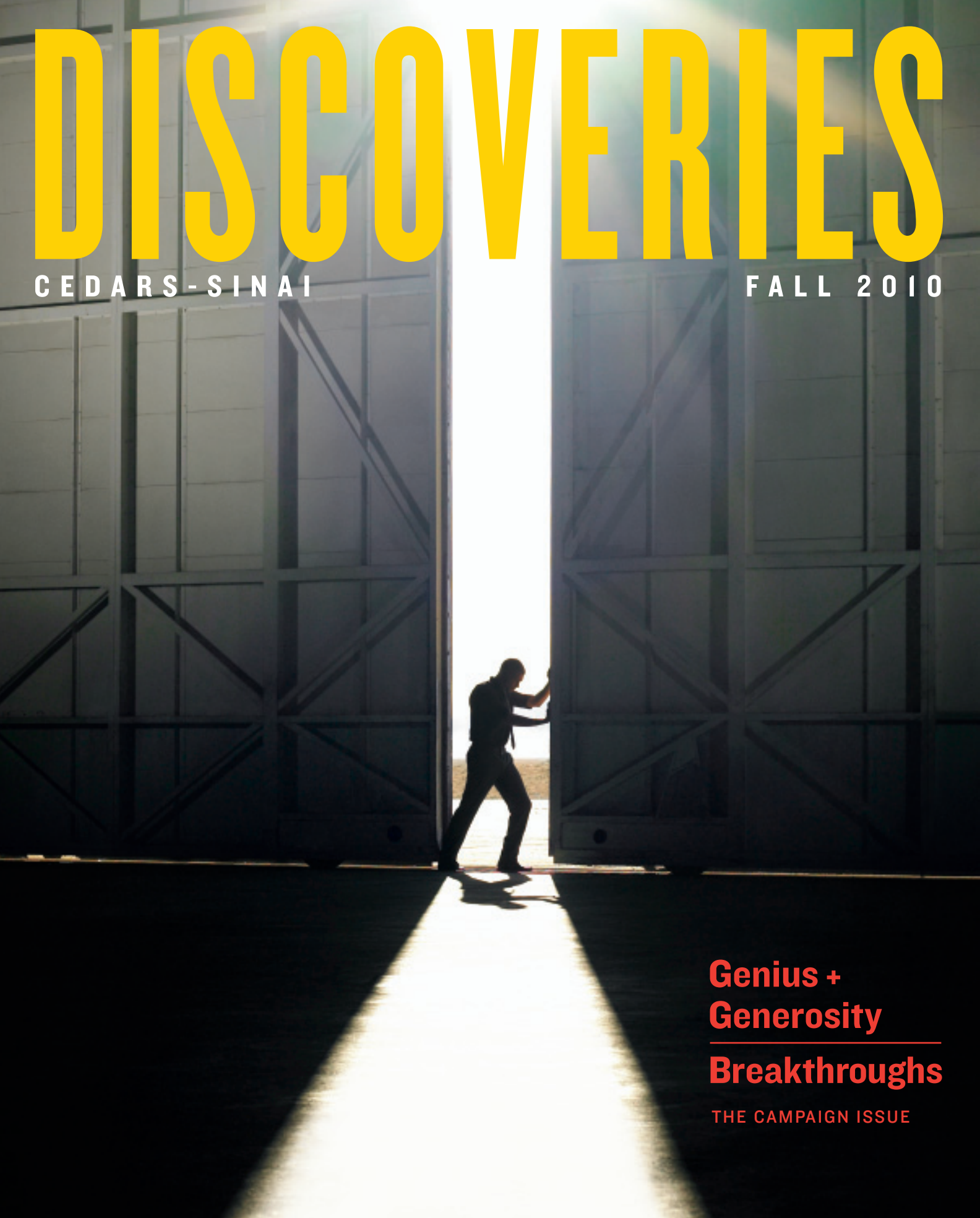
DISCOVERIES

CEDARS-SINAI

FALL 2010



Genius + Generosity

Breakthroughs

THE CAMPAIGN ISSUE

ABOUT RESEARCH PROGRAMS AT CEDARS-SINAI MEDICAL CENTER

Cedars-Sinai Medical Center is one of the largest nonprofit academic medical centers in the western United States. For more than 20 years, it has been named Los Angeles' "most preferred hospital for all health needs" in an independent survey of area residents. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthroughs in biomedical research and superlative medical education. It ranks among the top 10 non-university hospitals in the nation for its research activities. Biomedical research is an integral component of Cedars-Sinai Medical Center's mission. The Medical Center maintains the following goals for bio-medical research programs:

- Sustain a program of out-standing biomedical research, healthcare services, and nursing research by fostering basic and clinical investigation in the prevention and causes of medical illnesses, their pathologic mechanisms and diagnoses, and the development of cures for the ailments that afflict our society
- Translate research discoveries appropriately to a clinical setting
- Provide research training opportunities for graduate students and our professional teaching programs
- Foster the transition of biomedical discoveries to the realms of product development, patient care application, and marketing
- Provide cross-fertilization and interdependent synergy between the Medical Center and the biotechnology industry
- Protect the rights of human and animal subjects

To effectively implement its mission, Cedars-Sinai Medical Center recognizes the need to:

- Provide modern facilities and expert faculty support to encourage and stimulate new and ongoing meritorious research programs
- Encourage philanthropy and community support for such services, as well as community education programs

Cedars-Sinai Medical Center has been fully accredited by the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP) for assuring protection for our human subjects during research. Cedars-Sinai was the first institution in California to have received this designation. AAHRPP is a Washington, D.C.-based nonprofit organization that uses a voluntary, peer-driven educational model to accredit institutions engaged in research involving human subjects.

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CEDARS-SINAI DISCOVERIES

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In This Issue

From the Dean of Faculty

Shlomo Melmed, MD, MACP
Senior Vice President for Academic Affairs
Dean of the Medical Faculty
Director, Burns and Allen Research Institute
Helene A. and Philip E. Hixon Chair in
Investigative Medicine

Each member of our medical staff—each nurse, researcher, patient, or family member—has a unique story to tell about the important role of Cedars-Sinai in his or her life. My own Cedars-Sinai story began 30 years ago, in the basement of the old Schuman Building on Beverly Boulevard, where my laboratory was located. I would have never dreamed at that time that our medical center—with a very vibrant academic cardiology division and not much more—would today be well-established as one of the top comprehensive academic medical centers in the country.

Over the past 10 years, we have seen a metamorphosis in the academic stature, character, and culture of Cedars-Sinai. This medical center has transformed itself from an outstanding community hospital to an outstanding community-based academic hospital of national stature. This phenomenal growth was made possible by the unswerving support of our community. A transformation of that scope requires both vision and tangible support: We enjoy both.

The *Discovering for Life* campaign has enriched every single program and every area of care at the medical center, including heart, cancer, neurosurgery, gastroenterology, metabolism, pediatrics, lung, genetics, gene therapy, surgical technologies, and imaging, as well as our endowed chair and PhD programs. We have biomedical research programs of national repute all led by global clinical leaders, with well-established training programs for both physicians and scientists. We have leveraged philanthropic dollars into the strongest National Institutes of Health (NIH) support.

With this strong foundation in place, we are now ready for a new trajectory of growth with further expansion in imaging, the Regenerative Medicine Institute, innovative surgical subspecialties, genomics, and the construction of the state-of-the-art Advanced Health Sciences Pavilion.

We set out on this ambitious campaign because we realized that to excel in clinical care required us to be at the cutting edge of medical knowledge discovery. We know our community—and we knew it would support our goal. What we did not initially appreciate is that our supporters would embrace our vision with such enthusiasm and have such an appreciation for the importance of our research enterprise in delivering the finest clinical care. This strong partnership is what allows us to continue in our energetic quest to cure the diseases that afflict us all.

Contents

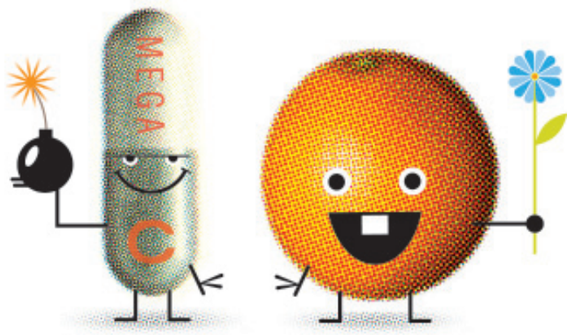
Bench Notes

Could Retinal Imaging Help Diagnose Alzheimer's Disease Earlier?

The nerve cell-damaging plaque that builds up in the brain with Alzheimer's disease also builds up in the retinas of the eyes—and it shows up there earlier. This hallmark discovery could lead to earlier diagnosis, intervention, and monitoring of the disease, according to new research conducted by a team of scientists in Cedars-Sinai's Department of Neurosurgery in collaboration with the Weizmann Institute of Science in Israel and the University of Southern California.

Scientists discovered characteristic amyloid plaques in the retinas of deceased Alzheimer's disease patients and used a noninvasive optical imaging technique to detect retinal plaques in live laboratory mice genetically modified to model the human disease. The combined results suggest the possibility that noninvasive retinal imaging may be helpful in early definitive diagnosis of Alzheimer's and monitoring disease progression in response to treatment.

Alzheimer's disease is a devastating condition that is becoming more prevalent worldwide as the baby-boom generation advances into its senior years, but there is no conclusive, noninvasive way to diagnose it in patients, especially at early stages of the disease. Previous studies have suggested that changes in the brain may begin years or even decades before symptoms occur—emphasizing the need for earlier, reliable detection for early therapeutic intervention to achieve effective remedy. The new study suggests the possibility of monitoring Alzheimer's disease through a simple retinal imaging approach.



High Doses of Antioxidant Supplements Can Lead to Cancer Formation

High doses of antioxidant nutritional supplements, such as vitamins C and E, can increase genetic abnormalities in cells, which may predispose supplement-takers to developing cancer, according to a new study from the Cedars-Sinai Heart Institute.

Cedars-Sinai Heart Institute director Eduardo Marbán, MD, PhD, and his team accidentally discovered the danger of excessive antioxidant doses while seeking a way to reduce the genetic abnormalities that occurred naturally when multiplying human cardiac stem cells in a Petri dish.

Marbán stressed that the study's finding applies only to excessive nutritional supplements and not to foods that are rich in antioxidants, such as milk, oranges, blueberries, and peanuts. "Taking one multivitamin daily is fine, but a lot of people take way too much because they think if a little is good, a lot must be better," says Marbán. "That is just not the case. If you are taking 10 or 100 times the amount in a daily multivitamin, you may be predisposing your cells to developing cancer, therefore doing yourself more harm than good."

Dr. Marbán is leading an ongoing, groundbreaking clinical trial in which heart attack patients undergo two minimally invasive procedures in an effort to repair and re-grow healthy muscle in a heart injured by a heart attack. The results of the trial are expected in early 2011. Recently, Marbán received a $5.5 million grant from the California Institute for Regenerative Medicine to continue developing cardiac stem cell therapies.

GPS Accuracy for Radiation Therapy

A new system that utilizes a precise GPS-like system to track prostate cancer tumors is now being offered to patients undergoing radiation therapy at Cedars-Sinai's Samuel Oschin Comprehensive Cancer Institute. The monitoring system, called Calypso, allows radiation beams to more precisely target the cancer as it gives real-time positioning information that allows the radiation beams to focus directly on the tumor.

Since many organs in the body are constantly moving—including the prostate gland—this technology provides a higher level of accuracy in the delivery of radiation to the cancer while minimizing potential damage to healthy tissue.

Cedars-Sinai's Samuel Oschin Comprehensive Cancer Institute is one of only a handful of cancer centers in Southern California to offer this advanced technology to its prostate cancer patients.

"This system allows us to deliver radiation more accurately directly to the tumor, minimizing the risk of sexual side effects and damage to other vital organs—a real benefit to patients," says Howard M. Sandler, MD, chairman of Radiation Oncology and the Ronald H. Bloom Family Chair in Cancer Therapeutics at Cedars-Sinai.

Dr. Sandler was the lead author of a clinical study published in *Urology*, which demonstrated that prostate cancer patients treated with radiation and monitored with the Calypso system reported significantly reduced prostate-related side effects than those whose radiation was not complemented by Calypso.

My Device

By Charles F. Simmons, Jr., MD

A Very Cool Baby Blanket

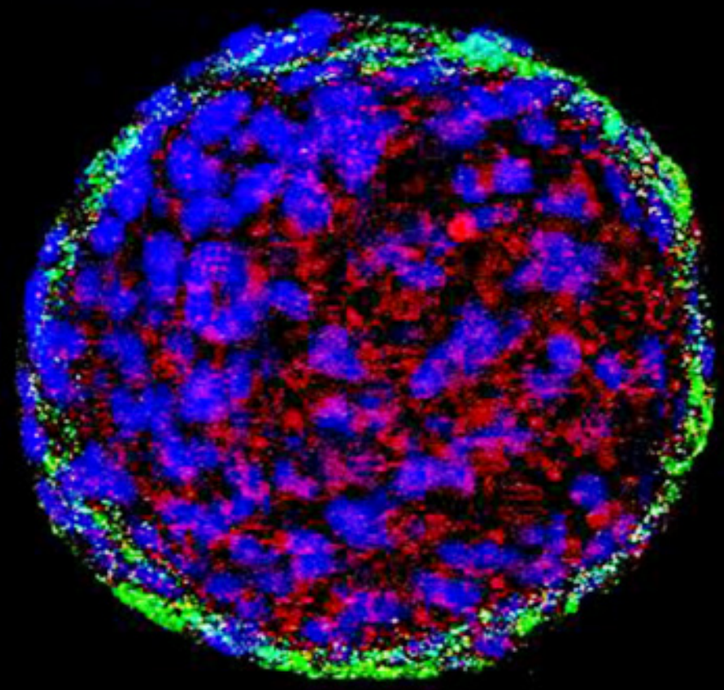
The neonatal cooling blanket system is the latest development in preventing and minimizing brain damage in babies who have been deprived of adequate oxygen before or during birth (a condition called hypoxic-ischemic encephalopathy).

In the past, no treatment was available for infants with this type of injury. It is based on groundbreaking research into why those who nearly drown in freezing water suffer less brain damage than other oxygen-deprived accident victims. The blanket lowers a baby's body temperature to 92.3 degrees, where it is maintained for 72 hours. Cooling works by slowing down brain metabolism and reducing the secondary phase of damage that occurs days after this kind of injury. The blanket then gradually warms the baby's body temperature back to normal.

Cedars-Sinai has a specially trained team of RNs who implement this therapy, guided by our neonatologists, Kurlen Payton, MD, and Asha Puri, MD. We use state-of-the-art neuromonitoring with continuous, 24-hour EEG that is monitored by neurophysiologists.

Dr. Simmons is chairman of the Department of Pediatrics and director of the Division of Neonatology

Imaging All the People



The image above is a cluster of cardiac stem cells and other supporting cell types, called a cardiosphere. The cells on the sphere's periphery labeled with the green marker are providing a protective environment for the cells in the sphere's center—labeled with the red marker. Each blue oval corresponds to the nucleus of a single cell. This cardiosphere contains a few hundred cells.

Cardiospheres are used in a groundbreaking study at the Cedars-Sinai Heart Institute, in which heart attack patients undergo two minimally invasive procedures in an effort to repair and re-grow healthy muscle in a heart injured by a heart attack. First, a biopsy of each patient's own heart tissue is used to grow hundreds of cardiospheres, which turn into millions of cardiosphere-derived cells. About a month later, the cells are injected into the patient's coronary artery, where they migrate into the heart muscle to start their beneficial repair work. The two-step procedure was completed on the first patient in June 2009.

