

UCLA Health David Geffen School of Medicine

PAIN LIKE NO OTHER

After millennia of struggle to cope with the crushing effects of migraine, science finally may have answers.



A publication of UCL A Health and David Geffen School of Medicine at UCLA

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BY ENRIQUE RIVERO



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Photo: UCLA Health

Shaping the Future

Visionary philanthropy can alter the course of science, education and patient care, and it is essential to our ongoing success.

In the last issue of U Magazine, I talked about our strategy to grow the UCLA health system through building alliances with health care partners who share our commitment to change and innovation. But making dramatic change that advances our goals as an institution takes significant and sustained funding. In that regard, I wish to talk about another critical partnership — the one between us and the generous men and women, foundations and corporations who support our mission.

Although National Institutes of Health funding now is slowly increasing after more than a decade of stagnation, there remains insufficient funding for the medical research community to reach its full potential. We are further challenged by declining insurance reimbursements for patient care, coupled with increasing operating costs for which we do not receive state funding. With such constraints, we have less latitude to do things that really are game changing. In this fiscal environment, the importance of philanthropy cannot be overstated.

We are so grateful to those who understand that, in the words of Martin Luther King Jr., "Life's persistent and most urgent question is 'What are you doing for others?" Through their support of the UCLA health system and the David Geffen School of Medicine at UCLA, our donors embrace the choice to make an indelible impact on health care to benefit the people — here in Los Angeles and around the world — whom we serve.

To meet the challenges of today and the future, we must become more proactive in our approach to philanthropy. In the past, we often waited to hear from potential donors about 2 what they were interested in supporting. But to achieve all that we desire, we now must become more engaged. Rather than donor-initiated giving, our leadership and department chairs and faculty have worked together to identify areas where we have needs and initiate focused fundraising campaigns to build philanthropic interest.

We have a solid development team for this effort. In the last fiscal year, we raised nearly \$276 million, and since 2012, we have raised \$1.4 billion toward our UCLA Campaign goal of \$2 billion. That is a solid foundation upon which to continue to build as we pursue our highest priorities.

While we often trumpet our biggest donations, we must recognize, too, the vital role that all donors play in helping to sustain the excellence of the UCLA health system and the David Geffen School of Medicine at UCLA. Relatively few can make a gift of seven or more figures. It is those smaller gifts that provide a consistent revenue stream that we can count on, and which often have a very direct and immediate effect on all of our missions. Giving at this level may help to offset the cost of a lifesaving organ transplant for a child who is underinsured or enable us to offer new chemotherapies for which insurance reimbursements have not yet been established.

Continuing the excellence of the UCLA health system and the David Geffen School of Medicine at UCLA and building toward the future require both leadership and investment. Exceptional philanthropy will help ensure that UCLA can continue unraveling the mysteries of diseases, make transformative discoveries and develop the next generations of physician and scientist leaders. It is what shapes the future.

John C. Mazziotta, MD (RES '81, FEL '83), PhD Vice Chancellor, UCLA Health Sciences CEO, UCLA Health

Rare Surgery Helps to Get LAPD Motorcycle Officer Back on His Bike

In July 2014, Officer Eric Holtz of the Los Angeles Police Department was riding his motorcycle in Van Nuys when a vehicle made a U-turn in front of him. Holtz collided with the rear of the vehicle and was thrown from his bike and over the vehicle, landing on his right side. He suffered bruises and soreness but no broken bones. But as the months went by, Holtz began to notice a shortness of breath, especially when he exercised. He didn't connect the accident with his symptoms. "I thought it was age-related," says Holtz, who now is 48.









Top Left: When LAPD Officer Eric Holtz was involved in an accident, the damage to his phrenic nerve almost ended his career. **Top Right:** Holtz and his wife at their daughter's wedding in 2017. **Bottom Left:** Illustration of the phrenic nerves (red). **Bottom Right:** Dr. Matthew Kaufman (left) and Dr. Reza Jarrahy (right) with Holtz in December 2017.

Photos: (Top Row) Courtesy of Eric Holtz; (Bottom Left) Shutterstock; (Bottom Right) Courtesy of UCLA Plastic and Reconstructive Surgery

Then, in December 2015, Holtz went to an urgent care facility for what he thought was a severe cold. Instead, a chest X-ray revealed that his diaphragm and right lung were paralyzed. The doctor told him he had a phrenic nerve injury. As a husband and father of three, he worried about how this condition would affect his family and his career.

The phrenic nerves, which originate in the neck and pass between the lung and heart to reach the diaphragm, transmit signals from the brain and spinal cord to cause the diaphragm to contract, resulting in expansion of the chest cavity and drawing of air into the lungs. Each year, approximately 5,000-to-10,000 Americans suffer an injury to their phrenic nerve, but many may not be aware of it. Neither may their doctors; the condition can be hard to diagnose. Though damage to the phrenic nerves is not always immediately apparent, the resulting scar tissue can, over time, compress the nerves.

Concerned that his physical condition might require him to take a desk job, or even early retirement, Holtz searched for a solution, finding UCLA Health's phrenic nerve program, which offers reconstructive surgery specifically to repair the paralyzed diaphragm. Even more promising, a 2016 UCLA study had shown that 89 percent of patients who underwent phrenic nerve repair surgery had significant improvement in breathing and an increase in regular physical activities.

Holtz underwent the 2½-hour surgery at UCLA in October 2016. The surgery was performed by Reza Jarrahy, MD (FEL '06), associate clinical professor of plastic and reconstructive surgery, and Matthew Kaufman, MD, a New Jersey surgeon who regularly volunteers as assistant clinical professor at the David Geffen School of Medicine at UCLA to team up with Dr. Jarrahy for the specialized procedure.

Together, they removed the scar tissue around the injured right phrenic nerve in Holtz's neck. Then they took a nerve from Holtz's right leg to use as a bypass around the injured area, creating a clear route for the nerve signal from the brain to the diaphragm. After that, the wait began for the new nerve to regrow and form connections in the body, a process that can take a year or more.

"During this time, patients are encouraged to maintain a pulmonary rehabilitation program, including cardiovascular exercise to rebuild the diaphragm muscle," Dr. Jarrahy says. "Also, a physical therapist with specialty training can help with diaphragm retraining to strengthen the muscle."

Before surgery, Holtz felt light-headed after jogging just one minute. But six months post-surgery, he was able to slowly run a couple of miles without noticing any breathing problems. With his recovery well underway, he's happy that he did his research and found treatment. Now, he can continue his career as a motorcycle officer.

Mirror Neuron Activity Predicts People's Decision-making in Moral Dilemmas

A UCLA study suggests that scientists can help predict how people will react to moral dilemmas based on the brain's response when they watch someone experience pain. Researchers analyzed mirror neurons, brain cells that respond equally when someone performs an action or simply watches someone else perform the same action. Mirror neurons play a vital role in how people learn through mimicry and feel empathy for others. When you wince while seeing someone experience pain — a phenomenon called "neural resonance" — mirror neurons are responsible.

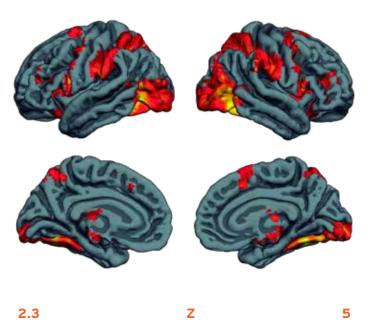
"The findings give us a glimpse into what is the nature of morality," says Marco Iacoboni, MD, PhD, director of the Neuromodulation Lab at UCLA's Ahmanson-Lovelace Brain Mapping Center. "This is a foundational question to understand ourselves and to understand how the brain shapes our own nature."

Dr. Iacoboni wondered if neural resonance might play a role in how people navigate complicated problems that require both conscious deliberation and consideration of another's feelings. To find out, researchers showed 19 volunteers two videos: one of a hypodermic needle piercing a hand and another of a hand being gently touched by a cotton swab. During both, the scientists used a functional MRI machine to measure activity in the brains of the volunteers.

Researchers later asked the participants how they would behave in a variety of moral dilemmas, including silencing a crying baby during wartime to prevent drawing the attention of enemy soldiers, torturing another person to prevent a bomb from killing several other people and whether or not to harm research animals in order to cure AIDS. Participants also responded to scenarios in which causing harm would make the world worse — inflicting harm on another person in order to avoid two weeks of hard labor, for example — to gauge their willingness to cause harm for moral reasons and for less-noble motives.

Dr. Iacoboni and his colleagues hypothesized that people who had greater neural resonance than the other participants while watching the hand-piercing video also would be less likely to choose to silence the baby in the hypothetical dilemma, and that proved to be true. Indeed, people with stronger activity in the inferior frontal cortex, a part of the brain essential for empathy and imitation, were less willing to cause direct harm, such as silencing

the baby. But the researchers found no correlation between people's brain activity and their willingness to hypothetically harm one person in the interest of the greater good — such as silencing the baby to save more lives. Those decisions are thought to stem from more cognitive, deliberative processes.



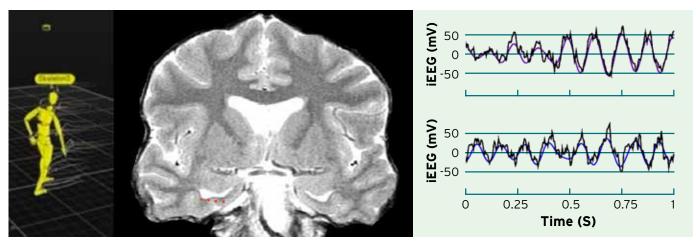
Rendering depicts areas of the brain that are activated by seeing another person in pain. The circled area, which is thought to contain mirror neurons, is more active in people who are more averse to harming others in difficult moral dilemmas.

Image: Courtesy of Dr. Marco Iacoboni

The study confirms that genuine concern for others' pain plays a causal role in moral dilemma judgments, Dr. Iacoboni says. In other words, a person's refusal to silence the baby is due to concern for the baby, not just the person's own discomfort in taking that action. Dr. Iacoboni's next project will explore whether or not a person's decision-making in moral dilemmas can be influenced by decreasing or enhancing activity in the areas of the brain that were targeted in the current study. The research could point to a way to help people with mental disorders such as schizophrenia that make interpersonal communication difficult.

"Deontological Dilemma Response Tendencies and Sensorimotor Representations of Harm to Others," *Frontiers in Integrative Neuroscience*, December 12, 2017

Deep Brain Waves Occur More Often during Navigation and Memory Formation



Real-time data downloaded from a patient's wireless implant reveal the deep brain waves that support spatial navigation and memory.

UCLA neuroscientists have shown that rhythmic waves in the brain called theta oscillations happen more often when someone is navigating an unfamiliar environment, and that the more quickly a person moves, the more theta oscillations take place — presumably to process incoming information faster. In an unexpected finding, theta oscillations were most prominent in a blind person who relied on a cane to move. The scientists hypothesized that a sightless person explores a strange environment through multiple senses, which would require more brain activity to process the extra sensory input.

Theta oscillations are one of several types of rhythmic waves in the brain that move, or oscillate, at different frequencies. Theta oscillations, which occur deep inside the brain, are named after the eighth letter in the Greek alphabet because they move up and down eight times per second. Scientists have long suspected that theta oscillations support our ability to learn new places and encode new memories, but no one had previously been able to test the hypothesis in humans.

The region responsible for regulating spatial navigation lies deep inside the brain. The inaccessible location has limited previous studies on the subject to rats or to people who were asked not to move because researchers needed them to be connected to hospital equipment. The study was the first to use a wireless

implant to directly record brain waves in real time as people moved freely through an environment.

The researchers — Nanthia Suthana, PhD, assistant professor of neurosurgery and psychiatry and biobehavioral sciences and associate director of the Neuromodulation Division in the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA, and Zahra Aghajan, PhD, a UCLA postdoctoral scholar in psychiatry and biobehavioral sciences — analyzed four volunteers, who previously had small wireless devices surgically implanted in their brains to prevent seizures. Dressed in motion-capture suits, the volunteers walked at different speeds in a large room as the implants recorded their theta oscillations. The UCLA team tracked the volunteers' movements and later correlated them to their deep brain waves.

The ability to navigate the world around us is a crucial part of daily life, and the study sheds light on the relationship of theta oscillations to human learning, memory and exploration. In addition, forgetting the route home is also one of the first clues of early Alzheimer's disease, and the new findings could help inform future studies and the development of new therapies for patients with memory disorders such as Alzheimer's.

"Theta Oscillations in the Human Medial Temporal Lobe during Real-World Ambulatory Movement," *Current Biology*, November 30, 2017

Stem Cells Offer Hope for Hair Growth

UCLA researchers have discovered a new way to activate the stem cells in the hair follicle to make hair grow. The research may lead to new drugs that could promote hair growth for people with baldness or alopecia, which is hair loss associated with such factors as hormonal imbalance, stress, aging or chemotherapy.

Hair follicle stem cells are long-lived cells in the hair follicle that are present in the skin and produce hair throughout a person's lifetime. They are quiescent, meaning they are normally inactive, but they quickly activate during a new hair cycle, which is when new hair growth occurs. The quiescence of hair follicle stem cells is regulated by many factors. In certain cases, they fail to activate, which is what causes hair loss.

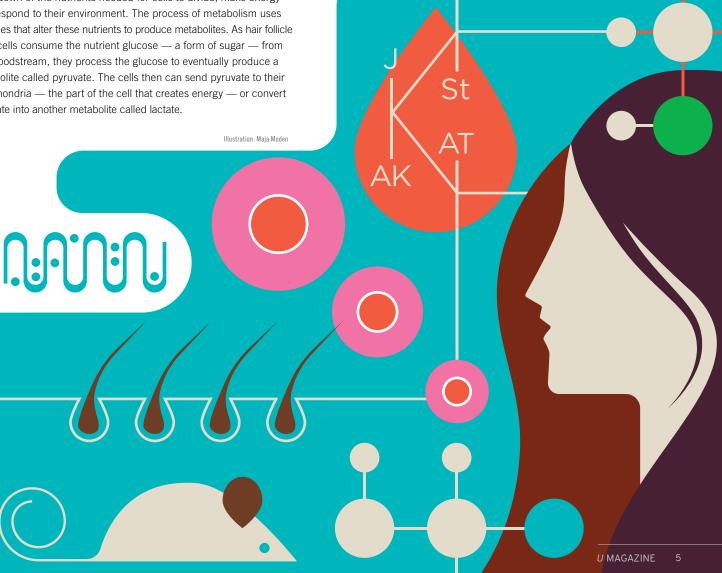
The study by Heather Christofk, PhD, and William Lowry, PhD, both of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA, found that hair follicle stem cell metabolism is different from other cells of the skin. Cellular metabolism involves the breakdown of the nutrients needed for cells to divide, make energy and respond to their environment. The process of metabolism uses enzymes that alter these nutrients to produce metabolites. As hair follicle stem cells consume the nutrient glucose — a form of sugar — from the bloodstream, they process the glucose to eventually produce a metabolite called pyruvate. The cells then can send pyruvate to their mitochondria — the part of the cell that creates energy — or convert pyruvate into another metabolite called lactate.

The research team first blocked the production of lactate genetically in mice and showed that this prevented hair follicle stem cell activation. Conversely, in collaboration with the Rutter lab at the University of Utah, they increased lactate production genetically in the mice, which accelerated hair follicle stem cell activation, increasing the hair cycle.

The team identified two drugs that, when applied to the skin of mice, influenced hair follicle stem cells in distinct ways to promote lactate production. The first drug, called RCGD423, activates a cellular signaling pathway called JAK-Stat, which transmits information from outside the cell to the nucleus of the cell. The research showed that JAK-Stat activation leads to the increased production of lactate, and this in turn drives hair follicle stem cell activation and quicker hair growth. The other drug, called UK5099, blocks pyruvate from entering the mitochondria, which forces the production of lactate in the hair follicle stem cells and accelerates hair growth in mice.

"Lactate Dehydrogenase Activity Drives Hair Follicle Stem Cell Activation."

