CATEGORICAL DENIAL

The distinction between male and female is not always clear, but understanding the biological origins of sexual orientation and gender identity is vital.
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It has been more than 30 years since I came to UCLA, after completing my MD, PhD and internship at Georgetown University. So much has transpired over those decades, both for me personally and for UCLA as an institution.

When I arrived for my residency in neurology, UCLA physicians had reported the very first cases of AIDS. Today, the UCLA AIDS Institute is among the world’s foremost research centers, seeking answers to the prevention and treatment of this illness. In the intervening years, we established our heart- and liver-transplant programs, and now we are recognized as world leaders in organ transplantation. The same can be said of our world-class reputation in imaging — enabling us to actually see the structure and function of the human body in health and disease. We are delivering better health and greater value to more people and deploying high-value innovations through collaborations such as UCLA’s Institute for Innovation. The school of medicine, at just 64 years old, is now among the country’s top-ranking institutions of medical learning. Our faculty have won a Nobel Prize and been elected to the prestigious National Academy of Sciences, among other high honors.

It was in this period of extraordinary growth that I completed my training and joined the faculty, established the Ahmanson-Lovelace Brain Mapping Center and became a department chair. I have been an associate vice chancellor and executive vice dean. All these perspectives have given me a clear view of what a unique and extraordinary institution and community we have here at UCLA.

Now, it is a great honor and privilege to assume the roles of dean of the David Geffen School of Medicine at UCLA, vice chancellor for UCLA Health Sciences and CEO of UCLA Health. My predecessors — Drs. A. Eugene Washington and David T. Feinberg, and those who came before them — have constructed an enduring foundation of excellence and a solid vision to carry forward our missions of teaching, research, patient care and community engagement. Their departure represents major changes for us, but, with the long-standing relationships we have built and our strategic plans, I am confident that this transition will be smooth, and we will move ahead with full momentum.

Change is always paired with opportunity. I look forward to continuing to work with my many colleagues at UCLA and our supporters and alumni throughout the community to continue building the future. People are the bedrock of all great institutions. Our faculty, trainees and staff are the reason for our success, producing the discoveries that transform medicine, teaching the next generations of scientists and physicians and providing the exceptional patient-centered and integrated care for which UCLA has become known. They connect us with our communities — with you, the readers of this publication — near and far.

I am excited and honored to serve in this new role, partnering with you as we continue our path forward to make UCLA the future of medicine.

John C. Mazziotta, MD (RES ’81, FEL ’83), PhD
Vice Chancellor, UCLA Health Sciences
Dean, David Geffen School of Medicine at UCLA
CEO, UCLA Health

Moving Forward
Under new leadership, UCLA’s health enterprise continues its drive to become the future of medicine.
When the Winter 2015 issue of U Magazine arrived at my home, your cover story entitled “What Makes Us Fat” (page 18) caught my eye and piqued my curiosity to read all the articles in the magazine on this subject. I have never had a weight problem myself, even after giving birth to two children. I have been blessed with a good metabolism and good genes while being committed to eating a healthy diet and exercising on a regular basis. That said, we all know someone who faces serious weight problems, and, sadly, some fall into the category of obese. I can only imagine how difficult and overwhelming it must be to think of losing substantial amounts of weight. The many psychological, behavioral and genetic components that come into play make this an extremely difficult and complicated issue. I applaud the scientists, doctors and researchers at UCLA and throughout the country for recognizing this as a dire public-health epidemic and for devoting time, energy and resources to gain more insight into the complexity and causes of obesity. It is encouraging to learn that strides are being made in this area of study. My hope is that people struggling with their weight have the opportunity to read these articles to better understand themselves and become more aware of the serious health risks associated with obesity. It is a difficult, if not impossible, subject to raise with a loved one or friend; therefore, the more information disseminated to the public, the better. Good health is a gift, and everyone is entitled to be the best they can be. At the same time, we, ourselves, are responsible for making it happen. Thank you for bringing such noteworthy and fascinating articles to our attention.

Janis Susskind
Los Angeles, California

It’s not easy! As the wife of Daniel Galorath, featured in “Appetite for Change” (Winter 2015, page 50), I want to thank you for educating people on the hard work and determination it takes to make changes to long-standing lifestyle habits that are required to lose unhealthy weight. For my husband, losing weight was life-changing; actually it changed the lives of our entire family — I have my husband back, and the children have their father back! Physically, the extra weight made him miserable — his feet hurt, his knees hurt. He didn’t even enjoy walking. There is no quick fix when you are overweight, but programs like the UCLA Risk Factor Obesity Program can provide the help, support and education that some people need to make healthy lifestyle changes. Hopefully, articles like this can help educate the public on the dangers of obesity and help provide reassurance that changes can be made to reverse this trend.

Judy Galorath
Rancho Palos Verdes, California

Thank you for the article “Appetite for Change” (Winter 2015). Eating and lifestyle habits are very personal, and the article by Dan Galorath opened a picture window on his victory.

Losing the weight is one thing, but keeping it off for nine years is a triumph. From what I understand, the UCLA Risk Factor Obesity Program is serious about weight loss, serious as a heart attack. Safely living on 920 calories a day requires professional oversight, but I suspect the most significant aspect is the training and emotional support to build a new lifestyle. The signals we get from our bodies about what and how much to eat seem to be all wrong. My take away from the article is that knowledge and disciplined mental exertion coupled with an understanding of habits and motivations coming together in a lifesaving collaboration have changed a life.

Sam Westover
Leesburg, Virginia

I appreciated the diversity of approaches discussed in the article “What Makes Us Fat?” (page 18). The old, simplistic paradigm of eat-less-and-exercise-more, while true in the case of certain individuals, cannot be depended upon to solve the overarching complexities of the obesity epidemic. I found it especially interesting that Dr. George A. Bray’s research, which points toward a high-protein diet as a part of the solution, seems to validate, at least in part, the recommendations of Dr. Robert Atkins, whose Atkins Diet has been alternately applauded and demonized over the past several decades. Even more remarkable were the results of the “Super-size Me”-style experiments performed on the hybrid-mouse diversity panel by Dr. Brian Parks. With body-fat-percentage increases ranging from 0-to-600 percent on the same diet, there can be no question that obesity is not a simple game of calories-in/calories-burned, good fats vs. bad fats or simple vs. complex carbohydrates. The breadth of the research presented in this issue substantiates the belief that the human conditions that contribute to obesity — both biological and psychological — are highly individualized; therefore, solutions to the epidemic need to be equally tailored to the individual. For both humanitarian and financial reasons, the current trend that leads to a majority of the U.S. population being overweight or obese by 2050 must be reversed.

Aostara Kaye
UCLA Transplant Services

Share Your Thoughts with Us

Like us or not, we want to hear from you. Your input is important, so please give us your comments and feedback. Include your name, e-mail address, city and state of residence and, if you are a UCLA medical alum (MD, PhD, Resident and/or Fellow), your degree(s) and graduation year(s). Letters and/or comments may be edited for clarity and/or length. Don’t be a stranger. Write to us, or post your comments on our social-media pages.

Submit letters to:
editormedicine@mednet.ucla.edu
uclahealth.org/getsocial
Same-day appointments now available

When you, or a loved one, need to see your doctor, the last thing you want to do is wait around. At UCLA Health, we want to ensure all of our patients receive the best care in the timeliest manner possible. That’s why we now offer same-day appointments in 27 specialties.

Call us before noon and we’ll schedule you for that day. Call us in the afternoon and we’ll schedule you for the next day. At UCLA, it begins with you. And now it begins today.
Only weeks after giving birth to fraternal twins in 2012, Alysia Padilla-Vaccaro felt something was wrong with one of her daughters, Evangelina. “I was told that it was the stress, or the fear of being a new mom, but I just knew something wasn’t right,” says Padilla-Vaccaro. “Then I was informed that Evangelina had absolutely no immune system, that anything that could make her sick would kill her. It was literally the worst time of my life.”

The baby had a genetic condition called adenosine deaminase-deficient severe combined immunodeficiency, or ADA-deficient SCID. Often called bubble baby disease — children born with SCID must be kept in controlled, isolated environments — the condition can, if untreated, be fatal within the first year of life.

Alysia and her husband Christian brought Evangelina from their home in Corona, California, to UCLA, where she underwent a new gene-therapy treatment developed by Donald Kohn, MD, professor of pediatrics and of microbiology, immunology and molecular genetics and researcher in the UCLA Eli & Edythe Broad Center of Regenerative Medicine & Stem Cell Research. The treatment aims to restore the immune systems of children with ADA-deficient SCID using their own stem cells.

It worked. Evangelina’s new immune system developed without side effects. Her T-cell count began to rise, and her ability to fight off illness and infection grew stronger. Then Dr. Kohn told Alysia and Christian the good news: For the first time, they could hug and kiss their daughter and take Evangelina outside to meet the world. “To finally kiss your child on the lips, to hold her, it’s impossible to describe what a gift that is,” Padilla-Vaccaro says.

Evangelina is among 18 children with SCID who have to date been cured after receiving the therapy in clinical trials at UCLA and the National Institutes of Health. “All of the children with SCID whom I have treated in these stem-cell clinical trials would have died in a year or less without this gene therapy,” Dr. Kohn says. “Instead, they are all thriving with fully functioning immune systems.”

The cells of children with SCID do not create ADA, an enzyme that is critical for producing the healthy white blood cells needed for a normal, fully functioning immune system. About 15 percent of all SCID patients are ADA-deficient. Currently, there are only two treatment options for children with the disease. They can be injected twice a week with ADA — a lifelong process that is expensive and often doesn’t return the immune system to optimal levels. Or they can undergo bone-marrow transplants from siblings, but bone-marrow matches are rare and can result in the patient’s body rejecting the transplanted cells, which then turn against the child.

To develop his therapy, Dr. Kohn and his team removed blood stem cells from the bone marrow of children with ADA-deficient SCID and genetically modified them to correct the defect. Using a virus-delivery system that he developed in the 1990s, Dr. Kohn inserted the corrected gene that produces the missing enzyme into the blood, forming stem cells in the bone marrow. The genetically corrected blood-forming stem cells then produced T-cells capable of fighting infection. With the newly transplanted cells now able to produce the needed enzyme, the research team harnessed the self-renewal potential of stem cells to repopulate the blood stream, and the children developed their own new, fully functioning immune systems.

The researchers’ next step is to seek U.S. Food and Drug Administration approval for the gene therapy, with the hope that all children with ADA-deficient SCID will be able to benefit from the treatment. Their research also lays the groundwork for the gene therapy to be tested for treatment of sickle cell disease; clinical trials are set to begin in 2015.
“We’ve been working for the last five years to take the success we’ve had with this stem-cell gene therapy for SCID to sickle cell,” Dr. Kohn said. “We now have the potential to take the gene that blocks sickling and get it into enough of a patient’s stem cells to block the disease.”

For Padilla-Vaccaro and her husband, what matters most is now seeing both of their children thrive. “I gave birth to my daughter,” Padilla-Vaccaro says. “But Dr. Kohn gave my baby life.”
New UCLA research indicates that lost memories can be restored, a finding that offers some hope for patients in the early stages of Alzheimer’s disease. The new study challenges the prevailing idea that memories are stored in the synapses — the connections between brain cells, or neurons — which are destroyed by Alzheimer’s disease.

“Long-term memory is not stored at the synapse,” says David Glanzman, PhD, professor of integrative biology and physiology and of neurobiology. “That’s a radical idea, but that’s where the evidence leads. The nervous system appears to be able to regenerate lost synaptic connections. If you can restore the synaptic connections, the memory will come back. It won’t be easy, but I believe it’s possible.”

Dr. Glanzman’s research team studies a marine snail called Aplysia to understand the animal’s learning and memory. They are particularly interested in its withdrawal reflex and the sensory and motor neurons that produce it. By giving several mild shocks to the snail’s tail, releasing the hormone serotonin into the central nervous system, they enhanced its withdrawal reflex. The enhanced reflex lasted several days, indicating long-term memory.

Long-term memory is a function of the growth of new synaptic connections caused by the serotonin, Dr. Glanzman says. As long-term memories are formed, the brain creates new proteins that are involved in making new synapses. If that process is disrupted — for example by a concussion or other injury — the proteins may not be synthesized, and long-term memories cannot form.