Massage Boosts Immune Response

People who undergo massage experience measurable changes in their body's immune and endocrine response. That is what researchers in Cedars-Sinai's Department of Psychiatry and Behavioral Neurosciences reported, following what is widely believed to be the first systematic study about the health benefits of massage in a larger group of healthy adults.

"There hasn't been much physiological proof of the body's heightened immune response following massage until now," says Mark Rapaport, MD, chairman of the Department of Psychiatry and Behavioral Neurosciences.

The study's results showed changes in numbers and percentages of lymphocytes (white blood cells that play a role in defending the body from disease) as well as a decrease in levels of the stress hormone cortisol after just one 45-minute massage.

"More research is ahead of us, but it appears that a single massage may deliver a measurable benefit," says Dr. Rapaport, principal investigator of the study and the Polier Family Chair in Schizophrenia and Related Disorders.

Who's Who

"A sweet and easy-going mutt." That's how Adam Mamelak, MD, describes his dog, Maya. If Maya could speak, she would probably say that her owner is "an especially kind man—
a renowned neurosurgeon who loves dogs and uses his expertise to save our lives."

Cushing's disease, a hormonal disorder caused by a tumor in the pituitary gland, is extremely rare in humans. In dogs, however, it is common—affecting 100,000 animals each year in the U.S. Because the pituitary is small and deeply lodged within the brain, tumors are not usually removed in veterinary medicine, and the disease is generally fatal for animals.

Enter Dr. Mamelak, who is best in show in his own way. An expert neurosurgeon who co-directs the Pituitary Center at Cedars-Sinai, Mamalek has mastered a novel endoscopic approach to pituitary surgery in humans. Until recently, the procedure required an incision in the lip and destruction of nasal structures. Mamelak uses a minimally invasive technique that is "as close to incision-less surgery as can be," he says. "There are no cuts, bruises, or unsightly scars, and the technology increases our ability to remove every last bit of tumor."

When Dr. David Bruyette at the VCA West Los Angeles Animal Hospital found out about the surgery, he called Dr. Mamelak to see if it could be applied to removing pituitary tumors in dogs. Surgeons in the Netherlands have performed this procedure but their methods proved too technically challenging for widespread use. Mamelak adjusted the procedure to work with a dog's anatomy—improving the effectiveness of the operation. So far, eight dogs and one cat have undergone successful surgery and returned to normal life with complete remission of their disease.

The best part: this collaboration isn't just good for man's best friend. Because Cushing's disease only affects one in a million individuals, there is little research into new treatments. The tumor tissue removed from the dogs' pituitary carries precious information for Dr. Mamelak and researchers at the Pituitary Center who study this tissue is the laboratory, hoping it may shed more light on Cushing's disease and help develop therapies for humans.

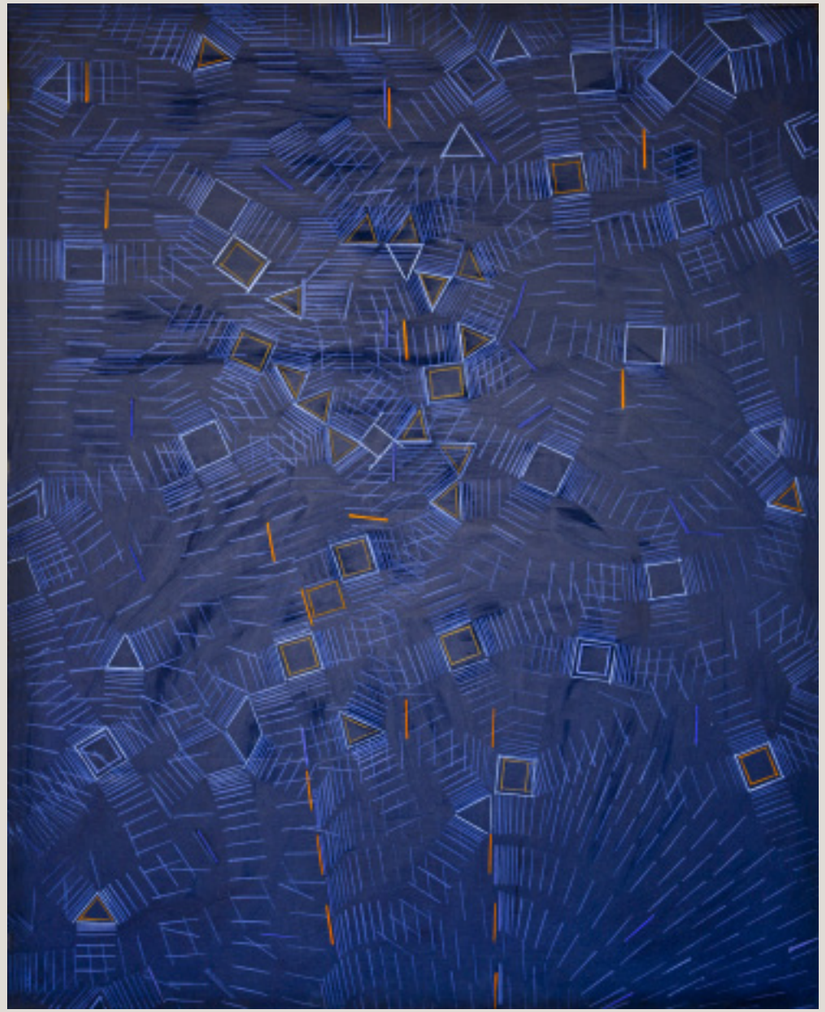
Dr. Bruyette couldn't be happier with the collaboration. "As veterinarians, we usually use advances in human medicine to develop animal treatments. In this case, the lifesaving treatments we are developing for animals may some day benefit humans."

Volunteer dogs from the hospital's pet visitation program, POOCH (Pets Offering Ongoing Care and Healing) surround Dr. Mamelak to thank him with tail wags and affectionate barks for his trailblazing veterinary efforts. Pictured from left are Venus, Pierre, Penny, Toby (in Dr. Mamelak's arms), Kelly, Moki, and Henry.

Gallery

"Whenever I walk by this painting, I have to stop for a minute. I always find something new to look at. It definitely distracts me: For a brief moment, I forget where I am."

—Julie H., Patient, 5th Floor, Cedars-Sinai Medical Center



Artist **Lee Mullican** (1919–1998) created paintings, drawings, and sculptures of great beauty for more than 50 years. A landmark, yet often overlooked figure in mid-century American modern art, Mullican's abstractions simultaneously engage the eye, the mind, and the heart. Through both his works and his teaching career at UCLA, the artist became a mainstay of the Los Angeles art community and a mentor to many younger artists. His paintings are in the collections of the Smithsonian American Art Museum, the Los Angeles County Museum of Art, New York's Museum of Modern Art—and now Cedars-Sinai Medical Center.

Artist: Lee Mullican
Title: Constellation [Taos]
Year: 1985
Medium: Oil on canvas
Dimensions: 50"h & 40"w
Donor: Luchita Mullican. Mullican's widow wanted to donate one of his paintings to Cedars-Sinai, but after taking a tour of the collection with her two sons, she was so impressed that she donated five works to make up a series—feeling that their display in the hospital created a great legacy for her husband's work. Lee Mullican married Luchita Hurtado in 1954. They had two sons, Matthew and John, who became artists as well. After surviving a plane crash, John—the author of a documentary titled ***Finding Lee Mullican***—asked his father how to heal his pain. "Go to your art," said Lee Mullican. "Because that's where the answers are."

For more information about the Cedars-Sinai art collection or to make a donation, call (323) 866.7798.

Genius + Generosity = *Breakthroughs*

A defining moment in the biomedical and bioengineering sciences. Intellectual firepower. A passion for education and discovery. An environment that seamlessly integrates research and clinical care. An urban setting that serves one of the largest, most diverse patient communities in the world. A bold vision for a healthcare mission that was born more than a century ago.

These are some of the elements that contribute to breakthrough discoveries in medicine. There is just one more critical part in the equation: the resources to recruit and retain extraordinary people, the infrastructure to support them, and the flexibility to sustain good work, even when times are tough.

In one of the most challenging economic times in recent history, Cedars-Sinai completed its most successful campaign in its history. Our community contributed generously to exceed the target, ultimately reaching $357 million in support of the Medical Center's academic mission. Along the way, our endowed chairs—key to recruiting and retaining research luminaries—grew from 30 to 50; we added new programs, centers, and institutes that focus on treating heart disease, brain disorders, lung disease, cancer, as well as metabolic and gastro-intestinal disorders; programs that address the needs of children, unravel genetic mechanisms that underlie disease, and train the next generation of skilled nurses.

A robust endowment is absolutely critical to sustaining new programs and propelling them forward. Five years ago, the *Discovering for Life* campaign left the drawing board. Today, the investment of a community of donors energized by our mission nearly doubled our endowment giving, making a long-term secure difference in Cedars-Sinai's capacity to translate research into new treatments and cures.

Throughout this issue, you will find success stories that demonstrate what happens when you infuse new resources into an institution staffed by extraordinary professionals and supported by visionary donors. The discovery of a gene responsible for Crohn's disease; an art therapy program for cancer survivors; a study that could shed light on heart disease's greatest mystery; or a mother's rare illness and the neurosurgeon that decided to help her when no one else would.

The anchors behind every scientific study, every technological advance, and every educational program are patients and their families. Our science is about babies who come into the world healthy and full of promise, about damaged hearts restored, cancers vanquished, another anniversary waltz, another birthday cake. There are bold scientific minds and generous donors behind all those happy outcomes.

We live in the era of possibilities that are turning into probabilities, building on the big discoveries of the past several years. Endowment resources sustain that engine. Every single donor and every single scientist was a key variable in a tested equation: genius, plus generosity *will* add up to breakthroughs.

THE POWER OF ENDOWMENT

Why, exactly, is an endowment so powerful? Here's what it can—and does—accomplish above and beyond operating funds.

Endowments set—and sustain—the pace

Promising research can be derailed by the ups and downs of year-to-year operating budgets. Endowments, which provide steady support, mean that progress does not slow or stop, even when operating budgets take a hit.

Endowments attract and retain great talent

There's no NFL or NBA draft for the best scientists. To field a powerful, productive team, an institution only has its reputation and its ability to provide sustained funding for equipment and laboratory work—enabling scientists to be scientists at their maximal capacity. Over the past five years, Cedars-Sinai has lured top talent from medical centers consistently ranked as the best in the country and from the finest institutions in the world (see page 57).

Endowments serve as venture capital

Can we predict adult health issues by understanding fetal health? Can we use a simple blood test to detect ovarian cancer in its earliest stages? Few of the research projects that ultimately answer questions like these start out as sure things. They begin as ideas worth exploring, and researchers need "seed money" to take them to the next step.

Endowments bring big ideas to life

Institutions with strong endowments generate progress. They create cultures where good ideas are vetted, explored, tested, and moved from the laboratory to the bedside. The big ideas today—using heart stem cells to "self-heal" a broken heart, the possibility of a vaccine to prevent the onset of Alzheimer's—are in the works, only because endowment funding was available to press on.

What was the most important scientific achievement of the past five years in your field? What's the next big idea around the corner? We asked some of Cedars-Sinai's best and brightest physicians and researchers to weigh in. You can find their answers throughout this issue of ***Discoveries***. Want more? Go to **www.discoveriesmagazine.org**.

CANCER

NEUROSCIENCE AND THE BRAIN

SURGERY AND TRANSPLANTATION

HEART DISEASE

WOMEN'S AND CHILDREN'S HEALTH

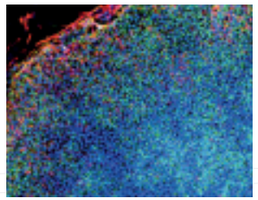
METABOLIC DISEASE

Cedars-Sinai: A Campaign Roadmap

The five-year *Discovering for Life* campaign brought unprecedented growth to Cedars-Sinai. Donors funded the latest biomedical research, the recruitment of the best and brightest scientific minds, and new approaches to patient care. Here are some of the profound transformations powered by community generosity that took place inside every building.

Institute for Inflammatory Bowel and Immunobiology Research
Thanks to a surge of private, foundation, and government support, the Pediatric IBD Center—under the direction of Marla Dubinsky, MD—is at the nexus of scientific research and patient care. Whether it is studying immune markers to predict which patients will respond to a certain class of therapies or opening the Al and Heidi Azus Foundation's Pediatric Infusion Center, every aspect is designed to ensure that children with IBD lead healthy, happy lives.

Regenerative Medicine Institute



The Regenerative Medicine Institute (RMI) is harnessing the power of stem cell technology via collaborations between basic scientists and clinicians across medical specialties. The RMI is exploring ways to treat life-threatening diseases by reprogramming a patient's own adult skin stem cells to an embryonic-like state to repair damaged, aged, or diseased tissue. See page 53

The Geri and Richard Brawerman Nursing Institute
In 2006, with the financial support of Richard and Geri Brawerman, Cedars-Sinai launched a unique professional development program for nurses. It is the only one of its kind west of the Mississippi and represents "the critical lynchpin of ensuring the availability of a qualified nursing force," says institute director Jane Swanson, RN, PhD. Accomplishments include specialty certification training. The certification of nurses at a higher training level ensures that they can provide better care, which results in better outcomes for patients.

Johnnie L. Cochran, Jr. Brain Tumor Center
Keith Black, MD, director of the Maxine Dunitz Neurosurgical Institute at Cedars-Sinai, and his team in the Department of Neurosurgery have developed a vaccine that teaches the body's immune system how to attack the most aggressive form of brain cancer, which makes chemotherapy more effective. With the opening of the Johnnie L. Cochran, Jr. Brain Tumor Center, this extraordinary research can reach patients more quickly and effectively, and extend their lives.

Women's Heart Center

Heart disease takes the lives of women more than all cancers combined. C. Noel Bairey Merz, MD, and her team at the Heart Institute's Women's Heart Center know that women suffer from specific heart problems that traditional cardiac research has overlooked in the past. The Center's pilot studies have led to large NIH grants. Specialists in women's heart health have been trained and national conferences organized, which have contributed to a radical outcome: Data shows that for the first time since 1984, we are seeing a decrease in cardiac-related deaths in female patients.

Wasserman Breast Cancer Risk Reduction Program
Women with a family history of breast cancer or concerned that their risk of developing breast cancer may be increased can go to the Wasserman Breast Cancer Risk Reduction Program at the Samuel Oschin Comprehensive Cancer Institute and receive comprehensive risk assessment services (including genetic testing) as well as medical and surgical management recommendations that are tailored to their particular level of risk.

The Campaign by the Numbers

GENIUS
GENEROSITY
BREAKTHROUGHS

Endowed chairs
30 (2005) → 50 (worth $134m) (2010)

Number of peer-reviewed publications
303 (2005) → 401 (2010)

NIH research funding ($m)
29 (2005) → 41 (2010)

Research projects
870 (2005) → 1,136 (2010)

Years
5

Contributions
$357 million

Gifts
32,710

Donors
22,546

New donors
13,438

Percentage of contributions to the research endowment
40

294
Number of kidney transplants made possible by IVIG therapy developed at Cedars-Sinai, including for Lakeisha Hall, who traveled 1,900 miles from Louisiana to seek it out.

30
Number of genes Cedars-Sinai researchers identified as being responsible for ulcerative colitis, a chronic digestive disorder and one of the most common types of Inflammatory Bowel Disease.

25,000
John Williams III, MD, has performed 25,000 chorionic villus sampling (CVS) procedures to determine chromosomal or genetic disorders in the fetus—the most by any physician west of the Mississippi.

73,584,000
John Heywood's heart took more than 73 millions beats since his mitral valve was repaired in October 2008 by Dr. Alfredo Trento using remotely guided robotic surgery.

50,380
Since 2005, run for her© participants have run 50,380 miles to support ovarian cancer research and awareness.