Nature Cell Biology, August 14, 2017



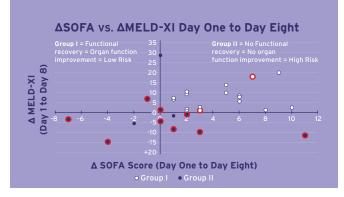
THE CUTTING EDGE

Genomic Blood Test Predicts Post-surgery Survival Rates for Advanced Heart Failure

An experimental blood test developed at UCLA that uses gene activity data from immune cells was 93 percent accurate in predicting survival rates for people with advanced heart failure who had surgery to implant mechanical circulatory support devices, such as ventricular assist devices and temporary total artificial hearts.

People with advanced heart failure often also suffer from multi-organ dysfunction syndrome, which is associated with atypical white blood cell activity and can lead to death after a device is implanted. When patients and doctors are considering a mechanical assist device, current clinical methods used to predict treatment results have limitations: They do not perform well in very sick patients, and they do not use molecular information. That lack of precision in predicting treatment outcomes can complicate the shared decision-making process between patients and their doctors.

Mario Deng, MD, professor of medicine in the Division of Cardiology, is a co-developer of a Food and Drug Administration-approved molecular blood test that is used to diagnose organ rejection in heart transplant recipients. The technology employed in the new study builds on the methods used in developing the molecular blood test. The study involved 29 people with advanced heart failure who underwent mechanical circulatory support surgery at UCLA from 2012 to 2014. Researchers collected blood samples one day before surgery and took clinical



Organ function and outcomes of 29 patients across five time points. Out of 29 patients with advanced heart failure undergoing mechanical circulatory support surgery, 17 had organ function improvement from preoperative day one to day eight, and 12 patients had no organ function improvement. Each purple line represents one one-year survivor, while each red line represents one one-year non-survivor.

Graphic: Courtesy of Dr. Mario Deng

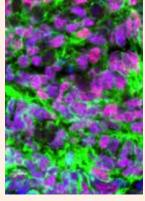
data both before surgery and eight days afterward. The patients were classified into two groups depending on their level of organ function. Seventeen patients showed improvement and 12 did not. One year later, 88 percent of the people in the "improved" group were still alive, compared with 27 percent in the other group.

The researchers identified a set of 28 genes from the pre-surgery blood samples that predicted how well the patients' organ function would recover shortly after surgery — and of those 28 genes, 12 helped predict whether or not organ function would improve after surgery and in forecasting if the patients would live at least a year after the surgery.

The researchers hope to study whether or not the test also can be used to accurately predict how people with advanced heart failure and declining organ function will fare after undergoing other types of heart surgery and catheter-based interventions. The test also could help patients and doctors make more informed decisions about treatment options; if it predicts a poor outcome, patients could choose to postpone surgery until their condition improves or could opt for another course of treatment. Ultimately, it could improve survival rates and the quality and cost-effectiveness of care.



"Association between Preoperative Peripheral Blood Mononuclear Cell Gene Expression Profiles, Early Postoperative Organ Function Recovery Potential and Long-term Survival in Advanced Heart Failure Patients Undergoing Mechanical Circulatory Support," *PloS One*, December 13, 2017



Human embryonic stem cell-derived neurons (green) showing nuclei in blue. Left: with retinoic acid added. Right: with retinoic acid and BMP4 added, creating proprioceptive sensory interneurons (pink).

Images: UCLA Broad Stem Cell Research Center/Stem Cell Reports

Scientists Create Cells that Enable Sense of Touch

UCLA researchers have, for the first time, coaxed human stem cells to become sensory interneurons — the cells that give us our sense of touch. The new protocol could be a step toward stem cell-based therapies to restore sensation in paralyzed people who have lost feeling in parts of their body.

Sensory interneurons, a class of neurons in the spinal cord, are responsible for relaying information from throughout the body to the central nervous system, which enables the sense of touch. The lack of a sense of touch greatly affects people who are paralyzed. For example, they often cannot feel the touch of another person, and the inability to feel pain leaves them susceptible to burns from inadvertent contact with a hot surface.

"The field has for a long time focused on making people walk again," says Samantha Butler, PhD, associate professor of neurobiology and member of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA. "Making people feel again doesn't have quite the same ring. But to walk, you need to be able to feel and to sense your body in space; the two processes go hand in glove."

How Diabetes in Pregnancy Affects Baby's Heart

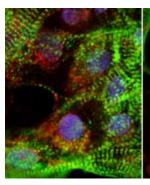
UCLA researchers have discovered how high glucose levels — whether caused by diabetes or other factors — keep heart cells from maturing normally. Their findings help explain why babies born to women with diabetes are more likely to develop congenital heart disease. When developing heart cells are exposed to high levels of glucose, the researchers found, the cells generate more building blocks of DNA than usual, which leads the cells to continue reproducing rather than mature.

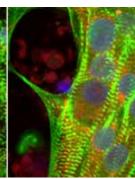
"High blood sugar levels are not only unhealthy for adults, they're unhealthy for developing fetuses," says Atsushi "Austin" Nakano, MD, PhD, associate professor of molecular, cell and developmental biology and member of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA. "Understanding the mechanism by which high blood sugar levels cause disease in the fetus may eventually lead to new therapies."

Although genetics plays a large role in the development of congenital heart disease, the leading non-genetic risk factor for the disease is a mother having diabetes during pregnancy. Babies born to women with high levels of glucose in their blood during pregnancy are two-to-five times more likely to develop the disorder than other babies. However, researchers have never been able to define the precise effect of glucose on the developing fetus.

Dr. Nakano and his colleagues used human embryonic stem cells to grow heart muscle cells, or cardiomyocytes, in the lab and then exposed them to varying levels of glucose. Cells that were exposed to small amounts of glucose matured normally. But cardiomyocytes that had been mixed with high levels of glucose matured late or failed to mature altogether and instead generated more immature cells.

The researchers discovered that, when exposed to extra glucose, the cardiomyocytes over-activated the pentose phosphate pathway — a cellular process that, among other things, generates nucleotides, the building blocks of DNA. In cells with high glucose levels,





Human heart cells grown from stem cells show less-robust muscle fibers (green) in the presence of high levels of glucose (left) than when glucose levels were lower (right).

Images: eLife/UCLA Broad Stem Cell Research Center

the pentose phosphate pathway made more nucleotides than usual. The scientists showed that the excess of building blocks kept the cells from maturing. "More nutrition is generally thought to be better for cells, but here we see the exact opposite," Dr. Nakano says. "By depleting glucose at the right point in development, we can limit the proliferation of the cells, which coaxes them to mature and makes the heart muscle stronger."

Dr. Nakano's group observed the same thing at work in pregnant mice with diabetes: The heart cells of fetuses divided quickly but matured slowly. Dr. Nakano says the finding could lead to better methods of making cardiomyocytes from stem cells. Today, most protocols for generating cardiomyocytes in the lab lead to immature cells, but targeting the pentose phosphate pathway could help generate more mature cells for regenerating heart cells or for research purposes.

"Gluc

"Glucose Inhibits Cardiac Muscle Maturation through Nucleotide Biosynthesis," *eLife*, December 12, 2017

When the researchers added a specific bone morphogenetic protein called BMP4, as well as another signaling molecule called retinoic acid, to human embryonic stem cells, they got a mixture of two types of sensory interneurons. DI1 sensory interneurons give people proprioception — a sense of where their body is in space — and dI3 sensory interneurons enable them to feel a sense of pressure. The researchers found the identical mixture of sensory interneurons developed when they added the same signaling molecules to induced pluripotent stem cells, which are produced by reprogramming a patient's own mature cells such as skin cells.

This reprogramming method creates stem cells that can create any cell type while also

maintaining the genetic code of the person from whom they originated. The ability to create sensory interneurons with a patient's own reprogrammed cells holds significant potential for the creation of a cell-based treatment that restores the sense of touch without immune suppression.

Dr. Butler hopes to be able to create one type of interneuron at a time, which would make it easier to define the separate roles of each cell type and allow scientists to start the process of using these cells in clinical applications for people who are paralyzed. However, her research group has not yet identified how to make stem cells yield entirely dl1 or entirely dl3 cells —

perhaps because another signaling pathway is involved, she says.

The researchers also have yet to determine the specific recipe of growth factors that would coax stem cells to create other types of sensory interneurons. The group is currently implanting the new dl1 and dl3 sensory interneurons into the spinal cords of mice to understand whether or not the cells integrate into the nervous system and become fully functional. This is a critical step toward defining the clinical potential of the cells.



"Deriving Dorsal Spinal Sensory Interneurons from Human Pluripotent Stem Cells," *Stem Cell Reports*, January 11, 2018

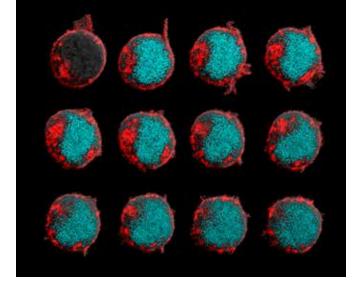
Cancer Defense Mechanism Could Be Turned Back to Attack Tumors

UCLA researchers have engineered a type of synthetic protein — a chimeric antigen receptor, or CAR, that responds to soluble protein targets. The advance shows promise for helping the body's immune system seek out and destroy cancer because it could boost the effectiveness of immunotherapies against solid tumors that are otherwise highly resistant to the body's immune response.

"We have generated the first example of a CAR that can help white blood cells — specifically T cells — convert tumor-produced proteins from suppressants, or 'downers' for our immune system, into stimulants that trigger robust attacks on the tumor cells," says Yvonne Chen, PhD, assistant professor of chemical and biomolecular engineering in the UCLA Henry Samueli School of Engineering and Applied Science. "This could lead to new therapeutic applications, particularly in the treatment of solid tumors."

Solid tumors — tumors that grow as masses in the body — are difficult to destroy because they have a variety of defenses, including an ability to secrete proteins that disable the immune system. Overcoming those defenses has been a major focus of cancer biology research. One promising method for doing that is CAR-modified T-cell therapy. In 2017, the Food and Drug Administration (FDA) approved such therapies to treat blood cancers such as leukemia or lymphoma. Since the FDA's approval, UCLA Health has launched a program to deliver CAR T-cell therapy to select patients with specific forms of lymphoma and leukemia for whom other therapies have not been effective.

While CAR-modified T-cell therapy has been approved for use against certain blood cancers, it has not been demonstrated to be as successful for treating solid tumors. That is because solid tumors have the ability to secrete soluble proteins called immunosuppressive cytokines, which inactivate immune cells, including T cells, that might otherwise neutralize harmful cells. This creates a microenvironment that is highly hostile to immune cells and protects the tumor. Based on that knowledge, the UCLA researchers hypothesized that they could overcome that defense mechanism by



In these time-lapse images, chimeric antigen receptors respond to a soluble cytokine, triggering T-cell activation.

Image: ZeNan Chang and Michael Lorenzini

altering the response of T cells to the immunosuppressive cytokines. Instead of shutting down, the engineered T cells would react to the cytokines by mounting an attack on the tumor cells.

Scientists knew that CAR signaling can trigger T-cell activation and anti-tumor effects, so the researchers proposed engineering CARs on the T cells to signal in response to immunosuppressive cytokines. However, CARs normally respond to antigens presented on the surface of cells, not to antigens that float around in the environment. The researchers discovered how to engineer CARs that could respond not only to surface-bound antigens, but also to soluble proteins, including immunosuppressive cytokines. The researchers placed the CARs they developed on T cells, and the modified T cells became activated in response to soluble antigens.

The new approach enabled T cells to convert the cancer's own defense mechanism into a weapon that could intensify the immune system's attack on tumor cells. The researchers also discovered that, in order for a T cell to activate, two of the CARs on its surface must both bind to a single soluble protein. And they demonstrated the versatility of their approach by engineering CARs that responded to several different soluble proteins, including transforming growth factor beta, or TGF-beta, a potent immunosuppressive cytokine. TGF-beta could be one target for future immunotherapies to treat cancer. The discovery follows a study published in December 2017 by another UCLA research team that created blood-forming stem cells, called hematopoietic stem and progenitor cells, or HSPCs, engineered to carry CAR genes that allow the production of immune cells that target cells infected with HIV.



"Rewiring T-cell Responses to Soluble Factors with Chimeric Antigen Receptors," *Nature Chemical Biology*, January 29, 2018

"Long-term Persistence and Function of Hematopoietic Stem Cell-derived Chimeric Antigen Receptor T Cells in a Nonhuman Primate Model of HIV/ AIDS," *PLOS Pathogens*, December 28, 2017



For more information about CAR T-cell therapy at UCLA, go to: uclahealth.org/car-t-cell-therapy

Studying Development of Embryonic Heart Cells in Mice, Scientists Hope to Regenerate Damaged Tissue

UCLA researchers used fluorescent-colored proteins to trace how cardiomyocytes — cells in heart muscle that enable it to pump blood — are produced in mouse embryos. The findings eventually could lead to methods for regenerating heart tissue in human adults.

"Our ultimate goal is to be able to regenerate cardiomyocytes after an injury like a heart attack," says Reza Ardehali, MD, PhD, associate professor of medicine in the UCLA Division of Cardiology and a member of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA. "But we're first trying to learn from the embryonic heart."

Cardiomyocytes make up most of the heart. During a heart attack, parts of the heart tissue are cut off from oxygen and nutrients. Cells in those regions of the heart die and slowly are replaced by scar tissue,

which reduces the heart's capacity to function. While it has been known that cardiomyocytes are formed during embryonic development, scientists have been unsure until now whether or not new cardiomyocytes are only created when existing cardiomyocytes divide, or if cardiac progenitor cells — a type of stem cell — create new cardiomyocytes.

Dr. Ardehali and his colleagues, including Ngoc Nguyen, a UCLA graduate student and the study's co-first author, used four different fluorescent-colored proteins to determine the origin of cardiomyocytes. When the cells divide, the resulting "daughter" cells maintain the same color as the parent cell. "The system lets us see, over time, which cell populations give rise to new cells," Nguyen says. "Compared to previous labeling methods that use only one or two different colors, this method allows us distinguish the role of different cells much more clearly."

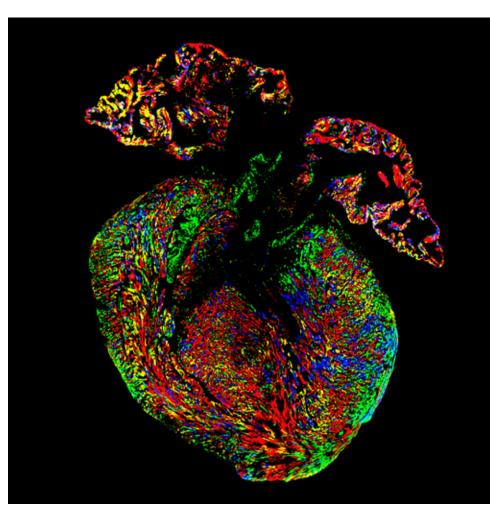
The team labeled different types of starting cells — including cardiomyocytes and cardiac progenitor cells — in mouse embryos by engineering the cells to contain genes for the fluorescent proteins. They turned the fluorescent labels on at different times during embryonic development and then watched how the colors spread through the developing heart as the embryos grew.

The scientists found that during early in utero development, most new cardiomyocytes come from cardiac progenitor cells rather than from existing cardiomyocytes. As a mouse fetus develops, however, the cardiac progenitor cells lose their ability, over the course of a few days or a week, to generate new cardiomyocytes.

The researchers also used the fluorescent proteins to study whether or not new heart cells arise after a heart injury. To do that, they simulated a heart attack in mice by surgically closing one of the heart arteries. They found that in newborn mice, the heart maintained a limited ability to regenerate cardiomyocytes after the artery was closed — even though its progenitor cells had matured. But when the heart attack was simulated in adult mice, the animals lacked that regenerative capability and couldn't recover.

The researchers have identified a handful of genes in the cardiomyocytes of newborn mice whose levels are different from those of adult mice; they are planning to study if any of those genes are responsible for giving the cells the ability to regenerate.

"Analysis of Cardiomyocyte Clonal Expansion during Mouse Heart Development and Injury," *Nature Communications*, February 21, 2018



Fluorescent colors spread through the developing heart as the mouse embryo grows.

Brain Trust

Linda M. Liau, MD (RES '97, FEL '98), PhD '99, MBA, is at the forefront of research to develop an effective treatment for brain cancer. Now, as the new chair of UCLA's Department of Neurosurgery, she faces the challenge of balancing administration among her many roles.