Dr. Glanzman’s team found the same mechanism held true when studying the snail’s sensory and motor neurons in a Petri dish. When serotonin was added to the dish, new synaptic connections formed between the sensory and motor neurons. But if the addition of serotonin was immediately followed by a substance that inhibits protein synthesis, the new synaptic growth was blocked; long-term memory could not be formed.

The scientists then examined what happens when serotonin was combined with sensory and motor neurons and followed 24 hours later with another pulse of serotonin — which acted as a “reminder” to trigger a new round of memory consolidation — and immediately afterward with the protein inhibitor; the synaptic growth indicating memory was erased.

If the prevailing wisdom were true — that memories are stored in the synapses — the researchers should have found that the lost synapses were the same ones that had grown in response to the serotonin. But that’s not what happened. Instead, they found that some of the new synapses were still present and some were gone, and that some of the original ones were gone, too. Dr. Glanzman says there was no obvious pattern to which synapses stayed and which disappeared, which implied that memory is not stored in synapses.

Dr. Glanzman believes the research could have significant implications for people with Alzheimer’s disease. “As long as the neurons are still alive, the memory will still be there, which means you may be able to recover some of the lost memories in the early stages of Alzheimer’s,” he says.

“Reinstatement of Long-term Memory Following Erasure of Its Behavioral and Synaptic Expression in Aplysia,” eLife, November 17, 2014
Obesity Accelerates Aging of the Liver

Using a recently developed biomarker of aging known as an epigenetic clock, UCLA researchers, working closely with a German team of investigators, have found that obesity greatly accelerates the aging of the liver. This finding could explain the early onset of many age-related diseases, including liver cancer, in people who are obese.

Although it had long been suspected that obesity ages a person faster, it hadn’t been possible to prove the theory until now, says Steve Horvath, PhD, professor of human genetics. The research showed that carrying excessive weight can negatively affect certain tissues in the body. “This is the first study that evaluated the effect of body weight on the biological ages of a variety of human tissues,” Dr. Horvath says. “Given the obesity epidemic in the Western world, the results of this study are highly relevant for public health.”

The epigenetic clock, which Dr. Horvath developed last year, uses a previously unknown time-keeping mechanism in the body to accurately gauge the age of various human organs, tissues and cell types. He and his collaborators focused on a naturally occurring process called methylation, a chemical modification of the DNA molecule. Dr. Horvath used the clock to measure the biological age of several tissues, and it proved accurate in matching biological to chronological age in leaner people. But liver tissues from obese people tended to have a higher biological age than the researchers expected. While obesity doesn’t affect the epigenetic age of fat, muscle or blood tissue, it was found that, on average, the epigenetic age of the liver increased by 3.3 years for every 10 body mass index, or BMI, units.

For example, a woman who is 5-foot 5-inches tall and weighs 140 pounds has a BMI of 23.3. A woman of the same height who weighs 200 pounds has a body mass index of 33.3. The study found that the heavier woman’s liver would be about three years “older” than that of the lighter woman. “This does not sound like a lot, but it is actually a very strong effect,” Horvath said. “For some people, the age acceleration due to obesity will be much more severe, even up to 10 years older.”

Dr. Horvath and his team now want to determine if the premature epigenetic aging of liver tissue in obese people can be prevented, which might help reduce their risk for diseases like diabetes and liver cancer. The researchers plan to work on models that allow them to determine the exact molecular mechanisms behind this aging process — which are not known at this point — in order to find targets for therapy and prevention.

“The increased epigenetic age of liver tissue in obese individuals should provide insights into common liver-related comorbidities of obesity, such as insulin resistance and liver cancer,” the study states. “These findings support the hypothesis that obesity is associated with accelerated aging effects and stresses once more the importance of maintaining a healthy weight.”


Illustration: Courtesy of Dr. Steve Horvath
‘NanoVelcro’ Captures Tumor Cells in Blood

UCLA scientists have led an international group in developing a new method for effectively extracting and analyzing cancer cells circulating in patients’ blood. Capturing these rare cells would allow doctors to detect and analyze the cancer so they could tailor treatment for individual patients.

In his laboratory at the UCLA California NanoSystems Institute, Hsian-Rong Tseng, PhD, professor of molecular and medical pharmacology, used a device he invented to capture circulating tumor cells from blood samples. The device, called the NanoVelcro Chip, is a postage-stamp–sized chip with nanowires that are 1,000 times thinner than a human hair and are coated with antibodies that recognize circulating tumor cells. When 2 milliliters of blood are run through the chip, the tumor cells stick to the Velcro-like nanowires.

Capturing the tumor cells was just part of the battle, though. To analyze them, Dr. Tseng’s team needed to be able to separate the cells from the chip without damaging them.

In earlier experiments with NanoVelcro, the scientists used a technique called laser capture microdissection that was effective in removing individual cells from the chip without damaging them, but the method was time-consuming and labor intensive, and it required highly specialized equipment.

Now, Dr. Tseng and his colleagues have developed a thermoresponsive NanoVelcro purification system, which enables them to raise and lower the temperature of the blood sample to capture (at 37 degrees Celsius) and release (at 4 degrees Celsius) circulating tumor cells at their optimal purity. Polymer brushes on the NanoVelcro’s nanowires respond to the temperature changes by altering their physical properties, allowing them to capture or release the cells. Because it could make extracting the cancer cells much more efficient and cost-effective at a time in a patient’s life when information is needed as quickly as possible, Dr. Tseng says it is conceivable that the new system will replace laser capture microdissection as the standard protocol.

“With our new system, we can control the blood’s temperature — the way coffeehouses would with an espresso machine — to capture and then release the cancer cells in great purity,” says Dr. Tseng, who also is a member of UCLA’s Jonsson Comprehensive Cancer Center. “We combined the thermoresponsive system with downstream mutational analysis to successfully monitor the disease evolution of a lung-cancer patient. This shows the translational value of our device in managing non-small-cell lung cancer with underlying mutations.”

“Nanostructure Embedded Microchips for Detection, Isolation and Characterization of Circulating Tumor Cells,” ACS Nano, August 11, 2014

Robotic Surgery Technique Treats Previously Inoperable Head and Neck Cancer

UCLA researchers have developed a robotic surgical technique to successfully access a previously unreachable area of the head and neck and safely remove tumors that may in the past have been considered inoperable or that required the use of highly invasive surgical techniques in combination with chemo or radiation therapy.

“This is a revolutionary new approach that uses highly advanced technology to reach the deepest areas of the head and neck,” the parapharyngeal space, says Abie H. Mendelsohn, MD ’06 (RES ’11, FEL ’11), director of head and neck robotic surgery. “Patients can now be treated in a manner equivalent to that of a straightforward dental procedure and go back to leading normal, healthy lives in a matter of days with few or no side effects.”

The parapharyngeal space is a pyramid-shaped area that lies near the base of the skull and connects several deep compartments of the head and neck. It is lined with many large blood vessels, nerves and complex facial muscles, making access to the space via traditional surgical options often impossible or highly invasive, such as splitting the patient’s jaw bone or areas close to the voice box.

The technique, transoral robotic surgery (TORS), was approved by the U.S. Food and Drug Administration in 2009. It utilizes the Da Vinci robotic surgical system; the surgeon operates with a three-dimensional, high-definition video camera and robotic arms that can navigate through the small, tight and delicate areas of a person’s mouth without the need for external incisions. A retraction system allows the surgeon to see the entire surgical area at once.

Over the course of the robotic program’s development, Dr. Mendelsohn refined, adapted and advanced the TORS technique to allow surgical instruments and the 3-D imaging
Uncorking Targets for Acne Treatment

It has long been suggested that an occasional glass of vin rouge can be good for our health, but now scientists are learning that an antioxidant derived from grapes and found in wine also can help to clear up one’s complexion. The compound in question, resveratrol, works to inhibit growth of the bacteria that cause acne, UCLA researchers have found.

The team also found that combining resveratrol with a common acne medication, benzoyl peroxide, may enhance the drug’s ability to kill the bacteria and could translate into new treatments. Resveratrol is the same substance that has prompted some doctors to recommend that adults drink red wine for its heart-health properties. The antioxidant stops the formation of free radicals, which cause cell and tissue damage. Benzoyl peroxide, on the other hand, is an oxidant that works by creating free radicals that kill the acne bacteria.

“We initially thought that since the actions of the two compounds are opposing, the combination should cancel each other out, but it didn’t,” says Emma J.M. Taylor, MD (RES ’10, FEL ’12), assistant clinical professor of medicine in the Division of Dermatology. “This study demonstrates that combining an oxidant and an antioxidant may enhance each other and help sustain bacteria-fighting activity over a longer period of time.”

The team grew colonies of the bacteria that cause acne and then added various concentrations of resveratrol and benzoyl peroxide, both alone and together. They found that benzoyl peroxide was able to initially kill the bacteria at all concentration levels, but the effect was short-lived and didn’t last beyond the first 24 hours. Resveratrol didn’t have a strong killing capability, but it inhibited bacterial growth for a longer period of time. Surprisingly, the two compounds together proved the most effective in reducing bacteria counts.

Scientists have long understood how benzoyl peroxide works to treat acne, but less has been known about what makes resveratrol effective. Using a high-powered microscope, the researchers observed that bacteria cells lost some of the structure and definition of their outer membranes, indicating that resveratrol may alter and possibly weaken the structure of the bacteria. The researchers also cultured human skin and blood cells with the two compounds to test their toxicity. They found that benzoyl peroxide was much more toxic than resveratrol, which could help explain what causes skin to become red and irritated when it’s used as a topical treatment in high dose or concentration.

“Resveratrol Demonstrates Antimicrobial Effects against Propionibacterium acnes In Vitro,” Dermatology and Therapy, September 2014

Left: The robotic arm moves directly through the mouth. Top Right: Under guidance of the surgeon, the robotically controlled instruments are able to take out only what is absolutely necessary, removing the tumor but leaving vital organs and tissues untouched. Bottom Right: After removal of the tumor, the throat is stitched up from the interior, with no external skin incisions.

“Transoral Robotic Assisted Resection of the Parapharyngeal Space,” Head and Neck, February 2015

Graphics: Courtesy of the UCLA Department of Head and Neck Surgery
Antidepressant Exposure In Utero Influences Anxiety Behavior Later in Life

Many women are prescribed medications during pregnancy to treat anxiety and depression, but little is known about the effect these drugs have on their children. It is an important question; 5 percent of all babies born in the U.S. — more than 200,000 a year — are exposed to antidepressants in utero.

A UCLA team studying early developmental exposure to two common antidepressants, Prozac and Lexapro, has found that although the two drugs were thought to work the same way — both are serotonin-selective reuptake inhibitors, or SSRIs — they have markedly different long-term effects on developing fetuses. The scientists studied the drugs’ effects in a mouse model that mimicked exposure to the medications during the third trimester of human pregnancy.

The mice exposed to Lexapro (escitalopram) had permanent changes in serotonin neurotransmission and were less anxious as adults than the mice exposed to Prozac (fluoxetine), says Anne M. Andrews, PhD, Richard Metzner Endowed Chair in Clinical Pharmacology at the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA. “This was quite surprising, since these medications belong to the same drug class and are believed to work by the same mechanism,” she says. “The implications of these findings suggest it may be possible to identify specific antidepressants that are safer for pregnant women.”

SSRIs like Prozac and Lexapro block the actions of a type of protein called a serotonin transporter, which removes the neurotransmitter serotonin from the signaling space between neurons. Dr. Andrews and her team also studied mice that had been genetically engineered to have a reduction or absence of serotonin transporters in the brain, so they were able to compare the effects of early exposure to antidepressants with the effects of the mice’s permanent reductions in serotonin transporter function.

In humans, genetic reductions in serotonin transporters are thought to be a risk factor for developing anxiety and mood disorders, particularly when combined with stressful life experiences. In fact, in Dr. Andrews’ study, the genetically engineered mice showed more anxiety as adults. “It might be possible that when mothers are treated for depression or anxiety during pregnancy, certain SSRIs taken by the mother may prevent the children from developing the disorders later in their lives,” Dr. Andrews says.

