are: What happens when we change that environment? Is it possible to promote more productive neurological connections? Can we rewire the brain?”

Elizabeth Sowell, PhD

Neuroimaging Research – A Team Sport

Neuroimaging research requires an interdisciplinary approach that includes biomedical engineering, neuroscience and physics, to name just a few of the specialties that consolidate into this area of inquiry. The tools are expensive, with the price of an fMRI machine in the millions, so it helps to have a number of scientists generating grants and philanthropic awards to pay for the equipment. Collaboration among several sites also allows more children to be imaged over a shorter time frame, producing faster results.

Elizabeth Sowell, PhD, has collaborated on many projects—with the University of Southern California; the University of California, Los Angeles; Emory University; the University of California, San Diego; Northwestern University; the University of Cape Town in South Africa; and many more. She explains the benefits this way: “It is a joy working with other people who have ideas. One good idea inspires another good idea.”

She sees mentoring as an important aspect of the collaborative process. “I think everyone needs a mentor,” she says. “You learn so much from people who have been there before you.”

Sowell has two graduate students and two post-doctoral fellows. One of those grad students, Suzanne Houston, MA, was a project coordinator in Sowell’s lab for six years. Like her mentor, Suzanne has selected a niche that is still relatively new, leaving her room to make a name for herself.

“I’m working in the area of educational neuroscience,” says Houston. “Right now, I’m studying reading disability with the plan to segue into educational intervention. Eventually my goal is to be a professor doing research or be on an NIH policy panel.”

She has made a great start on those plans. Just one semester into a PhD program, she has been an author on five papers, and a sixth paper, where she will be first author, is in the works.

“The people I mentor tend to be productive, creative, ethical and team players,” Sowell says. “Mentoring is one of my favorite, and most important, jobs. We need to help guide the next generation to build on what we know, so they can bring their own innovations into the future.”



Spotlights – A Culture of Mentoring

Helping tomorrow's medical and research leaders find the path to success includes making sure they have what they need to thrive at one of the best children's hospitals in the U.S. Here's a look at three people leading the way at Children's Hospital Los Angeles.

Charles Gomer, PhD



Success takes the work of many, especially in academic medicine. That couldn't be truer for Charles Gomer, PhD, and the numerous junior faculty he has helped mentor over the last decade.

As vice chair of Pediatrics for Faculty Development at Children's Hospital Los Angeles, Gomer routinely meets with new faculty recruits, guiding them to mentors—the people who will best help them pursue their academic and clinical interests. With feedback from his Faculty Development cabinet, and assistance from Valerie Ortiz-Campana, administrative director of the program, the goal is to provide all faculty with the resources they need to succeed academically at one of the largest and best pediatric medical centers in the country.

"Together, we provide new faculty with the opportunity to succeed," Gomer says. "And by doing this, we ensure that we're helping the next generation of academic pediatric leaders."

Faculty development at Children's Hospital is three-pronged, including career development workshops and presentations, junior faculty mentoring and appointment and promotion counseling. Through this infrastructure, new arrivals to the hospital are greeted with a formatted orientation and are introduced to a team of mentors tailored to their specific areas of

research interest. Teams consist of a primary mentor in the junior faculty's academic interest area, along with two others that can serve to fulfill clinical guidance as well as networking opportunities.

"It seems very logical to provide this support to someone who is new to the hospital," Gomer says, "but often these needs can be forgotten in the stress of day-to-day work."

The program also supplements the learning process with mentorship brochures that explain the program goals, along with ongoing sessions on applying for grants, how to write manuscripts and even checklists for mentees to ensure that the new recruits maximize their interactions and relationships with mentors. What's more, mentors themselves are provided with the support they need to help the next generation. That includes mentorship recognition through best practices, training and faculty mentoring awards, including one named after Robert McAllister, MD, past director of Research at Children's Hospital—and Gomer's former mentor.

"We have outstanding pediatric faculty with great passion," Gomer says. "Everyone involved is in some phase of being mentored or mentoring others."