Linda M. Liau, MD (RES '97, FEL '98), PhD '99, MBA

Chair, Department of Neurosurgery

Director, Brain Tumor Program
Professor, Department
of Neurosurgery

Linda M. Liau, MD (RES '97, FEL '98), PhD '99, MBA, has never been one to sit idly. Or even to sleep. "Everyone tells me it's going catch up to me — that I'll die of a heart attack or something," she says. "So I'll go to bed, but I just wind up lying there, thinking about all the things that I need to do." If she manages four hours, that's a good night.

And there indeed is plenty for Dr. Liau to do. This past August, she was named chair of the UCLA Department of Neurosurgery — only the second woman in the country to chair an academic department in neurosurgery. So now, in addition to her schedule as a surgeon and researcher in brain cancer, she must handle the administrative tasks of a prominent and busy department.

Dr. Liau's research is on glioblastoma, the most aggressive and lethal form of brain cancer, and she is the principal investigator of a \$11.4 million National Cancer Institute Specialized Program of Research Excellence (SPORE) grant for brain cancer studies. Her work over the past two decades — motivated by her own mother's death from metastatic cancer — has focused on developing a vaccine against the disease. The vaccine, which fights glioblastoma by triggering the patient's immune system to attack cancer cells that remain in the brain after the tumor has surgically been removed, now is in multicenter

phase-3 clinical trials. "I have a huge drive to prove that things that seem impossible can actually work," she says. "When I first started working on brain tumor immunotherapy, everyone told me that you can't mount an immune response in the brain. Now we know that's not true."

Dr. Liau talked with *U* Magazine contributor Kathy Svitil about her work and her new administrative role.

As chair, what are your goals for the department?

Dr. Linda Liau: One of the great things about being a physician-scientist is that you see both worlds what goes on in the laboratory and what goes on within the hospital. Because of the proximity of the research and clinical enterprises at UCLA, there is a wonderful potential to take discoveries that are made in the lab directly to clinical application and then back again. But since becoming the chair of neurosurgery, I've come to realize that there are some cultural barriers between clinicians and basic scientists; it is my hope that these can be broken down to bring people together and further enhance these collaborations. I have been doing that within my own niche of brain cancer, but it can be done throughout the various subspecialties of neurosurgery. Sometimes, it's just a matter of meeting people and knowing who does what, and



Dr. Linda Liau.
Photo: Courtesy of UCLA Department of Neurosurgery

why. And since I've been here so long, I know a lot of people at UCLA.

Resources are another concern. Funding from the National Institutes of Health (NIH) is tighter now, and clinical profits are much smaller than they used to be. In the past, clinical departments used to fund research just on the surplus that they made from clinical revenues. Now that surplus doesn't exist. It is not enough anymore for young physicians or scientists to just do great science; they need the resources to help them with that. I feel it is my role as department chair to help get those resources for them.

Another of your responsibilities is to educate medical students, residents and fellows who come through the department. Do you feel that today's trainees need a level of training that was not available to you when you first started?

Dr. Liau: The field of medicine has grown so much in the last 25 years in terms of medical knowledge, as well as engagement in clinical performance metrics, quality improvement projects, electronic medical records, et cetera. We never had to do those things

to this extent when I was in training. We just went and saw the patients; we practiced medicine and did surgeries. It used to be that you would go on rounds, and then you'd be tested on certain facts about certain diseases. Now, you can get many of those facts just by looking them up on your phone. So, in order to excel, a student must know not just the facts, but also how to integrate them clinically and also simultaneously manage various different priorities. Information is easier to come by, but along with that, the expectations are higher. Ultimately, I believe that the role of an academic neurosurgery department is to produce future leaders in the field of neurosurgery, and that could be in the form of basic or translational research in terms of developing new diagnostics or new treatments, but it also can be leadership in other areas — hospital operations, quality improvement, public health issues.

What distinguishes UCLA's neurosurgery program from other programs?

Dr. Liau: UCLA traditionally has been a very strong clinical neurosurgery program, but we also have

"In order to excel, a student must know not just the facts, but also how to integrate them clinically and also simultaneously manage various different priorities." "It is not enough anymore for young physicians or scientists to just do great science; they need the resources to help them with that. I feel it is my role as department chair to help get those resources for them."

"The concept is to take tumor cells, create a vaccine against them in the lab and then inject them back into the patient to activate his or her immune system's T cells so that they get into the brain and attack the cancer cells when they start coming back."

very strong research programs in pretty much all of the major areas of neurosurgery: neurosurgical oncology — brain and spine tumors; functional neurosurgery — epilepsy and movement disorders; spine – degenerative spine disease and spinal cord injury. These programs are well-funded by the NIH. It is important for us to be able to compete and to be successful for peer-review funding.

You are the second woman to chair an academic department of neurosurgery in the U.S. How does that feel?

Dr. Liau: When I started medical school, people told me that women shouldn't be neurosurgeons because it's too challenging of a profession. It has been very fulfilling for me to break these stereotypes. So, from that standpoint, I don't really think about being only the second woman to chair an academic neurosurgery department; I think of myself as a neurosurgeon, like everybody else here. The first woman to be appointed chair of an academic neurosurgery department was Dr. Karin Muraszko at the University of Michigan, and that was 13 years ago. It took more than a decade for there to be a second woman chair. This is becoming apparent in many fields — you get the first woman to crack the glass ceiling, but then there's not a lot of traction until you get more and more women in leadership roles. I am hoping that we will have a third and a fourth and a fifth woman chair within the next year or two - not just breaking the glass ceiling, but also breaking it wide open so that it's not unique to have a woman chair of a neurosurgery department, or to have a woman in any other position of leadership.

Your research focus is on the development of a vaccine for brain cancer. How did you come up with that idea and how it works?

Dr. Liau: When I started thinking of how to better treat glioblastoma, one thing that I noticed as a surgeon was that we would take the tumor out and the surgery would go great, but the tumor would come back six months later. That probably was from cells that were in areas we didn't see while doing the surgery. I thought immunotherapy would be a good way to get to these cells. The concept is to take tumor cells, create a vaccine against them in the lab and then inject them back into the patient to activate his or her immune system's T cells so that they get into the brain and attack the cancer cells when they start coming back.

We have a subgroup of patients, maybe 25 or 30 percent, who do really well after the treatment. What is puzzling is why the other 70 to 75 percent don't do as well. What's different? Their tumors look the same. Figuring out the reason for this variation in response has been the focus of my lab over the last 10 years, and we are moving toward new ways to personalize treatments based on predictors of response.

Is there a time frame for when you feel such a vaccine might be in widespread use?

Dr. Liau: Twenty-five years ago, I thought it would happen in 10 years. I am still waiting. But we've come a long way in the last 20 years in how we think about glioblastomas. When I was a resident, the outcome for a patient with glioblastoma was very dismal. We really didn't have much hope that these

patients would live beyond a year or so. Now, we have patients out 10 to 15 years. I can't say that every patient lives a long time, but my approach to patients is much more hopeful. They could potentially be in the group that responds.

One thing that I hope also will change is the way the Food and Drug Administration approves drugs. Right now, it's such a long and tedious process that can take 10 to 15 years before you are able to get a drug approved. So, there are scientific questions that need to be answered as well as regulatory trialdesign issues that then need to be fixed before we actually can get new treatments approved.

How do you balance your time as a chair, as a neurosurgeon, as a researcher, as a teacher and as a person with a life?

Dr. Liau: Balancing my time is the most difficult part of this job; I'm still trying to figure it out. There are certain things that are priorities at different times. At one point, someone asked me, "Can you have it all? Can you do it all?" And I think my answer to that is "Yes, but not at the same time." I don't think you can be the best mom and the best surgeon and the best researcher all on the same day, or even all in the same week or month or year. It is a balancing act, but the balance changes over time and under new circumstances. I'm still trying to find the right balance.

You have been affiliated with UCLA for nearly 30 years, beginning as an intern in 1991 and through your residency and fellowship training. Why have you stayed in one place for so long?

Dr. Liau: I grew up in Southern California, so initially one of the reasons I came here was because my mom was diagnosed with breast cancer while I was in medical school (at Stanford University School of Medicine), and I wanted to be close to home to be with her during that period of time. She died from her cancer while I was a resident, but throughout the time I've been here, I've felt such collaborations and friendships that it's been very hard to leave. There have been other offers, but when it comes down to it, nothing else really felt like home.

Do you think you'll reach a point at which you will be satisfied with what you've accomplished and allow yourself to take a break?

Dr. Liau: Oh, no. I think I'm one of those type-A people. I feel like I have to do this and do that. I thought that maybe after becoming a chair, I'd think, "OK, this is the final point of my career." But now, I think, "No! There's so much still to do."

"When I was a resident, the outcome for a patient with glioblastoma was very dismal. We really didn't have much hope that these patients would live beyond a year or so. Now, we have patients out 10 to 15 years."









Photos: Ann Johansson

Gene Chaser

Leonid Kruglyak, PhD Chair, Department of Human Genetics

ILLUSTRATIONS BY KENT BARTON



Dr. Leonid Kruglyak is a leader in the quest to understand how changes in the genome are shaped by molecular and evolutionary forces and how these changes lead to all the observable differences among individuals within a species. His research, using the gene-editing tool CRISPR, has helped to pinpoint regions of the genome that play key roles in common diseases.

Dr. Kruglyak steps into the *U* Magazine Spotlight.

When did you begin to think about science?

If you asked me in second grade what I wanted to do, I would have said I want to be a scientist. I was interested in math and science, but what I was *really* interested in first was astronomy and astrophysics and the solar system and the planets. My interest began as soon as I realized there is a bigger world out there and that people have been trying to understand how it all works.

What was your first experiment?

Anything that I did experimentally when I was a kid generally was a total failure. For a science project in high school biology, I was going to investigate the effect of acid rain on plants. I had these plants, and I was going to water them with solutions with different acidity. But I think I wasn't very good at watering any of them and so they all died, which made it hard to see any results.

Who is your science hero?

Gregor Mendel. I'm a geneticist, and he is the founder of genetics. I feel that a lot of the questions we ask today are exactly the same questions that he asked back in the middle of the 19th century.

Where are you happiest?

I really like being out on the trails in the Santa Monica Mountains on my mountain bike. I enjoy the combination of physical exertion and challenge and natural beauty.

What is your defining characteristic?

I'm extremely competitive. That runs through everything I do. It certainly translates into a desire to be first in science, to come up with a new idea and execute on it before anybody else does.

What are the qualities that go into being a great scientist?

Problem choice: What are you going to work on? You have to be able to recognize that it is a question that hasn't really been addressed, that it is worth addressing and that the impact is going to be large. And, also, it has to be attainable. It can't be the kind of problem where the answer is 50 years away.

What is your greatest virtue?

I have a pretty good recollection of what it was like for me to be at different career stages, and I remember how different folks higher up the ladder treated me and what I liked and what I didn't like. I try to act toward others in ways that I would have appreciated when I was at that stage.

What is your greatest fault?

I am impatient and easily bored.

When don't you think about science?

If I'm on my bike going downhill and the trail is technically challenging, then I'm definitely not thinking about science — or anything else.

To which superhero do you most relate?

I've watched all the Marvel movies, and I don't know if there's a specific superhero that I identify with, but it would definitely be the more human and vulnerable ones. It is hard for me to identify with the all-powerful ones like Superman.

Where does your inspiration come from?

A lot of it comes from conversations with members of my group and other scientists.

What is the best moment of your day?

I ride my bike to work, and the route I take drops down to the ocean and goes along the beach path for a while. When you're riding your bike right by the ocean and the weather is beautiful — especially if it's in January! — it's pretty great.

What has been your biggest "aha" moment?

I saw a connection between [a problem I was trying to solve] and the fast Fourier transform, which is an algorithm used in engineering and physics. I saw that the computation I was trying to do in genetics was analogous to that. Once I saw the connection, I was able to write about 10 lines of code that solved the problem. When I first started to describe the results at conferences, people would be like, "Did you just say you can calculate this? That's impossible."

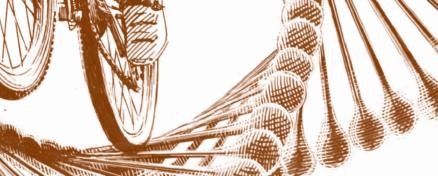
What music do you listen to while you work?

When I was in school, I would play rock music fairly loud while I was trying to do hard math. Now I need peace and quiet to concentrate.

Whom would you like to have at your dinner table?

Charles Darwin, Gregor Mendel and William Bateson, the English biologist who coined the term "genetics." That would be one heck of a dinner party.

To read a fuller transcript of
Dr. Kruglyak's responses to these
and other questions, click on
the link to this article at:
uclahealth.org/u-magazine



The L.A. Generation Xchange Project

Generation Xchange is a partnership among the UCLA Department of Medicine Divisions of Geriatrics and General Internal Medicine, the Los Angeles Urban League and principals from several L.A. Unified School District elementary schools. The project is an inter-generational program that places older volunteers into kindergarten through third grade elementary school classrooms to help students improve reading and math skills. Its goal is to improve academic and behavioral outcomes for the children while simultaneously offering health promotion for older adult volunteers.

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For more information about Generation Xchange, go to: medschool.ucla.edu/community-generation-xchange



Photos: Courtesy of Generation Xchange Project











PAIN LIKE NO OTHER

BY VERONIQUE DE TURENNE • ILLUSTRATIONS BY NOMA BAR

We have struggled for thousands of years to understand and relieve the agony of migraine. Now science offers increased understanding and the hope for improved treatment.

MY HEAD DOTH ACHE,
O SAPPHO! TAKE
THY FILLET,
AND BIND THE PAIN,
OR BRING SOME BANE
TO KILL IT.

- Robert Herrick "The Head-ake" (1648)*

early 3,000 years before the English poet Robert Herrick evoked the torment of a crushing headache and the yearning of its sufferer for relief, scientists and philosophers had deliberated over the mysteries of a pounding cranium. Throughout human history, people have struggled in the throbbing grip of migraine — a particularly vicious form of headache. It only is recently, however, that researchers have begun to

fathom the biological mechanisms of the complaint. With their increased knowledge, they now are better able to offer sufferers real hope for a cure.

Andrea Alsberg knows too well how migraines can hijack a person's life. She was 28 years old when the first attack hit. Like most people, she had, over the years, dealt with off-and-on headaches, but this one was frighteningly different. "I was living in New York City and had just been to see a play," she recalls. "Afterward, I went out with some friends, and suddenly I got this splitting headache — pain like never before in my life."

When she got home, she took some over-the-counter pain meds and lay down for an hour. The headache, a directed, driving pain that took over the entire right side of her head, finally passed. This same approach worked with the next monster headache, which struck a few months later, and with the ones that came after that. But by the time Alsberg moved to Los Angeles, a few years later, the migraines had become more frequent. At the same time, the increasingly potent medications that doctors prescribed for her weren't working.



While quiet, meditative moments help Andrea Alsberg to soothe her migraines, the only thing that truly works is medication.

Photo: Ann Johansson

"During one attack, my husband wasn't home, and I was bathing our two little ones," says Alsberg, who worked as a curator and later served as head of programming for the UCLA Film & Television Archive. "I leaned over to put them in the tub and had such an extreme wave of pain that I thought I was going to pass out."

As often happens to migraine sufferers, Alsberg's primary care physician soon ran out of treatment options. But instead of this being a dead end, it wound up opening a door. Her doctor referred her to Andrew Charles, MD '86 (RES '90, FEL '92), a neurologist and professor at UCLA who is widely recognized as a leader in the field of migraine research. "Until that point, I had been alone in this," Alsberg says. "And suddenly here was Dr. Charles, someone who understood every aspect of what I was going through and who gave me hope for the future."

MIGRAINE IS A COMPLEX NEUROLOGICAL

DISORDER in which headache is just one symptom among a web of symptoms. In addition to the crushing pain, which often throbs or pulsates, sufferers can experience nausea; dizziness; neck pain; sensitivity to light, smell or sound; visual disturbances; sensory hallucinations; mental confusion; depression; difficulty speaking; and acute

exhaustion. With so many interlocking symptoms, it is not always easy to describe what a migraine actually feels like. Several years ago, the news and blog website Huffington Post asked followers on its social communities to try to put into words their experience of a migraine. "Like my brain is exploding, someone took a baseball bat and beat the base of my skull and neck with it, and there's an ice pick jabbed into my right eye and temple," one reader responded. "Every bright spot of light and every minor sound sets the entire back of my head on edge. The source of the noise or light becomes irritating and aggravating to me beyond anything else I ever experience," wrote another. "Thunder and lightning inside of your head combined with a serious need to toss your cookies," another reader wrote.