42
The two-year survival of patients suffering from the most aggressive form of brain cancer increases from 8 to 42% with a vaccine pioneered by researchers in the Department of Neurosurgery.

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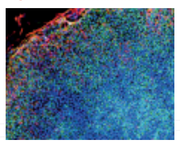

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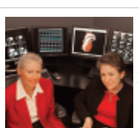

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Graduate PhD Program
The Graduate Program in Biomedical Science and Translational Medicine is merging scientific research and clinical medicine to give graduate students the opportunity to focus on the translation of scientific discoveries into the application of therapies, treatments, and cures.

COACH Mobile Unit at the Cedars-Sinai Maxine Dunitz Children's Health Center
The COACH for Kids and Their Families® mobile unit visits medically underserved communities throughout the greater L.A. area, providing an array of free medical services to at-risk children. It is part of a commitment to meeting the health needs of vulnerable, underserved populations in LA County. Since 2005, the hospital's annual community benefit contribution has grown from $130 million to $350 million.

The Board of Governors Heart Stem Cell Center at the Cedars-Sinai Heart Institute
Scientists at the Heart Institute have designed and implemented the world's first clinical trial exploring the use of a patient's own adult stem cells to re-grow healthy tissue after a heart attack. This revolutionary study may alter the course of cardiac medicine. See page 7

The Sports Spectacular Endowed Fellowship Program
Each year, this program supports the training of five physicians or scientists of exceptional promise and demonstrated accomplishment who wish to pursue the study and practice of their area of specialization. See page 37

Comprehensive Transplant Center
It has earned a reputation as one of the most successful transplant facilities in the world, and today it supports fully integrated surgery for lung, heart, liver, and kidney/pancreas transplantation. Internationally renowned physicians, surgeons, and research scientists have tested and pioneered techniques that are used the world over, while contributing to an outstanding record of superior outcomes. The Center's survival statistics consistently exceed national and international averages. The Immunology and Immunogenics Laboratory conducts wide-ranging research into organ rejection.

Women's Guild Lung Institute
The most comprehensive resource of its kind in the western United States, the Women's Guild Lung Institute is dedicated to medical and surgical treatment of—and research into—emphysema, asthma, lung cancer, and other pulmonary diseases that affect more than 30 million Americans.

Labor and Delivery Expansion Project
Cedars-Sinai launched an expansion and remodel project for the Labor and Delivery rooms, increasing the total from II to 20 (including one sized for multiple births.) With additional space and a design makeover, Cedars-Sinai will be better equipped than ever to tend to mothers and babies with both the latest in medical technology and the ultimate in comfort and care.

The Samuel Oschin Cancer Center
The Center provides complete outpatient cancer services for children and adults in a single location. It is open 24 hours a day, seven days a week to provide a full spectrum of care, including diagnostic evaluation, multidisciplinary treatment teams, genetic cancer risk assessment, cancer prevention and hospice care.

Bloodmobile

Getting to the hospital to give blood can be a challenge, so Cedars-Sinai is bringing blood collection to the community. Since 2007, the Mobile Blood Collection Program has conducted mobile blood drives from Atwater to Westchester and collected 7,450 units of blood, increasing the hospital's blood supply by 33 percent. The results: countless lives saved, rising public awareness, and a new, cost-effective model for mobile blood collection.

The Board of Governors Infusion Center at the Samuel Oschin Cancer Center
The redesigned and expanded infusion bays, where chemotherapy is administered, reflect a commitment to a more integrated approach to healing. This focus on total well-being brings 9,000 patients to the Cancer Center every year.

The O.R. of the Future
The "Operating Room of the Future" combines the latest in design and technology to enhance patient safety and operating room efficiency. It is equipped with the latest in robotic surgical systems, advanced mobile high-definition imaging, and fixed C-arm (180 degree) radiography.

Cedars-Sinai Endowed Chair Program
In just five years, the Endowed Chair Program has united 20 of the world's best and brightest clinicians and researchers with the most visionary philanthropists to support scientific inquiry, education, and patient care.

AROUND THE CORNER:
The Advanced Health Sciences Pavilion
"Research-to-patient" will become a reality in this revolutionary healthcare destination for Los Angeles, where scientific research and clinical care will find a home beneath one sustainably designed roof. Not to mention added parking spaces. See page 49

TRACKING THE GI GENES

The systematic and measured discovery of genes and proteins linked to Crohn's disease could reveal the cause for the condition. Armed with the patience and determination of forensic detectives, gastroenterologists and researchers are hoping to expose the genetic culprit for IBD.

By Idelle Davidson

Imagine being constantly exhausted because pain keeps you awake at night. Or being unable to leave your home, much less go to work, because you may not be able to control the effects of your disease. Imagine losing weight and developing malnutrition because your body is not able to absorb nutrition from the food you eat.

This is inflammatory bowel disease (IBD) a debilitating and often devastatingly painful chronic inflammation of the gastrointestinal (GI) tract that affects about two million children and adults in the United States. For more than 25 years, scientists at Cedars-Sinai have been painstakingly collecting blood samples from IBD patients in an effort to understand the disease. Nine thousand permanent cell lines are kept frozen and available to researchers for extracting DNA and linking genes to altered biologic functions. Ultimately, the hope is that these efforts will converge to defeat the disease.

There are two common forms of IBD: Crohn's disease and ulcerative colitis. Of the two million people with IBD, about half suffer from Crohn's, which can affect any part of the GI tract, and half suffer from ulcerative colitis, which is limited to the large intestine.

"For some people, the disease is fairly benign, but for others, it causes terrible pain every day and every night, and their whole life is consumed by this illness," says Stephan R. Targan, MD, director of the Inflammatory Bowel and Immunobiology Research Institute and the Division of Gastroenterology at Cedars-Sinai.

There is little doubt that genetics and ethnicity play a role in IBD. About 25 percent of IBD patients report having a close relative with the disorder. So it runs in families. And Ashkenazi Jews, or American Jews of European ancestry, are four to five times more likely to develop IBD than the general population. The question is *why?* Dr. Targan thinks the answer can be found in a newly discovered protein.

People with IBD have immune systems that overreact to bacteria normally found within the intestine. That, in turn, causes inflammation. Crohn's disease and other inflammatory bowel diseases often elude diagnosis for many years, while patients suffer and physicians search for clues. The early identification of defective genes helps physicians identify individuals who are at risk for developing the disease and enables the development of targeted drug therapies.

In 2006, the Inflammatory Bowel Disease Genetics Consortium linked a gene mutation to the development of Crohn's disease. The multicenter research team confirmed the involvement of a gene called NOD2 and discovered that a defect of another gene also led to the development of Crohn's. The Consortium is composed of IBD genetics research groups from six centers in North America, including one at Cedars-Sinai led by Kent Taylor, PhD, and Jerome I. Rotter, MD, of the Medical Genetics Institute.

"There has been an explosion of understanding in genomics, and we know that many genes may have a role in the diseases," says Dr. Targan. The discovery is being done several genes at a time, but with each discovery comes a new set of questions. "Every gene produces a different protein," he explains. "How do variations in that gene affect the protein? Is the protein even being produced? If so, is too much protein produced? Is there a non-functioning or defective protein produced? What part do these malfunctions play in the disease?"

What Dr. Targan is referring to is an approach called integrated science. Integrated science brings together multiple disciplines like proteomics, genomics, and phenomics. In order to understand how genes actually work, the functions of the proteins they produce have to be studied. Proteomics is a natural follow-up to the mapping of the human genome. It is the study of an organism's proteins, just as genomics is the study of genetic material. Phenomics studies the unique changes in organisms in response to genetic variations or the environment. Used together, these approaches help to develop treatment plans that are individually and precisely suited to a patient's specific disease.

This is all relatively new science: One of the key proteins implicated in IBD was unknown until 2002. A biotechnology company had cloned a gene with the protein and asked Dr. Targan to advance the research. "We have since done most of the biologic and genetic analyses and have discovered how this protein works," he says. "We know this protein plays a very important role in intestinal inflammation." For many of the 5,000 patients followed at Dr. Targan's Inflammatory Bowel Disease Center, this single research effort on one small molecule could actually be a big game-changer.

The next challenge is to test how these findings apply to people. In a preliminary study using blood samples from patients, Dr. Targan's team found that patients with a certain gene variation produced a high level of protein, while patients with a different gene variation produced smaller amounts. "These discoveries will set the stage for us to test an antibody that can be used in treating patients who produce large amounts of our protein," says Dr. Targan.

"Inflammatory bowel disease is an umbrella term that includes a variety of disorders," he adds. "The more specific we can be in diagnosing a particular subtype of IBD, the more specific we can be in prescribing an appropriate therapy."

After years spent focusing tightly on cancer cells, researchers are realizing they are dealing with a moving target and need to broaden their aim. A leading scientist's pioneering research is targeting the tumors as well as the cells outside the tumors—a new approach that promises to explain why life-threatening cancers can grow and spread, and could yield lifesaving treatments. **By Dan Gordon**

Taking New Aim

In March 1889, Stephen Paget, a self-effacing 34-year-old assistant surgeon at West London and Metropolitan hospitals, published a visionary breast cancer study in the journal *Lancet*. "When a plant goes to seed," he wrote, "its seeds are carried in all directions. But they can only live and grow if they fall on congenial soil." Paget's botanical premise is now known as the "seed and soil" theory of metastasis. At its heart is the idea that a cancer's metastasis depends on the communication between the tumor cells and the cells of the target organ. Paget's theory languished in the shadows for many years, but it's now at the center of a rare scientific time warp: Today, this 120-year-old theory drives one of the most forward-thinking and promising approaches in cancer research.

With over nearly a quarter-century as a cancer researcher, Leland W. K. Chung, PhD, has built a reputation for being ahead of the scientific curve. So it comes as no surprise that today, when the hottest two words in cancer are *targeted therapy,* Dr. Chung is pioneering an even bolder approach.

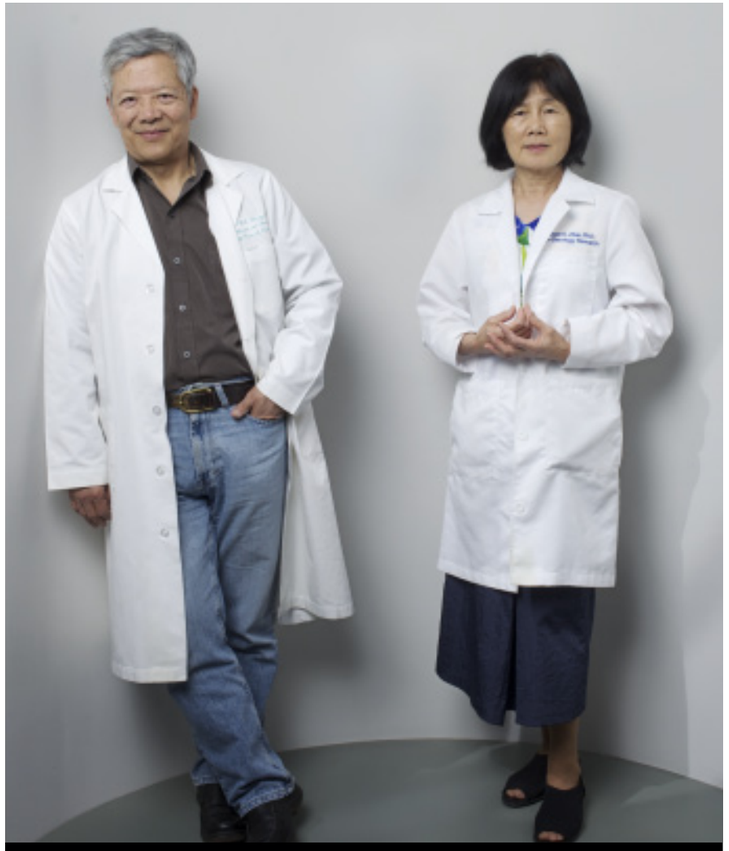
A professor of Medicine and director of the Uro-Oncology Research Program at Cedars-Sinai's Samuel Oschin Comprehensive Cancer Institute, Dr. Chung heads a prostate cancer research program that focuses on not just the cancer cell but its microenvironment: the surrounding cells that interact with the tumor and can promote its growth. The soil in Paget's theory. The strategy, known as *co-targeting,* is rapidly gaining momentum.

Cells outside the tumors play a key role in the development of malignant cancers, helping them to grow and spurring them to attack. "With targeted therapy, the concept has been to fix our eyes solely on the tumor," says Dr. Chung. "Now we are beginning to understand that the behavior of tumor cells—their ability to grow, invade, and migrate to another organ—is not only determined genetically, it is also affected by the cells surrounding the tumor."

Cancer cells can be described as "the body's terrorists." The cancer cells need to recruit members—other cells—to their group before wreaking havoc on the body. This recruiting involves sending signals through the blood, sometimes as distant as the bone marrow.

And just as terrorist cells thrive in the sanctuary of a friendly government, prostate cancer cells are more likely to thrive when the microenvironment is hospitable, as Dr. Chung and colleagues have shown. Thus, they reason, the optimal therapeutic approach goes after both the cancer cell and its hospitable host. It takes aim at the cancer while also isolating the microenvironment and its ability to rev up and propel the tumor cells.

However, certain cellular changes are not preordained by DNA, Dr. Chung explains. "Genetics is like the hardware of a computer. But a computer needs software to run. We call that 'epigenetics.'" That means learning how cancer



Drs. Leland Chung and Haiyen Zhau: The husband-and-wife team lead a research effort focused on targeting prostate cancer tumors as well as their microenvironment.

cells and normal cells communicate—and how those interactions change the biology and behavior of each. It also means understanding how the different cell types in the tumor constellation talk to one another.

"This is another step toward personalized oncology," says Dr. Chung, who suspects the principles adhered to by his lab apply to many cancers. "If we can understand more specifically the behavior and intercommunication of each patient's cancer, we are on our way to making this a treatable chronic disease."

This year, approximately 217,000 men in the United States will be diagnosed with prostate cancer, according to the American Cancer Society, ranking it behind only skin cancer as the most common malignancy among men. When the disease metastasizes to the bone, treatment options are limited and the prognosis is poor. But for many, the cancer will never pose a threat. "It is clear that some prostate cancers are not lethal and we are overtreating them, while others should be treated aggressively," explains Dr. Chung. "We need to improve predicting which patients fall into which categories." (*see sidebar*)

A little more than a year has passed since Dr. Chung and his team changed residence—moving from Emory University School of Medicine in Atlanta, Georgia, to Cedars-Sinai. Stuart Holden, MD, director of Cedars-Sinai's Louis Warschaw Prostate Cancer Center, describes it as "a coup" for the institution. "He is one of the premier prostate cancer cell biologists in the world," says Dr. Holden, who has supported Dr. Chung's work since the early 1990s in his capacity as medical director of the nonprofit Prostate Cancer Foundation.

At first glance, the new space occupied by Dr. Chung's team of 12 looks like a typical laboratory, albeit one cutting-edge enough to boast state-of-the-art equipment. Quiet and roomy, it suggests a sterile environment, with the exception of the solarium-like feel of the conference room located at the building's core. But when populated, the space begins to take on its own character. It starts with Dr. Chung, whose unassuming nature belies his stature: Recruited from Emory University by way of the University of Virginia and the University of Texas MD Anderson Cancer Center, he is the author of more than 300 scientific papers, reviews, and book chapters, and has edited several books.

The lab draws individuals from all over the world. Bright young scientists from 12 countries have ventured to work on Dr. Chung's team—India, Japan, China, Taiwan, New Zealand, and Turkey are currently represented. "You learn so much from working here; not just about science, but about different cultures," says Gina Chu, a doctoral student born in Taiwan and educated in New Zealand.