Charles Gomer, PhD, with his mentee, Douglas Vanderbilt, MD, and Valerie Ortiz-Campana

Rima Jubran, MD, MPH

Since 2006, Rima Jubran, MD, MPH, has served as fellowship program director for the Division of Hematology-Oncology at Children's Hospital Los Angeles. And now, as director of all pediatric subspecialty fellowships at the hospital, she hopes to provide the foundation for fellows to become leaders in their fields. Effective mentorship and faculty development are important cornerstones for this foundation.

"The two go hand in hand," Jubran explains. "You can't do one without the other."

Working with Charles Gomer, PhD, vice chair of Pediatrics for Faculty Development at Children's Hospital Los Angeles, and the Faculty Development Program at the hospital, Jubran is helping to create a program that mirrors those efforts already in place while tailoring it to the future leaders in subspecialties. Trainees develop through seminars, innovative educational opportunities and comprehensive academic and career development.

For Jubran, it's important to create an environment that fosters exchange between individuals at Children's Hospital and the University of Southern California (USC). Specifically, she's aiming to bridge the gap that sometimes exists between scientists and clinicians, a goal set by D. Brent Polk, MD, vice president of Academic Affairs and director of The Saban Research Institute of Children's Hospital, and chair of the Department of Pediatrics at the Keck School of Medicine of USC.



"Exposure to dialogue between scientists in the lab and collaborating clinicians is something that is very important for our trainees," Jubran says. "They need to be able to see all the different points of view people can bring from the research and clinical arenas."

Acting as an example, Jubran, medical director of the Retinoblastoma Program in the Children's Center for Cancer and Blood Diseases at the hospital, is working with a team of clinicians and scientists to promote research in the field. The team includes Gomer; A. Linn Murphree, MD, director of the Retinoblastoma Program at The Vision Center at Children's Hospital; Thomas Lee, MD, division head of The Vision Center; Susan Lee, PhD, of the Proteomics Core Laboratory; and members of their labs and clinical research teams.

"We meet regularly, working to make the research as relevant and beneficial for patients as possible," Jubran says. "Exposing our trainees to this kind of process will only serve to improve their training and the health of our patients."



Rima Jubran, MD, MPH, (right) meets with a team of clinicians and scientists to promote research that's relevant and beneficial for patients.

Niurka Rivero, MD



At Children's Hospital Los Angeles, being a good physician also means being a good leader. For the last seven years, the Anesthesiology Critical Care Medicine (ACCM) Leadership Program has been teaching new department faculty how to be more effective clinicians.

"In the end, it's a matter of patient safety," says Niurka Rivero, MD, director of the Critical Care Fellowship at Children's Hospital. "There's more and more evidence linking the lack of leadership to patient outcomes—patients do worse, nursing retention is worse and errors happen more when there isn't a team leader. It really reveals the responsibility of a physician in that role."

Under the leadership of Randall Wetzel, MD, ACCM department chair, the three-year course aims to increase professional effectiveness by focusing on leadership and professionalism. Together, with co-lead instructor Samuel Yanofsky, MD, MEd, Rivero helps trainees at Children's Hospital think about how their influence in the medical context comes from their credibility and the ability to effectively lead and develop alignment with others. Participants also look at dimensions of leadership, including character, emotional intelligence, community, culture, organizational context and uses of power, as well as effective styles of leadership.

All of these topics focus upon the person as leader and the organizational structure that supports his or her leadership—building leadership competence and professional maturity through personal change and leading organizational structures to patient and organizational health. In addition, training in professional networking and development of a career plan are offered.

Delivered by faculty in the ACCM Department and assisted by other invited outside speakers, the sessions are taught in large groups, small groups with mentors, individually with mentors and via evaluation activities. Along with Yanofsky, Rivero and Wetzel, course instructors include Rambod Amirnovin, MD; Sylvia Del Castillo, MD; Barry Markovitz, MD, MPH; David Moromisato, MD; Lara Nelson, MD; and Beth Zemetra, RN.