Despite centuries of inquiry, the physiological origins of the condition that lead to such excruciating descriptions have been elusive. Today, Dr. Charles is a leader in the effort to more fully understand and treat migraine. He holds the Meyer and Renee Luskin Chair in Migraine and Headache Studies, the only endowed chair in the U.S. that is dedicated to migraine, and he also serves as director of the UCLA Goldberg Migraine Program in the David Geffen School of Medicine at UCLA. As both an active researcher and a clinician who sees patients, he is a rarity in the field.

"One of the biggest challenges of migraine is that the whole field has long been filled with so many misconceptions," Dr. Charles says. "Migraine is the third-most common of all disorders on the planet, and it is the second leading cause of time spent disabled over a lifetime, yet its mechanisms have been misunderstood, and its consequences have been greatly underestimated."

In the U.S., about 100 million people suffer from chronic headache. Of those, close to 40 percent have migraine as defined by strict criteria, although it is likely that the actual percentage is much higher. The disorder, which is believed to have a genetic component, is three times as common in women as it is in men. According to the World Health Organization, as many as 20 percent of all women and 8 percent of all men worldwide suffer from migraine. That translates not just to several days per week or month spent in unrelieved pain, but also to a significant loss of quality of life and productivity.

"Tally up the time you spend disabled by this disorder over a lifetime, and it really is quite extraordinary," Dr. Charles says. "Even for the luckiest individuals who have one migraine attack per month and lose just one day, over the course of 40 years, they have lost close to 500 days to a problem that they often aren't bringing to the attention of a medical practitioner."

Patients who do discuss migraine with their family doctor often don't get very far, Dr. Charles says. That is because, despite it being one of the most common of all medical disorders, the subject of headache, in all of its permutations, including migraine, merits just a few hours of lecture in medical school. Thanks in part to this information vacuum, migraine has become a common pathway for dependence on prescription opioids.

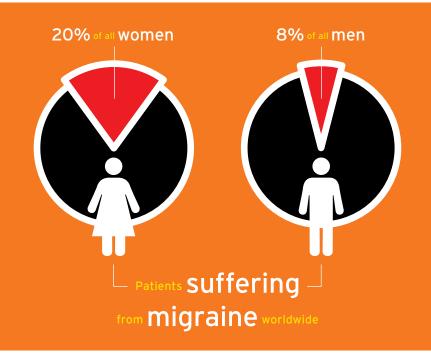
UNTIL QUITE RECENTLY, MIGRAINE WAS BELIEVED TO BE A VASCULAR DISORDER

caused by the dilation and constriction of blood vessels in and around the brain. As a result, migraine treatments were for decades focused on vascular effects. Most current migraine therapies initially were licensed to treat other medical conditions, such as seizures, depression and high blood pressure. It was only by chance that they were discovered to offer benefits to migraine patients. Greater understanding of the basic mechanisms of migraine has led to major changes in the focus of the development of new therapies.

The search for answers goes back thousands of years. Migraine shows up in medical writings in ancient Egypt as early as 1200 BC. In 4000 BC, Hippocrates accurately described both the visual disturbances that often precede a migraine attack and the nausea that can accompany it. Attempts at

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"With monoclonal antibodies, you are able to target mechanisms far more specifically. You can design antibodies that act as a sponge to soak up badacting molecules or to block a selected receptor or channel that is causing trouble."

a cure have included drilling holes into the skulls of sufferers in 7000 BC; acupuncture in ancient China; and blood-letting, hot irons and witchcraft during the Middle Ages. The first use of vasoconstrictors emerged in the 1920s in the form of ergotamine, a substance derived from fungi such as mushrooms. As is true of virtually all migraine treatments developed since the 20th century, the application of ergotamine for migraine was a secondary use; its original purpose was to lessen bleeding in childbirth.

Today's seismic shift in migraine research is taking place, in part, thanks to the advent of sophisticated imaging technologies, advanced approaches for the analysis of genetic factors and the development of antibodies that can act with remarkable specificity on individual therapeutic targets. With these new tools, researchers can study migraine at the molecular and cellular levels, as well as visualize specific changes in the function of the nervous system that take place during a migraine attack. These studies are helping migraine to shed its status as a forgotten stepchild of medicine and become a disorder for which there are precise and targeted therapies.

In recent years, imaging studies have disproven the vascular theory of migraine, Dr. Charles says. Instead, scientists now see fluctuations in brain chemicals, as well as abnormal electrical activity in specific brain regions, as a likely cause. Another misconception that has been swept aside is that the throbbing nature of migraine pain is caused by the heartbeat, or vascular pulse. "What's fascinating is that it turns out that the throb rate of a patient's migraine pain is not the same as his or her vascular pulse," Dr. Charles says. "So there has to be something else generating the throbbing nature of migraine other than the pulsation of a patient's blood vessels."

One possibility is that the pulsing pain mirrors the slow oscillations of brain activity itself. "That's part of what we're very interested in figuring out," Dr. Charles says. "But it's something we don't have a clear understanding of just yet."

What scans do show is that patients in the throes of a migraine are experiencing waves of abnormal activity that spread across the surface of the brain. There also is unusual stimulation of nerve centers deep within the brainstem. The ultimate treatment goal is a means to reduce, or even short-circuit, these abnormal patterns of brain activity before they can begin to cause symptoms.

In that regard, memantine, a drug used to treat moderate-to-severe confusion associated with Alzheimer's disease, has shown promise. The drug inhibits the type of brain activity that researchers suspect to be a migraine trigger, and it has brought relief to some of the patients under Dr. Charles's care. On the horizon are stimulation devices that would stop a budding migraine via an electrical or magnetic pulse sent to specific nerves or regions of the brain.

Another breakthrough that Dr. Charles believes has great potential is the use of monoclonal antibodies. These are laboratory-produced molecules designed to target or bind to precise sites within the body. In this case, the targets are certain peptides, or chains of amino acids, that are released during the earliest phases of a migraine attack.

"The idea is that with traditional drugs, you basically are trying to target some sort of receptor or channel on a nerve cell or blood vessel, but it is rarely possible to design a drug that is 100 percent specific to the target. These off-target effects may lead to unwanted side effects," Dr. Charles says. "With monoclonal antibodies, you are able to target mechanisms far more specifically. You can design antibodies that act as a sponge to soak up bad-acting molecules or to block a selected receptor or channel that is causing trouble."



Game Changer

For anyone who has white-knuckled his or her way through the explosive pain of a migraine attack, the craving for release can be extreme. Yet current avenues for relief have offered mixed effectiveness. That may soon change as the first generation of drugs that have been developed specifically for the prevention of migraine become available. The Food and Drug Administration approved one such drug, erenumab-aooe, this May.

Known as monoclonal antibodies, erenumab-aooe and several other similar drugs still in late-stage testing have been so effective in clinical trials that some experts in the field of migraine are using exuberant language like "game changer."

Like the naturally occurring antibodies in our bodies, which help to power our immune systems, lab-made monoclonal antibodies are proteins that pursue specific targets. But because the lab-made antibodies are produced by clones derived from one parent cell, they can be designed to bind to and neutralize a single, highly specific target. As scientists continue to decode a growing number of diseases at a molecular level, they increasingly are turning to monoclonal antibodies for precision therapies.

In cancer treatment, for example, monoclonal antibodies are used to carry substances like drugs or radiation directly to specific types of cancer cells. In recent Ebola research, they have shown promise in delivering a gene that will jump-start a patient's immune response to the deadly virus. And in the migraine-prevention breakthrough, scientists have created monoclonal antibodies that target calcitonin gene-related peptide (CGRP), a neuropeptide that is known to play a role in migraine.

Researchers have found that serum concentrations of CGRP become elevated during a migraine attack, and they normalize when the attack resolves. Infusion of CGRP in patient volunteers provokes migraine attacks that are very similar to those that occur spontaneously. Small molecule drugs binding to the CGRP receptor were able to abort migraine attacks. It was this body of evidence that led researchers to suspect that by blocking CGRP receptors, or targeting the neuropeptide itself, a migraine attack could be prevented.

According to results from late-stage clinical trials of erenumab-aooe and other anti-CGRP antibodies, the researchers were right. For a subset of patients, these treatments are remarkably effective in preventing migraine, and they work quickly and have a long duration of action.

"The notion that we would be using antibodies to treat migraine is really quite a radical concept," says Andrew Charles, MD '86 (RES '90, FEL '92), Meyer and Renee Luskin Chair in Migraine and Headache Studies and director of the UCLA Goldberg Migraine Program.

Antibodies bind to CGRP or its receptor to block its effect Antibodies CGRP CGRP CGRP CGRP CGRP

Monoclonal antibodies specifically bind to the peptide CGRP or its receptor, thereby selectively neutralizing CGRP and its migraine-causing effects.

CGRP Receptors

Images: Courtesy of Dr. Andrew Charles

"This is a very different approach because, in contrast to other treatments that we've used in the past, which often have been developed for other reasons and we've borrowed them as migraine treatments, this has been developed based on our understanding of the chemistry of migraine and what is going on during a migraine attack."

Sufferers anxious for a therapy that can head off an attack before it becomes incapacitating are understandably eager. So, too, are the physicians who will treat them. "It has all of us very excited, and we are looking forward to getting our hands on these new medications to help our patients," Dr. Charles says.

— Veronique de Turenne



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Dr. Andrew Charles. "In contrast to other treatments that we've used in the past ... this has been developed
based on our understanding of the chemistry of migraine and what is going on during a migraine attack."

Photo: Ann Johansso

based on monoclonal antibodies to prevent migraines.

And three other pharmaceutical companies are completing phase-3 clinical trials or awaiting FDA approval of similar medicines. Known as anti-CGRP (calcitonin gene-related peptide) drugs, all are compounds that target a specific protein in the brain that causes severe headache.

"The CGRP story is very exciting; we have been working on aspects of it in our laboratory here," Dr. Charles says. "We are gearing up to deliver these new therapies to patients in our clinic,

been working on aspects of it in our laboratory here," Dr. Charles says. "We are gearing up to deliver these new therapies to patients in our clinic, where quite a number of them are already asking about the treatment."

The anti-CGRP therapies — the first treatments

In fact, the Food and Drug Administration (FDA)

this May approved erenumab-aooe, the first drug

The anti-CGRP therapies — the first treatments ever to be developed primarily and specifically for migraine — are intended to be preventive, Dr. Charles says. "We have seen remarkable results from the clinical trials, with a subset of patients for whom the response is a dramatic reduction in the number of migraine attacks," he says. "A smaller percentage have shown complete remission, which is unlike what we've seen with other therapies."

migraine science and migraine therapy. Now that we have powerful tools like monoclonal antibodies and functional imaging studies ... we're coming ever-closer to finding definitive therapies."

ADDITIONAL ADVANCES ARE TAKING PLACE IN DR. CHARLES'S LAB, where he and his colleagues are doing research with mice that have been genetically engineered to express human migraine genes. Other research takes place at UCLA's imaging centers, where patients volunteer to have the course of their migraine attacks mapped or their anatomy characterized. Dr. Charles and his research team also collaborate on a variety of studies with other institutions.

Even as the science has advanced, lack of significant monetary support has hindered the development of new migraine therapies. "When it comes to the migraine field, there historically has been very little funding," Dr. Charles says. It largely has been left to pharmaceutical companies to support research to bring new therapies forward. Today, that is changing, Dr. Charles says. "Thanks to philanthropy, we now are able to take control of the translation of basic science into new treatments."

That effort is being significantly propelled by a gift from Wendy Goldberg, an author and philanthropist, and her husband Leonard Goldberg, an award-winning film and television producer and executive. The couple recently gave \$10 million to support research at UCLA, with the bulk going to migraine research. It is the largest private donation ever to support migraine research.

Meanwhile, as these promising treatments progress from laboratory bench to bedside, Dr. Charles and his clinical staff work to help their migraine patients manage their conditions. New patients give a detailed oral history and fill out a medical questionnaire. They receive educational materials and undergo a physical exam. Based on the information gathered, Dr. Charles and his team formulate individualized treatment plans.

Migraine education is important. Dr. Charles and his staff teach patients to recognize migraine triggers like skipped meals, irregular caffeine intake, irregular sleep, changes in the weather, air travel and emotional or physical stress. Foods like chocolate, nuts, aged cheese, fermented foods, alcohol in general and red wine in particular can be problematic for migraine sufferers. Birth control pills and anti-depressants also can play a role in migraine. Ironically, so do over-the-counter pain medications, which can ease discomfort but then cause a "rebound" headache.

On patients' to-do lists are aerobic exercise, which has been shown to reduce the frequency and severity of attacks. However, migraine patients often feel too unwell to exercise, which sets up a distressing Catch 22. Also included is a list of helpful vitamins and supplements such as Vitamin B2, magnesium, Coenzyme Q10 and melatonin.

This confluence of primary research with clinical care makes UCLA's migraine program noteworthy, says Amy Gelfand, MD, assistant professor of pediatric neurology at UC San Francisco and director of the UCSF Pediatric Headache Program. Dr. Gelfand also is a leader in the field of migraine research; her recent breakthroughs include identifying a connection between migraine and colic in babies.

"The number of programs where people can get great clinical care and that also are doing original investigative research is small. Andy Charles's program is one of the strongest in the field," Dr. Gelfand says. "He and his group are moving the science forward and improving our understanding of migraine."

Among the recent advances in how researchers think about migraine is the idea that headache pain is preceded by far subtler symptoms like irritability, foggy thinking or scent sensitivity. Learning to identify these early-warning signals allows patients to take medication at the earliest possible moment in a migraine attack, which is key to successful pain relief.

In UCLA's Department of Neurology, Angel Moreno, NP, helps Dr. Charles's patients work on this, as well as identifying drug-free alternatives for coping with migraine pain and symptoms. "I work with them on all aspects of their treatment — how they're sleeping, what they're eating, whether or not they're exercising, what medications they are taking," Moreno says. "We work on identifying their triggers and on how to avoid them in the future."

Moreno teaches his patients about healing herbs and essential oils, showing them how, when and where on the body to use them. "For example, if someone has the migraine start in their temples or the back of their head, we may work with peppermint — a drop of it over the areas that are affected," he says. "If it's facial pain, I've found that frankincense rubbed over the area that's affected can help."

With precision health and targeted therapies coming into their own, Dr. Charles foresees a golden age of migraine research. "These are incredibly exciting times in migraine science and migraine therapy," he says. "Now that we have powerful tools like monoclonal antibodies and functional imaging studies to visualize what's happening in people's brains at the various stages of an attack, we're coming ever-closer to finding definitive therapies."

For his patients, the potential for new cures is, indeed, exciting. Says Alsberg, Dr. Charles's longtime patient, "He doesn't have an answer for everyone. But the reason I love him is that he instills hope that someday there will be an answer."

Veronique de Turenne is a freelance writer in Los Angeles.

*EDITOR'S NOTE: In "The Head-ake,"

Robert Herrick — familiar to many readers for the line "Gather ye rosebuds while ye may" — conjures the torment of a sufferer in the throes of a headache, but it is, in fact, a metaphor for the pain of an aching heart. This does nothing to diminish the power of its evocation. Says Jonathan F.S. Post, PhD, Distinguished Research Professor in the UCLA Department of English: "The headache points to a real thing — pain — even if in the service of a greater thing — love; both are images of human suffering. It's a wonderful little wisp of a poem that might go some distance to relaxing the reader and curing a headache." Here is Herrick's poem in total.

MY HEAD DOTH ACHE, O SAPPHO! TAKE THY FILLET. AND BIND THE PAIN, **OR BRING SOME BANE** TO KILL IT.

BUT LESS THAT PART THAN MY POOR HEART **NOW IS SICK; ONE KISS FROM THEE WILL COUNSEL BE** AND PHYSIC.