Based on the findings, Dr. Andrews and her team suspect that early exposure to Lexapro might alter the way serotonin neurons innervate brain regions involved in mood and anxiety behavior — a concept they plan to investigate in the future. They also plan to evaluate other SSRIs such as Paxil and Zoloft. “Current antidepressant therapies are ineffective in treating anxiety and depression in large numbers of patients, and advances in predicting individual responses are hindered by difficulties associated with characterizing complex influences of genetic and environmental factors on serotonergic transmission in humans,” the study states. “Highly controlled animal models, such as those studied here, represent avenues by which to identify factors potentially influencing behavioral domains associated with emotion-related disorders.”

“Antidepressant Exposure In Utero Influences Anxiety Behavior Later in Life,” Neuropsychopharmacology, December 2014
New Regulations Proposed for Off-label Drugs and Devices

The off-label use of drugs and medical devices — using approved remedies in unapproved ways — has long been a part of medicine, providing public-health benefits but also presenting some risks to patients. For the most part, the U.S. Food and Drug Administration (FDA) allows physicians to prescribe drugs and devices off-label in the same way they are prescribed for their approved uses, requiring healthcare providers to make their own decisions about using drugs off-label, often in the face of uncertain evidence.

Researchers from the David Geffen School of Medicine at UCLA and Yale University now have proposed a system combining reporting, testing and enforcement regulations and allowing interim periods of off-label drug prescriptions. Their recommendations would give patients more treatment options, while providing regulators with evidence of the drugs’ safety and efficacy.

Much off-label prescribing of medications and medical devices is beneficial, but without rigorous study, it is difficult to know what works and what doesn’t, says Ryan Abbott, MD, JD, visiting assistant professor of medicine. “Even though a drug or device has been approved for one indication, physicians can prescribe it for other uses as well; it’s been part of medical practice for a long time,” Dr. Abbott says. “Our proposals are important, because there is a tension between providing access to the drugs and devices that could benefit patients in untested ways and the need to prevent harmful uses.” The authors’ proposal is comprised of three elements:

• Improved reporting of off-label use through the disclosure of diagnostic codes in reports to the FDA, in detailing data that pharmaceutical companies obtain on physicians’ prescribing habits, and in reports to the FDA and Medicare/Medicaid reimbursement requests.

• Expansion of post-market testing requirements for off-label use of drugs and medical devices.

• A tiered labeling system for drugs consisting of “red-box” warnings that prohibit certain off-label uses; informed consent from patients receiving prescriptions for off-label use of some drugs that currently carry “black-box” warnings, which identify drugs that pose a significant risk of serious or life-threatening adverse effects; and the creation of a new “grey-box” warning that blocks Medicare Part D and Medicaid reimbursements by the Centers for Medicare and Medicaid Services.

“The improved reporting, testing and enforcement regulation would work together to produce a more layered range of regulatory responses,” the authors write. “The FDA, armed with better information about the extent of off-label use and adverse effects, would be in a better position to require post-market testing and to discourage off-label use with new types of warnings.”

“It’s time for the FDA to impose more serious or life-threatening adverse effects,” says Dr. Abbott. “If we don’t, we run the risk of patients suffering and dying from the use of a drug that should be regulated.”

Iron-overload Disease Causes Bloom of Potentially Deadly Bacteria

Every summer, there are people who sicken, and some die, after eating raw shellfish that is tainted with a bacterium called Vibrio vulnificus or who have an open wound and come in contact with bacteria-laden saltwater. People with a weakened immune system, chronic liver disease or iron-overload disease are most at risk for severe illness.

Researchers at UCLA have figured out why those with iron-overload disease are so vulnerable: The overabundance of iron in their blood and tissue provides prime growth conditions for Vibrio vulnificus. The study also found that minihepcidin, a medicinal form of hepcidin — the iron-regulating hormone that is deficient in people with the disease hereditary hemochromatosis — that lowers iron levels in blood could cure the infection by restricting bacterial growth.

Researchers compared the fatality of Vibrio vulnificus infection in healthy mice with mice that lacked hepcidin, modeling human hereditary hemochromatosis. The results showed that the infection was much more lethal in hepcidin-deficient mice because they could not decrease iron levels in the blood in response to infection. Giving minihepcidin to susceptible hepcidin-deficient mice to lower the amount of iron in the blood prevented infection if the hormone was given before the Vibrio vulnificus was introduced. Additionally, mice given minihepcidin three hours after the bacterium was introduced were cured of any infection.

The next stage of research is to understand why Vibrio vulnificus bacteria become so lethal when iron levels are high.

“Hepcidin-Induced Hypoferremia Is a Critical Host Defense Mechanism against the Siderophilic Bacterium Vibrio vulnificus,” Cell Host and Microbe, January 2015
Members of the community voted, and now the results are in. Five projects will each receive a $20,000 award to advance collaborations between UCLA faculty and community partners that aim to improve the health and the quality of life for residents of Los Angeles and beyond. The Helping U Help the Community competition was sponsored by UCLA Health and the David Geffen School of Medicine at UCLA. A panel of judges identified the first round of finalists, and the final selection was made by voters from throughout the community. The award-winning projects are:

Youth Opportunities for Life Options (YOLO)
YOLO is a comprehensive intervention targeting obesity among inner-city youth. It brings youth, families, schools, academic institutions and community partners together to address the epidemic at the individual level, while advocating for healthier environments.

Summer Urban Health Fellowship
This health-professional pipeline program engages family medicine residents and medical, college and high school students to work to improve health and well-being through community-based research, health fairs, shadowing physicians and forming long-term mentorship relationships.

UCLA TIES for Families
The mission of UCLA TIES for Families is to reduce barriers to successful adoption of children in foster care who have special needs. UCLA TIES provides pre-placement education and state-of-the-art multidisciplinary services and support for these children and their resource parents.

Community Partners in Care (CPIC)
CPIC has demonstrated that partnered depression care across health and community agencies improves the mental-health quality of life for its clients and reduces the risk factors for homelessness and behavioral-health hospitalizations.

UCLA Breathmobile
The Breathmobile is a specialty-based asthma clinic “on wheels,” serving public schools in high-risk, urban communities where barriers to specialty asthma care exist. Missed school days and missed work days due to asthma are minimized by treating children at the school site.

To learn more about the winners and the competition, go to: changemakers.com/ucla
UCLA pediatrics — the right start for kids

What’s the only thing more important than your health? If you’re like most people, it’s your child’s. At UCLA, we understand. We offer complete pediatric care for infants, children and teens at our hospitals and offices throughout the area. It’s the world-renowned care UCLA is known for, right in your neighborhood — for the ones you care about most.

- General Pediatrics
- Allergy/Immunology
- Cardiology
- Craniofacial
- Endocrinology
- Gastroenterology
- Genetics
- Hematology/Oncology
- Nephrology
- Neurology/Neurosurgery
- Ophthalmology
- Orthopaedics
- Otolaryngology (ENT)
- Pulmonology
- Urgent Care
- Urology

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uclahealth.org/mattel uclahealth.org/getsocial
Earlier in his life, John C. Mazziotta, MD (RES ’81, FEL ’83), PhD, thought about becoming an architect. With a keen eye for form and function, he would apply his skills to the construction of great buildings. Instead, he chose medicine. Now, after more than 30 years at UCLA — where he has been chair of the Department of Neurology, an associate vice chancellor and executive vice dean, and founding director of the Ahmanson-Lovelace Brain Mapping Center — that style of visual thinking will serve him well in his new roles as vice chancellor for UCLA Health Sciences, dean of the David Geffen School of Medicine at UCLA and CEO of UCLA Health. “There are many parallels between architecture and construction and what we do in medicine and the building of a large medical enterprise,” he says. “And, on a purely administrative level, it doesn’t hurt to have some interest in the subject when you are managing millions of square feet of space and renovating a giant building. Having some interest and experience about how these things work is helpful.” Dr. Mazziotta spoke with U Magazine editor David Greenwald about his new roles and his aspirations for the future of the medical school and health system.

As vice chancellor, dean and CEO, you bridge the worlds of the health system and the medical school. How does each of these worlds inform the other?

Dr. John C. Mazziotta: We have one health organization with two big pieces to it: the health system — the hospitals, the clinics, the doctors and nurses and support staff — and the David Geffen School of Medicine at UCLA. The overarching goal of our medical enterprise is its academic purpose — to excel in research and education. To achieve that, we have to be excellent in all areas. We have to be good at the business of medicine — which has become very complicated over the years — in order to have the opportunities for our students, residents and fellows to have a place to train and to have the financial resources to support research and education. We have a responsibility to the citizens of California and Los Angeles, and to society in general, to produce great scientists and doctors and to develop new and effective treatments and, ultimately, cures for disorders of the human condition. Having one person over these arenas helps to ensure the correct balance and laser focus on our academic mission.

What are the opportunities that this presents?

Dr. Mazziotta: When there is a significant change in leadership, involving more than one individual, as is the case now, there is the opportunity to actually review the governance structure of the organization. It is like starting with a clean slate and makes it possible to ask questions such as, “What are the functions we actually need?” and “How do we change the structure to become more effective, efficient and responsive?” It has been, perhaps, 20 years since the overall structure of this organization has been examined, so this is a great opportunity to look at it in a new way.
opportunity for us to do just that. Chancellor Gene Block has assembled a task force to do exactly that, to look at the governance of the health sciences — not just medicine, but all of the health-science schools — as well as the health system. Change is healthy. It is good to have a chance to engage in self-examination and to think about whether or not we have the ideal approach to the governance structure. It is an exciting opportunity. When Thomas Watson Jr. was the CEO of IBM, he said, in the early 1960s, "I believe that if an organization is to meet the challenges of a changing world, it must be prepared to change everything about itself, except its beliefs." Like the business-machine and early computer industry of Watson’s time, today’s healthcare environment is undergoing dramatic change, and we need to be prepared to adapt without changing the beliefs that are embedded in our core academic missions.

As you assume your new roles, what are your priorities?

Dr. Mazziotta: I’ve traveled all around the world in my career. What do you think is the first thing people mention when they identify someone as being from UCLA? Basketball. That is the one thing you will find that UCLA is known for pretty much anywhere in the world. So that makes me think we can work toward establishing a John Wooden-like dynasty of excellence in health science. In the future, people will say “basketball and medicine.” I believe that is possible. We should strive to be the best in the world at the things we choose to do. We can’t be the best in the world at everything, but, when we pick a subset of those things, we should pick the ones in which we can be the very best. When I first became chair in neurology, the faculty said, “We want to be the best in research.” So we constructed a strategic plan, and we executed the plan down to the most minute detail, and in a short period of time, we were No. 1 in the United States in research funding, and we maintained that distinction for nine consecutive years. Five years ago, the faculty wanted to enhance philanthropy. So we developed an approach and implemented it. Last year, neurology raised more philanthropic dollars than any other department on campus.
“Change is healthy. It is good to have a chance to engage in self-examination and to think about whether or not we have the ideal approach to the governance structure. It is an exciting opportunity.”

“We want to be the best in the world in specific areas. For the health system, that means being the role model nationally for enabling an academic medical center to truly deliver patient-centered and integrated care to heal humankind one patient at a time.”

**The strategy worked well for the department. How would that be applied to achieve similar results on a broader scale?**

**Dr. Mazziotta:** We have a strategic plan for the health system and the medical school, and we will continue to implement the plan, particularly in this time of change. We have great teams in place. Our previous leadership left their legacy in the people who served with them. Our people are ready and, without question, able to execute on these plans to enhance our momentum. That is in the short term. For the long term, we want to be the best in the world in specific areas. For the health system, that means being the role model nationally for enabling an academic medical center to truly deliver patient-centered and integrated care to heal humankind one patient at a time. Instead of being compartmentalized into the “department of the eyeball” and the “department of the nervous system,” where the patient must go from one center to another to receive care, we want to create a system where whatever is needed for the patient surrounds him or her in a cost-effective way. No one has done this in academic medicine. The first one to do it will be the role model for the rest of the country, perhaps for the rest of the world. I want UCLA to be that role model. For the school of medicine, we have identified six research themes in which we want to particularly invest and excel. These areas are non-departmental; they are thematic: cancer; immunology; cardiovascular medicine; neuroscience; metabolism; and degeneration, regeneration and repair. In education, through the enormous generosity of David Geffen and the David Geffen Medical Scholarships, we attract the brightest medical-student applicants, and they can attend UCLA without financial burdens. Dr. Clarence H. Braddock, our vice dean for education and chief medical-education officer, will continue to restructure our pre- and post-graduate medical training. Our new Bioscience Graduate Program ensures optimal education for biomedical scientists. With this clear focus, we will be the future of medicine.