"It's a real personal transformation for the trainees," Rivero says. "It helps them to see that being a great physician also includes their effectiveness in shaping culture and understanding the role of the leader within it." ○



Niurka Rivero, MD, (right), mentoring L. Nelson Sanchez-Pinto, a first year fellow in critical care medicine, at a patient's bedside

A black and white portrait of Richard Koch, MD, an older man with wavy hair, wearing a striped shirt and a tie. The background is a solid green color.

Research Hero

Richard Koch, MD, early advocate for the developmentally disabled and founding director of the Frank D. Lanterman Regional Center, spent his career at Children's Hospital Los Angeles.

Born in North Dakota, Richard Koch and his family moved to Petaluma, Calif., where he earned a scholarship to the University of California, Berkeley in 1941. His college plans were cut short one year later when he enlisted in the Army Air Corps and was trained as a bombardier. On April 9, 1944, his B-24 was shot down, and he spent the next 13 months as a prisoner of war at Stalag Luft 1 in Germany.

This event, which might have derailed another person, provided the inspiration for a truly extraordinary life and career. The POW camp where Koch was held had a meager library that happened to include a medical biography titled "The Doctors Mayo." The book, published in 1941, was the story of the Mayo family of physicians and how their lives and careers became entwined with the history of medicine. It also served as a roadmap to a lifetime of achievement for the young Koch.

Following the war, he finished college and graduated from the University of Rochester School of Medicine in New York in 1951. After interning at Children's Hospital Los Angeles, Koch joined the Medical Genetics staff and later became professor of Pediatrics at the Keck School of Medicine of the University of Southern California (USC).

Photo courtesy of the Koch family archives

Advocating for the developmentally disabled, he instituted traveling clinics that provided services so that children could remain at home with their families instead of being institutionalized, which was customary at that time. In 1955, Koch was named director of the newly established clinic for the study of mental disabilities at Children's Hospital. His research focused on preventing disability caused by phenylketonuria, or PKU. Babies with this genetic disorder lack the enzyme that processes the amino acid phenylalanine, causing it to build up in the infant's blood and damage the developing brain.

Koch successfully lobbied for mandatory screening and established one of the first programs in the country, allowing PKU babies to be identified soon after birth by a simple blood test. Early diagnosis led to prevention of complications, including intellectual disability. Koch was principal investigator on the National Institutes of Health (NIH)-funded "Collaborative Study of Treatment of Children with Phenylketonuria," which lasted 16 years. These babies were placed on a diet low in the amino acid phenylalanine and kept on the diet until about age 10, when their brains were sufficiently developed.

By the late 1960s, it appeared that the problem had been solved. This relatively simple intervention prevented children from life-long disability. However, a decade or so later, PKU mothers who had been saved from disability were delivering babies with neurological and other disorders. Koch proposed another study to the NIH and became principal investigator on the "International Maternal Phenylketonuria Collaborative Study." Children's Hospital became the primary site for this effort at collecting data on adult PKU patients who went back on the low-phenylalanine diet to maximize their chances of delivering a healthy baby.

Over a career spanning more than 50 years, he became an internationally recognized expert on PKU, with more than 200 articles published in peer-



Richard Koch, center, known to the hospital as "Dr. PKU," was internationally recognized for his landmark research in phenylketonuria.

reviewed journals. He also established the model that became the Regional Center system in California and was named the first director of the Frank D. Lanterman Regional Center in Los Angeles.

Like the Mayo physicians Koch had studied as a young man, he had become a physician who dedicated his career and his life to advocacy, service, research and clinical care. And like the Mayo physicians, his career serves as a model for younger doctors.

A colleague from the Division of Medical Genetics, Richard Boles, MD, remembers him this way: "Dr. Koch was the true physician-scientist and an inspiration to me. He leveraged his dual role, using cutting-edge science to provide superb clinical care to his patients and allowing that clinical experience to guide his groundbreaking research. He literally saved thousands of people from mental disability."

Koch passed away peacefully at his home on Sept. 24, 2011. ◉

"Dr. Koch ... leveraged his dual role, using cutting-edge science to provide superb clinical care to his patients and allowing that clinical experience to guide his groundbreaking research. He literally saved thousands of people from mental disability."