Wendy and Leonard Goldberg. Photo: Courtesy of Wendy and Leonard Goldberg

WHY THEY GIVE

Recognizing the need to find new therapies to alleviate the debilitating effects of migraine, Wendy and Leonard Goldberg made a visionary gift to endow the UCLA Goldberg Migraine Program. News of the Goldbergs' gift, which has enabled the program to treat a greater number of patients and accelerate research of promising migraine therapies, caught the attention of many experts in the field who have reached out to UCLA. This endowment gives scientists the flexibility to investigate the most innovative avenues and allows them to change course if new exciting therapies emerge, more quickly bringing treatments from bench to bedside.

"Leonard and I have seen firsthand in friends and family members how debilitating migraines can be. We are eager to help find better treatments and, ultimately, a cure."

- Wendy Goldberg



MARCELA ZHOU HUANG WAS BORN IN MEXICO AND HAS

THIS

LIVED IN THE UNITED STATES SINCE AGE 15. SHE GRADUATED

IS

HIGH SCHOOL, EARNED A COLLEGE DEGREE AND NOW IS A

HER

MEDICAL STUDENT AT UCLA. BUT MARCELA IS UNDOCUMENTED,

STORY

AND THE POSSIBLE END OF DACA THREATENS HER FUTURE.

hen I was 7 years old and growing up in Mexico, a robber held me hostage and hushed my cry with a knife he pressed against my throat. Two years later, when I was 9 and developed a mass on my neck, a doctor told me that I had three months left to live. I am 27 now, and it has been more than a decade since I've seen my father and my sister. I don't know when we will see each other again.

There has been much love and joy in my life, but also trying times. In many ways, I am fortunate to be alive. So when I woke up on the morning of September 5, 2017, to the news that the current administration would terminate the Deferred Action for Childhood Arrivals — DACA program, I wasn't terribly afraid.

I sent a text to everyone I knew who I thought might reach out to me that day. I told them not to worry, that I was turning off my phone and heading to the hospital for my clinical rotations. I wanted to stay fully present for my patients, and insulating myself from the life-changing announcement that now was dominating the news was the best way I knew how.

In a strange twist, the stress and fear that had engulfed my life since the 2016 presidential election subsided. Although my American dream and legal status in this country had a potential end date, I felt calm and composed. Suddenly, I had concrete answers and a clear path forward. Now it was time to work toward a solution for me and for the nearly 800,000 other DACA recipients like me.

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in the U.S."

According to the American Medical Association (AMA), there are an estimated 70-to-100 DACA recipients in training to become doctors nationwide, and more than 5,400 previously ineligible physicians could enter the health care system in the coming decades because of DACA. At the same time, there is a growing physician shortage in the U.S. In a letter to congressional leaders after the announcement to end DACA, the AMA noted the potential for "severe consequences" for many in the health care workforce, patients and the overall health care system. The AMA cited an independent study by the Association of American Medical Colleges that projected the total physician deficit to grow between 61,700 and 94,700 physicians by 2025. The AMA argued that DACA helps address these shortages and ensures patients access to care, saying, "Those with DACA status help contribute to a diverse and culturally responsive physician workforce, which benefits all patients."

MY PARENTS EMIGRATED FROM CHINA TO

MEXICO in the early 1980s, settling in the town of Mexicali, just south of the California border. My father Yin and my mother Hua worked in restaurant kitchens while they raised my older sister Claudia and me

My parents always have been huge advocates for education, a path to progressing in life. They spent what little money we had on private schooling in Mexico, where my sister and I learned to speak and read and write in Spanish and English. When an opportunity arose to attend a better school in the U.S., my parents arranged for us to live with our uncle and his family across the border in Calexico, California. We took advanced classes, participated in extracurricular activities and made new friends. Claudia and I were very close. We shared the same room growing up in Mexico, and in the U.S. we even shared the same bed. We spent every day together, developing the type of bond that only sisters understand. That all changed in January 2007.

We had returned to Mexico to stay with our parents over the winter holidays. But while we were

there, one or the other of my parents would drive us back across the border nearly every morning so that my sister could complete a school project. The one day I decided to stay at home with my mother was the day that everything went awry. Immigration officers stopped my father and sister at the border for a random secondary inspection and detained them for 12 hours. The officers revoked both my sister's and father's visas. Our family was in shock.

When they got home that night, tears and sobs shattered the somber silence at our dinner table. My sister had just started to receive college acceptance letters, including from UCLA and UC Berkeley. She would never be able to attend. My visa, however, still was valid. My parents sat me down and gave me, a 15-year-old whose world had just turned upside down, the most difficult choice of my life: stay in Mexico or return to school in the U.S. If I chose to return to school, I would not be able to see my father and sister again until their immigration status changed. I felt like I was thriving in school, and I wanted to get the most out of my academics, so I decided to go back to the U.S. I said goodbye to Claudia and my father. That was the last I have seen of them.

The average medical student in the U.S. graduates with almost \$200,000 in debt. For most students, the availability of low-interest loans can help offset the high cost. DACA students, on the other hand, are not eligible for federal loans and must rely on scarce state and local resources or philanthropy. While private loans are available, interest rates often are high, and a U.S. citizen or permanent resident must act as a cosigner.

For those who do earn a medical degree, residency training is required to obtain a medical license and practice in a given specialty. However, acceptance into residency training — which typically lasts three-to-six years — is difficult in many states outside of California that do not recognize DACA participation as sufficient for a medical license. This also raises the possibility that prospective employers may have doubts about whether or not to offer a qualified candidate a spot because, if they cannot fulfill their training, this could potentially waste medical education funds and leave spots vacant.

AS A TRILINGUAL TEENAGER WHO LIVED IN MEXICO AND THE U.S., I often struggled with how to identify. I never wanted my mom to speak Chinese to me in public in Mexico as I tried to blend in with my Spanish-speaking friends and classmates. Now Border Patrol agents and immigration officers were my neighbors in the U.S., and their presence made the potential for discovery and deportation a constant threat.

I lived in disguise for many years, learning to protect my identity by assimilating as an Americanized Chinese. I also had the privilege of looking a certain way, and I didn't fit the typical picture of what some might think of as an "undocumented" person. No one suspected that a little Asian-looking, English-speaking girl who worked hard to become valedictorian of her high school class might lack the proper paperwork.

But some things were beyond my control. Shortly after I finished high school, I was walking down the street one day when a dog charged and bit my foot. When I checked in at an urgent-care facility, the woman at the front desk asked if I knew the owner of the dog. I told her I did not. She continued to press for details and insisted the clinic would file a police report about the incident. Until then, I had no idea that something as unremarkable as a dog bite might trigger the undesired attention of law enforcement officials.

When I started to walk out after telling the receptionist that I lacked identification, she understood my hesitation. Thankfully, I received the care I needed and continued to live my life.

A 2014 study in Public Health Reports found that racial and ethnic minorities are at a disproportionate risk of being uninsured and lacking access to care, as well as experiencing worse health outcomes from preventable and treatable conditions. DACA students, meanwhile, often are bilingual and come from diverse cultural backgrounds, making it easier for them to relate to the challenges of these communities.

Because of their experiences, medical students from underrepresented minority backgrounds are more likely to work in underserved areas, according to a study of 20,000 U.S. medical students published



Marcela Zhou Huang (center) at home in Mexico with her older sister Claudia and mother Hua. Photo: Courtesy of Marcela Zhou Huang

in the journal JAMA in 2008. That study also showed that Caucasian students at more racially diverse medical schools rated themselves better prepared to care for racial and ethnic minority patients than students at less diverse schools.

UNDERSTANDING THE VALUE OF ACCESS TO QUALITY HEALTH CARE was instilled in me at an early age. When I was 9 and developed a mass on my neck, my family set off on a hunt for answers, traveling up to eight hours from home to seek help. Uninsured and unable to get comprehensive medical care, I experienced the burdens as a helpless patient limited by financial barriers.

We sought care from a dermatologist, who referred us to an ear, nose and throat specialist. We lacked insurance and were charged for every visit and every lab draw. My mother didn't speak Spanish well, so I was left to communicate with the doctor. During one examination, the doctor told me that if the mass turned white, I would have three months to live. Years later, I had a biopsy performed in the U.S. that confirmed it was nothing to fear, and eventually I had the mass drained. The small scar on my neck serves as a visible reminder of the inadequate medical care and poor communication that highlighted the nightmare my family faced.

These experiences taught me invaluable lessons that have shaped my ideas about what constitutes quality medical care. I learned the importance of doctor-patient communication and the value of

"No one suspected that a little Asian-looking. **English-speaking** girl who worked hard to become valedictorian of her high school class might lack the proper paperwork."



Marcela Zhou Huang and her mother during the White Coat Ceremony for incoming first-year students in the David Geffen School of Medicine at IICLA 2015

Photo: Courtesy of Marcela Zhou Huang

a patient understanding his or her health status, regardless of the treatment availability or diagnosis. My experience as an uninsured and low-income immigrant showed me the health disparities that come in the wake of financial hardship and sparked my desire to help bridge the gap for the underserved.

The David Geffen School of Medicine at UCLA, along with the broader University of California system, has been committed to providing the most qualified students an opportunity to pursue their dreams, regardless of their immigration status. Kelsey C. Martin, MD, PhD, dean of the David Geffen School of Medicine at UCLA, and Clarence Braddock III, MD, MPH, vice dean for education, are among those who have taken strong public stances supporting DACA recipients. In an article published last year in U.S. News & World Report, they wrote: "These students are here not because of their DACA status, but because they are exceptionally qualified intellectually and because of their genuine desire to care for, and heal, the sick."

Drs. Martin and Braddock noted how the David Geffen School of Medicine at UCLA has become one of the most competitive medical schools in the country, with more than 14,000 applicants vying for 175 spots. "To achieve one of those spots is a monumental and arduous feat, all the more so for DACA students whose future — unlike other medical students — has been ever shrouded in doubt," they wrote.

I FOUND MY PASSION FOR MEDICINE WHEN I WORKED AT A FREE CLINIC while

an undergraduate student at the University of California, San Diego. The work gave me a sense of purpose and motivation to do the most that I can for the community. Yet I had mixed emotions in the lead-up to graduation. Despite the fact that I was about to receive a degree in human biology from a top-10 public university, my legal status made it challenging to apply to medical school or pursue a career path of my choice. I felt like I had put my family and myself through too much to do some other job that did not merit all of the sacrifices we had made.

But then, on June 15, 2012, the day before graduation, President Obama announced DACA. The policy, established by the Department of Homeland Security, made it possible for young undocumented immigrants like me to pursue our dreams. It was an amazing experience to walk across the stage at graduation knowing that there was this possibility that I could study and work in my chosen field. I also could finally get a driver's license, open a bank account and apply for a credit card — simple things that are a rite of passage for most young people but major milestones for someone who never before had access to them.

I earned acceptance into the PRIME Program at the David Geffen School of Medicine at UCLA, where I hope to graduate in 2020. As part of the program, I will spend next year at Harvard University working toward a master's degree in public health, with an emphasis on health policy. I eventually hope to practice internal medicine in underserved communities. While the academic challenges are great, I know they are within my control. Other things about my life are not.

Recent years have posed constant threats to the continued presence of many immigrants in this country, including myself. There are days I go to bed wondering if I will be forced out of the country that I love and call home. I know there are some people who would rather see me deported. I try to listen to their point of view and understand why they feel the way they do, because this discussion is not just about people like me. I feel that we all are contributing to this country in different ways. Similarly, I do not feel that I ought to be put on a pedestal as a model person who should be allowed to stay in the U.S. simply because I am educated, multilingual and working to become a health care provider. There are millions of others who are contributing in different ways and who too often are not a part of this discussion.

I frequently wonder: What do we define as being worthy to be in the U.S.? Why are some people unworthy? And who defines who is and who is not worthy? What kind of standards are we setting? Because here's the thing — I wouldn't be who I am without my parents, two immigrants who are quite the opposite of me, who are uneducated, who work in kitchens and who don't really speak English or Spanish. Their horizons were limited by many factors, but they were able to raise me and my sister — who now is pursuing an environmental sciences career

in Canada — to be educated and motivated and caring young adults. Parents and families like mine often are lost in the noise of the immigration discussion. I am actively seeking these difficult conversations, trying to give a voice to those who are socioeconomically disempowered.

While the future of DACA is held up in court proceedings, UCLA has developed infrastructure to support the estimated 600-to-700 undocumented students on campus. The Chancellor's Advisory Council on Immigration Policy created DACA-renewal workshops and distributed educational materials should immigration enforcement occur at UCLA. The council also recommended additional psychological and legal services and reached out to campus police and other groups.

At the David Geffen School of Medicine at UCLA, faculty and administration have continued to lend support to DACA recipients. Additionally, the UCLA medical student group UndocuMed has brought the campus community together to advocate for undocumented medical students. The group's mission is to support medical students by increasing funds, such as loans and scholarships; educating students and faculty about how immigration status affects students, patients, providers and the greater community; and advocating for policy changes that lead to sustainable solutions for undocumented students pursuing careers in medicine.

FIGURING OUT WHAT TO DO IF I COULD NOT COMPLETE MEDICAL SCHOOL and become

a practicing physician in the U.S. is perhaps something I should plan for, but I'm hopeful that the situation won't get to that point. Many of us stuck in the political limbo of the immigration debate have been through a lot already and have survived. I went through college without financial aid. My family exhausted savings and borrowed money. I know many others who have had their own unique journey filled with obstacles. I think the resilience of the community has taught us that even if things don't work out at that moment, another opportunity will open up. We just have to be

ready for it. Maybe I won't have the chance to be a practicing physician, but I know I can do something else with my medical knowledge.

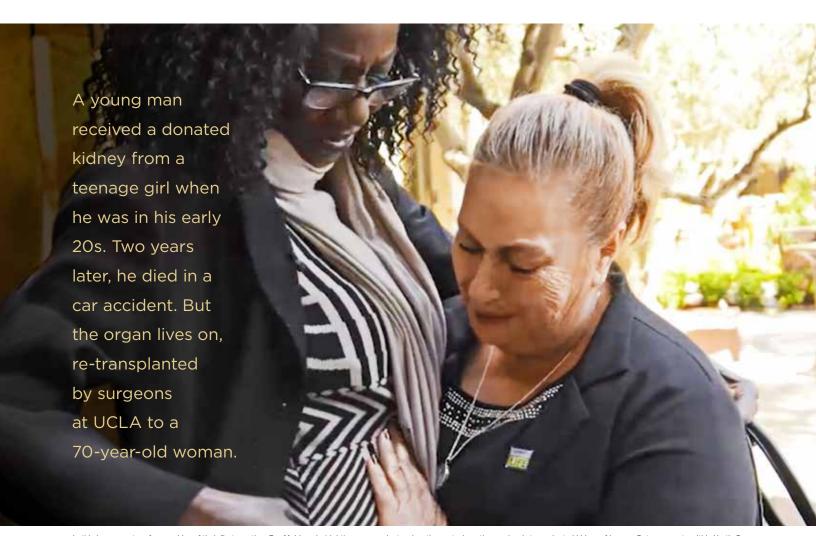
I've been told plenty of times that I'm not Chinese enough, I'm not Mexican enough and I am not American enough. Everyone tries to categorize me as one or the other. As I've gotten older, I've come to appreciate being able to identify with multiple cultures. I've learned to not allow people to define me and to accept myself for who I am and what I can be. I'm proud of where I come from, and I'm excited about the positive differences I can make in this country, my home.

Marcela Zhou Huang is a third-year student in the David Geffen School of Medicine at UCLA/UCLA PRIME program. She is on track to receive her MD and MPH degrees in 2020. Antonio Gonzalez is research and news editor of U Magazine and a former writer for the Associated Press. "I'm proud of
where I come from,
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my home."



TWICE BLESSED

BY ENRIQUE RIVERO



In this image capture from a video of their first meeting, Eva Maldonado (right) weeps as she touches the spot where the previously transplanted kidney of her son Beto now rests within Vertis Boyce.

Photo: Courtesy of UCLA Health

hen Vertis Boyce first meets Eva
Maldonado and Maldonado's daughter
Linda, the three of them barely speak.
They exchange hugs and Eva reaches out and holds
her hand over Boyce's abdomen. It lingers there,
and tears flow from Eva's eyes.

"Mi hijo" — my son — Eva Maldonado says softly in Spanish.

Her hand presses over the spot where a kidney from her son Beto, who was in his 20s when he died in 2017, now rests in Boyce. "He lives on. He lives on," Boyce says. "I'll take good care of myself so I can take good care of this."