**What are some examples of how we already excel in the research areas you have identified?**

**Dr. Mazziotta:** There are many, but let’s highlight one: cancer. Within this past year, three new cancer therapies developed at UCLA have been approved by the U.S. Food and Drug Administration. These therapies are the results of years of investigation led by UCLA researchers, and they offer new alternatives for patients with such cancers as melanoma, non-small-cell lung cancer and estrogen-receptor-positive breast cancer. (See “Turning the Tables,” page 26.) I will highlight one other. In the area of cardiovascular research, our scientists have developed an entirely novel therapeutic approach to fighting vascular plaques — a synthetic protein that is designed to mimic HDL, or “good cholesterol.” This therapy was brought to clinical trial, which resulted in...
“There’s a proverb that I like: ‘In the struggle between the river and the rock, the river always wins, not through strength, but through perseverance.’ That was a good lesson for me to learn. I believe every problem has a solution.”

We are speaking in your office in the Center for the Health Sciences building, what used to be the old UCLA Medical Center, before the hospital moved to Ronald Reagan UCLA Medical Center. This building has been undergoing a significant transformation. What is happening here?

Dr. Mazziotta: This has been the single-largest renovation project in the history of the University of California, to transform this building into a space for high-intensity-research laboratories. The building has been seismically retrofitted, and now it is being reassembled into clean, open spaces with all-new infrastructure. That phase is scheduled to be completed this June. The final phase will be outfitting the labs, which will be customized to serve different purposes — there will be a floor devoted to each of the six research themes that I previously mentioned. That phase will take another six-to-nine months. Other areas will be used to facilitate different kinds of partnerships — public-private partnerships. We will partner with established organizations and businesses in the private sector to do joint research projects, possibly startup companies. As a university, we’re not a bottom-line organization that focuses only on the money that can be made from these opportunities. Rather, we will pursue intellectual property that can lead to societal benefit, even if it isn’t necessarily a financial winner. That’s going to be a very exciting activity.

What have been the most pivotal moments in your life and career leading up to where you are now?

Dr. Mazziotta: I will go back to my childhood, growing up outside of New York City. My father was an individual who was a pretty structured guy. And whenever I would want something, for example, “Dad, I need a car,” his response was to say, “If you want it bad enough, you’ll figure out how to get it.” So, I would come up with a proposal for how to accomplish what I wanted. He would look at it and say, “You’re getting there. You’ll figure it out.” I would have to be creative, knowing that I had a certain amount of money, and maybe I could borrow some from him and perhaps earn extra money doing more jobs. And he would just say, “You’ll figure it out.” That taught me perseverance and to try to think in a variety of different ways to solve a problem. Rather than to just say I want something and get it, I had to come at it from five or six different directions. Eventually, I knew, some combination of those different approaches would be successful. There’s a proverb that I like: “In the struggle between the river and the rock, the river always wins, not through strength, but through perseverance.” That was a good lesson for me to learn. I believe every problem has a solution.
“It’s not just black or white” is an adage heard so often that it borders on cliché. It underscores life’s complexities; wherever a gray area exists between two opposing endpoints, it asks us to consider the diverse realities and experiences that make life both more interesting yet harder to comprehend. But that gray area brings with it a certain unease. We are most comfortable when we can neatly categorize our environment. It helps make the world seem more manageable, more familiar.

When it comes to sex and gender, that “gray area” remains murky and mysterious — often undiscussed and even taboo. Pitted against familiar “black-or-white” stereotypes of what it means to be male or female, masculine or feminine, society struggles to accept what lies in between. At UCLA, however, and elsewhere in the small but growing field of sex and gender biology, science is shedding light on this unfamiliar terrain.

People often are unaware of the biological complexity of sex and gender, says Eric Vilain, MD (RES ’98, FEL ’99), PhD, director of the Center for Gender-Based Biology at UCLA, where he studies the genetics of sexual development and sex differences. “People tend to define sex in a binary way — either wholly male or wholly female — based on physical appearance or by which sex chromosomes an individual carries. But while sex and gender may seem dichotomous, there are in reality many intermediates.”

Dr. Vilain says that understanding this complexity is critical, as misperceptions affect the health and civil liberties of those who fall outside perceived societal
norms. “Society has categorical views on what should define sex and gender, but the biological reality is just not there to support that,” he says.

Even at the most basic physical level, Dr. Vilain explains, there is a spectrum between male and female that often goes unrecognized and risks being obscured by stigma. Among his many lines of research, Dr. Vilain studies differences and disorders of sex development (DSDs), an umbrella term that encompasses genetic variation and developmental differences of “intersex” individuals — those whose physical characteristics are not completely male or female but somewhere in between. This includes genetic variations in the complement of sex chromosomes — for example, a mix of XX (female) and XY (male) sex chromosomes in the same body, or an extra or missing sex chromosome (XXY, Klinefelter syndrome, for example, or monosomy X, Turner syndrome). DSDs also include variations in the development of the genitals or the gonads. Individuals can be born with both testicular and ovarian gonadal tissue or with ambiguous genitalia — female genitalia that is enlarged enough to resemble a male penis or exceptionally small male genitalia.

Conditions that affect hormone levels also fall into this category. Examples include androgen insensitivity syndrome, which impairs the male body’s ability to recognize male hormones, and congenital adrenal hyperplasia (CAH), which causes females to produce unusually high levels of male hormones.

A number of genetic factors have been associated with DSDs, and, in recent years, whole-exome sequencing — analysis of the parts of the genetic code that control protein-coding regions of the human genome — has made it possible to diagnose the genetics at play in many intersex cases.

A GROWING BODY OF RESEARCH also is showing how biology influences gender expression, sexual orientation and gender identity — characteristics that can also fall outside of strict, socially defined categories. “Toy-preference tests,” a popular gauge of gender expression, have long shown that boys and girls will typically gravitate to toys that are stereotypically associated with their gender (cars and guns for boys, for instance, or plush toys for girls).

While one might argue that this could be the by-product of a child’s environment — parental influence at play, or an internalization of societal norms — Melissa Hines, PhD, a former UCLA researcher and current professor of psychology at the University of Cambridge, in England, has shown otherwise. In 2008, she demonstrated that monkeys given the toy-preference test exhibit the same sex-based toy preferences as humans — absent societal influence. Dr. Hines later found that
girls with CAH tended to prefer masculine toys compared to their non-CAH sisters, suggesting that hormones heavily influence gender expression.

Sexual orientation (whether one tends to be attracted to men or women) has also been shown to have biological roots. Twin studies and genetic-linkage studies have shown both hereditary patterns in homosexuality (attraction to one’s own sex), as well as genetic associations with specific parts of the genome.

And while gender identity — the sense one has of oneself as being either male or female — has been harder to pinpoint from a biological standpoint, efforts to understand what role biology may play are ongoing.

In the 1960s and ’70s, UCLA psychiatrists Richard Green, MD, JD, and the late Robert Stoller, MD, conducted groundbreaking research on the early expression of significant cross-gender behavior in males, then termed “gender-identity disorder” and now known as “gender dysphoria,” a condition where one identifies with the gender that doesn’t match the sex assigned at birth. The researchers studied boys whose cross-gender behaviors matched those retrospectively reported by adult males seeking sex-change hormones and surgery. They tracked the youths over some 15 years, gaining a better understanding of the course of early cross-gender behaviors. Most of the boys matured into homosexual, not transgender/transsexual, young adults.

Today, cross-gender childhood behaviors that distinguish later transgender/transsexual from homosexual adults remain a research puzzle. Dr. Vilain says that most promising approaches to understanding the development of gender identity include genetics and the study of the environment, including epigenomics — combining the effects of environmental factors on gene expression. His lab recently found a connection between hormone exposure early in life and long-term sexual development. In their study, female mice exposed to high levels of testosterone at birth later exhibited more masculinized gene-expression patterns. Dr. Vilain’s team is looking at the location of these epigenomic changes for clues about which regions of the genome may be influencing gender expression and possibly gender identity.

WHAT THE SONGBIRD TELLS US

Some of Arthur P. Arnold’s scientific epiphanies — pivotal observations on the biological roots of sex differences — came from studying songbirds. In the mid-1970s, Dr. Arnold, who holds a PhD in neurobiology and behavior, was at The Rockefeller University investigating the neurological circuits that control singing behavior in zebra finches, when he and colleagues noticed something: Regions of the brain that controlled singing behavior were much larger in male finches than in their female counterparts. At the time, major sex differences hadn’t been observed in the structure of vertebrate brains, but in the years that followed, consistent differences were uncovered in other major vertebrates, including monkeys, mice and humans.

Now director of the Laboratory of Neuroendocrinology at UCLA’s Brain Research Institute and editor-in-chief of the journal Biology of Sex Differences, Dr. Arnold studies the biology underlying these sex differences. He says that, for decades, the prevailing theory about the source of these differences centered on sex hormones — hormones produced in the male testes and female ovaries. “However, there were eventually problems with the hormone theory,” Dr. Arnold says.

If the theory held true, he explains, then adjusting hormone levels in animals (giving male hormones to females, for instance) should have resulted in corresponding changes in brain structure. That, however, didn’t happen in all cases; other ideas were needed to explain sex differences.

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SQUEAMISHNESS ABOUT SEXUAL BIOLOGY and adherence to long-held gender stereotypes have masked just how diverse sex and gender are across the population. The Intersex Society of North America estimates that as many as one in every 100 people is born intersex, and a 2011 study by the Williams Institute at the UCLA School of Law reported that approximately 9-million Americans identified as lesbian, gay, bisexual or transgender (LGBT).

Despite the prevalence of this variance, we remain uncomfortable with the subject. That discomfort feeds an ignorance that affects patient health. Doctors, patients and caregivers alike need to be aware of the implications of a condition and willing to discuss the patient’s needs. These may be medical. For instance, fertility issues often accompany DSDs, and some of these conditions carry a higher risk of diseases such as breast, ovarian or testicular cancers. Hesitance to discuss the issues could put patients at physical risk or add to the psychological burden of being part of an often-persecuted minority.

Clinical psychiatrist Vernon Rosario, MD (RES ’00, FEL ’02), PhD, counsels intersex patients and their families at the Clark-Morrison Children’s Urological Center at UCLA. He says...
that the accessibility of information and studies about these conditions are helping clinicians and patients and their families make informed choices. For instance, he has witnessed an increasing willingness to accept the ambiguity that accompanies DSDs; parents are less likely to impose a gender on their child, opting to wait several years until their son or daughter expresses a clearer gender behavior. As recently as the 1980s and early 1990s, it was not uncommon to assign a sex at birth and to surgically alter the child to physically conform.

Dr. Rosario, whose PhD is in the history of science, suggests it also is important to put intersex and LGBT health in cultural and historical context; he advises clinicians to be aware of the ethnic, religious and cultural values that patients and families bring with them to the clinic.

"I try to stress to patients that the gender norms they are dealing with are societal constructs and are not something that were determined scientifically. We have these categories, but practitioners need to help patients and parents recognize that everything doesn’t have to all fit together in one particular way that we conventionally call 'normal.' There's a lot of diversity, and that’s okay,” he says.

This is all the more important because pressure to conform comes with a psychological cost — one that the healthcare community has struggled to address. Those who fall outside of sex and gender norms face stigma, hostility and outright violence. Many endure bullying and rejection that can lead to psychological scars or even suicide. A 2014 study from the Williams Institute and the American Foundation for Suicide Prevention found that 41 percent of transgender individuals and 10-to-20 percent of gays and lesbians have attempted suicide. That risk jumps dramatically for those who have faced violence, familial rejection or homelessness.

Suicide attempts also increase among transgender individuals who have been turned away by medical professionals — a surprisingly common experience, experts say, and one that often is noted on LGBT advocacy websites. "I think more times than not, health providers shy away from seeing transgender individuals because they don’t want to offend them, or they don’t really understand

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Scientists speculated that sex chromosomes — the two X chromosomes that make an animal female (XX) or the single X and Y chromosomes found in males (XY) — might be influencing the development of sex differences. However, since sex chromosomes determine if an organism has testes or ovaries (and, therefore, how much of each sex hormone is produced), teasing out whether or not sex chromosomes were independently causing sex differences was a challenge.