Richard Boles, MD

Mentoring the Future



Cheryl Saban, PhD, and Haim Saban are longtime advocates of advancing scientific causes and health care for pediatric patients. Their support of Children's Hospital Los Angeles and its research center has culminated in donations totaling nearly \$50 million, making the Saban family the largest individual benefactors of research at the hospital.



Cheryl Saban, PhD



Cheryl Saban, PhD, (center), with the young women of the 2011 Latino & African-American High School Internship Program (LA-HIP) class

In 2003, after their transformational gift of \$40 million, The Saban Research Institute was named to honor the Sabans and their mission to foster innovative scientific studies that translate into better clinical outcomes for patients. Dr. Saban also is an honorary trustee of Children's Hospital and serves on the Research Committee of the Board of Trustees.

As a trained psychologist, Dr. Saban has studied and written about personal empowerment for women and children. She has found that the positive influence of a role model can create life-long benefits for members of the younger generation who carry on and expand the work of their predecessors. In a recent interview, Dr. Saban shared her thoughts about the role of mentoring in medicine and, specifically, how it influences the next generation of scientists.

"The data is in on this—studies show that when you have a mentor, your prospects for success are so much greater," she says. "I can't think of any field where the presence of a mentor would be more significant than in science and medicine. The curriculum is difficult, and it's helpful to have the benefit of someone else's experience as students navigate the transitions from high school to university to professional school and then to the workplace. A mentor can provide not just knowledge and experience but also the passion and enthusiasm that can encourage a young person to stick with it." ○

"To all the MDs and PhDs who are reading this, I'm extending a challenge to you: Take the time to share what you know, and to be a role model for younger generations. The future of science and medicine depends upon it."

Cheryl Saban, PhD

Honor Roll of Donors

From July 1, 2010 to June 30, 2011

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 Children's Hospital Los Angeles. The dedicated investigators at The Saban Research Institute of Children's Hospital Los Angeles would like to extend our deepest gratitude for the support of all of our donors. We offer our deepest gratitude to Cheryl Saban, PhD, and Haim Saban, without whom our dream of a world free from 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.

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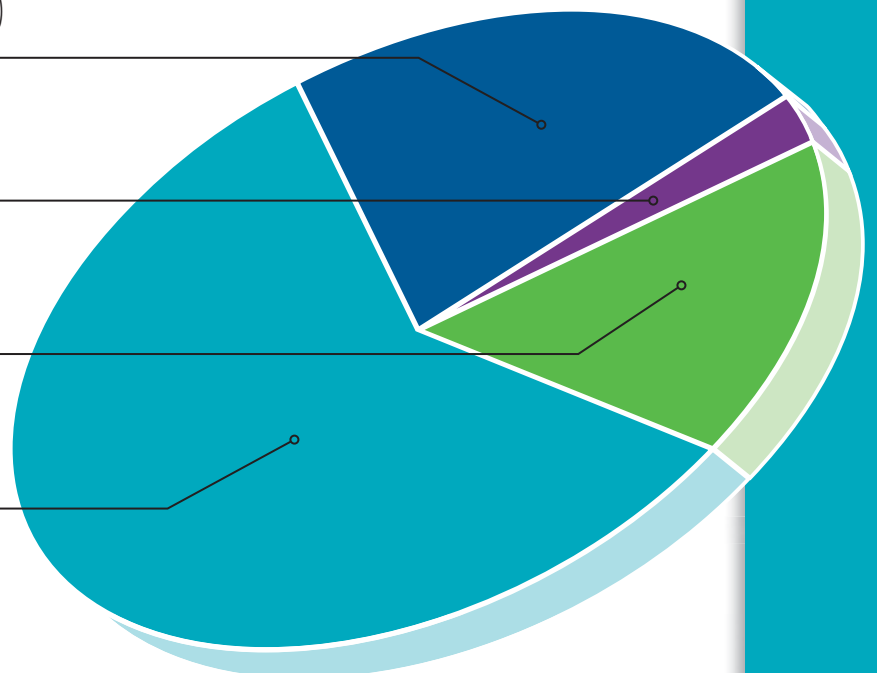
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