It wasn't the kidney with which Beto was born. He had suffered from kidney disease and received two transplants during his short life, the final one in 2015 from a deceased teenage girl. Two years later, however, the young man died in an automobile accident. Rather than discard the still viable organ, the man's family agreed to donate it to someone who might not otherwise have received a kidney.

"Kidneys don't go with you to heaven," says Linda Maldonado. "Why not give somebody else a second opportunity?"

Her brother's transplanted kidney went to Boyce, age 70. "I'm just so grateful to this family," she says. "It's just like a blessing. That's the best way I can explain it."

Boyce had been on dialysis for nearly 10 years when Jeffrey Veale, MD (FEL '06), director of the UCLA Kidney Exchange Program, called her at home in Las Vegas, Nevada, last July to inform her that there was a kidney for her and to tell her about its unusual history. Up until then, Boyce didn't believe she ever would receive a transplant. "I thought, I'm 69 years old — when could I get a second chance?" she says. Now, "I feel freer, and I know I'm on the road to a more fulfilled life," she marvels. "I have a 6-year-old grandbaby who I thought I wouldn't live to see grow up. I think I will be there now."

Boyce benefited from "re-gifting," an approach to organ donation with an untapped potential for saving lives by re-transplanting a previously donated kidney. According to a study published in October 2017 in the *American Journal of Transplantation*, 38 kidneys had been re-transplanted between 1988 and 2014 in the United States. Boyce's re-transplant was the second that Dr. Veale had performed; he has since performed a third.

Re-gifting may extend to other organs, as well. The *American Journal of Transplantation* noted that



Beto Maldonado had received two transplanted kidneys before he died in an automobile accident and his family re-gifted his donated organ.

Photo: Courtesy of UCLA Health

26 livers and three hearts had been re-transplanted during the time frame studied. UCLA performed two liver re-transplants during that period, and UC San Diego, in 2015, re-transplanted a heart. "This clearly offers a viable option for liver and some other organ transplantation — dictated by a variety of clinical factors that will vary from case to case," says Ronald W. Busuttil, MD (RES '77), PhD, executive chair of the UCLA Department of Surgery, William P. Longmire, Jr. Chair in Surgery and founding chief of the Division of Liver and Pancreas Transplantation. "I have learned that in the field of transplantation, anything is possible. Practices that seemed wildly impossible 30 or 40 years ago have evolved into today's standard of care."

RE-GIFTING IS NOT A MAGIC BULLET THAT WOULD DRAMATICALLY REDUCE

the chronic shortage of donor organs, but its potential could have a lifesaving impact for some select patients, Dr. Veale says. "Twenty-to-25 percent of those who receive a donated kidney die while their transplanted kidney is still functional. Re-gifting that viable organ to another patient on the waiting list gives new hope to patients who otherwise may not be considered for a transplant," he says.

Currently, less than 20 percent of the some 100,000 patients on the kidney transplant list in the U.S. receive a kidney each year, while 13 people on the waiting list die each day. Broadening the potential pool with re-gifted organs would not mean a sudden flood of available donor kidneys, however. Like any organ that is being considered as a donation, not all previously donated kidneys are suitable for transplantation. A kidney recipient who, for example, dies from cancer would not be

"I feel freer, and I know I'm on the road to a more fulfilled life. I have a 6-year-old grandbaby who I thought I wouldn't live to see grow up. I think I will be there now."

able to pass on his or her organ. On the other hand, a recipient who dies from a heart attack or stroke or accident still might be a viable re-donor.

There are many other issues that stand between a once-used donated organ and a successful second transplant, notes Richard Formica, MD, a nephrologist at Yale University and secretary of the American Society of Transplantation. Before listing the many potential hurdles, Dr. Formica is quick to add that, "in any given circumstance, when a group — and UCLA is excellent — is able to make use of an organ, it's always a good thing." But the list of impediments to success is lengthy. "It is not a fruit cake that can be re-gifted over and over," he says. A kidney that is considered for retransplantation already has gone through a number of significant insults. In the case of a deceased donor, it begins with the circumstances around the death of that donor. "Maybe that person had varying degrees of comorbidity," Dr. Formica notes. "Maybe they had hypertension or maybe they were older. So right there, the kidney already is suffering some disease while being in that person." Then the kidney is removed and put on ice, "so there's injury there," he says. Then when it is transplanted into a recipient "the restored blood flow rips through that kidney again — ischemia reperfusion injury. So that kidney's already been bashed around a bit." Follow that with exposure to immunosuppression medication, and perhaps some episodes of rejection, Dr. Formica continues, and then a second death and the process starts all over again. "There's already so much injury to the kidney, it's unlikely that most would be usable in a meaningful way by a second recipient," he concludes.

In Boyce's case, however, Dr. Veale felt that the kidney was in excellent condition to be retransplanted. The donor's creatinine levels, which measure kidney function, were within appropriate range, and the organ was functioning well — "The donor was making plenty of urine," Dr. Veale notes. The kidney "had been working very well in the original 17-year-old donor and was functioning perfectly for two years inside a 25-year-old man before he died in a car crash," Dr. Veale says. "The nephrologist and I consulted, and together we felt that there were unrealized life-years left on that kidney, so why discard a valuable organ?"

Because two years had passed between the first and second transplants, there was a good deal of scarring, which would make the procedure

more complex. Dr. Veale addressed that issue by taking iliac arteries, which descend from the lower abdomen, from Beto Maldonado and transplanting them, along with the kidney from the original donor, into Boyce. "I sewed the first donor's kidney, along with the second patient's vessels, and they all kind of work together to help the third person get off dialysis," Dr. Veale says.

KIDNEY DISEASE RAN IN BOYCE'S

FAMILY. Both her mother and grandfather died from it. When her own kidneys failed shortly after she turned 60, she didn't think she had much longer to live. She signed onto the deceased-donor waiting list, on which she would likely remain for years before receiving a kidney — if ever. "I had to resign myself to the fact that I probably would never receive a kidney, that I would spend the rest of my remaining days, which I was thinking wouldn't be long, on dialysis," she says.

Then, last year, "A miracle happened," she says. "I received a call: There was a possibility I was in line for a kidney transplant. I just couldn't believe it. Still, right now, it just seems so surreal."

She met with Dr. Veale and the rest of the UCLA kidney transplant team, and Dr. Veale explained the unusual journey of the hand-me-down kidney they had for her. It also was unusual that, in this case, two years had passed between the first and what would be the second transplant for this particular organ. In most prior re-transplant cases, the interval between first and second transplant was only a matter of hours or days, not years, Dr. Veale notes.

"They gave me the decision as to whether or not I wanted to accept the kidney, and I'm thinking, how can I say no? Nothing ventured, nothing gained, so, OK!" she says.

She considers herself "living proof" that kidney re-gifting can be a viable option. "If someone can have a second chance to receive a kidney that normally would've just been discarded, it would make a big difference," she says.

While Dr. Formica views re-gifting as having limited potential to address the chronic shortage of donor organs, he firmly believes that the procedure sends a significant positive message. "The value, in my mind, is in what it says to the community of people who are signed up as deceased donors, and, more important, to the community of family members of deceased donors. It says to them that the transplant profession takes its fiduciary duty very

"We thought, someone gave my brother that gift, so why not us give that gift to somebody else — why not help another family if we can?"



Dr. Jeffrey Veale (center rear) with (from left) Linda Maldonado, Eva Maldonado and Vertis Boyce. Photo: Courtesy of UCLA Health

seriously, and, therefore, if there is an opportunity to make sure that a person's organs can help someone else, we've got to do it."

IT HAD NOT OCCURRED TO LINDA MALDONADO AND HER FAMILY TO

DONATE her brother's functioning organ to someone else. But when a health care worker brought up the possibility, they recognized that the gift Beto had received from the unknown teenage girl helped to extend his life and the time he had with his loved ones, and so it made sense to give his kidney to someone else who was in need. "We thought, someone gave my brother that gift, so why not us give that gift to somebody else — why not help another family if we can?" she says.

And re-gifting her brother's kidney helps, in its way, to keep Beto Maldonado alive for his family. "A person's never truly gone until he's forgotten, until you don't remember him anymore, and now that we were able to meet his recipient, it's very rewarding for us," Linda Maldonado says. "It's a very good feeling to know that we have somebody that kind of still represents him now, even though we can't see him anymore."

Enrique Rivero has been writing about health care and other topics for more than 25 years as a newspaper reporter and senior media relations officer for UCLA Health.

"A person's never truly gone until he's forgotten, until you don't remember him anymore, and now that we were able to meet his recipient, it's very rewarding for us."



For Dr. Jean-Pierre Hubschman, practicing the Israeli martial art of Krav Maga is about more than perfecting the aggressive fighting style; it has taught him to focus and stay calm under pressure and makes him a better doctor.

Photo: Ann Johansson

Combat Medic

By Robin Keats

Jean-Pierre Hubschman, MD (FEL '08), is a study in contrast. As an associate professor-in-residence at the UCLA Stein Eye Institute, he is a skilled ophthalmic surgeon whose deft fingers can carry out the delicate task of repairing a retinal tear. But as a practitioner of a military-style form of self-defense, he might try to gouge out an attacker's eyes with his thumbs.

The latter, of course, might happen only in practice sessions as he rehearses the moves of Krav Maga — literally contact-combat — a fighting style that developed prior to World War II in Eastern Europe as a form of Jewish self-defense and later was refined and adopted as the martial art of the Israeli military and security forces. For Dr. Hubschman, perfecting this aggressive fighting technique helps, he says, to make him a better doctor.

"Practicing Krav Maga, combining it with yoga classes, has taught me to focus and stay calm under pressure," he explains. "It trains my body and brain to work together to achieve balance and control in the surgery room, where every motion has to be precise and done at the exactly perfect time."

Dr. Hubschman trains with a Krav Maga instructor about four times a week, usually for an hour each session. Together, they work through a series of threatening scenarios: An "attacker" holds a (mock) knife against his throat or presses a (dummy) gun to his head or swings a (real) fist at his jaw. He sweats and grunts as he throws an uppercut with his left hand while shoving his right knee upward in sync to neutralize his attacker's left hand and his right hand rises in defense of his face. Disarming an opponent, taking control of whatever weapon an attacker might be using, makes use of coordination skills that he hones during his workouts. "Anatomy plays a significant role; one needs to know where the body's pressure points lie," he says as he squeezes between the thumb and forefinger of his plasticknife-wielding trainer's hand, forcing the ersatz weapon to drop from his grip.

Dr. Hubschman grew up in Arras in northern France, in a home that was steeped in both science and athletics. His father is an endocrinologist and his mother a pharmacist. He has an older sister who also is a doctor. During his childhood, Dr. Hubschman accompanied his father on rounds, and he was an avid tennis player and skier during his school days. His first ambition was to be a professional tennis player; the practice of

Krav Maga offers him a way to keep athleticism a significant part of his life.

After graduating medical school at the University of Lille, close by his childhood home, Dr. Hubschman married. He and his wife, an interior designer, moved to Marseille, where he completed his residency. He then practiced for a number of years in the Basque city of Biarritz before coming to UCLA in 2007 for a research fellowship. The couple have three children — a daughter in medical school, a son at university and another daughter in high school — and it was the kids who first prompted his pursuit of Krav Maga about 10 years ago.

"I came to Los Angeles, which was a dream of mine," he says. But he was concerned about the potential dangers of the city. "I wanted my kids to learn how to protect themselves, so I enrolled them in Krav Maga classes." He thought learning such skills would help them to be more confident and to be more aware of their surroundings and able to respond in the face of a threatening situation. His daughters eventually lost interest, but Dr. Hubschman became a devotee. "I used to do boxing when I was a kid, and I loved the concept of Krav Maga as a martial art as soon as I discovered it," he says. Now he often works out in tandem with his son. "It has strengthened our bond," Dr. Hubschman says.

Physics, Dr. Hubschman says, is the key to Krav Maga. That, he says, is what comes into play "to overcome an attacker who may well be bigger and stronger. Leverage and bio-mechanics more than level the playing field; their interplay is a huge advantage." For one hour, after his day is done at UCLA, he spars with his trainer. The immersion is so complete that, he says, it clears his mind as well as exercises his body. "You exercise so much, you forget everything. After a day at work, I need the buffer of the workout session before I head home."

His training regimen gives him physical satisfaction; his work with patients gives him intellectual satisfaction. "I love the research, I love the teaching that I am doing, but the clinical activity — meeting the patients, doing surgery, seeing the patient after surgery — is really important to me," he says.

With that, Dr. Hubschman returns to his sparring session, fending off a ferocious volley of punches and kicks. He's winded, yet he seems so energized and focused that his sense of being totally centered is palpable — ready for whatever challenges may come, be they in the practice studio, on the street or in the OR.

Robin Keats is a frequent contributor to U Magazine.





After finishing his day's work at UCLA, Dr. Hubschman hones his Krav Maga moves with his trainer.

Photos: Ann Johansson

Awards & Honors

Dr. Utpal Banerjee,

Distinguished Professor of biological chemistry and co-director of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA, was elected to the National Academy of Sciences.

Dr. Carrie Bearden,

professor of psychiatry and biobehavioral sciences, received the Joel Elkes Research Award from the American College of Neuropsychopharmacology.

Dr. Mario Deng, professor of medicine in the Division of Cardiology, was named by *Forbes* magazine as one of 27 cardiologists recognized as an exemplary physician in the field.

Dr. Arjun Deb, associate professor of medicine

and of molecular, cell and developmental biology, was elected as a member of the American Society for Clinical Investigation.

Dr. Joann Elmore, professor of medicine, was named director of the UCLA National Clinician Scholars Program.

Julie Friedman, MPH, director of the Iris Cantor-UCLA Women's Health Education and Research Center, was appointed to the Los Angeles County Commission for Women.

Dr. Gregg Fonarow (MD '87, RES '90, FEL '93), Eliot Corday Professor of Cardiovascular Medicine and Science, received the 2017 Chairman's Award from the American Heart Association.

Dr. Lara Ray, professor of psychiatry and biobehavioral sciences and director of the

UCLA Addictions Laboratory, received the Eva King-Killam Research Award from the American College of Neuropsychopharmacology.

Dr. Rhonda Voskuhl,

Jack H. Skirball Chair for Multiple Sclerosis Research, received the Berlin Institute of Health's Excellence Award for Sex and Gender Aspects in Health Research

Dr. Karol Watson (RES '92, FEL '97, PhD '98), professor of medicine in the Division of Cardiology and director of the UCLA Women's Cardiovascular Health Center and the UCLA-Barbra Streisand Women's Heart Health Program, was named the Elliot Rapaport Cardiologist of the Year by the California chapter of the American College of Cardiology.

In Memoriam

Dr. Donald G. Mulder, emeritus professor of surgery and former vice chair of the Department of Surgery, died April 4, 2018. He was 94 years old. After graduating from Johns Hopkins School of Medicine and completing two years of residence, Dr. Mulder came to UCLA to complete his surgical training. He joined the UCLA surgical faculty in 1957 and went on to become chief of the Division of Thoracic Surgery, acting chair of the Department of Surgery and vice chair of surgery from 1988 until his retirement in 1991. He conducted early research in the use of cardiopulmonary bypass and devised and tested the first pump oxygenator used at UCLA, Dr. Mulder and his wife endowed a medical scholarship, the Dr. Donald and Barbara Mulder Scholarship Fund.

Dr. Bernice Wenzel, professor emeritus of physiology and psychiatry and biobehavioral sciences and assistant dean for educational research, died on January 31, 2018. She was 96 years old. Dr. Wenzel came to UCLA in 1956 as a junior assistant research anatomist in the anatomy department and then was a postdoctoral fellow in the National Institute of Mental Health training program. She was appointed assistant professor of physiology in 1959. She and her husband endowed the Wendell Jeffrey and Bernice Wenzel Term Chair in Behavioral Neuroscience in the UCLA Department of Psychology.

RAP Stars







Left: Drs. Dayana Carcamo-Molina and Ricardo Molina today practice in Northern California, where she is a gastroenterologist and he an orthopaedic surgeon. Middle and Right: Drs. Carcamo-Molina and Molina during their student days at UCLA.