Again, a songbird pointed the way.

In the 1990s, Dr. Arnold’s lab came across a rarity: a gynandromorphic zebra finch. Gynandromorphs, most commonly seen in the insect world, are organisms that have both female and male characteristics. This particular bird was genetically male on the right side of its body and genetically female on the left. However, the bird’s hormone levels were the same throughout its body.

If the hormone theory had held true — if hormone levels controlled the development of brain structure — then both sides of the bird’s brain would have been morphologically the same. But the gynandromorph’s male and female sides showed the same structural differences that Dr. Arnold had previously observed in other finches.

"Studying the songbirds told us that the sex chromosomes were playing a larger role in biological sex differences than we realized,” Dr. Arnold says.

Dr. Arnold’s lab now develops animal models that help investigate the roles that sex chromosomes and hormones play in the development of sex differences. It’s an endeavor that has taken on greater urgency in recent years, as evidence has mounted that differences exist in the way males and females experience disease. Researchers have found sex differences in disease susceptibility (autoimmune diseases afflict far more women than men, for instance, while men are more vulnerable to diseases of mental development). Differences have also been noted in the way some diseases progress in men and women, and symptoms and side effects of diseases and treatments can vary depending on the sex of the patient.

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what all the issues are,” says Gail Wyatt, PhD, clinical psychologist and director of the UCLA Sexual Health Program.

It is essential, she says, for clinicians to maintain an open dialogue with transgender patients, to maintain trust and not inadvertently compound the rejection and denial they often face. “Health professionals should encourage the individuals to talk freely about their life as one sex, as well as the process of transitioning to a different sex or gender. A lot of people have never asked these questions,” she says. (In 2014, UCLA Health was recognized as one of the “Leaders in LGBT Healthcare Equality” by the Human Rights Campaign Foundation, which is the educational arm of the country’s largest lesbian, gay, bisexual and transgender civil rights organization.)

Dr. Wyatt says that health professionals should also be aware of transgender-specific issues they might not encounter regularly in their clinic. She and colleagues from Planned Parenthood in New York City recently adapted an intervention program originally designed for abused, HIV-positive women, called “Healing Our Women,” for use with transgender women. The process brought important issues to light about the needs of transgender patients. A session on preventive care, for instance, had to be adapted to address a spectrum of male and female physical characteristics. Since many transgender patients do not follow through with sex-reassignment surgery, either by choice or because of financial or procedural barriers, the individuals in the program represented various stages of transition. Transgender individuals needed to be educated about both male and female anatomy, including tips on sex-specific hygiene and self-exams for breast and testicular cancer. Such topics can be neglected when doctor or patient is hesitant to discuss the transition.

“This is something we need to do more about in the training phase of health professionals’ careers so that they are better equipped to care for transgender men and women,” Dr. Wyatt says.

**WHEN PATIENTS ARE ALIENATED BY HEALTH PROFESSIONALS**, they are denied basic access to care. This not only happens at the doctor-patient level, but also often is systemic. Many insurance carriers won’t cover sex-reassignment surgery. Health professionals lack training about LGBT issues. And in some places, patients are steered toward controversial “treatments” like sex- or gender-conforming surgeries or conversion therapies.

Ironically, one way for LGBT populations to be assured access to care would be to fit neatly into another category — a “suspect class.” Legally speaking, if a population is defined by inborn and immutable characteristics (as with women
or African-Americans), they can be deemed a “suspect class,” with special protections against unfair discrimination.

U.S. courts have thus far skirted the issue, but legal actions over the past half-century have still resulted in civil rights gains. As early as the 1970s, Dr. Green’s pioneering work on gender identity — he has edited or authored several books, including *Transexualism and Sex Reassignment* (Johns Hopkins Press, 1969), *The “Sissy Boy Syndrome” and the Development of Homosexuality* (Yale University Press, 1987) and *Sexual Science and the Law* (Harvard University Press, 1992) — made him a sought-after expert in civil rights cases, including job-discrimination lawsuits and child-custody battles involving lesbian mothers. He later earned a law degree to help lead such cases, where he argued that sexual orientation should be protected against discrimination under the U.S. Constitution.

“The arguments we used were based on a growing body of evidence pointing to sexual orientation as innate and immutable, as well as evidence that efforts to change sexual orientation were rarely successful,” he explains in a telephone conversation from London, England, where he now lives and teaches.

Dr. Green says that scientific evidence on the biological origins of sexual orientation and gender identity, like that which is being amassed at UCLA, will continue to be critical in fighting discrimination, both legally and socially. “When I started my career, homosexuality was considered a mental illness by American psychiatry and a crime in many U.S. states. Now,” Dr. Green says, “the conversation is, ‘Which state will become the next to allow same-sex marriage?’”

**Veronica Meade-Kelly is a science writer at the Broad Institute of MIT and Harvard.**

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In July 2014, Dr. Eric Vilain gave a TEDxUCLA talk on the subject of gender and athletics. To read about this issue, click on the link to this article at: magazine.uclahealth.org

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In 1993, such findings spurred the National Institutes of Health (NIH) to mandate that both men and women be included in all NIH-funded clinical research, a move designed to address persistent underrepresentation of female subjects. In 2014, the NIH went even further and is developing plans to balance the two sexes in funded studies on animal models and cell lines. NIH director Francis Collins and Janine Clayton, director of the NIH’s Office of Research on Women’s Health, explained their reasoning in a May 2014 *Nature* commentary. Disparities in representation in preclinical research, they said, threatened to “[obscure] key sex differences that could guide clinical studies.”

A third of the studies cited by the directors were authored by investigators at UCLA, where researchers have been blazing trails in the study of sex differences in disease. The commentary also singled out one of Dr. Arnold’s animal models for its utility in advancing research in the field.

At UCLA, that model and other approaches have led to groundbreaking findings. Studies led by Karen Reue, PhD, professor of human genetics, have shown that sex chromosomes play a role in weight gain and obesity, and a team led by Mansoureh Eghbali, PhD (FEL ’01), assistant professor of anesthesiology at UCLA, has shown that sex chromosomes make a difference in cardiovascular and pulmonary disease. For instance, they found that having two X chromosomes hampers recovery from heart attacks.

Neurology professor Rhonda Voskuhl, MD, has shown in mice and humans that sex chromosomes and hormones both play roles in multiple sclerosis (MS), a disease that appears four times more often in women but progresses more severely in men. Her findings have spawned two clinical trials: One uses a key estrogen of pregnancy to treat women with MS, and a second uses testosterone to achieve the protective effects of higher male-sex-hormone levels for men with the disease.

The advancement of this work from basic biological findings to clinical trials underscores the ultimate goal of sex-difference research: to use what we’re learning about the mechanisms underlying these differences to develop new treatments for disease. A field that first took its lead from bird brains is now making a difference in human health.

— Veronica Meade-Kelly
Nearly 45 years after the launch of the War on Cancer, immunotherapies are revolutionizing our approach to treating this dreaded disease.

In the spring of 2012, Tom Stutz was a man without a future. Just getting through the day took all of his energy and determination. The retired attorney from Sherman Oaks, California, had been diagnosed with metastatic melanoma the previous year. He had tumors in his lung, liver, spine and shoulder. He could no longer walk. His wife Sophia had just died after a long illness, and Stutz, at age 71, was depressed and hopeless. Struggling to breathe, nighttime became almost unbearable. “I had to sleep sitting up and could only get cat naps,” Stutz recalls. “I used to dread the night.”

But in the midst of this misery, Stutz had the good fortune to meet with Antoni Ribas, MD (FEL ’98, ’01), PhD, professor of medicine, surgery and pharmacology at UCLA, and secure one of the last spots in a Phase 1 clinical trial Dr. Ribas was conducting on an experimental medication for advanced melanoma. The study was designed to assess the drug’s safety at various doses and look for some signs of effectiveness. Stutz, wheelchair bound and tethered to an oxygen tank, had tried every other available therapy, but the disease had progressed relentlessly. “I figured this was my last shot,” he recalls. “I wasn’t optimistic.”

Today, Stutz is in excellent health. He travels, plays tennis and cycles. What’s remarkable is that he’s not an exception — one of those rare cases of someone who survives seemingly terminal cancer for reasons unknown. Rather, Stutz is among a growing number of cancer patients who are being snatched from the precipice by novel immunotherapy treatments. Immunotherapy is the catchall word for treatments that enlist the body’s own immune system to fight cancer. Unlike chemotherapy, which poisons cancer cells but also can damage healthy tissue, immunotherapies provoke the body into doing to cancer what it does naturally to viruses, bacteria and other foreign invaders: attack and destroy.

Because of its stunning success, the medication that Stutz received, pembrolizumab, received “fast-track” approval by the U.S. Food and Drug Administration (FDA) last fall and now is prescribed under the brand name Keytruda. It’s among the first in a new class of immunotherapies known as checkpoint inhibitors. Another drug, nivolumab (Opdivo), was approved by the FDA in December 2014 for metastatic melanoma and, two months later, for patients with metastatic squamous non-small-cell lung cancer. Several other drugs with similar mechanisms are in the pharmaceutical pipeline.
T-lymphocytes, or T cells (round), play an important role in the body’s immune system, tracking down and destroying foreign bodies and infected cells. Now, the evolving science of immunotherapy seeks to unleash the power of T cells against cancer.

Image: Stefan Diller/Science Photo Library
Pembrolizumab and nivolumab represent a jaw-dropping burst of progress in the field of cancer immunotherapy. Today, many experts believe immunotherapies will emerge as primary treatment modalities for many types of cancer, perhaps, in some cases, even relegating chemotherapy to the sidelines. “I’ve been working in the field of immunotherapy for lung cancer for 25 years,” says Steven M. Dubinett, MD, chief of the Division of Pulmonary and Critical-care Medicine and director of UCLA’s Jonsson Comprehensive Cancer Center’s lung-cancer-research program. “I think we had all hoped that there would come a point where our knowledge about human immunotherapy would be sufficient to overcome critical obstacles. That has come to pass, and, although many questions remain to be addressed in further research, optimism is certainly warranted.”

The checkpoint inhibitors “have been one of the biggest stories in cancer in the last 10 years, and they are the biggest advance in cancer immunotherapy ever,” adds John Timmerman, MD, associate professor of medicine in the Division of Hematology/Oncology.

UNTIL RECENTLY, SCIENTISTS DEBATED whether or not the finely balanced immune system could be harnessed to kill cancer. For many years, James P. Allison, PhD, now chair of immunology at the University of Texas MD Anderson Cancer Center in Houston, studied why the immune system, so efficient at protecting the body from microbes and chemicals, was no match for cancer. “Immunotherapy has gone through a lot of peaks and valleys,” he says. “In the 1960s, the notion was that the reason we had an immune system was to kill early cancers arising in our bodies. But then, people began to doubt that.”

In the 1980s, the hope that immunotherapies could conquer cancer rose with the advent of two drugs: interferon and interleukin-2. Both are cytokines, proteins secreted by immune cells that communicate and coordinate the immune response. During a normal immune response, cells called lymphocytes are summoned into action; B-cell lymphocytes manufacture antibodies, proteins that bind to the surface of the foreign invader, while T-cell lymphocytes attack the target.

But excitement over those inaugural immunotherapies faded. A decade’s worth of studies showed the drugs benefited fewer than 10 percent of people with kidney cancer and melanoma and had little impact on other cancers. Another immunotherapy approach — cancer vaccines to propel the immune system into action — also did not pan out at that time. Dr. Allison remembers the pall over the field. After he submitted a research paper on cancer immunotherapy to a
The problem was that we were trying to turn on that the AT FIRST, TOM STUTZ CONCLUDED

This T-cell braking mechanism serves an important (Yervoy), which was approved in 2011 for metastatic (PD-L1), that applies a brake to the body’s immune 22 percent of patients. Pembrolizumab works without being out of breath,” and he had to undergo realigned afterward was that we needed to take off the melanoma. The drug, which binds to the CTLA-4 response. Pembrolizumab, a PD-1 inhibitor, disables myosin activity and a lot of side effects,” Dr. Ribas explains.