The new arrivals find an atmosphere that is both collaborative and nurturing. "We are not just focused on paper generation and grant dollars," says Haiyen E. Zhau, PhD, a collaborator of Dr. Chung's since 1978. "Years later, they tell us that their time studying with us was the happiest of their life." Contributing to the nurturing environment is the fact that Dr. Zhau is more than a key collaborator: She and Dr. Chung are married and have two children and three grandchildren.

From the scientific standpoint, the international and collaborative nature of Dr. Chung's laboratory reflects and enhances his research perspective. Since 1986, Dr. Chung's approach has been to direct studies in the lab with the potential for clinical payoff, and to collaborate with clinicians—locally, nationally, and internationally—toward that end. "One of our motivations in moving to Cedars-Sinai was the institution's emphasis and expertise in the design and implementation of clinical trials and a different kind of research focused on patient care," he says.

Traditionally, basic researchers often spend years focusing on a single gene or genetic pathway—a process that may lead to therapies and drug development, but often at a glacial pace and a high cost. The research model at Cedars-Sinai, on the other hand, enables physicians to collaborate with scientists and design studies that address a clear clinical issue, and to translate research findings into treatments quickly and efficiently.

At Cedars-Sinai, Dr. Chung has established a program that allows physicians—some of whom are taking a year or two away from clinical practice to focus on research—to work alongside the PhDs and doctoral students. This formula has produced powerful model systems to study prostate cancer progression. "Usually in a research lab, you are working exclusively with pure scientists," says Chu, who was recruited to join Dr. Chung's lab at Cedars-Sinai. "Here, we all exchange ideas, and it really helps me to better understand the clinical side of what I am doing."

The Guessing Game

Predicting whether a prostate tumor will remain indolent or turn lethal is currently an uncertain proposition. The most commonly used prognostic marker, the Gleason score, is accurate only about 70 percent of the time. Dr. Chung and his team at the Louis Warschaw Prostate Cancer Center are looking at this issue in much finer detail and have developed a new method that could ultimately enable better-informed treatment decisions.

The laboratory is testing specific proteins or molecules, known as biomarkers, for their role in pathways discovered by the laboratory to promote distant cell proliferation, or metastasis. The method employs a first-of-its-kind instrument that detects multiple markers at the level of a single cell in a tissue sample, using powerful image software. A fluorescent nanoparticle allows researchers to tag and simultaneously follow the plight of specific biomarkers. "It is improving our understanding of the biochemical and molecular properties of the cancer cells," explains Dr. Zhau, who is spearheading the initiative.

In collaboration with the Cedars-Sinai Pathology Department, which is under the leadership of world-renowned prostate pathologist Mahul Amin, MD, Dr. Zhau and her colleagues are studying archived tissue specimens from prostate cancer patients to test whether the specimens can accurately predict which tumor would turn out to be the most virulent.

What's Now, What's Next

CANCER

Mark Greene, MD, PhD

Director of Basic Science, Distinguished Scientist at the Samuel Oschin Comprehensive Cancer Institute and the Department of Biomedical Sciences; Vera and Paul Guerin Chair in Pulmonary Disease Research

Most important scientific achievement of the past 5 years: The most interesting idea is that resistance to cancer therapies can happen either through genetic change in the cancer cell or through changes in its microenviroment. These changes make cancer cells take on different behaviors, which lead to resistance to treatment. We call this change "adaptive"—there are no obvious mutational genetic changes. The reason this discovery is important is that it will allow us to target resistance to therapy in different ways.

The next big thing: The next big thing will be new targeted therapies for prostate cancer, lung cancer, and double and triple negative breast cancer.

GAMMA KNIFE RADIOSURGERY

HOW IT WORKS

Gamma Knife® surgery is a bloodless surgical method that is recognized worldwide as the preferred treatment for selected lesions, tumors, and conditions that afflict the body's most important organ: the brain. The Gamma Knife Center at the Samuel Oschin Comprehensive Cancer Institute is one of only a handful of facilities in the Los Angeles area to offer Gamma Knife surgery.

Radiation distorts the DNA in cancer cells. The cells then lose their ability to reproduce. Conventional radiotherapy usually involves the delivery of large volumes of radiation, which may affect normal brain tissue as well as cancer tissue. Gamma Knife technology allows radiation to only touch very small tumors or lesions deep within the brain, leaving healthy brain cells alone.

This treatment is safe, accurate, and effective. There is no "knife" in Gamma Knife: because no incisions are made, it avoids the risks and complications associated with traditional surgery. The treatment is performed in one day and usually does not require an overnight stay in the hospital.

Going Under the Knife: A Patient's Experience

On an unusually cool day last summer, Mary V. enjoyed a meal at her Los Angeles hotel, checked in with friends via Facebook, and answered the phone in a clear, upbeat tone. Amazingly, just 24 hours earlier, she had been, in effect, "under the knife"—the Gamma Knife, that is—in a procedure aimed to destroy any lingering cells from a brain tumor that had been removed two weeks earlier.

"The team at The Gamma Knife Center did a wonderful job," says Mary, while getting ready to fly home to Houston. "I'm up and about. My face is swollen, but I feel great." She had been awake but sedated during the half-hour procedure, which was performed by John S. Yu, MD, neurosurgical director of the Center.

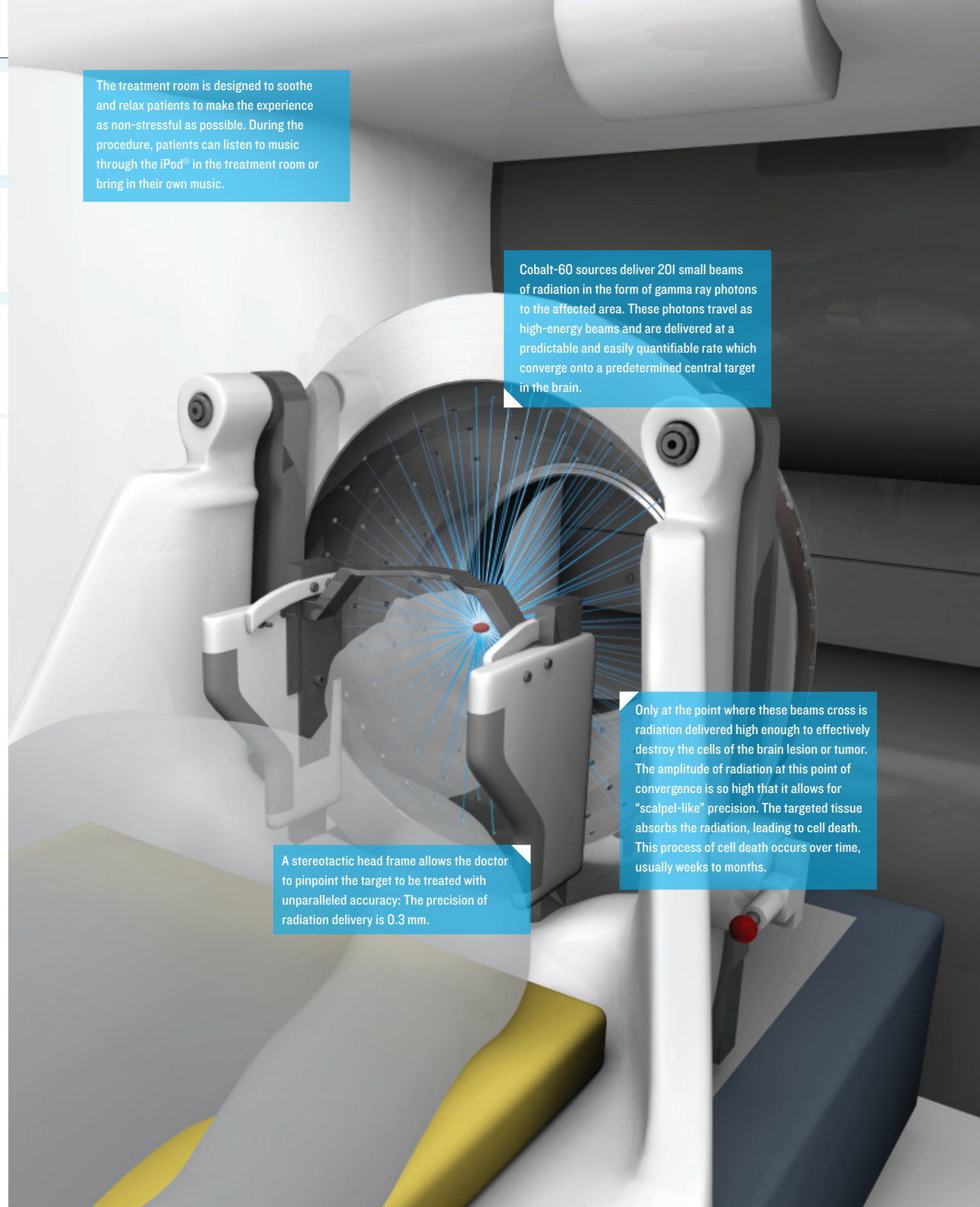
Mary had come all the way to Los Angeles to see Edward M. Wolin, MD, co-director of the Cedars-Sinai Carcinoid and Neuroendocrine Tumor Program, about chemotherapy for her neuroendocrine cancer, a rare form of cancer. While in his office, she suffered a seizure, and it was then discovered that the malignancy had metastasized to her brain.

Dr. Yu surgically removed the tumor in Mary's left temporal lobe, just in front of her speech center. Given her vocation as a speech therapist, it was crucial to remove the tumor with precision. Yu explains that the normal standard of care after surgery for brain cancer is whole-brain radiation, which carries a significant risk of dementia. Mary was a good candidate for the Gamma Knife, he says, because her cancer carried a low risk of developing additional brain tumors.

What was not rare, however, was how quickly she rebounded from her experience with the Gamma Knife. "Patients tend to tolerate it very well, and often can go back to their regular activities right after the procedure," says Dr. Yu. "We treat 150 patients each year, and the vast majority of them immediately resume their lives, even the same day."

Dr. Yu is teaming up with radiation oncologist Amin J. Mirhadi, MD, to study the use of Gamma Knife surgery for the treatment of glioblastoma multiforme, the most prevalent form of brain tumor. "We think treating patients aggressively with surgery and then with Gamma Knife is a novel and effective approach," says Yu. "Gamma Knife does not kill the residual tumor little by little like other types of radiation—it simply obliterates it."

—ROBIN HEFFLER



THE MYSTERIOUS *and* CASE OF A MOTHER'S HUGS VANISHING DELAYED BONES

By Sandy Van and Kevin McClanahan

Cooing in her mother's lap, Sky Meadow Harms is the center of the universe. And when it's time to hit the floor crawling, she is picked up, hugged and turned loose by dad, Ryon, for whom the birth of his daughter and the life of his wife are nothing less than miracles.

Laurie Harms, 31, suffers from a disease so rare that fewer than 200 cases have been recorded worldwide. She endured nearly two decades of pain and uncertainty before reaching Cedars-Sinai Medical Center and the care of Frank L. Acosta, Jr., MD. Four other neurosurgeons had already given up on her care

Fortunately for Laurie, Ryon and Sky, Dr. Acosta tends not to look back at what has been, but to imagine and explore what may be. The director of Spine Deformity in the Department of Neurosurgery, Dr. Acosta trained in complex and reconstructive spine surgery, and studies such intricacies as tissue engineering to repopulate worn out spinal disks with

healthy cells. But Laurie's case was unlike anything he had ever seen.

"Her condition was quickly going downhill," recalls Dr. Acosta. "Her head had actually collapsed over her shoulder because of bone loss in her neck. We could not send her home like this."

Laurie was 13 when she began to experience progressively debilitating pain in and around her left ear. Doctors dismissed the symptoms as ear infections, sinus problems or muscle spasms, but after years of emergency room visits, a CT scan revealed disintegration of her neck bones and an undetermined tumor mass.

The pain, bone loss, and questions kept coming, and at age 22, Laurie was told she had what amounted to a broken neck. She needed bone fusion surgery right away.

Single, and facing major surgery and an uncertain future, a shaken Laurie thought of Ryon. They had worked together at a small café three years earlier, but their lives went in different directions. Though she had rarely seen him since they parted ways, she picked up the phone and punched in his number.

"I'd always loved Ryon, and he was the first person I wanted to call," explains Laurie. "He knew from my voice that it wasn't good news."

Ryon appeared on her doorstep the next day, leaving his apartment and job behind, and he was at her side at a major Los Angeles-area hospital where surgeons fused the bones in her neck.

"Doctors gave her just two years to live," says Ryon, who, searching for a way to counter the bleak prognosis, decided to propose marriage. "I really believe it was our love that helped Laurie make it through that first surgery."

By the time they were married in 2003 the rate of her bone loss had slowed. Except for periodic emergency room visits and the chronic pain she suffered, they lived a fairly normal life for a while.

They also got a better understanding of the enemy they faced when an oral surgeon finally identified the mysterious disease—a decade after the original onset of Laurie's pain. Gorham-Stout syndrome, also known as vanishing bone disease, is characterized by the body's inability to normally

"Doctors gave her just two years to live," says Ryon, who, searching for a way to counter the bleak prognosis, decided to propose. "I really believe it was our love that helped Laurie make it through that first surgery."

—Ryon Harms, husband

regenerate bone. It also is associated with the formation of painful, fluid-filled tumors, a condition related to lymphangiomatosis. Bone deterioration can start, stop and start again and travel to adjacent structures, resulting in profound disability and even death.

"When I read the symptoms, they fit me to a T, and I realized what I had experienced for so long suddenly made sense," Laurie remembers. "It was a relief to know but, at the same time, I realized it was going to be a struggle in the years ahead."

Laurie defied the two-year survival predictions but experienced a major setback and a new round of treatments in 2008. Eventually, her oncologist arranged for her to try a new type of chemotherapy, but at the last minute she opted out. A week later she discovered she was pregnant. "Ecstatic but terrified" at the prospect of this surprise and potentially high-risk pregnancy, Laurie and Ryon chose to proceed despite the odds. Sky Meadow was born premature but healthy at 4 pounds, 8 ounces on September 28, 2009.

The new year brought another series of medical crises. Laurie's spine collapsed and she was rushed to an emergency room. When Ryon walked into his wife's hospital room, he saw her head resting on her shoulder. "As soon as I saw her I knew that her neck was broken," he recalls. The bones had literally crumpled under the weight of her skull.

She lay helpless in a hospital bed—neck broken, arms limp and useless, and voice muted by tubes that kept her alive. Pressure on nerves in her neck and shoulder triggered intense pain and paralysis in her arms. Normally petite, at little more than 100 pounds on a 5-foot-2-inch frame, Laurie had dropped to 85 pounds. Holding her baby was out of the question, and her doctors gave up hope.

In desperation, an aunt called her neurologist, Hart Cohen, MD, at Cedars-Sinai, who put her in touch with Dr. Acosta. By that afternoon, family members were rushing X-rays to his office for review.

"Dr. Acosta called us the next morning—a Saturday—to tell us he thought he could help Laurie. It was the most amazing feeling because all of a sudden we had hope again," Ryon recalls. "Other doctors told us they couldn't do anything, that nobody could help her. Without even knowing us, Dr. Acosta agreed to see us."

Dr. Acosta asked neurosurgeon J. Patrick Johnson, MD, to assist with the surgical plans and procedures. "I have encountered many complex cases, but I had never seen anything like this," recalls Dr. Acosta. "The whole concept of fusion depends on bone growing across the hardware we place along the spine, so the bone loss of Gorham-Stout syndrome presents a major challenge. You can place any type of screw and rod but if fusion doesn't occur, the procedure is not going to solve the problem."

During two complex surgeries, the neurosurgeons repositioned an existing plate and extended the previous fusion with rods along the thoracic spine, anchoring the hardware in solid bone. They also adjusted disk spacing between two vertebrae and placed a protective plate over the hardware. After a week's recovery, Laurie went home with a virtually rebuilt upper spine and 36 staples in her head and back.