Photos: (today) Courtesy of Drs. Dayana Carcamo-Molina and Ricardo Molina; (students) Courtesy of the David Geffen School of Medicine at UCLA

In 2001, several University of California medical schools established RAP (Re-Application Program), a program to help students from educationally and economically disadvantaged backgrounds gain admission to medical school after they were not successful in their first attempts. Ricardo Molina, MD '05, and Dayana Carcamo-Molina, MD '08, were participants in one of the first RAP classes. Nearly a decade later, the husband-and-wife physicians have returned to their RAP roots in establishing the Carcamo-Molina Scholarship.

Before completing her undergraduate degree at UC Irvine, Dr. Carcamo-Molina knew that she wanted to pursue a career in medicine. But as a first-generation graduate, she encountered several obstacles along her journey, starting with her transition from high school to college. A lack of guidance, mentorship and financial resources made it difficult for her to hit the benchmarks necessary for acceptance to medical school. "I asked others about applying, and they would say, 'It's really hard to get in,'" she says. But in spite of such discouragement and other setbacks, she was not ready to give up on her dream.

Then a friend of Dr. Carcamo-Molina's who already had been accepted to medical school received a letter regarding the new University of California RAP program. He passed the letter on to her. "He said, 'I already got in. Why don't you call?" she remembers. Dr. Carcamo-Molina took the information and ran with it, applying and being admitted to the first RAP class at UCLA.

Among the criteria for acceptance to RAP, which is an intensive 11-month-long preparatory program of review, mentorship and coursework, is a commitment to practice medicine in an underserved community. "It opened my mind to this community of all these other people that I could relate to," Dr. Carcamo-Molina recalls of the program. "I just needed somebody to tell me I could do it. I would not be a doctor today if it were not for RAP." Dr. Carcamo-Molina's husband, Dr. Ricardo Molina, also recalls a similar experience, "What was so great about the RAP program was that everyone was so different. We all had different reasons why we did not gain admission the first time. For some, a more well-rounded application was needed. For others, they needed more of the science curriculum. The RAP program was able to tailor the curriculum to each and every one of us to improve our individual applications."

First-year UCLA medical student and RAP graduate Eden Patton shares a similar affinity for the program. "Not only did RAP provide the tools and resources necessary to meet the academic requirements for applying to medical school, it also provided mentorship and compassion throughout the entire process," she says. Applying to medical school is very taxing physically, mentally, financially and emotionally, and RAP was there every step of the way."

Not only does the program academically prepare students to reapply to medical school, it also provides weekly mentorship and RAP alumni shadowing opportunities. Monica Perkins, interim director of diversity, inclusion and outreach for the David Geffen School of Medicine at UCLA, says that "it's important for the students in this program to interact with someone like them. RAP gives students the space and opportunity to bond with other students from similar backgrounds and experiences."

Throughout medical school, Drs. Molina and Carcamo-Molina served as RAP student mentors. However, their involvement with the program diminished when they left UCLA to begin her internship (in Kansas City, Kansas) and his residency (in Kansas City, Missouri). "We always told one another that once we were 'there,' we had to help out somehow," Dr. Carcamo-Molina says. When they returned to California and settled into their current practices in Northern California, where she is a gastroenterologist and he an orthopaedic surgeon, they decided to give back by establishing the Carcamo-Molina Scholarship, a fund dedicated to supporting UCLA RAP students in their medical school application process.

Patton is among those students who have benefited from the scholarship. "Because of RAP, I was a very successful applicant when I was ready to apply again to medical school. I was elated to have so many offers to interview but was often unsure how I could afford to pay for the travel to these institutions." The Carcamo-Molina Scholarship was essential to enabling her to complete her application process. "I was able to travel to all interview locations

and make the best decision for me as far as my medical school education. Fortunately for me, I was offered a slot at UCLA."

Reflecting on his own time at UCLA, Dr. Molina explains, "For Dayana and me, it holds a special place in our hearts because that's where we met each other. Now, after almost 17 years of marriage, moving to the Midwest, coming back to California, UCLA is where it all began." Having such a strong personal connection to the medical school, he and Dr. Carcamo-Molina always felt they needed to give back in some way. "We both work with underserved communities in our different specialties," and that, he says, was one of their goals when they chose to become physicians. Helping medical students with similar goals, interests and experiences was a key driver for him and his wife in starting their scholarship fund. "Now that we are both settled in our careers, we think of the scholarship as a very small way to pay back for all of the help we received while in RAP," Dr. Molina says.

Since 2001, the UCLA RAP program has graduated 142 students, and the Carcamo-Molina Scholarship, since its inception, has supported four prospective medical students. Drs. Molina and Carcoma-Molina plan to continue funding their scholarship for years to come. "It's a small way that is easy for us to give back," Dr. Carcoma-Molina says. "We can't forget how we got to where we are now, and we can't forget where we came from."



For more information about UCLA RAP, go to: medschool.ucla.edu/current-ucla-rap



Students in 2017-18 RAP cohort are (from left) Adolfo Hernandez, Rubi Galarza, Guilda Hernandez Garcia, Slesha Thapa, Marisol Solis and Brandon Rogers.

Photo: Courtesy of RAP

The Indelible Mark of the Rosenfeld Family

Eugene and Maxine Rosenfeld have continued their long-standing dedication to UCLA with a \$20 million commitment to health sciences. The funds will strengthen simulation training at UCLA by expanding and revitalizing the Learning Resource Center. Soon to be renamed Eugene & Maxine Rosenfeld Hall, the building at 700 Westwood Plaza is across the street from Ronald Reagan UCLA Medical Center. Renovating this space, which includes the UCLA Simulation Center and will create a new home for the Center for Advanced Surgical and Interventional Technology and a new state-of-the-art facility for standardized patient training, is one of the most urgent priorities of the health enterprise and is critical to attracting and preparing future leaders in health care to serve Los Angeles and communities beyond its borders.

Over the course of more than 50 years, Eugene and Maxine Rosenfeld's philanthropy has made a significant mark on education and on UCLA. Their previous generous gifts established the Rosenfeld Library at the UCLA Anderson School of Management and the Maxine and Eugene Rosenfeld Chair in Medical Education, which is currently held by Dr. Clarence H. Braddock, vice dean for education at the David Geffen School of Medicine at UCLA. Their giving to UCLA College includes more than 270 scholarships for students with disabilities and those in need of financial assistance. They also have given to the Chancellor's Greatest Needs fund, UCLA Alumni Affairs, UCLA Athletics, UCLA School of the Arts and Architecture and UCLA Health Sciences.

"Gene and Maxine have made a profound difference in our ability to achieve our important missions through their generosity, and we are grateful," said Dr. John C. Mazziotta (RES '81, FEL '83), vice chancellor of UCLA Health Sciences and CEO of UCLA Health. "This transformative investment in the continuous training of future and practicing physicians and other health care professionals will prepare them to meet the challenges of modern medicine for decades to come."

The son of Russian immigrants, Eugene Rosenfeld received a scholarship to attend UCLA and was the first in his family to graduate from college. A leading real estate investor, he is sole proprietor of Forest Lane Management, LLC, a major investor in and developer of commercial and residential real estate in the United States and Europe. Maxine Rosenfeld serves on the David Geffen School of Medicine at UCLA Board of Visitors.

Rosenfeld Hall will emerge as one of few destinations in the nation that unites mock



Maxine and Eugene Rosenfeld
Photo: Courtesy of the Rosenfeld Family

clinical experiences, surgical and procedural simulation and interprofessional emergency and hospital team training in a central location under one roof. "This philanthropic partnership will revolutionize UCLA's facilities to maximize knowledge, giving the David Geffen School of Medicine a competitive advantage and leading to greater health care efficiencies and more personalized patient care," said Dr. Kelsey C. Martin, dean of the David Geffen School of Medicine at UCLA and Gerald S. Levey, MD, Endowed Chair.

The activities at Eugene & Maxine Rosenfeld Hall will engage learners with simulation, visualization and problem-based learning

scenarios; enable them to apply scientific principles of health and disease through virtual patients and other digital learning activities; and facilitate collaborations among students, residents, faculty, patients, thought leaders and the community. Rosenfeld Hall's proximity to Ronald Reagan UCLA Medical Center, which includes UCLA Mattel Children's Hospital and the Stewart and Lynda Resnick Neuropsychiatric Hospital at UCLA, makes it an ideal location for physicians, residents, trainees, nurses and clinical researchers.



For more information, contact Judy Land at: 310-206-9995

An Evening Remembering Leonard Nimoy

More than 125 community members came together on November 29, 2017, for a reception and screening of the documentary, *Remembering Leonard Nimoy: His Life, Legacy and Battle with COPD*," at the California NanoSystems Institute at UCLA. The film provides an intimate look into the life and legacy of Leonard Nimoy, who died on February 27, 2015, from complications arising from chronic obstructive pulmonary disease (COPD).

Nimoy and his wife Susan were generous supporters of UCLA, and, following his death,
Susan Nimoy made contributions to the
Division of Pulmonary and Critical Care
Medicine in the David Geffen School
of Medicine at UCLA. Nimoy's daughter
Julie Nimoy and her husband David Knight
continued this spirit of giving by hosting the event, in
partnership with Sunovion Pharmaceuticals, Inc., to raise
funds for the division's COPD research.

Nimoy's family and friends and donors and friends of UCLA enjoyed a reception before the screening. Also in attendance were staff members of the UCLA Division of Pulmonary and Critical Care Medicine, including Dr. Steven Dubinett (RES '84), associate vice chancellor for research and chief of the division. Dr. John Belperio, associate professor of medicine in the UCLA Division of Pulmonary and Critical Care Medicine and Guitiara



(From left): Leonard Nimoy's son Adam Nimoy, actress Terry Farrell, Julie Nimoy and David Knight.

Photo: Steve Resich

Pierpoint Endowed Chair in Interstitial Pulmonary Fibrosis, provided opening remarks. He shared fond memories of Nimoy and spoke about the importance of philanthropy in advancing COPD research.

The documentary celebrates Nimoy's life and his personal journey with COPD and features UCLA's COPD team as instrumental in his care.



For more information, contact Lauren Davis at: 310-267-1844

Inaugural C.G. Jung Symposium Explores Trauma and Healing



(From left): Drs. Nancy Furlotti and Peter Whybrow, presenters Margaret Wilkinson, Dr. Morten Kringelbach and Dr. Ruth Lanius.

Visitors, scholars and the local community of analytical psychology practitioners affiliated with the C. G. Jung Institute of Los Angeles and the Pacifica Graduate Institute, along with UCLA faculty, came together on January 27, 2018, for the inaugural C.G. Jung Endowed Symposium, "Jung, Trauma and Neuroscience: Pathways to Healing." Held at the UCLA Meyer and Renee Luskin Conference Center, the event featured guest speakers and an open discussion on research and analytical psychology.

Dr. Nancy Furlotti, past president of the C.G. Jung Institute of Los Angeles and the Philemon Foundation,

serves as the co-chair — with Dr. Peter Whybrow, Judson Braun Chair in Biological Psychiatry and director of the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA — of the Carl Jung Professorial Endowment in Analytical Psychology board (in the Semel Institute), which she established through the Pettit Foundation in 2013 to celebrate and advance the analytical psychology work of Dr. Jung. Through Dr. Furlotti's philanthropy, the endowment supports scholarship and research and expands Dr. Jung's teachings at the interface of neuroscience, the mind, the body and society.

Dr. Whybrow and Dr. Furlotti welcomed guests and introduced the speakers, who were selected as a tribute to Dr. Jung's lifelong curiosity and wide-ranging scholarship.

In the first presentation, Margaret Wilkinson, from the Society of Analytical Psychology in London, asked the question: "How Do People Change? A Whole-Person Approach to Psychotherapy," which focused on the relevance of contemporary neuroscience, trauma theory and attachment theory in daily treatment sessions and outlined how psychoanalytic therapists can help distressed clients achieve a more confident approach to living.

Dr. Ruth Lanius, director of the post-traumatic stress research unit at the University of Western Ontario, Canada, presented on, "Challenging Moments in the Treatment of Trauma: Towards a Recovered Self." She explored strategies on how to predict and recognize trauma-related alterations in consciousness and how to effectively overcome them, while considering how those changes are represented in the patient's mind, brain and body.

Dr. Morten Kringelbach, director of the Hedonia: Transnational Research Group, based at the universities of Oxford, England, and Aarhus in Denmark, presented, "The Tragic Miracle of Consciousness: Impact of Trauma and Stress on Unbalancing the Brain, Mind and Body," which examined how recent access to whole-brain activity in health and disease can be described using physics-based modeling and allows an understanding of how the brain is making up the mind.

For several decades, the Semel Institute, together with the UCLA Brain Research Institute, has been building a broadly based neuroscience history archive. It houses several collections, including the professional papers of distinguished analyst Dr. Leo Rangell, who served twice as the president of the International Psychoanalytic Association and American Psychoanalytic Association. Through the UCLA Neuroscience History Archives, led by Dr. Joel T. Braslow (FEL '92), psychiatrist, historian and Frances M. O'Malley Administrative Chair in Neuroscience History, the goal is to embrace the history and development of neuropsychiatry, psychological theory and psychoanalytic practice, which has been defined over the past century, and weave it together with the accelerating understanding of neuroscience. The pioneering work of Carl Jung in analytical psychology will play an essential role in this effort, which led to the Jung Endowment being established at UCLA.



For more information, contact Alan Han at: 310-825-1546



Photo: iStock

UCLA Promotes Empowered Aging with TEDxUCLA Salon

TEDxUCLA, an event that brings people together to share a TED-like experience and "ideas worth spreading," hosted a salon at Ronald Reagan UCLA Medical Center on October 26, 2017, on how to achieve health and well-being across the lifespan. Through the efforts of the Board of Advisors of the Stewart and Lynda Resnick Neuropsychiatric Hospital at UCLA, UCLA Residential Life and UCLA Extension, the salon, themed "Empowered Aging," highlighted novel scientific discoveries, as well as valuable lifestyle practices and emotional tools to promote successful aging and longevity.

Dr. Thomas B. Strouse (RES '91), medical director of the Resnick Neuropsychiatric Hospital and Maddie Katz Endowed Chair in Palliative Care Research and Education, moderated the event, UCLA National basketball champion, author and motivational speaker Andrew Hill and Primetime Emmy Award-winner and Oscar-nominated television writer and producer Norman Lear were featured speakers. Other speakers included UCLA researchers Dr. Gary Small (FEL '83), Albert F. Parlow-David H. Solomon Chair for the UCLA Program on Aging and director of the UCLA Longevity Center and the UCLA Division of Geriatric Psychiatry; Dr. Robert Bilder, Michael E. Tennenbaum Family Endowed Chair in Creativity Research in the Department of Psychiatry and Biobehavioral Sciences; and Dr. Linda Ercoli, director of geriatric psychology in the UCLA Division of Geriatric Psychiatry.

Prior to the main event, Dr. Karen Miller, associate clinical professor at the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA, led an interactive training session on methods to improve memory, while Tai Chi and Qi Gong Master Peter Asco demonstrated effective Tai Chi techniques to modulate stress and the nervous system.



For more information, contact Alan Han at: 310-825-1546

NEWS + NOTES friends

UCLA Department of Neurosurgery Welcomes New Chair



Dr. Linda Liau.

Photos: Reed Hutchinson

On Thursday, February 15, 2018, UCLA friends, donors, faculty members and staff gathered together in the Dr. S. Jerome and Judith D. Tamkin Auditorium at Ronald Reagan UCLA Medical Center to celebrate the appointment of Dr. Linda M. Liau (RES '97, FEL '98, PhD '99, MBA) as chair of the Department of Neurosurgery, David Geffen School of Medicine at UCLA.

A welcome was provided by Dr. John C. Mazziotta (RES '81, FEL '83), vice chancellor of UCLA Health Sciences and CEO

of UCLA Health. Featured speakers included Dr. Kelsey C. Martin, dean of the David Geffen School of Medicine at UCLA and Gerald S. Levey, M.D., Endowed Chair, and Dr. Liau. A question-and-answer period followed the presentations.

"The UCLA Department of Neurosurgery has established worldclass clinical programs covering every area of neurosurgery, from brain tumors, epilepsy and movement disorders to spine diseases, brain trauma, neurocritical care and pediatric neurosurgery," Dr. Mazziotta said. "In the research labs, our investigators work tirelessly to understand diseases of the brain and accelerate new treatments for patients. In fact, Linda developed one of the first human applications of a personalized brain tumor vaccine, DCVax-L, which is currently being tested in multicenter clinical trials in the United States and Europe. I am certain that now, as the new chair of the department, Linda will lead the department forward as our neurosurgery faculty members continue achieving medical and scientific discoveries."