Dr. Allison’s work ultimately led to the first immune checkpoint inhibitor, ipilimumab (Yervoy), which was approved in 2011 for metastatic melanoma. The drug, which binds to the CTLA-4 molecule on the surface of T cells, helps about 22 percent of patients. Pembrolizumab works on a different tumor-defense mechanism, called programmed cell death 1 (PD-1). Cancer hides by expressing a protein, programmed death-ligand (PD-L1), that applies a brake to the body’s immune response. Pembrolizumab, a PD-1 inhibitor, disables this brake, allowing T cells to attack cancer cells.

When he launched his clinical trial, Dr. Ribas was hopeful the drug would work in 10-to-15 percent of patients with advanced melanoma.

Then, one night, one of his fitful cat naps stretched into a blissful 16 hours of uninterrupted sleep. Gradually, he found he could breathe easier. He took small walks outside his house, adding a few more steps every day. By June, he no longer needed oxygen therapy. In July, a scan showed the two main tumors in his liver and lung had shrunk by half.

Stutz continues to receive pembrolizumab infusions every three weeks. There is a shadowy spot in his lung that may be a small tumor, the remnants of a tumor or scar tissue. He doesn’t really care what it is; he’s alive and thriving, spending precious time with his children and grandchildren.

“In the beginning, I was stunned. I would say to myself: I can’t believe I’m still here,” he says. “The wonderful thing about this treatment, besides the result, is you can live pretty much a normal life. The side effects are minimal.”

Dr. Ribas’s clinical-trial data, published in the July 2013 issue of the New England Journal of Medicine, showed that one-third of patients with advanced melanoma experienced long-term responses to pembrolizumab. Another third had some tumor shrinkage, but the disease eventually progressed. Only 12 percent of patients had a significant side effect, such as fatigue or joint pain.

“I honestly didn’t think it would work this well,” Dr. Ribas says. “When we started the clinical trial, sometimes we tried to select patients who we thought would be more likely to benefit. Then we started giving it to patients with more aggressive metastatic melanoma, even patients who were at the limit of eligibility for the clinical trial, where a day or two more and they wouldn’t have been eligible. Some of those patients responded. Those were patients where, if we didn’t do anything, life expectancy would have been weeks.”

The therapy also appears to attack cancers that have spread throughout the body, including the brain. “If you get an immunotherapy that works really well, it can work all over,” Dr. Ribas notes.

Now, similarly stunning results are being seen with other checkpoint inhibitors and in other types of cancer. Thirty-two percent of melanoma patients receiving nivolumab experienced a reduction in tumor size, and more than one-third had an effect that lasted for more than six months. In people with advanced squamous non-small-cell lung

scientific journal, a peer reviewer wrote on the paper: “Immunotherapy has never worked, will never work and we shouldn’t waste pages in these precious journals on it,” he recalls.

In 1997, however, the FDA approved a drug called rituxumab for patients with non-Hodgkin’s lymphoma. The drug was an antibody that targeted a specific protein on the surface of B cells and unleashed the immune system to fight some types of cancer. Meanwhile, Dr. Allison and another group independently showed that a molecule on the surface of T cells performed like a brake, or checkpoint, on the immune system’s attack cells. This T-cell braking mechanism serves an important function by preventing the immune system from becoming overactive, attacking healthy tissue. But it also allows cancer to thrive. Dr. Allison’s next insight was a game-changer: Could blocking the checkpoint free the immune system to attack cancer?

“When interferon and interleukin-2 were approved for the treatment of melanoma, but they had low activity and a lot of side effects,” Dr. Ribas explains. “The problem was that we were trying to turn on the immune system against the cancer. What we realized afterward was that we needed to take off the brakes instead of trying to turn it on.”

Dr. Allison’s work ultimately led to the first immune checkpoint inhibitor, ipilimumab (Yervoy), which was approved in 2011 for metastatic melanoma. The drug, which binds to the CTLA-4 molecule on the surface of T cells, helps about 22 percent of patients. Pembrolizumab works on a different tumor-defense mechanism, called programmed cell death 1 (PD-1). Cancer hides by expressing a protein, programmed death-ligand (PD-L1), that applies a brake to the body’s immune response. Pembrolizumab, a PD-1 inhibitor, disables this brake, allowing T cells to attack cancer cells.

When he launched his clinical trial, Dr. Ribas was hopeful the drug would work in 10-to-15 percent of patients with advanced melanoma.

AT FIRST, TOM STUTZ CONCLUDED that the infusions of pembrolizumab he received every three weeks at UCLA weren’t working. “I got quite a lot worse,” he says. “I couldn’t turn over in bed without being out of breath,” and he had to undergo a procedure to drain fluid from his lungs.

But given this huge, quantum leap in immunotherapy ... we feel we can get away from chemotherapy for some forms of cancer.”

Top: Dr. Steven M. Dubinett: “I’ve been working in the field of immunotherapy for lung cancer for 25 years. I think we had all hoped that there would come a point where our knowledge about human immunotherapy would be sufficient to overcome critical obstacles. That has come to pass.”

Bottom: Dr. John Timmerman: “For the majority of common cancers ... chemotherapy is still very important. We’re not ready to replace the conventional treatments yet. But given this huge, quantum leap in immunotherapy ... we feel we can get away from chemotherapy for some forms of cancer.”
cancer, nivolumab produced tumor shrinkage or the complete disappearance of the tumor in 15 percent of patients, many with long-lasting results.

And, in a highly anticipated presentation in April at the American Association for Cancer Research annual meeting in Philadelphia, Pennsylvania, UCLA researchers reported evidence of positive responses to pembrolizumab in about 20 percent of patients with non-small-cell lung cancer. The study — which will be published in the New England Journal of Medicine — also demonstrated the potential for measuring the expression of PD-L1 to help select patients who are most likely to respond to the therapy; nearly half of patients with high-level staining for PD-L1, a target of PD-1, responded to the drug.

“These results have the potential to very substantively change the way that lung cancer is treated,” says Edward B. Garon, MD (FEL ’06), director of the thoracic oncology program at UCLA, who presented the data. “The prolonged duration of the response with this class of drugs has been particularly appealing to patients. It’s quite exciting.”

THERE ALSO IS EVIDENCE that checkpoint inhibitors are most effective in tumors with a high number of genetic mutations, such as lung cancer in cigarette smokers, says Dr. Garon, who also co-authored a study published recently in the journal Science on tumor mutations and immunotherapy.

Melanoma also is a cancer with many mutations. “Melanoma has the highest instance of DNA aberrations of any cancer,” Dr. Ribas says. Usually, if patients have a lot of alterations in the cancer, that’s bad. But, for this therapy, a lot of gene alterations may allow the immune system to differentiate normal from disease.”

The question of how well the checkpoint inhibitors may work on other types of cancers, including those with fewer mutations, has emerged as one of the most pressing issues to resolve. Clinical trials are underway around the world to assess the drugs on a number of cancers. In January 2015, Dr. Timmerman and his colleagues published data in the New England Journal of Medicine showing a whopping 87 percent of patients with Hodgkin’s lymphoma responded to nivolumab. Moreover, at a December meeting of the American Society for Hematology, the group reported a response rate between 30 and 40 percent in patients with non-Hodgkin’s lymphoma.

Some cancers, such as colon cancer, appear less responsive to immunotherapies, but researchers are studying those cancers to understand the less-robust response and how potential barriers might be circumnavigated. “We’re still trying to understand why some of these cancers are resistant,” Dr. Timmerman says. “There are plenty of theories. These cancers could be using a different set of checkpoints.” About a half-dozen other checkpoints are being explored, he adds.

Researchers also are examining whether or not checkpoint inhibitors should be used for earlier-stage cancers. Dr. Dubinett is exploring how the immune system responds to early abnormalities in the lung.

“The assumption is that as the tumor moves from premalignancy to cancer, the immune system has missed the ability to kill the cancer,” he explains, adding that the key “is to learn when to intervene.”

Work also is underway to evaluate immunotherapies used in combination with drugs that target specific mutations, such as the BRAF mutation that allows cancer to become resistant to drugs. Dr. Ribas and his colleagues have already demonstrated the success of such combinations in patients with advanced melanoma.

MANY OTHER HIGHLY CREATIVE IMMUNOTHERAPIES are under investigation. For example, only about half of lung-cancer patients have lymphocytes in the tumor. That’s a problem because lymphocytes must be present for drugs like the checkpoint inhibitors to work. To get around that obstacle, Dr. Dubinett and his team are injecting molecules called chemokines into tumors. Chemokines are signaling molecules; they attract immune-system cells to the site of infected or damaged tissue. In this case, the chemokines shepherd T cells and dendritic cells (cells that also help induce an immune response) into the tumor.

In a Phase 1 trial in patients with advanced lung cancer, Dr. Dubinett and his UCLA colleague, Jay M. Lee, MD ’97, chief of thoracic surgery, injected a chemokine called CCL21, a protein that is typically found in human lymph nodes, into the tumor via a bronchoscope or a needle through the chest wall.
The protein was able to draw lymphocytes to the tumor. The therapy was safe, and some patients’ tumors stabilized. “The therapy is intended to activate the immune response not just at the local site but is designed to work systemically — all over the body,” Dr. Dubinett says. “Thus the therapy is designed to treat metastatic disease as well as the local tumor.”

Meanwhile, Dr. Dubinett is collaborating with Leonard Rome, PhD, associate director of UCLA’s California NanoSystems Institute, on a treatment that combines CCL21 with nanotechnology drug delivery. The drug is packaged in biological particles called vaults, which were discovered by Dr. Rome in the 1980s. The CCL21-vaults are injected into the tumor to allow the slow release of the chemokines. Last fall, the researchers received a $1-million grant from the National Cancer Institute's Small Business Innovation Research Program to advance the project.

The therapy may be most effective when used with a drug like pembrolizumab, Dr. Dubinett says. “We think that by getting lymphocytes into the tumor, more patients will have a durable response.”

Researchers also are studying immunotherapies that target specific tumor targets. Madhuri Wadehra, PhD, assistant professor of pathology and laboratory medicine, is studying a protein called EMP2 that is present in a number of cancers affecting women, especially breast cancer, with the goal of making an antibody to target that protein. “What the PD-1 story tells us is we can use a specific subset of the immune system to target cancer,” Dr. Wadehra explains. “We don’t want to elicit a massive inflammatory environment. We need to just tap into the part of the immune system we need to use.”

Other promising immunotherapies include adoptive cell therapies in which cells taken from a patient are engineered in the lab to recognize and attack tumors and then returned to the patient. In another variation, called chimeric antigen receptors therapy (CARs T-cell therapy), T cells taken from a patient’s blood are genetically engineered to produce receptors on their surfaces. CARs receptors allow T cells to recognize cancer and destroy it. In a study at Children’s Hospital of Philadelphia, CARs T-cell therapy eradicated leukemia in 27 of 30 patients treated, according to a study published in October in the New England Journal of Medicine. Dr. Ribas is among the UCLA researchers who are working on adoptive cell therapies.

It may not be long before immunotherapies begin to take the place of chemotherapy in some cases, Dr. Timmerman says. For lymphoma, care is turning toward targeted therapies in combination with checkpoint inhibitors. “Those treatments are looking to be just as effective as traditional chemotherapy,” he says. “For the majority of common cancers, such as breast and gastrointestinal cancers, chemotherapy is still very important. We’re not ready to replace the conventional treatments yet. But given this huge, quantum leap in immunotherapy, which continues to move at a faster and faster pace, we feel we can get away from chemotherapy for some forms of cancer.”

Immunotherapy is emerging as the “fourth pillar” of cancer treatment, joining surgery, radiation and chemotherapy, says Dr. Ribas. “I don’t think there’s much research going on in the development of new chemotherapy drugs — which are nonspecific toxins — without knowing why they work or not,” he says “The majority of cancer drugs in development now are based on understanding specific targets.”

That means that cancer patients today, perhaps more than ever before, need to ask questions about emerging treatments, even therapies that are still in clinical trials. “In many communities, doctors are not aware of how fast this is moving,” Dr. Timmerman notes. “Patients need to be aggressive and be aware that some new medications are available.”

Shari Roan wrote about healthcare and medicine as a staff writer for the Los Angeles Times.