"Laurie has done really well since the surgery, regaining a good deal of arm and hand function, and she continues to make progress," says Dr. Acosta, who expects to perform additional surgery in the coming months. "She isn't out of the woods yet—and the bone loss has to be stopped."

While there is still no cure for Gorham-Stout syndrome, Laurie remains optimistic. She is back up to weighing nearly 95 pounds and full of energy. She has started driving again, and is working hard in physical therapy to increase her upper body strength and mobility. She improves almost weekly and is now able to lift up 20-pound Sky by herself.

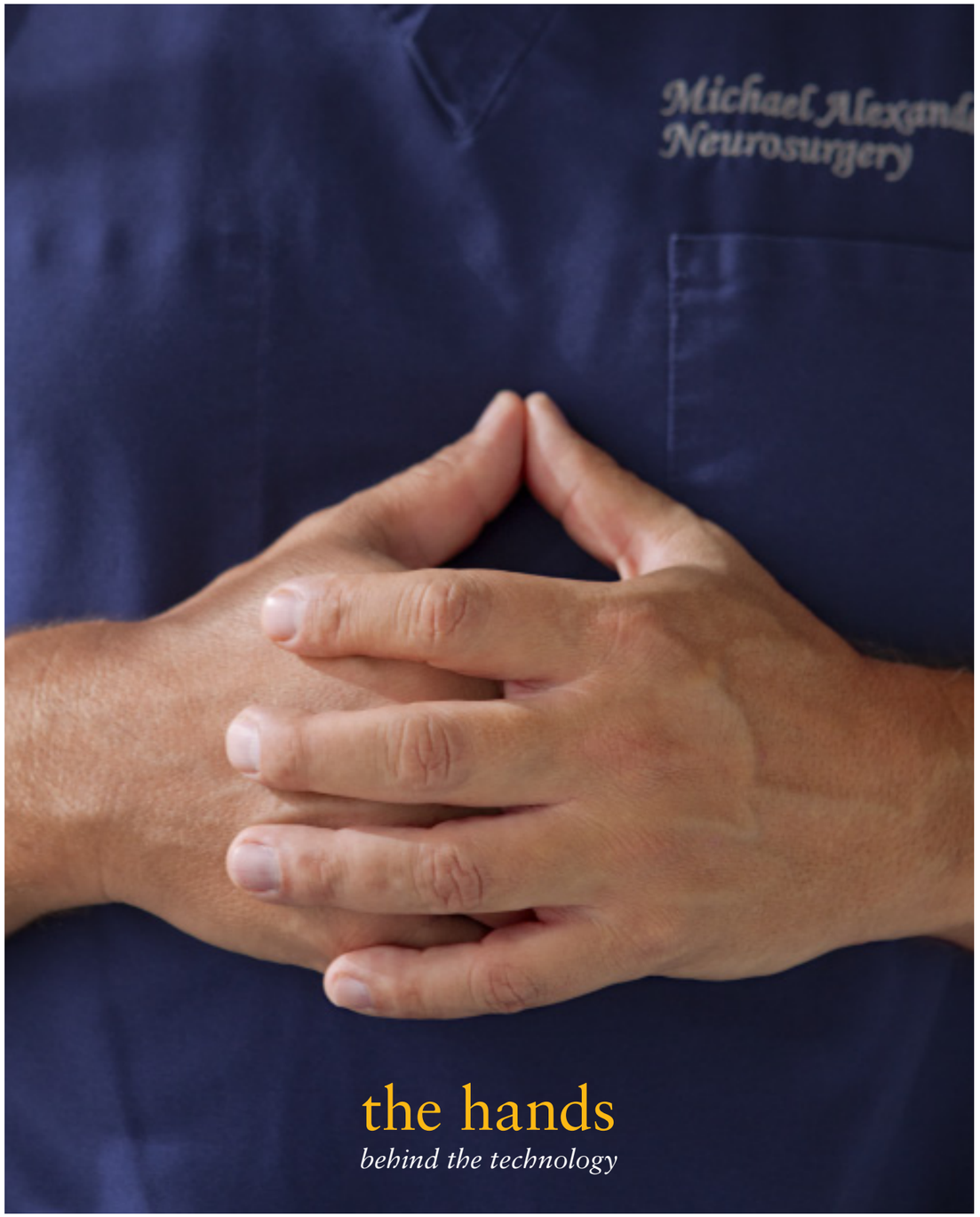
"I have this beautiful little treasure and she's all the motivation I need," says Laurie. "I already feel so blessed—every little accomplishment is simply a bonus."

What's Now, What's Next
NEUROSCIENCE AND THE BRAIN

Keith L. Black, MD
Chairman and Professor, Department of Neurosurgery; Director, Maxine Dunitz Neurosurgical Institute; Ruth and Lawrence Harvey Chair in Neuroscience

Most important scientific achievement of the past 5 years: Our progress with the dendritic cell vaccine for brain cancer is one of our more important scientific achievements in the past five years. We have shown an increase in two-year survival of patients with Glioblastoma Multiforme (GBM), the most aggressive form of brain cancer, from 8 to 42 percent. We have also correlated that dendritic cell vaccination and chemotherapy work in synergy to improve treatment.

The next big thing: We are currently working on a project we call the "Brain Window," a non-invasive imaging technique to diagnose early stage Alzheimer's disease thru the eye. Our team of researchers has shown in animal studies that nerve-cell damaging amyloid plaques appear earlier in the retina than in the brain. Using this knowledge, we are developing a noninvasive optical imaging technique to potentially detect early stage Alzheimer's disease.



the hands
behind the technology

THE MEDICAL ADVANCES created by modern surgical technology in the past 5–10 years—robotics, microsurgery, high-definition cameras, and miniaturized endoscopes—are astonishing, even as their use has become an established fact of today's operating rooms. As with all tools and technologies, they are only as good as the hands that use them and the skills and experience behind them. Two expert Cedars-Sinai surgeons discuss how these advances are impacting their practices and their patients. By Bob Barnett

The Brain Man

"Even our sutures are very fine, the size of a hair."

MICHAEL J. ALEXANDER, MD
Director, Neurovascular Center
Director, Endovascular Neurosurgery

From the neck up: As a neurovascular and skull base surgery specialist, Dr. Alexander's practice focuses on strokes, aneurysms, tumors at the base of the brain, and blockages in arteries of the neck or brain that restrict blood flow to the brain.

How it works: There are many options for treating a blockage of a brain artery. They include sending a stent, or tube, from the groin artery up through the carotid artery to open the blockage, or performing an open surgical bypass: operating around the blocked section in the artery itself and reconnecting normal artery on both sides.

Outcomes: "It's amazing to see how quickly some patients recover. You see a patient with a blockage come in who can hardly talk or may have acute paralysis. We remove a clot or perform a bypass and they may return back to work in a few weeks. I've seen patients in their 80s and 90s who, without treatment, would have been headed for a nursing home but go back to their normal activities with these therapies."

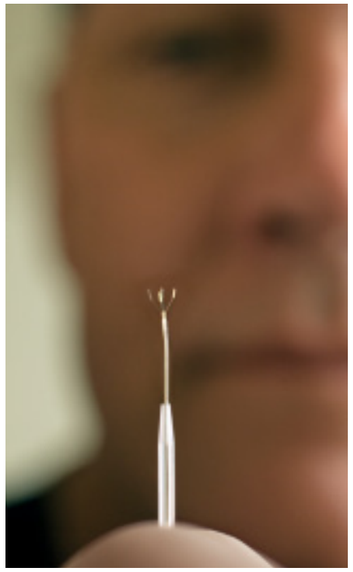
Steady hand: Alexander uses micro-instruments, including micro-scissors. Each instrument performs a different function. "Even our sutures are very fine, the size of a hair. You have to have a steady hand and good hand-to-eye coordination."

On the bookshelf: Alexander authored a textbook on pediatric neurovascular disease, published in 2006, in addition to over a hundred other publications. "There really wasn't anything out there on the subject before. It is used primarily as a reference by residents and students."

The next big thing: Laser-assisted surgery. "Lasers can now be used to help connect one artery to another in bypass surgery. They can also be used to burn away diseased tissue, in the case of tumors."

The first time: "I was a second year medical student when I observed my first open brain surgery in a patient with a benign brain tumor. I was always interested in the anatomy of the arteries and the brain, but this elegant surgery really fascinated me. I can still remember my first time seeing the pulsing brain during surgery."

Conversation starter: "When I tell people I'm a brain surgeon, they don't believe me. They'll ask, 'No, really, what do you do?'"



The Minimalist

"...as you move your fingers, the robotic arms mimic your movements..."

HYUNG LAE KIM, MD
Associate Director, Surgical Research, Samuel Oschin Comprehensive Cancer Institute
Director, Academic Programs, Urology

Specialty: Cancers of the prostate, testis, bladder, and kidney.

I robotics: "Urology was one of the first specialties to incorporate robotics in surgery. I use the da Vinci Surgical System® to perform laparoscopic prostate or bladder removal." At Cedars-Sinai, 95 percent of radical prostatectomies are performed robotically, versus 70 percent nationally.

Surgical benefits: "We operate through six keyhole-sized openings." In open surgery, the incision goes from the belly button to the pubic bone. Because robotic surgery is minimally invasive, it results in less blood loss and a shorter hospital stay. It may enable the surgeon to better preserve urinary and erectile functions in patients.

A new perspective: "We use a fiber-optic laparoscopic lens, so not only do we have greater magnification and a much closer picture than we could have in traditional surgery but we also have a much better overall perspective on what we are doing."

How it works: "I sit at a robotic console that has a high-definition screen with a 3D view of the surgical field. The fingers on both my hands fit into three rings. When I move my fingers, the robotic arms mimic my movements. The robotic instruments have wrists and elbows that allow them to work in very small spaces. In fact, they can even enhance movements of the human hand."

Some history: Some of this technology was originally developed for battlefield surgery when a surgeon can't be on the frontline. The idea was that the surgeon would be able to operate from another location, possibly a safer location, through telesurgery. The technology proved too delicate for use in war zones, but it is extremely useful in the modern hospital environment.

Margin of confidence: The role robotics can play in treating bladder and kidney cancers is still being defined through research. "We want to be sure that all cancer tissue is removed, when possible. We have enough information to believe that robotic surgery is very effective for treating prostate cancer. We want to be equally confident with bladder and kidney cancers before it becomes the accepted standard of care."

Looking ahead: "Robotics is the wave of the future. I think we will be surprised by what surgery will look like in 10 years. It might not look like anything we know now."

What's Now, What's Next
SURGERY AND TRANSPLANTATION

Andrew S. Klein, MD
Director, Comprehensive Transplant Center;
Esther and Mark Schulman Chair in Surgery and Transplantation Medicine

Most important scientific achievement of the past 5 years: Many patients who could be helped by an organ transplant are unable to receive one due to antibodies which exist in their blood that would immediately attack and destroy the transplanted organ. A major advance is the development of treatments that are allowing people previously thought to be untransplantable to receive a lifesaving organ. These novel strategies have been pioneered by doctors in the Cedars-Sinai Comprehensive Transplant Center.

The next big thing: The techniques used to restore function to people who suffer from organ failure will transition from organ replacement to organ rejuvenation via cell-based therapies. Instead of transplanting entire organs we will inject cells to repopulate diseased organs, or stimulate the bodies own cells to multiply and replenish the failed organ. Where structural elements are required (such as heart valves, bladders, and external body parts), cell-based therapies will be used to prime the growth of new body parts that can subsequently be transplanted.

An

ELECTRICIAN

for the

HEART

It's the black box of cardiology: an unexpected and catastrophic collapse of the heart's electrical system that causes instant death. One researcher is looking at very large populations and very small genes to solve the mystery of sudden cardiac arrest.

By Denise Gellene

Sumeet Chugh, MD, was completing his medical residency at Hennepin County Medical Center in Minneapolis when a young woman was brought to the emergency room. She had collapsed at a discotheque. Dr. Chugh and the medical team labored for an hour to restore the young woman's heartbeat. Their efforts failed. The cause of death: sudden cardiac arrest. The woman was only 19.

The autopsy revealed that her heart was perfectly normal.

Why would the heart of an apparently healthy young person suddenly stop? The young doctor was shaken and perplexed. "It was devastating to me," recalls Dr. Chugh, now an esteemed member of the Cedars-Sinai Heart Institute. "I thought, 'Here I am in the USA, on the cutting edge of medicine, and I can't explain something like this.' "

For Dr. Chugh, that painful moment launched a career devoted to finding an explanation for this mysterious and seemingly merciless condition. He initiated and continues to lead the Oregon Sudden Unexpected Death Study (Ore-SUDS), an ambitious and far-reaching epidemiological study aimed at identifying those most at-risk for sudden cardiac death. In a result that defies conventional medical wisdom, the Ore-SUDS is showing that the only currently accepted clinical gauge for assessing the risk of sudden cardiac death misses more than two-thirds of fatal cases.

Sudden cardiac arrest leaves few survivors. Mortality exceeds 95 percent; each year, 200,000 to 250,000 Americans die as their hearts are abruptly brought to a halt. Better predictors are sorely needed. Like the young patient Dr. Chugh tried to save during his residency, nearly half of the people taken by sudden cardiac arrest have no prior warning. Others may experience palpitations or chest discomfort, but these symptoms are not clear danger signs because they are also

associated with other heart conditions, such as congestive heart failure.

For the past decade, Dr. Chugh, 46, has been using the Portland, Oregon, metropolitan area as his study population. With his team, he has meticulously logged, probed, and analyzed every single case of sudden cardiac death—over 3,000 so far—that has occurred among the region's 1 million residents.

In a field where scientists often limit their research to rigorously measured questions and narrow patient populations, this is a strikingly different model: A large-scale epidemiological study with few or no living patients to follow. But it is working. The project has already demonstrated that lower socioeconomic status increases the risk of sudden cardiac death, as does taking methadone, a prescription drug used to treat addictions and relieve pain. The study holds new promise: By understanding the hidden forces that lead to sudden cardiac death, we may be able to prevent it.

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Sudden cardiac arrest is triggered by what can only be described as electrical chaos in the heart. The ventricles—the main pumping chambers of the heart—quiver uselessly, and brain cells begin to die because little blood is able to reach them. Within 10 minutes without effective resuscitation, all hope of survival is gone. (Cardiac arrest often is confused with heart attack, in which a blockage restricts the flow of blood to the heart, causing heart muscle to die for lack of oxygen.)

The only way to restore a normal heartbeat is with an electric shock. Emergency workers use paddle-like external defibrillators that, when placed on the chest, deliver a jolt to the heart. People thought to be at very high risk for sudden cardiac arrest receive automatic internal defibrillators. These devices, which are implanted in the chest or abdomen, continually monitor the heart and deliver electrical shocks when an irregular heartbeat is detected.

Internal defibrillators can be lifesavers; however, the challenge for cardiologists has been figuring out who should get one. Clinical standards call for cardiologists to measure the pumping action of the left ventricle, the chamber that pushes blood to the rest of the body. Weak pumping action is a sign of heart muscle damage, which can lead to disrupted electrical activity and sudden cardiac arrest.

Unfortunately, this gauge is a woefully inadequate predictor of risk. Dr. Chugh found that only one-third of the 121 individuals in the Oregon Study who had their ventricular function evaluated before dying had met the criterion for receiving a defibrillator. He also found that the vast majority of those who die of sudden cardiac arrest—nearly 80 percent of women and 65 percent of men—are ineligible for defibrillators under existing guidelines.

Paradoxically, many of the people who receive defibrillators don't need them. For every 15 to 20 patients with defibrillators, only one ever receives a life-saving jolt. "We just aren't very good at choosing the patients at the highest risk," Dr. Chugh says.