Dr. Liau received her MD from Stanford University in 1991, and, after completing her residency and fellowship training in neurosurgery at UCLA, she joined the faculty at the David Geffen School of Medicine at UCLA. In 1999, she received her PhD in neuroscience from UCLA, and her MBA from the UCLA Anderson School of Management in 2016. Board-certified in









Top: (From left) Dr. Christopher C. Giza (RES '94, FEL '96, '00), director of the UCLA Steve Tisch BrainSPORT Program; longtime UCLA supporter Phyllis Easton; and Dr. John Mazziotta. Middle: (From left) UCLA Neurosurgery Board members Jack and Maggy Simon, Sylvia Cheatham and Dr. Mel Cheatham. Bottom Left: UCLA donors Elka Weiner (left) and Shirley Familian. Bottom Right: (From left) UCLA donor Gregory Mueller and UCLA Neurosurgery Board members Loic Bailly and Ted Gagliano.

neurosurgery, Dr. Liau is a tenured professor of neurosurgery and has both an active research laboratory and a busy clinical practice in the field of brain tumors and neurosurgical oncology. Dr. Liau also serves as co-director of the UCLA Brain Tumor Center and as the principal investigator and director of the National Cancer Institute-designated UCLA Brain Cancer SPORE (Specialized Program of Research Excellence) P50 grant. Over the past 20 years, Dr. Liau has been the principal investigator on several National Institutes of Health research grants. Clinically, she developed novel ways to map brain function during awake brain tumor surgeries and is an internationally recognized expert in intraoperative brain mapping for brain tumors.

"It is an honor to chair this prestigious department," Dr. Liau said. "I have a huge drive to prove that things that seem impossible can actually work. When I first started working on brain tumor immunotherapy, everyone told me that you can't mount an immune response in the brain. Now we know that's not true. I'm looking forward to the work we can do in this department that will push even more boundaries."



For more information, contact Karen Colimore at: 310-267-0496

Grey Matters: Unveiling Mysteries of Brain Disease

Brain diseases present one of the greatest challenges to medical science in the 21st century. On Wednesday, March 21, 2018, at an event called "Grey Matters: Unveiling Mysteries of Brain Disease," UCLA physicians and scientists who are experts in brain diseases and conditions, such as autism, depression and Parkinson's and Alzheimer's, discussed breakthroughs in research and what the future holds for treatments.

Held at the Dr. S. Jerome and Judith D. Tamkin Auditorium in Ronald Reagan UCLA Medical Center, Grey Matters was presented by the UCLA Neuroscience Research Theme, a research priority of the David Geffen School of Medicine at UCLA. The Neuroscience Research Theme comprises multidisciplinary scientists and physicians across the UCLA campus who collaborate to accelerate investigations aimed at unlocking the mysteries of the brain.

During the opening reception, faculty members, program directors and department chairs who are part of the Neuroscience Theme were on hand to field questions at "Meet the Experts" stations for autism, depression and Alzheimer's and Parkinson's diseases.

The evening proceeded with a welcome from Dr. Kelsey C. Martin, dean of the David Geffen School of Medicine at UCLA and Gerald S. Levey, MD, Endowed Chair. Dr. Larry Zipursky, Jerome J. Belzer Chair for Medical Research and chair of the UCLA Neuroscience Research Theme, served as the moderator of a panel discussion with three scientists: Dr. Daniel Geschwind (RES '95, FEL '97), senior associate dean and associate vice chancellor for precision health, Gordon and Virginia MacDonald Distinguished Chair in Human Genetics and an expert in the genetic basis of autism; Dr. Ming Guo (RES '01, FEL '02), P. Gene & Elaine Smith Chair in Alzheimer's Disease Research, whose research focus is Parkinson's and Alzheimer's diseases; and Dr. Jonathan Flint, Wilder Chair in Psychiatry and Neuroscience, whose area of expertise is depression.

The panelists discussed how they began doing research in their field, what motivated them to investigate these areas, breakthrough moments in their research programs, what roadblocks they face in studying these diseases, what strategies are in development that will overcome those roadblocks and changes on the horizon for these conditions. A question-and-answer period followed, along with an opportunity for informal discussions.



For more information, contact Karen Colimore at: 310-267-0496



For more information on the UCLA Neuroscience Research Theme visit: giveto.ucla.edu/fund/neuroscience-research









Top: (From left) Panel moderator Dr. Larry Zipursky and panelists Drs. Ming Guo, Jonathan Flint and Daniel Geschwind. **Middle:** (From left) UCLA alumna and donor Renee Luskin, Dr. Kelsey C. Martin, panelists Drs. Jonathan Flint and Daniel Geschwind, and UCLA alumn and donor Meyer Luskin. **Bottom Left:** Dr. Nancy Glaser, psychiatrist and founding chair of the board of advisors of the Stewart and Lynda Resnick Neuropsychiatric Hospital at UCLA (left), and Dr. Zipursky. **Bottom Right:** (From left) Dr. Jeff M. Bronstein (MD, PhD '88, RES '92), who served as one of the Parkinson's disease panelists at the event; Laurie and Steven Gordon, UCLA friends and supporters of the UCLA Depression Grand Challenge; and Dr. Nader Pouratian (PhD '01, MD '03), who served as a Parkinson's disease and depression panelist.

Photos: Reed Hutchinson

Golden Portal Fundraiser Recognizes Tenacity



Top Left: (From left): Dr. Judith C. Gasson, Loic Bailly, Dr. Linda Liau, Ted Gagliano and Johnese Spisso, president of UCLA Health and CEO of the UCLA Hospital System. **Bottom Left:** (From left): UCLA neurosurgery residents Drs. Bayard Wilson, Matthew Sun and Giyarpuram Prashant. **Right:** Tenacious Bravery Award honoree Jamil Newirth (left) and Dr. Linda Liau. Photos: Vince Bucci

More than 250 people gathered at the Griffin Club in Cheviot Hills on January 6, 2018, for the 5th Annual Golden Portal Awards. The fundraiser brunch, hosted by Ted Gagliano, president of post-production at 20th Century Fox Film Corp., and former Fox colleague Loic Bailly, raises money to benefit brain cancer research in the Department of Neurosurgery at the David Geffen School of Medicine at UCLA.

The event joins movies and medicine, and this year's theme of "tenacity" was recognized in characters who exhibited great tenacity

in the movies *Battle of the Sexes*, *Dunkirk*, *The Mountain Between Us* and *Murder on the Orient Express*. Original props and small vignettes of each film were shown, creating an interactive setting for guest photos.

Medical honorees included Jamil Newirth, who received the Tenacious Bravery Award. Diagnosed with a stage-four glioblastoma, a rare and aggressive form of brain cancer, he was the first patient to receive the glioblastoma vaccine from Dr. Linda Liau (RES '97, FEL '98, PhD '99, MBA), director of the UCLA Brain Tumor Program and chair of the UCLA Department of Neurosurgery, and successfully complete the trial.

Dr. Liau presented Dr. Judith C. Gasson, director of the David Geffen School of Medicine Technology Accelerator and former director of the UCLA Jonsson Comprehensive Cancer Center, with the Tenacious Discovery Award for her work to purify a hormone-like substance that increases the speed of bone marrow cell reproduction. This purified substance is used to help prevent infections in cancer patients and allow patients to tolerate more chemotherapy and radiation than had previously been possible.

Guests enjoyed a mini-fundraiser called "Adopt A Resident," with UCLA neurosurgery residents on hand to talk about their research interests with guests and what it is like to be a resident in the UCLA Department of Neurosurgery.

Since its inception in 2012, the Golden Portal Awards have raised more than \$2 million to help UCLA patients receive the most innovative brain cancer therapies available.



For more information, contact Porcha Dodson at: 310-267-9472

Gifts



Eli and Edythe Broad.
Photo: Courtesy of The Eli and Edythe Broad Foundation

The Eli and Edythe Broad Foundation

has awarded \$1.2 million to the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases in the David Geffen School of Medicine at UCLA. Under the direction of Dr. Charalabos "Harry" Pothoulakis, director of basic research in the UCLA Center for Inflammatory Bowel Diseases (IBD) and Eli and Edythe L. Broad Foundation Chair in Inflammatory Bowel Disease Research, the Broad Foundation's gift will capitalize on its decade of support by providing resources for early-career scientists pursuing new discoveries in the understanding and treatment of IBD. This funding is vital to investigators launching their careers as they pursue early-stage IBD research. In the 10 years since its founding, the UCLA Center for IBD has made significant advances in the field and, in collaboration with Dr. Dimitrios Iliopoulos, director of the UCLA Center for Systems Biomedicine, discovered two new drugs to treat IBD.



Dr. Stephen Smale, vice dean of research for the David Geffen School of Medicine at UCLA (left), and Shaobo Cheng.

Photo: Courtesy of Shandong Longlive Bio-Technology Co., Ltd.

Shaobo Cheng, president of
Shandong Longlive Bio-Technology
Co., Ltd., has made a \$500,000
contribution to the UCLA Center for
Human Nutrition. The gift, under the
direction of Dr. Zhaoping Li
(FEL '94), Lynda and Stewart
Resnick Endowed Chair in Human
Nutrition, chief of the Division
of Clinical Nutrition and director
of the Center for Human Nutrition,
will establish The Shandong
Longlive Nutrition Training Fund to
support the center's postdoctoral
training program.

Karyn Jackson set up a charitable remainder trust to benefit the Division of Thoracic Surgery in the David Geffen School of Medicine at UCLA. The gift will establish The Kariel Butner Huff and Bernard "Mac" McMorrow Fund for Lung Research. The fund will support lung and heart research under the administration and direction

of Dr. Jay M. Lee (MD '97), associate professor of surgery and chief of the UCLA Division of Thoracic Surgery.

The Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA has received a gift of \$200,000 from Marlene and Donald Kottler to support innovative research of Lewy body disease, one of the most common causes of dementia in the elderly. This contribution will enable Dr. David Merrill (RES '08, FEL '10) and his colleagues in the UCLA Cognitive Health Clinic, in the UCLA Division of Geriatric Psychiatry, to study, test and identify novel treatments for this debilitating disease and improve the quality of life for patients and their families.

The UCLA Jonsson Cancer Center Foundation has received distributions totaling more than \$3 million from the estate of **Beverly McLaughlin** to support highest priority research at the **UCLA Jonsson Comprehensive** Cancer Center (JCCC). McLaughlin was a steadfast supporter of the JCCC for 15 years. She enjoyed keeping informed of the latest research breakthroughs made at UCLA and their positive impact on cancer patients around the world and their families. Her bequest will help to continue this life-changing work well into the future.

Helene Spiegel and the Thomas Spiegel Family Foundation have contributed \$265,800 to the UCLA Kidney Transplant Program to support postoperative on-campus housing for qualified UCLA kidney transplant patients. Under the direction of Dr. Gabriel Danovitch, medical director of the UCLA Kidney Transplant Program, and Dr. Hans A. Gritsch (RES '91), surgical director of the Kidney Transplant Program, the Spiegel family's gift will provide housing on campus to patients who travel long distances, enabling UCLA to provide optimal postoperative care, which will facilitate patient recovery.

Dr. Jim Truchard has made a gift of \$500,000 to benefit the UCLA Department of Neurology. Funds will be used for translational studies in preclinical models of Alzheimer's disease. Investigations, led by Drs. Greg Cole and Sally Frautschy, will include studying the role of ApoE genes. This contribution also will support the molecular analysis of various projects based on the findings from research on the role that curcumin plays in scientific models. Curcumin is an amyloid-binding molecule that has been shown to block several potential disease pathways in Alzheimer's disease.



For more information, contact Health Sciences Development at: 844-474-4387 **EPILOGUE**

Leo & Me



I SPENT 10 MINUTES WITH LEO IN JANUARY 2017.

He and I are nothing alike, so looking at us you would never guess it was a meaningful encounter. Leo wore a blue bandana and exuded a sense of calm while I wore baggy teal pajamas and was manic. Leo is a golden retriever. I was, at the time, a patient in the Stewart and Lynda Resnick Neuropsychiatric Hospital at UCLA. It has been more than a year now, but I still think about those 10 minutes.

In the weeks before I met Leo, I rang in the New Year at the peak of euphoric mania. My thoughts were messy and fleeting; every idea seemed undeniably brilliant. I was so up that I forgot a basic principle of gravity: What goes up must come down, sometimes destructively. So I was admitted to the hospital, and that is where I spent my 25th birthday.

I was terrified. I feared for my well-being and for my future. But I feared judgment even more. Judgment is inescapable when you are a psychiatric patient. It is not just the cultural stigma or the social estrangement; the act of treating mental illness involves judgment that is not present with other illnesses. Psychiatrists don't study bones and blood pressure; they study behavior and feelings. It weighed me down. It felt somehow personal, like my soul itself was sick. I went to group therapy, and I watched television, but even once-automatic tasks like getting dressed felt too ambitious. I measured time in pudding



cups — chocolate pudding with lunch, maybe vanilla pudding after dinner. Even 10 minutes seemed to take an eternity. I felt exhausted. Ashamed. Alone.

One morning, the patients in my ward were told that a therapy dog from the UCLA People-Animal Connection (PAC) program would be coming to visit us. The news filled the day room with an electric hum of excitement and a question: What does a therapy dog actually do? A woman walked in with an older golden retriever at her side. Her name was Lynne, and her smile was warm and familiar. She introduced us to her dog, and we reacted like fans





in the presence of an A-list celebrity. We started to pet him. His fur was so soft. We rested our hands on his head and back. Suddenly, we were not patients uprooted by our illnesses; we were just a bunch of people petting a dog. He was gentle and surprisingly zen.

He easily tolerated the many hands stroking his coat. His temperament was the exact opposite of dogs I grew up with — rowdy Labradors who would gobble up entire potlucks — and yet I felt instantly at home, as if I'd grown up with this dog as well. I caught the dog's eyes as I petted his head, and I felt calm — more calm than I'd felt in weeks. I didn't have to say anything. I didn't have to explain myself. It was just nice to see a friendly face.

I stayed in the hospital for another week or so.

I got healthy enough to appreciate the structure of its routine. I talked with my doctors about how I'd stay well after my release. I continued going to group therapy, and I continued to measure time in pudding cups. Ten minutes still felt like an eternity. More dogs came to see us, a black lab named Bubbles and a big grey sheepdog named Blizzard. They looked at me without judgment; they didn't pity me or worry about my prognosis. During their visits, 10 minutes passed in an instant.

I thought about the dogs a lot after I was discharged, but I only talked about them in passing. Mentioning cute dogs gave levity to otherwise awkward conversations about the hospital, but it felt silly to elaborate on their impact. Getting discharged came with its own set of anxieties. How would I get my life back on track? How would I make my loved ones proud? How would I stay healthy? Progress was slow, and I didn't want to look back. In November, I pulled my discharge paperwork out of a folder, intending to stuff it in a drawer where I could forget about it. A card fell out. I laughed: It was a dog's business card. I don't have a business card! It pictured

I sent an email to PAC to let Leo's handler Lynne Grande know how much I appreciated her. I was so stunned and excited when I found out I could see Leo again if I wanted. I was also a little nervous. I wasn't sure how to put my gratitude into words.

I saw Leo for a second time in February, just over a year after we met. I doubt he recognized me, but I immediately remembered his kind eyes and his gentle patience. He had the same calming effect on me, but now I possessed a calmness of my own. I realized how far I'd come since my release. I was able to stay with Leo much longer than 10 minutes this time. It still didn't feel like enough.

My gratitude didn't need words because it was clear that receiving thanks or applause has nothing to do with PAC's mission or the work of Lynne and Leo and of the many other volunteers and their dogs. What they do is an act of heroic kindness. My life is one of frequent disruption, of ups and downs, but I find strength in such kindness. Leo has shown me kindness the way only a good dog can, with a wagging tail, a slobbery tongue and a reminder that to stay healthy I must be kind to myself.



Beth May (with PAC volunteer Lynne Grande and Leo) is a playwright, dog lover and mental health advocate

Photos: Ann Johansson





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