“Mutational Landscape Determines Sensitivity to PD-1 Blockade in Non-small-cell Lung Cancer,” Science, March 2015


“Anti-programmed-death-receptor-1 Treatment with Pembrolizumab in Ipilimumab-refractory Advanced Melanoma: a Randomised Dose-comparison Cohort of a Phase 1 Trial,” The Lancet, September 20, 2014


WHY I GIVE

As president of The Saul and Joyce Brandman Foundation, Joyce Brandman has provided vital support to hundreds of medical, educational and Jewish communal causes and organizations. She and her late husband Saul provided long-standing support for the UCLA Division of Pulmonary and Critical Care Medicine.

“I’ve been impressed with Dr. Steven Dubinett and his innovative approach to research. I appreciate how he keeps me updated on all the latest developments, and he frequently invites me to visit his facility, allowing me to ask questions and see how my money is being spent.”

– Joyce Brandman
By Lyndon Stambler • Illustration by Otto Steininger

Our frenetic, wired lives keep us on the edge and, in some cases, make us crazy. But the prescription for relief is clear: take a deep breath, turn off the cell phone and slow down.
A mericans are overwhelmed. Living in chronic-stress mode, our days running 24/7, our senses assaulted by the pinging of smart phones and our attention diverted by relentless tweets, texts and emails, we are in constant quest of all that is new and different and exciting. All this more, better, bigger, faster, sooner, now, now, NOOOWWW is driving us to the edge. Our bodies surge with adrenalin, hearts pumping, muscles twitching. That served us well when we were hunters and gatherers, but no longer. The constant strain of our modern lives leads to anxiety, depression, insomnia, obesity and a host of other illnesses.

Peter C. Whybrow, MD, executive chair of the Department of Psychiatry and Biobehavioral Sciences and director of the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA, has a high-stress job, and yet he keeps his smart phone switched off in his briefcase. “Every time your phone rings, somebody else is providing you with a priority that wasn’t your own before the phone rang,” he explains. We all want to control our environment. When we lose our capacity to control our future as we see it, stress begins to mount.”
Most of us live in a mindless haze of non-stop activity. But UCLA researchers have studied the impact of stress and are designing ways to cope. “Universities are supposed to be the places where you learn not only physics, but also how to live,” Dr. Whybrow says.

Philanthropists Jane and Terry Semel, whose gift in 2004 endowed the Jane and Terry Semel Institute of Neuroscience and Human Behavior at UCLA, also provided the support in 2011 to create the healthiest campus in the nation. The Healthy Campus Initiative (HCI) seeks to support the 85,000 students, faculty and staff at UCLA to eat healthy (Eat Well), exercise (Move Well), improve mental health (Mind Well), live in a healthier environment (Be Well) and thrive in a smoke-free campus (Breathe Well). Integrating the five facets can reduce stress and foster healthy lifestyles, says Assistant Vice Provost Wendy Slusser, MD, who directs HCI. “It’s caught on like wildfire. People want to eat healthfully. They want to have a balanced, high-quality life, especially the youth on campus. It’s leading to a whole culture of wellness.”

The British-born Dr. Whybrow, who has lived in the U.S. for 40 years, is a Tocqueville-esque observer of American society. In his book American Mania: When More Is Not Enough (W.W. Norton & Co., 2005), he observes Americans’ stress-inducing drive for material wealth. Now he posits a remedy for that mania in The Well-Tuned Brain: Neuroscience and the Life Well-Lived (W.W. Norton & Co., 2015). The remedy involves re-engineering society to address the problems confronting Americans. HCI created a living lab at UCLA for his ideas. The hope is that people will take the lessons beyond the campus and promote healthy living in their families and the workplace. The Semels and UCLA Chancellor Gene D. Block, whose office now oversees HCI, see the program as a beacon for others. “Whether it’s about diet, exercise, transportation or sustainability, our goal is to lever age our unique strengths in the health sciences and as a leading research university to encourage healthier outcomes for individuals and for society as a whole,” Chancellor Block says.

HCI has already spread beyond UCLA. In July 2014, University of California President Janet Napolitano, inspired by the Eat Well program, created the UC Global Food Initiative, creating programs and projects throughout the UCs.

**THE ABILITY TO MANAGE STRESS** and develop greater powers of resilience will be “the most important cornerstone of advancing human health in general over the next 50-to-100 years,” says Robert Bilder, PhD, Tennenbaum Professor of Psychiatry and director of Mind Well.

Technology and social media have “led to a net decrease in well-being,” Dr. Bilder says, disrupting the balance between our willed intentions and responsiveness to external stimuli. “As we see people walking around the streets with their cell phones, they’re constantly responding to signals that they’re getting from others: e-mails, text messages, phone messages, tweets. That’s hijacking people’s behavior and making them responsive to these devices in a way that prevents them from implementing their own willed intentions. It’s a cause of a lot of stress because people are now acting based on external signals that they consider valuable in part because of their social meaningfulness.”

Dr. Bilder would prefer that people use technology to reduce stress or bolster creativity. “UCLA is well-poised to do exactly this and to provide people with the measurement tools that they need to be able to understand our own stressors and the life tools they need to manage our stressors,” he says.

UCLA cognitive researchers, who have studied how people learn, might provide a key for managing those stressors. Their research may help students learn more efficiently. The Mind Well program also is developing a co-curriculum at UCLA to emphasize life skills, recognizing students for studying subjects like mindfulness in addition to physics and chemistry. And the Semels made another gift in Fall 2014 to help create a food-studies minor for undergraduates and a food-studies certificate program for graduate students, recognizing the importance of nutrition to well-being.

**UCLA’S MINDFULNESS AWARENESS RESEARCH CENTER (MARC)** was created a decade ago, in part by a gift from the Petit Foundation, to conduct studies of and teach the powerful tool for reducing stress: mindfulness. Over the years, there has been a surge in interest for the
practice, which can be defined as paying attention to present-moment experiences “with openness, curiosity and a willingness to be with what is.”

MARC Director Michael Irwin, MD (RES ’85), Cousins/MARC Professor of Psychiatry and Biobehavioral Sciences, says that more than half of the population has incorporated some form of mindfulness into their lives at some point. Dr. Irwin began practicing yoga in 1980, while finishing medical school. But it wasn’t something he crowed about. “Quite frankly, with most of us in medicine, we kept it a secret. We didn’t talk to our colleagues about what we were doing with mindfulness or yoga.”

Now he is the co-author of a study published in February in *JAMA Internal Medicine* on the efficacy of mindfulness meditation in the treatment of sleep problems in older adults. “If you had asked me, ‘Do you think that a paper on the mindfulness topic would be published in *JAMA*?’ I would have said no. We actually tried to do it, without success, but that was in 2007,” Dr. Irwin says.

Ten years ago, most of the therapies targeting stress involved cognitive behavioral therapy, Dr. Irwin notes. “The use of mind-body interventions was dismissed as irrelevant to the practice of medicine when we began exploring its role in treating stress-related conditions like insomnia, depression and anxiety.”

But through randomly controlled studies of more than 600 subjects over the last decade, funded mainly by the National Institutes of Health, Dr. Irwin and his colleagues have shown not only that mind-body interventions, such as mindful meditation, yoga and Tai Chi, improve mental and physical outcomes, but also how these interventions work to reduce stress, improve sleep and possibly prevent chronic illnesses like hypertension, cancer, cardiovascular disease, dementia and rheumatoid arthritis. Mind-body interventions target behavioral and biological pathways and, within weeks, can “alter the molecular expression of genes that are involved in the regulation of inflammation, and inflammation is a principal pathway linked to many chronic diseases,” he says. “Ten years ago, we knew very little about how it was producing those effects.”

Moreover, Dr. Irwin has shown that the benefits of mindfulness, Tai Chi and yoga exceed the benefits of exercise. “Part of it has to do with the ability of the brain to control how we perceive stress, with effects on our body’s physiology,” he says.

“If you’re on the treadmill and you’re working out, certainly the physical activity is producing some benefit. But if you’re also stressing about all of the things you have to get done that day and continue to be upset by these things when you step off the treadmill, then all of those stressors just continue to have an impact on you throughout the day.”

One of Dr. Irwin’s studies controlled for the physical activity of Tai Chi and found that the main benefit came from mindfulness. “You may feel overwhelmed, but there are tremendous opportunities to empower yourself by these simple practices to promote health in the midst of the stresses that we all experience. We can’t change what’s happening in the world, but we can change our own internal experiences,” he says.

Diana Winston, UCLA’s director of Mindfulness Education, began meditating 25 years ago. She has seen an explosion of interest in mindfulness in the past five-to-10 years. *Time* magazine ran a cover story on the topic, 60 Minutes
aired a story and Winston regularly is interviewed by mainstream women’s magazines. “When I first started, it was a very hidden thing. You did not tell people that you meditated,” she says.

MARC reaches several thousands of people a year through its training sessions, and an average of 120,000 to 130,000 people a month access guided meditations from the MARC website. Winston co-authored the book *Fully Present: The Science, Art and Practice of Mindfulness* (De Capo Lifelong Books, 2010) with Emeritus Professor Susan Smalley, PhD, who founded MARC. Winston says that people who take the classes are dealing with stress-related illnesses: depression, anxiety, attention-deficit issues, back pain, migraines or high blood pressure. She often hears from people who face crises and find comfort from the online mindfulness recordings, such as a woman recently diagnosed with stage-four colon cancer.

“Mindfulness is about paying attention in the present moment, not being lost in the past, not being lost in the future, but coming into this moment and finding a place of ease and well-being with things as they are,” Winston says. “Mindfulness is both a meditation practice and a quality of attention that you can bring to any moment in your day or life.”

Using mindfulness to cope with information overload is particularly difficult. Winston encourages people to “unplug” but finds that most have a love-hate relationship with technology. “I hear it again and again. ‘I’m overwhelmed by e-mail, I’m overwhelmed by my phone. But I love it.’ People also have a love-hate relationship with quiet. They want it, but it’s scary, or it’s hard or they can’t imagine how to get it into their lives.”

**ONE REASON TECHNOLOGY IS SO STRESSFUL** is it’s addictive, tapping into the most primitive part of the brain. “It ties into the nature of the central nervous system, which is to be terribly attuned to novelty,” Dr. Whybrow says. If it pings, hums or blurs, we are compelled to respond. And now, Dr. Whybrow says, “we give [smart phones] to children. When I was a kid, I used to get on my bike in the summer, ride off with a friend and come back at suppertime. Now children are tethered to their parents and their friends 24/7.”

Dr. Bilder embarrasses his own children when he happens to see two kids texting each other while sitting together on a bench. Rather than walk by, he’ll confront them: “Hey dudes, do you realize that right next to you is a three-dimensional representation of a human being, and you could actually talk to him? You can’t believe the bandwidth available to you if you just put down the phone and actually look at, listen to and maybe even touch that person.”

Although mindfulness is a simple concept, it’s not as if you can just do it once and experience the benefits. It’s a practice. And Drs. Bilder and Irwin would like to see it encouraged throughout the UCLA Health network. Dr. Irwin, for one, would like to see his primary-care physician encourage the use of mindfulness meditation and other mind-body practices, along with other lifestyle factors such as diet and exercise. “I would hope that research and the support of the institution over time will continue to foster the national leadership of our physicians as we implement these practices throughout the UCLA healthcare system,” he says.

In fact, Dr. Irwin says, mind-body approaches will be essential in this evolving age of healthcare reform for promoting wellness and reducing costs. “I’m very optimistic,” he says. “No country can sustain the huge costs of healthcare treatment that we see now. Prevention is key. Lifestyle interventions like yoga, Tai Chi and mindfulness, exercise and diet, along with not smoking or not drinking to excess, are all lifestyle factors that have robust effects upon health.”

In the future, UCLA doctors perhaps may prescribe mindfulness before they prescribe drugs for certain conditions. Dr. Bilder says that the Semel Institute, Department of Psychiatry and Biobehavioral Sciences and the David Geffen School of Medicine at UCLA are organizing a primary-care division with the goal of spreading behavioral-health programs throughout UCLA’s growing primary-care network. Prevention is the watchword. Indeed, in April 2013, UCLA became the first University of California campus to ban smoking throughout its grounds, eliminating a major environmental stressor. (UCLA Health had earlier banned smoking in and around all its facilities.)