More than 90 percent of those killed by sudden cardiac arrest have a heart muscle abnormality or coronary artery disease. "Either their hearts look terrible or their arteries look terrible," Dr. Chugh says. The remaining 5 to 10 percent may not have obvious reasons for sudden cardiac arrest, which suggests a genetic cause. This data is an important starting point for Dr. Chugh's research. This is where he thinks an accurate predictor could be hiding.

Born in Punjab in northwestern India, Sumeet Chugh received his medical degree from Government Medical College, Patiala, also in Punjab, in 1988. He says he came to the United States because he "wanted to be on the cutting edge of science." He was completing his internal medicine residency in Minnesota in 1992 when his 19-year-old patient died.

The tragic experience prompted him to study cardiovascular medicine at the University of Minnesota and cardiac electrophysiology at the Mayo Clinic. In 1999, he joined the faculty of the Oregon Health & Science University and set about organizing his community study. It took nearly two years for him to persuade funders and the community that his audacious plan offered a real opportunity to unravel the mystery of cardiac arrest and ultimately save lives.

"It was considered complete madness," Dr. Chugh says, chuckling. The Framingham Heart Study, the largest cohort study funded by the National Institutes of Health, tracks 20,000 people, he explains. "Here we were, saying we would treat a population of 1 million as a human heart disease laboratory. It was craziness!" he says. He clearly enjoys having proved those early doubters wrong.

Today the study involves 16 hospitals, a network of medical examiners, and all fire and ambulance crews in the Portland metro area. To make this research possible, he has so far raised $9 million from foundations and government agencies such as the Centers for Disease Control and Prevention and the National Institutes of Health.

Dr. Chugh aptly calls himself an electrician for the heart. At Cedars-Sinai since 2008, he is associate director for Genomic Cardiology at the Heart Institute, professor of Medicine, section chief of Clinical Cardiac Electrophysiology, and director of the Heart Rhythm Center of Excellence. He holds the Pauline and Harold Price Chair in Cardiac Electrophysiology Research.

In his quest for more accurate risk measurements, his team has been scrutinizing, among other things, electrocardiograms (ECG), which trace electrical patterns in the heart. Dr. Chugh found that an abnormally long delay in the time it takes heart muscle cells to recharge—what cardiologists call a prolonged QT interval—multiplies the risk of sudden cardiac death by five. Importantly, the increased risk was seen in patients who were not candidates for defibrillators under standard practice.

This year, Dr. Chugh received a new, $1.7 million grant from the National Heart, Lung and Blood Institute to develop a more accurate clinical risk measurement using another ECG pattern called the QRS duration. Preliminary results indicate the specific electrical impulse measured by the QRS duration travels more slowly in people who later experience sudden cardiac arrest.

Following his recruitment to the Cedars-Sinai Heart Institute, Dr. Chugh moved to expand his research beyond Oregon. He is working with an international research team that identified novel genetic variations that appear to increase the risk of rhythm disturbances that lead to cardiac arrest after a heart attack. A separate collaboration with researchers at six U.S. institutions recently uncovered evidence of genetic variations that protect against cardiac arrest.

Dr. Chugh has also been assisting researchers at Fuwai Hospital in Beijing to develop a community study based on his Oregon model. The project should provide insight into possible race-based risk factors for sudden cardiac arrest. Similar studies in South Africa and India are under discussion.

"We are now thinking bigger and have a broader vision," he says. "The Heart Institute has become the focal site for global arrhythmia assessment."

Dr. Chugh's goal is to take the risk factors he and others identify and use them to develop a battery of screening tests, a checklist for physicians that will better predict who is likeliest to suffer sudden cardiac arrest. "If we combine what we find in the community, what we find in the patients, and what we find in the genome, we will do a much better job at predicting who is the best recipient of a defibrillator, and who gets a chance at survival," he says.

What's Now, What's Next
HEART DISEASE

Eduardo Marbán, MD, PhD
Director, Cedars-Sinai Heart Institute; Mark Siegel Family Foundation Chair

Most important scientific achievement of the past 5 years: Heart attacks and heart transplants may someday be a thing of the past, thanks to the discovery of an entirely new treatment for repairing damaged heart tissue: using a patient's own heart stem cells. We are well into a Phase 1 clinical trial in which a patients' heart stem cells are used to grow millions more stem cells that are then reinserted into their heart. The hoped-for result? That these stem cells will generate new muscle and blood vessels and return the patients' hearts to improved functioning.

The next big thing: Today, inoperable patients who have aortic heart valve problems that interfere with the flow of blood have no truly effective option for treating their condition. That may change in the future. We are currently engaged in a clinical trial in which patients undergo a less traumatic procedure to implant a replacement valve—through an artery in the thigh. With the new valve in place, patients are expected to have better heart function and fewer symptoms of heart disease.

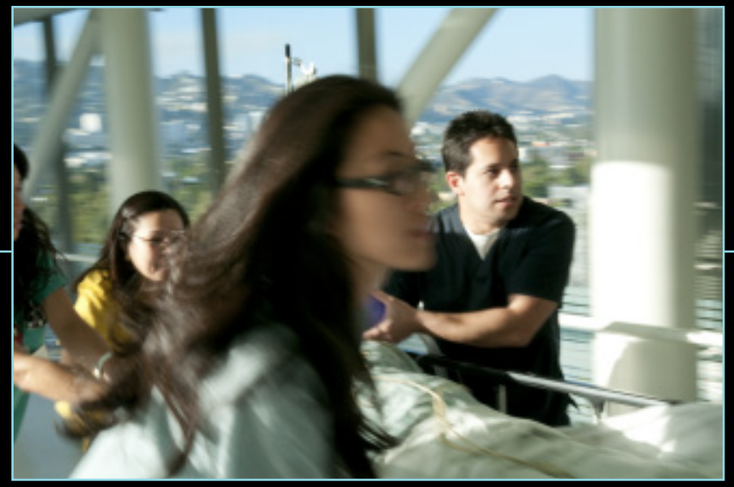
A young surgical resident. An accomplished attending surgeon. A shared portrait.

Photographs & Text by Rick Nahmias

Even with the many demanding years of schooling it takes to become a doctor, there is no way to complete the training through textbooks, testing, and trial and error alone. The process of mentoring is core to this intense journey.

For the next generation of doctors, mentoring has become something of a science unto itself, allowing those in training the opportunity to spend a great deal of time studying under a lineage of experienced physicians as they work their way up from medical school to the OR. What may be news to many is that Cedars-Sinai is at the forefront of creating and administering cutting-edge programs that support the mentoring process and skills improvement of tomorrow's medical professionals.

Danny Shouhed is a third-year surgery resident who specifically chose to do his residency at Cedars-Sinai for this very reason. Danny and Shirin Towfigh, MD—associate professor in the Division of General Surgery and the Center for Minimally Invasive Surgery, and the director of the Medical Student Education Program—have forged a deep mentoring relationship since his arrival here. Photographer Rick Nahmias followed them across the stretch of a normal day, recording each individually as well as during shared moments. This story was shot at a time when Danny was at a significant crossroads in his career: deciding which surgical specialty he wanted to pursue, while Dr. Towfigh was in the throws of a busy summer performing numerous operations, teaching a new class of residents and students, overseeing research projects, and inspiring a whole new corps of surgeons-in-training. The following story looks at a day in the life of these two tireless individuals and how their intersecting paths have brought a greater depth of knowledge and sensitivity to their own lives, as well as to their patients and the greater Cedars-Sinai community.



5:13a Danny gets up and prepares for his day as the on-call junior resident for the Trauma Service.

6:38 Within an hour of arriving, Danny attends to a patient suffering from sudden internal bleeding due to a ruptured spleen.

8:12 Dr. Towfigh debriefs with a group of summer research students who have traveled from universities across the nation to study under her.

Surgery

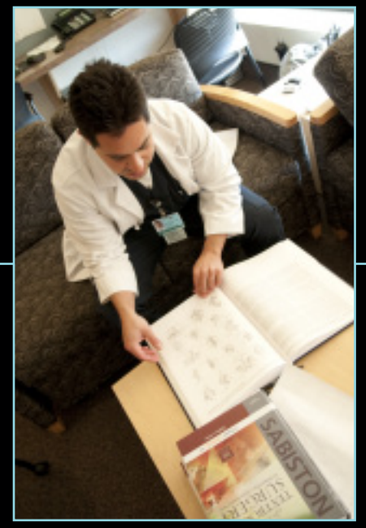
9:08 With his trauma patient stabilized after an emergency splenectomy, Danny joins Dr. Towfigh at a pre-operative visit with a patient about to have a laparoscopic hernia repair. The patient, a woman from Arizona, came to Cedars-Sinai for her procedure because of the reputation and expertise of Dr. Towfigh, a nationally recognized leader in complex hernia surgery.

9:25–12:35p Under the direction and guidance of Dr. Towfigh, Danny delicately inserts the laparoscopic camera. However, it soon becomes clear that the patient's condition requires the surgical team to convert to open surgery for repair of the hernia.

12:42 From real surgery to simulation, Danny heads to the Surgical Skills Simulation Lab to work on his laparoscopic techniques.

Surgical Skills

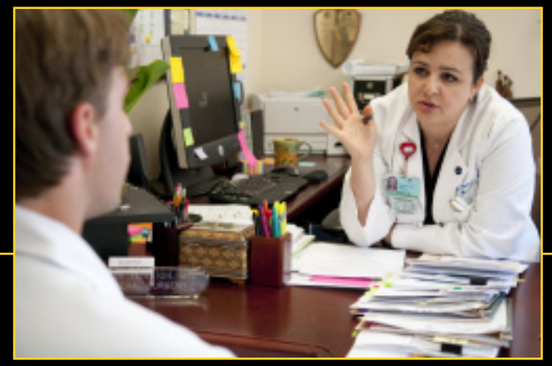
1:25 In the Surgical Skills Simulation Lab, Danny and other residents hone their skills with the aid of high-tech simulators. These extremely sophisticated machines replicate the near-exact sensations and steps related to specific laparoscopic techniques: from suturing and knot tying to organ handling. In between these one-on-one demos, Dr. Towfigh tests a group of UCLA medical students on surgical instruments.



2:04 Prior to his next operation, Danny studies up on surgical technique and anatomy.

2:30 Danny meets with Bruce Gewertz, MD, surgeon-in-chief and chair of the Department of Surgery, who takes an active role with hands-on mentoring of all surgical residents. They discuss lifestyle, work hours, environment, and the future of various specialties he is considering.

3:30 Dr. Towfigh counsels a visiting senior medical student taking part in Cedars-Sinai's highly competitive sub-internship program in surgery. After hearing details of his background and application for surgical residency, she advises him on revising his personal statement and creating a four-month plan to improve his chances of finding a good residency match.

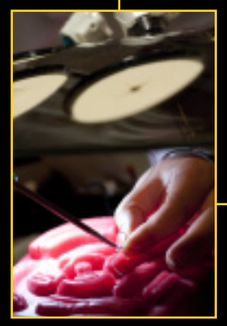


4:11 Making his twice-a-day rounds, Danny stops in on one of his patients, a man suffering from end-stage kidney disease who needed permanent access for dialysis. Danny, who took part in the procedure that was performed to place the arteriovenous fistula, is pleased to see that it remains open and operational.

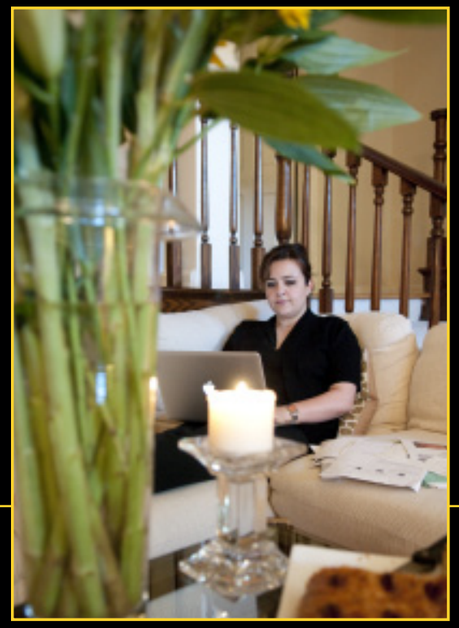
4:11 Dr. Towfigh visits with the patient on whom she and Danny operated earlier. She is recovering well after the complex open surgery.

4:39 Dr. Towfigh catches up with Danny over coffee. Dr. Towfigh brings up key issues Danny needs to consider when making his final choice, including the future advances in his field and the patient populations he'll be interacting with. As their conversation winds down, Danny is leaning heavily towards merging surgical oncology and minimally invasive laparoscopic surgery—two areas he enjoys.

6:15 Dr. Towfigh finishes her day at Cedars-Sinai in her research lab. Using a bariatric model, she is testing laparoscopic suturing and other surgical techniques aimed at solving the challenges operating on patients with varying body fat levels.



Watch the day unfold: more pictures and exclusive interviews at **discoveriesmagazine.org**



7:12 Danny and his girlfriend arrive at his parents' home. After catching up with his father, Danny unwinds from a long day as the entire family gathers for their weekly Shabbat dinner.

9:30 Dr. Towfigh continues work on her manuscript, "Can You Cut It: What It Takes to Get into a General Surgery Residency," in which she offers surgical residency candidates step-by-step directions and insider information to ensure they obtain a perfect residency match. This type of information is currently unavailable to most candidates she mentors. She takes her detail-oriented, delicate approach to the canvas as she unwinds by working on her painting.

"People who knew I had blood cancer expected me to look a certain way, but I didn't look emaciated," says Jeanette Tersigni, pictured above. "I looked fine. What my family and friends couldn't see was the isolation and anxiety I felt on the inside."

The Art of Survival

REMISSION: *what every cancer patient hopes for as they triumph over the disease. Yet, after innumerable trips to the doctor's office, painful procedures, and dealing for months with undesirable side effects, remission marks only the beginning of a cancer survivor's challenging journey.*

By Louise Cobb

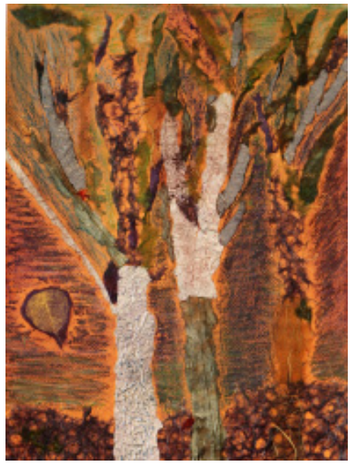
When 70-year-old Jeanette Tersigni went into remission from multiple myeloma, a chronic but incurable cancer of the white blood cells, she thought, "I did it!" But it wasn't long until she realized she was always "waiting for the other shoe to drop."

"People who knew I had blood cancer expected me to look a certain way, but I didn't look emaciated," says Jeanette, a soft-spoken grandmother of seven. "I looked fine. What my family and friends couldn't see was the isolation and anxiety I felt on the inside."

A mere 10 years ago, the word *cancer* often alluded to a death sentence. Research breakthroughs, innovative treatments, and better early detection methods have made it possible for more and more men and women to survive cancer. Whereas only three million people with a cancer history were alive in 1971, the population of survivors now approaches 12 million—approximately 3 percent of the U.S. population, according to the National Cancer Institute. Currently, the overall five-year relative survival rate for all cancers combined is 67 percent. Cancer may not always be entirely vanquished, but it is increasingly becoming a chronic disease rather than a fatal one.

Cancer survivors often must cope with physical, emotional, psychological, and financial problems during remission—including depression, anxiety, forgetfulness, and short-term memory loss associated with cancer and its treatment (commonly known as "chemobrain"). Survivors describe it as a general sense of not feeling like oneself. These various issues, however, often go unchecked.





Artistic representations based on the prompt: "I am the Tree of Life." Cedars-Sinai's weekly art class, part of the hospital's new Cancer Survivorship and Rehabilitation Program, helps cancer survivors find meaning in their experience through art.

"There is a significant subset of patients who are not fully healed when they go home, but because they look reasonably healthy or healthier than they used to, their family and friends think they are back to normal," explains Arash Asher, MD. "But cancer survivors have to face many residual issues. Even if you are disease free, it doesn't mean you're free of your disease." Dr. Asher is director of Cancer Survivorship and Rehabilitation at Cedars-Sinai's Samuel Oschin Comprehensive Cancer Institute.

He spearheaded the program in 2008, the first systematic and sustained effort of its kind at Cedars-Sinai. His own trailblazing efforts prompted him to veer from studying physical medicine and rehabilitation to designing his own training path with a cancer rehabilitation fellowship at MD Anderson Cancer Center in Houston, Texas. He aimed to "heal the whole cancer patient—physically and emotionally—to get them back to their highest quality of life," he says.

Dr. Asher's initial effort at Cedars-Sinai was to implement "Expressions of Hope and Healing," a weekly art class for survivors taught by artist and cancer survivor Flori Hendron. Together, they implemented an eight-week program to help survivors heal through artistic expression.

"Many patients struggle to find meaning in their experience and grapple with their new identity as survivors," says Flori. The course structure aims to facilitate a reflection process based on Joseph Campbell's 1949 influential best-seller, *The Hero with a Thousand Faces*.

Flori explains, "We use the Hero's Journey to move through different steps so we don't get stuck talking about diagnosis, and we can examine getting through cancer survival in steps that cycle back into living your life."

She is all too familiar with this process, having been a survivor herself for the past 14 years—a commonality with her students that creates an emotionally honest atmosphere, according to Dr. Asher. In the midst of her own cancer battle, Flori and the people around her thought she was close to death, but her health steadily improved when she began to paint and conquered a big mental hurdle.

"Healing is directly related to expression," she shares. "I was scared to death of dying and worrying about it, and then I realized my process had value and I had to handle it with grace and dignity."

"The people sharing their stories and the art projects all wrapped into one was like medicine to me."

—Shelden Blevins, cancer survivor

She quickly found that the more time she spent painting, the less time she spent in fear. She wanted to help others come to this realization and master "the mental game of cancer." Flori says, "I am every woman who has thrown up in the bathroom, stood in front of the mirror, breast-less and bald, putting on the war paint."

Flori's classroom is a makeshift safe haven that's far from clinical. Soft, uplifting music plays in the background and hot tea and fruit are available for snacking. Along the perimeters of a large table covered with various art supplies, a group of nine women, focused on the mixed media art piece of the day, drift in and out of conversation. Their dialogue seamlessly flows from adverse side effects of medications, to locating a dark green pastel, to everyday family troubles, and to who has seen what at the movies. In the center of the table, there's a box of pastels and a box of tissues, two necessities for every session.

When Shelden Blevins began taking the class, she was in a heavy round of radiation following three surgeries and chemotherapy to treat her breast cancer. She's a woman in her mid-40s with a bright, friendly smile and calming presence. As she speaks, she brushes away the few wisps of dark hair she has remaining after her treatment.

"I actually looked forward to going to radiation on Fridays because the art class helped me through the process. It was exciting—it was like going on a date!" she says. "The people sharing their stories and the art projects all wrapped into one was like medicine to me."

While Shelden is at the beginning of her journey as a survivor, the class boasts a tightly knit community of men and women at different points in their survivorship.

Next to Shelden sits Jeanette Tersigni, working on her tree of life piece. "My experience in the workshop surprised me," she says. "I thought I had done what I needed to do for healing, but I realized I isolated parts of myself, and this workshop gave me an inner strength for more comprehensive healing. It was very powerful and it gave me a renewed sense of control and hope."

Dr. Asher explains why patients are able to find meaning in their challenges through art by likening the cancer experience to an emotional abscess. "When you have gone through something as devastating as cancer, it really affects all facets of your life and brings up serious existential issues. But it's hard for people who have cancer to honestly and fully express everything to their loved ones. When you put a group of strangers in a safe environment, they can let everything out and are guided through art and discussion. The poison must be expressed for the abscess to clear and the integrated healing process to succeed."

Other Survivorship Programs at Cedars-Sinai

Cancer Rehabilitation program: A personalized, supervised exercise program designed to give cancer patients the strength, endurance, and independence necessary to function at their maximum level.

Emerging from the Haze: This six-week series to combat "chemobrain" is designed to educate, inform, and empower patients experiencing problems with memory and concentration after cancer treatments.

Qigong: A program that explores the form of traditional Chinese mind-body exercise and meditation to improve balance, flexibility, muscle strength, and overall well-being.

What's Now, What's Next
WOMEN'S AND CHILDREN'S HEALTH

Sigfried Rotmensch, MD
Director, Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology

Most important scientific achievement of the past 5 years: The development of new fetal imaging modalities, which allow us to understand fetal development and intrauterine life in unprecedented ways.

The next big thing: The number of bacteria that peacefully coexist with us in our healthy bodies is far greater than our own cells. Many pregnancy complications, including preterm labor, are caused by infection and inflammation, but it is unknown why some women develop these conditions and others do not. We are hoping to develop a "roadmap" to bacterial compositions that might explain why the most serious complications of pregnancies occur.

The Advanced Health Sciences Pavilion

GROUND BREAKING

How will healthcare be delivered as the 21st century unfolds? That question is anything but hypothetical: As knowledge explodes and creates new possibilities, a growing patient population and evolving healthcare needs are also creating new challenges. Cedars-Sinai found answers. Now, it's building them.

It is a challenge as old as the medical profession: harness scientific possibility and translate it into treatments and cures that make a meaningful difference in patients' lives.

With the Advanced Health Sciences Pavilion, Cedars-Sinai is taking a fundamental part of its mission—integrating research and clinical care—and turning it into an innovative physical space. When the doors open in 2013, the Pavilion will bring together leading clinical scientists to conduct advanced research and to accelerate the pace of discovery. Together, they will transform patient care.

Patients, physicians and researchers, partnering to strengthen outcomes and advance the medical frontiers. *Discoveries* takes you on a tour of the healthcare facility of the future.

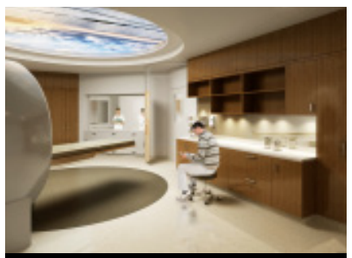
Enhancing Patient Experience

First and foremost, Cedars-Sinai is dedicated to patient-centered care. Housing outpatient services for the Cedars-Sinai Heart Institute, neurosciences, and other clinical specialties, as well as outpatient procedure suites, the Pavilion places the highest priority on patient convenience: procedures performed by different specialists can now be consolidated into a single visit.

❶ The pedestrian bridge serves as an open and convenient gateway to the Medical Center.

❷ Ample parking (six of the Pavilion's II stories), elevators that go directly to patient care floors, and user-friendly directions ensure smooth and easy access while minimizing the amount of time (and stress) a visitor experiences.

Patients will benefit from the stress-free access to outpatient services, and feel welcome in the open, light-filled exam rooms.



The Plaza level features a new, high-tech Educational Center, a café, a pharmacy, a blood lab, and imaging facilities.

Supporting Collaboration

Strong partnerships drive effective medicine. This idea informs the design of the Pavilion, which joins scientists and physicians together to foster close working relationships that yield lifesaving clinical results.

An open design for research areas, as well as comfortable lounges and lobby areas, enhances informal interaction and allows physician scientists to collaborate closely in developing new procedures and treatments. Doctors and researchers can gather easily under one roof to expand partnerships across medical disciplines.

Improving Research Efficiency

The Pavilion brings laboratories and clinics under one roof. The proximity of the clinical and research components simplifies the day-to-day operations and allows doctors to bring new treatments and therapies to their patients with maximum safety and efficiency.

❸ A research pavilion occupies the two top two floors and enables physicians to move easily between their laboratory and the clinics located on the lower levels.

Going Green

In keeping with Cedars-Sinai's commitment to responsible environmental design, the architectural firm HOK has designed the Pavilion as a model of green architecture.

❹ The exterior enables recycling, as accumulated storm water is captured, filtered and reused for landscape irrigation. Façades control the effects of sun and weather, save energy, and promote a comfortable environment inside the building. Lighting controls work with natural exterior light to limit the use of artificial light.

Environmentally friendly and energy-saving building materials lower the construction's carbon footprint.

THE BODY REBUILDERS

A Conversation in Real Time

Alzheimer's, Parkinson's, and macular degeneration have chipped away at patients' lives and mystified scientists for generations. New therapies can sometimes slow progression of the damage, but there is still no cure.

Clive Svendsen, PhD, has both the passion and the means to change that. A world-renowned stem cell expert, he heads the Cedars-Sinai Regenerative Medicine Institute (RMI), where clinicians and scientists are about to thwart life-threatening diseases by using patients' own cells to repair and re-grow damaged tissue. Dr. Svendsen has assembled a think tank of clinicians and researchers in diseases that affect most organs—from the eye to the liver.

Discoveries asked Dr. Svendsen and his core team to sit down and talk about regenerative medicine and the future of this revolutionary science.

The Big Idea

Clive Svendsen The big idea behind regenerative medicine is that rather than prescribing a drug, we focus on regenerating tissue or cells to replace the ones that are lost due to a specific disease.

How It Started

Clive Svendsen Being a neurobiologist, I got into this through Parkinson's disease while at the University of Wisconsin. In Parkinson's, you lose specific neurons in the brain, those responsible for releasing dopamine. Studies done using fetal tissue showed that cells could be transplanted into patients with Parkinson's disease, integrate in their brain, and release serotonin. When I saw that, I thought, "Wow, that's fantastic." The question is, where do you get the cells? Therapies using fetal and embryonic tissues are very controversial and limited, and replacing these cells that are lost to Parkinson's disease with adult stem cells seemed to be a realistic alternative. Then, naturally, we got very interested in other diseases for which replacing cells permanently in patients would allow them to function normally again. This is quite a phenomenal idea.

Terrence Town For me, it was through my research on Alzheimer's. It's a terribly debilitating illness and anyone who has a family member that has suffered from it realizes what a tragic disease it is—and no drug is available to effectively treat it. While certain medications are prescribed, these drugs were developed based on a 30-year-old understanding of the disease, and they simply don't have a major effect on reducing dementia progression. So I was just enthralled by this idea that—instead of drugs—we could focus on stem cells as a potential treatment. The beauty of this approach is that these stem cells could theoretically be placed into the brain, where they could take over the function lost by the dying neurons in the brain of an Alzheimer's patient.

Jeffrey Fair With transplantation, we replace organs to treat diseases, but the limitations are extreme. Many patients can't tolerate the procedure because they are too sick and there are just not enough donor organs. For example, hepatitis: We believe we can reprogram the molecular machinery inside the cells before we implant them back into the patient, then allow those cells to repopulate the liver, and treat the hepatitis in that way. That is really what urged me to become a part of this field.

Yaron Rabinowitz Ophthalmologists are very spoiled. We get instant gratification. Somebody has myopia, we do LASIK


Jeffrey Fair, MD


Terrence Town, PhD


Clive Svendsen, PhD


Yaron Rabinowitz, MD

surgery, they see. They have a cataract, we take it out, they see. They have a scarred cornea, we do a transplant, they see. So it's very frustrating when we encounter certain diseases for which there isn't a cure and for which we cannot instantly improve vision.

For example, macular degeneration, glaucoma, and permanent corneal blindness affect millions of people worldwide. A transplant can't provide a cure for any of these diseases. Stem cell therapies and regenerative medicine offer the potential to cure these diseases for which, currently, we really have no reasonable therapy, and that is why I felt it was important for me to be part of this effort.

From Lab to Patient

Terrence Town The concept is that we can, in fact, take a treatment or therapy from humble beginnings in the laboratory to the patients, with the help of clinicians. For that reason, it makes complete sense to partner with specific clinicians here and to focus on a particular disease.

The Collaboration

Yaron Rabinowitz I have very little expertise with stem cells in the lab, but luckily, Dr. Svendsen has expertise in pluripotent cells, and he's working with us to help us develop these cells that could be used on patients with corneal blindness or macular degeneration, which affects 30 percent of all Americans over the age of 70. So I'm learning a lot from you, Clive.

Clive Svendsen Thank you for that. I think it's a very exciting collaboration. On my own front, I've learned a lot about immunology and the work that Jeff is doing on the liver. I knew nothing about the liver, really, until we started working together. There is a lot of cross pollination. For instance, Terrence and I submitted a grant application with the California Institute for Regenerative Medicine (CIRM). It was a very quick collaboration, which turned out to be incredibly fruitful: We were awarded $1.5 million just a few weeks ago.

Terrence Town Yes, it has been a really wonderful collaboration. It's a natural thing for us to collaborate to take on complex diseases. We're both working on degenerative brain diseases, but looking at the brain from slightly different perspectives. I have a neuro-immune background. Clive comes from neurobiology and stem cell backgrounds, and the collaborative synergy really works. When you realize that these tissues, organs, and organ systems are all built from the same general cellular constituents, you can actually see a lot in other organs that is quite applicable to the particular organ system that you are studying. I think we're going to be able to learn a great deal from each other in moving forward.

Patient Stories

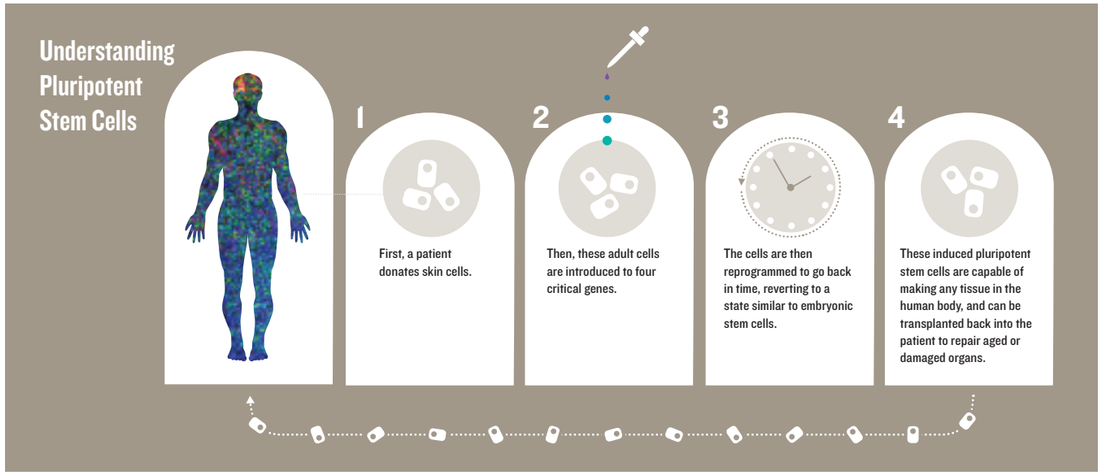
Jeffrey Fair A few years ago, I was caring for a young family whose child was found to have a devastating metabolic disease. It affects the brain, even though the disease is in the liver. We knew we would have to perform a liver transplant on this child. As we were getting them ready for the transplant, the child developed severe brain damage and was in a vegetative state, no longer transplantable. That was very tragic. Had we been able to intervene with stem cells at the time, we might have been able to head off that type of tragic outcome.

Yaron Rabinowitz The patient that comes to mind is a little baby that I operated on when it was 2 weeks old. I performed corneal transplants on both eyes. I wasn't very optimistic—not that you can't perform transplants at two weeks. In fact, we do that all the time but she also had stem cell deficiency. The part of her cornea that produced stem cells was damaged. Over the years, I have performed about three transplants on each eye, and just really given her vision temporarily. She's 11 years old now, and she's still blind, but the rest of the eye works very well. So, if we can provide a good stem cell environment for her cornea, the cornea transplant would definitely work, and she could end up seeing.

Clive Svendsen I think we all have stories like that. We just have to get the research going quickly and efficiently. Cedars-Sinai is the place where we can do that.

Hopes

Terrence Town The tragic thing about Alzheimer's is that after a certain point in the progression of the disease, the caregivers and the family members are actually the ones who suffer the most. There's a precarious drop-off that often occurs within about three or four years after diagnosis. Patients lose all short-term memory. They can't remember who their



children are or who their spouse is. My hope is that we would be able to develop a form of personalized stem cell therapy to intervene before that precarious drop off the cliff. I think that is possible. I certainly have a strong belief that it is or I would not be here.

The Payoff

Clive Svendsen I think Cedars-Sinai will pioneer the techniques that are going to lead to personalized medicine. But perhaps the first legacy of this approach is that we will be developing safer and more specific drugs for each patient.

The Future

Clive Svendsen The big thing in stem cells is now modulation: If you put young, fresh stem cells into any organ, it appears that the stem cells can modulate your own cells. If a cell is dying because of a disease, it is very responsive to its environment. It's a little like being in a hospital. The hospital would be dysfunctional without nurses and doctors. So, think of you as the dying cell: stem cells are the doctors and nurses, and they are modulating your health. Stem cells are not replacing dying cells, but they are caring for them, modulating them, and making sure they continue to have a healthy life. That's actually the direction we are taking with ALS: we introduce new modulating stem cells to stop neurons from dying. It's quite exciting, and I think there is a lot of potential in the brain—also the eye and the liver—to slow down your own cells' dying process through stem cell modulation.

Jeffrey Fair I see dramatic changes in the way we would treat patients. Instead of patients coming in for the very difficult and death-defying procedures of organ transplantation, maybe they come in as outpatients, receive some cells, have those followed, and achieve a cure. It seems within our grasp.

Clive Svendsen I think the chance of one of these being successful over the next 5 to 10 years is very high. We are right on the brink of exponential growth in studies for stem cell biology. There are now about 20 stem cell institutes (including the RMI) in California alone. This is going to revolutionize medicine; however, it's still a young field. We are standing at the edge of a cliff, wondering, "Am I going to fly or am I just going to fall?" But I am convinced it's going to change medicine. What shape and form it takes is what we are discovering here.

To watch more of the conversation go to **discoveriesmagazine.org**

What's Now, What's Next
METABOLIC DISEASE

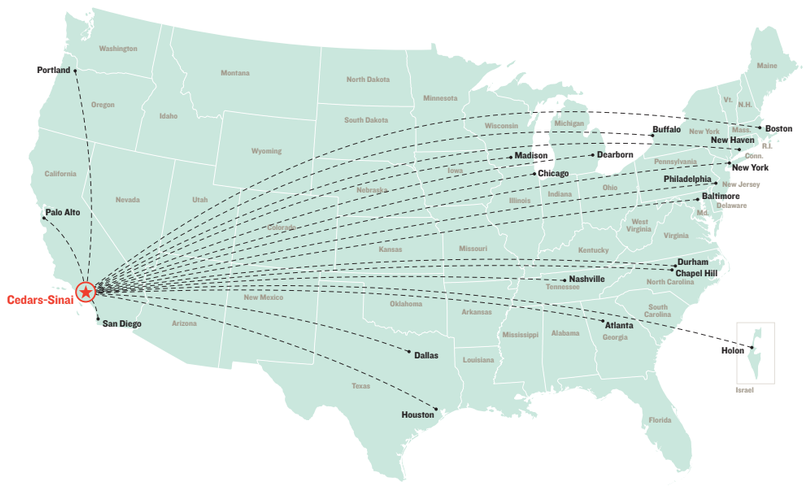
Marla C. Dubinsky MD
Director, Pediatric Inflammatory Bowel Disease Program;
Abe and Claire Levine Chair in Pediatric Inflammatory Bowel Disease

Most important scientific achievement of the past 5 years: The discovery of susceptibility genes for Inflammatory Bowel Disease (IBD). The advances in genomic techniques using Genome wide association studies has revolutionized the road to genetic discovery in complex genetic disorders such as IBD.

The next big thing: The next big idea is gaining an understanding of the role of the gut flora or intestinal bacterial milieu and how it interacts with one's underlying genetic susceptibility to result in a diagnosis of IBD. In addition, genetic and immune markers will be used to predict the natural history and treatment responses in patients at the time of diagnosis. Individualized medicine is just around the corner in IBD.

All Roads Lead to Cedars-Sinai

When we can recruit some of the greatest minds in the country, we can conduct research that challenges the frontiers of biomedical science. These are just a few of the outstanding scientists and physicians from all over the world recruited during the *Discovering for Life* campaign—and the route that led them to Cedars-Sinai where they are now leading scientific studies, training tomorrow's physicians, and breaking new medical grounds.



Michael J. Alexander, MD
Director of the Neurovascular Center
Expertise: Minimally invasive treatment of complex aneurysms, artery angioplasty and stenting for stroke prevention
Origin: Duke University, Durham, NC

Arash Asher, MD
Director of Cancer Survivorship and Rehabilitation
Expertise: Rehabilitation of cancer patients to restore maximal functional capacity and quality of life after treatment
Origin: MD Anderson Cancer Center, Houston, TX

Kenneth E. Bernstein, MD
Director of Experimental Pathology, Departments of Biomedical Sciences and Pathology and Laboratory Medicine
Expertise: Experimental and renal pathology
Origin: Emory University

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Research Scientist,Uro-Oncology Research Program
Expertise: Cancer Biology and Pharmacology
Origin: Vanderbilt University, Nashville, TN

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Associate Director for Genomic Cardiology, Cedars-Sinai Heart Institute; Chief of Clinical Cardiac Electrophysiology; Pauline and Harold Price Chair in Cardiac Electrophysiology Research
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Expertise: Cardiac stem cell research
Origin: The Johns Hopkins University School of Medicine, Baltimore, MD

Sandra Orsulic, PhD
Director of Women's Cancer Biology
Expertise: Molecular characterization of ovarian cancer, and pathway-targeted therapy
Origin: Harvard University and Massachusetts General Hospital, Boston, MA

Kurlen S. Payton, MD
Neonatologist, Neonatology Intensive Care
Origin: The Johns Hopkins Hospital, Baltimore, MD

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Expertise: Design and analysis of clinical trials for cancer research
Origin: Johns Hopkins School of Medicine, Baltimore, MD

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Expertise: Prenatal diagnosis
Origin: Edith Wolfson Medical Center, Holon, Israel

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Expertise: Prostate cancer and emerging cancer treatment technologies
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Expertise: Reconstructive microneurovascular surgery
Origin: University of Southern California

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Origin: University of Wisconsin, Madison, WI

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Expertise: Movement disorders, Deep brain stimulation
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Terrence Town, PhD
Research Scientist, Department of Biomedical Sciences and the Maxine Dunitz Neurosurgical Institute
Expertise: Neuroimmunology for Degenerative Diseases
Origin: Yale University/Howard Hughes Medical Institute, New Haven, CT

Magdalena Uhart, MD, PhD
Attending Physician, Division of Endocrinology, Diabetes and Metabolism
Expertise: Genetic determinants of the stress response and alcoholism
Origin: The Johns Hopkins University School of Medicine, Baltimore, MD

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Director of the Center for Hypertension; Associate Director, Clinical Research, Cedars-Sinai Heart Institute; Burns and Allen Chair in Cardiology Research
Expertise: Hypertension research for high-risk population
Origin: University of Texas Southwestern Medical Center, Dallas, TX

Faculty News

Robert Figlin, MD, has joined the Samuel Oschin Comprehensive Cancer Institute as director of the Division of Hematology/Oncology and as associate director of the Institute's Academic Development Program.

Dr. Figlin specializes in urologic and lung cancer treatments. He will help manage the Institute's growing clinical trials program and oversee breast, prostate, lung, blood, and bone cancer programs. Figlin previously served as chair of the Department of Medical Oncology and Therapeutic Research at City of Hope.

Shlomo Melmed, MD, has been appointed by Gov. Arnold Schwarzenegger to the Independent Citizen's Oversight Committee, the governing board of the California Institute for Regenerative Medicine.

Dr. Melmed, a prominent endocrinologist, is senior vice president for Academic Affairs and dean of the Medical Faculty at Cedars-Sinai.

David L. Rimoin, MD, PhD, chair of the Medical Genetics Institute and director of the International Skeletal Dysplasia Registry at Cedars-Sinai Medical Center, received the American College of Medical Genetics Foundation second annual Lifetime Achievement Award in March.

Dr. Rimoin was recognized at the college's annual meeting for his decades of contributions to genetic medicine, his research into skeletal dysplasias and heritable disorders of connective tissue, and helping to organize the field of medical genetics into creditable associations.

The College of American Pathologists honored **Mahul B. Amin, MD,** chairman of the Department of Pathology and Laboratory Medicine and one of the nation's leading authorities in oncologic pathology, with two awards for outstanding leadership and contributions in the field of pathology. Dr. Amin was recognized for his work in developing the CAP Cancer Protocols, which ensure standardization of pathology reporting throughout the world. As the role of pathologists in diagnosing cancer expands with personal medicine advances, the protocols allow data to be more easily shared and compared, which supports research efforts and better patient care.

Clive Svendsen, PhD, director of the Cedars-Sinai Regenerative Medicine Institute, received the American Academy of Neurology Sheila Essey Award for his research on ALS (Lou Gehrig's disease).

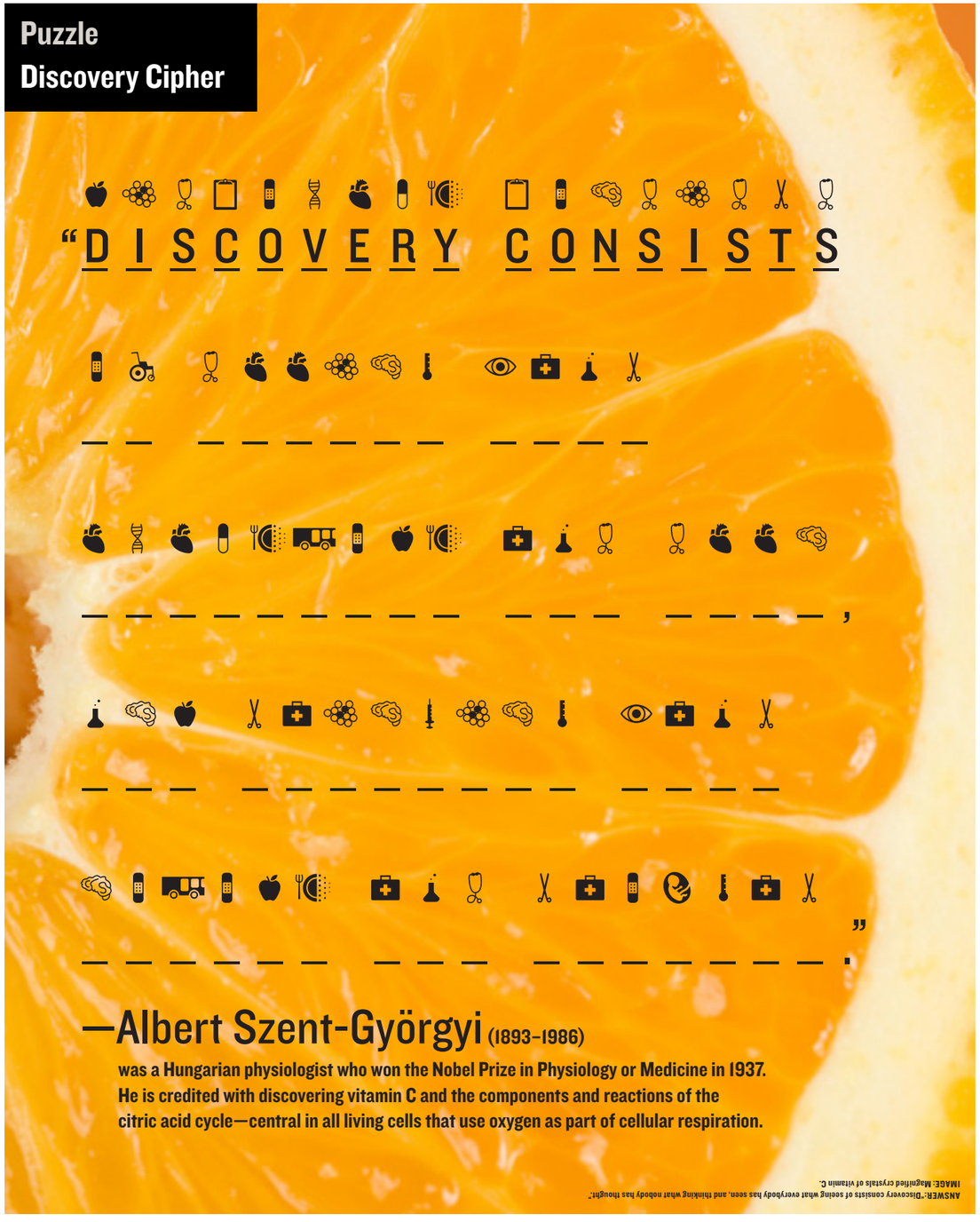
The innovative research on which Dr. Svendsen and his team of scientists have focused for eight years involves developing specifically engineered stem cells that, when injected into spinal cords, stall the degeneration of nerve cells. The specialized stem cells are manufactured to release a growth factor that has been shown to support the survival of dying motor neurons.

The Sheila Essey Award carries a $25,000 grant. This award will be used to continue developing novel gene therapy approaches. "In particular," says Svendsen, "we are close to completing work on a cell bank that will allow us to move ahead to clinical trials on humans and may provide another step forward in the treatment of ALS."

Terrence Town, PhD, and his team of Cedars-Sinai Regenerative Medicine Institute researchers have been awarded a three-year, $1.47 million grant from the California Institute for Regenerative Medicine to fund research into how the human immune system rejects or accepts transplanted brain stem cells.

The results from this study will help develop new stem cell therapies for patients with ALS, Parkinson's disease, and other neurological disorders. Solving the immune issue ensures that stem cells transplanted into the brains of patients with neurological diseases are not being rejected, can generate new, healthy cells, and re-grow diseased tissues.

Puzzle
Discovery Cipher



CEDARS-SINAI
DISCOVERIES

Cedars-Sinai Medical Center
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Los Angeles, California 90048

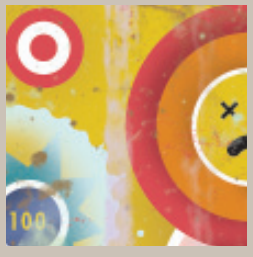
IN THIS ISSUE

Genius + Generosity = Breakthroughs

Five years, $357 million, an unprecedented surge of generosity, a research endowment campaign closes and exceeds its goal: find out what happens when generosity meets vision.

24 Hours

From the morning debriefing to final rounds in the hospital, an insightful, photographic, around-the-clock look into the lives of a young surgical resident and his physician mentor.



Taking New Aim

A new approach to cancer research broadens the scope of traditional studies to target not only tumors but also the cells that feed them.

The Body Rebuilders

Get introduced to the new face of medicine where diseases are fought from the inside and adult stem cells are programmed to re-grow organs. Four leading researchers and physicians discuss the dramatic changes that this science is bringing to medical treatments.

An Electrician for the Heart

An ambitious study of sudden cardiac arrest yields valuable insights into what triggers this deadly electrical chaos in the heart and who's most at risk for it.

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