In addition to banning smoking on campus and promoting stress reduction through MARC and HCI,
UCLA is embarking this spring on a Depression Grand Challenge Project to identify risk factors and prevent a substantial number of people from becoming depressed. Nelson B. Freimer, MD, director of the Center for Neurobehavioral Genetics and professor of psychiatry and biobehavioral sciences, will coordinate the project, which will involve more than 100 faculty from across the campus. Depression has a complex causation, involving genetic, social and environmental predispositions. “Extreme stress is one of the main things that can tip someone from health to depression,” Dr. Freimer says. “If you can help people be more resilient to stress, certainly you are removing one of the factors that tips susceptible people into depression.”

Everything from stress in interpersonal relationships to climate change, he says, is a byproduct of our “hell-for-leather” drive to produce without any concern for the consequences. He laments that his daughter’s generation has more anxiety and depression than did his generation, and the trend continues. Dr. Whybrow cringes at a request for statistics on the issue. “That’s another problem America has. We want to put everything into metrics. We’ve lost the sense of humanism. Life is not about metrics,” he says. “Life is about other people. If we lose that connection, we lose what life is really all about. It’s a life that is no longer well-lived.”

Americans, in order to de-stress, need to re-tune their habitat, educational systems and food consumption and rediscover social conventions — in short, the things that make us human, like attachment, love and face-to-face communication. Dr. Whybrow hopes that the Healthy Campus Initiative will be a start, with roots and branches that extend beyond the confines of the UCLA campus.

“Change doesn’t occur in one fell swoop,” he says. “It occurs with individuals beginning to see opportunities for themselves and intellectual excitement around the changes that can occur. Those islands of opportunity begin to grow and then eventually coalesce, and you’ve got a cultural movement.”

Freelance writer Lyndon Stambler teaches journalism at Santa Monica College.

To learn more about the UCLA Mindful Awareness Research Center and to access guided meditations, go to: marc.ucla.edu
Surfin’ Safari
By Marina Dundjerski

One sunny morning on the sand at Venice beach, Noah Federman, MD (RES ‘05, FEL ’08) traded his white coat for a wet suit. With him were a stack of surfboards and more than a dozen of the young sarcoma patients he treats as a pediatric oncologist.

For a day, these teens and young adults left their illness behind and waded into the rolling waves to participate in an activity they normally might be advised against. "In some ways, these kids are my family," Dr. Federman says. "They are the kids I see when I am away from home. Being with them like this, interacting with them like this, helps to make me a better doctor. They see that I’m not that scary — the guy who only gives them bad news — that I’m a human being, too.”

The surf event in October was the latest of several Teen Adventure Program activities that Dr. Federman has put together over the past four years to instill a sense of confidence and camaraderie and to help meet the unique psychosocial needs of his patients, who occupy that uncomfortable space between pediatric and adult oncology. With help from nurse Marjorie Weiman, social workers, child-life specialists and a member of the UCLA Department of Athletics adaptive-recreation program, the outings have included a ropes challenge, rock-wall climbing, kayaking and wheelchair basketball in Pauley Pavilion.

Often, a barrier exists between physicians — particularly oncologists — and their patients, Dr. Federman acknowledges. "We tend to try to not get too close because we see a lot of death," he says. But away from the hospital and out on the sand, everyone got a chance to just be who they are and have fun. Indeed, the young patients are determined to learn how to stand on their boards for the first time, and they also take a certain delight in seeing their doctor wipe out in the waves.

"I was excited to go surfing and surprised to see Dr. Federman there," says Carleigh Williams, 17, who is in remission after suffering from an ovarian germ-cell tumor. "He surfed a lot and was there encouraging us.” It’s a side to the doctor-patient relationship that Carleigh appreciates. "It’s more than just a job to him," she says. "He really cares. And he always talks with me like an adult; he has a light way of explaining things that are heavy, but without being super serious.”

Dr. Federman’s interest in medicine started early. When he was just 4 years old, growing up in Brooklyn, New York, he already could name all the bones in the...
During his residency in pediatrics at UCLA, he gravitated toward oncology. In particular, he was drawn to the multidisciplinary efforts to fight pediatric bone and soft-tissue sarcomas. After completing a fellowship in 2008, Dr. Federman was appointed as assistant professor and director of the Pediatric Bone and Soft Tissue Sarcoma Program in UCLA’s Jonsson Comprehensive Cancer Center, and he holds joint appointments in the departments of pediatrics and orthopaedics.

His immediate goal as a clinician is to alleviate suffering and save lives; as a researcher, Dr. Federman hopes to discover more effective and less toxic treatments for metastatic sarcomas. Specifically, he is researching new therapeutics that target cancer nanoparticles or compounds that don’t cause unnecessary damage to the body. “My aim is to get better at killing cancer without affecting the entire body — without irreparably damaging the heart muscle, hearing, the kidneys or the bone marrow or causing infertility,” Dr. Federman says. “I think we’re headed in that direction, and in the next decade or so, we will see some major improvement in survival.”

Meanwhile, out on the beach, the teens are having a chance to bond and enjoy the day. After a half-dozen tries, Carleigh is able to get up on her board and surf through a small wave, a huge smile spreading across her face. “It’s so great to see her board and surf through a small wave,” says Carleigh Williams, who joyfully caught a wave at the patient surf event.

Marina Dundjerski is a regular contributor to U Magazine.
In His Own Words: Douglas J. Hopper, MD ’64 (RES ’68)

Douglas J. Hopper, MD ’64 (RES ’68), completed a rotating internship at the Los Angeles County + USC Medical Center. Upon finishing his psychiatry residency at the UCLA Neuropsychiatric Institute, Dr. Hopper started a private practice and worked as an inpatient physician at Olive View-UCLA Medical Center. He missed the hands-on aspect of medicine and completed a second residency in family practice. He practiced full-service family medicine, including obstetrics, until 2000. He has been active in managed-care systems, has worked in multiple low-income clinics and student-health centers, and he continues to practice outpatient family medicine in Santa Monica.

Rewind the clock 60 years. It was the very beginning of the Civil Rights Movement, and Dwight D. Eisenhower was president. I won the governorship of California Boys State, a summer leadership and citizenship program sponsored by the American Legion and the American Legion Auxiliary for high school juniors, and was selected to participate in the weeklong Boys Nation in Washington, DC. For the first time, I was involved with individuals and ideas from across the nation. In Washington, I was able to develop my oratory skills and was elected as the president of Boys Nation. On July 28, 1955, I led the delegation of the American Legion’s 10th Annual Boys Nation to the White House Rose Garden to present President Eisenhower with a Suitland Tractor motorized rototiller for his Gettysburg farm and “pin him” with an Honorary Boys Nation label. The president shook my hand as I left the Rose Garden. It was a proud moment. I wasn’t nervous at all. Shortly after I returned home to Glendale, California, I received a thank-you letter from President Eisenhower, dated July 28, 1955.

Dear Douglas:

I am grateful to you and to the members of Boys Nation for bringing me this morning a motorized rototiller for use in the garden at Gettysburg. I am sure it will prove to be a very important part of our equipment up there, and I am most appreciative of your thoughtfulness. Won’t you please express to those in your group once again my warm thanks for your kindness?

It was a great pleasure to meet you all.

With best wishes.

Sincerely,
President Dwight D. Eisenhower

This last summer, I was inducted into the California American Legion Hall of Fame, which recognizes members of the Legion family and U.S. citizens for their significant and ongoing contributions to the American Legion and its organizations.
Rishi Manchanda, MD (RES ’07), MPH, is president and founder of HealthBegins, a social enterprise that provides innovative training, technology and consultancy services to healthcare professionals and community partners to improve care and the social determinants of health. A public-health pacesetter with real-world expertise in improving care-delivery models for vulnerable communities, Dr. Manchanda focuses on improving primary care, the social and environmental conditions that make people sick and health and human rights. In 2008, he started RxDemocracy, a nonpartisan coalition of healthcare and civil-society groups that registered more than 26,000 voters in doctors’ offices and hospitals. In The Upstream Doctors (TED Books, 2013), he introduced a new model of the healthcare workforce that includes clinical “upstreamists” and urges patients and providers to focus on the “causes of the causes” of public-health challenges. Dr. Manchanda is a dual-board-certified internist and pediatrician and was the first graduate of the UCLA Combined Internal Medicine and Pediatrics Residency Program. He leads a program for homeless veterans in Los Angeles, and he was selected as a fellow in the California Healthcare Foundation’s Health Care Leadership Program. In 2014, Dr. Manchanda was recognized in The Atlantic magazine as one of 20 leading healthcare innovators in America.

We all think we know what good medicine looks like: smart doctors, stethoscopes, imaging machines, high-tech tests and the best prescriptions and procedures money can buy. But that picture is vastly incomplete, perhaps fatally so. Our health may depend even more on our social and environmental settings than it does on our most cutting-edge medical care. The future of our health, and our healthcare system, depends on growing and supporting a new generation of healthcare practitioners who look upstream for the sources of our problems, rather than simply going for quick-hit symptomatic relief. These upstreamists, as I call them, are doctors and nurses on the frontlines of medicine who see that health, like sickness, is more than a chemical equation that can be balanced with pills and procedures administered within clinic walls. They see, rather, that health begins in our everyday lives, in the places where we live, work, eat and play.

Upstreamists know that asthma can start in the air around us or in the mold in the walls of our homes. They understand that obesity, diabetes and heart disease partly originate in our busy modern schedules, in the unhealthy food choices available in our stores and even in the way our neighborhoods are designed. They recognize that depression, anxiety and high blood pressure can arise from chronically stressful conditions at work and home and that such conditions can even affect our DNA. And, just as important, these medical innovators understand how to translate this knowledge into meaningful action in their clinics. The upstreamist considers it his/her professional duty not only to prescribe a chemical remedy, but also to tackle sickness at its source. The few upstreamists working in healthcare today — in small practices and community health centers, hospitals and large healthcare systems — struggle daily against a system that wants to push them downstream. In the process of helping their clinics address upstream causes of disease, the upstreamists also help create a higher-value system that can achieve the triple aim of improved outcomes, better quality and lower costs.

Everyone, from patients to fellow doctors to legislators to educators, has a role to play in supporting clinical upstreamists. The United States spends more per capita on healthcare than any other nation; however, the U.S. ranks 37th in health status. If our high-cost sick-care system is to become a high-value healthcare system, the upstreamists will show us the way.

To learn more about HealthBegins, go to: healthbegins.org
An evening of moving tributes to patients, family members and friends highlighted the UCLA Department of Neurosurgery’s Visionary Ball 2014. The annual gala, which raises awareness and crucial research funds for brain and spine disorders that affect millions of Americans, took place at the Beverly Wilshire Hotel on October 30, 2014. The event raised more than $2.25 million to fund innovative investigations aimed at curing brain cancer, reversing strokes, repairing traumatic injuries and re-engineering the central nervous system.

Hosted by entertainer Arsenio Hall, the special evening featured a performance by the group Wilson Phillips, dinner and multiple awards. Steve Tisch, honored in 2013 with the Visionary Award, was recognized during the evening for his gift of $10 million, committed in 2014, to establish the UCLA Steve Tisch BrainSPORT Program, which focuses on sports concussion prevention, outreach, research and treatment for athletes of all ages, especially youth. This year’s honorees included:

**Dr. Patrick Soon-Shiong — Medical Visionary Award**
Dr. Soon-Shiong’s vision as a physician, surgeon and scientist has contributed to breakthroughs in the treatment of diabetes and cancer. Among his many accomplishments, Dr. Soon-Shiong performed the world’s first encapsulated-human-islet transplant and the first pig-to-man islet-cell transplant in diabetic patients. He put the David Geffen School of Medicine at UCLA in the global spotlight when he performed the school’s first whole-pancreas transplant. His invention and development of the drug Abraxane for the treatment of metastatic breast cancer and lung cancer have doubled the response rate in patients with these diseases. The drug has since been approved for treatment of pancreatic cancer and melanoma.
Susan and Jonathan Dolgen — Courage Award
Jonathan Dolgen has had a long and distinguished career as an executive in the entertainment industry, where he held a variety of positions, such as president of Fox, Inc., and chair of 20th Century Fox TV; president of Columbia Pictures; and chairman of the Viacom Entertainment Group. He currently runs Wood River Ventures. Susan Dolgen is an education advocate and philanthropist and was appointed by Govs. Pete Wilson, Gray Davis and Arnold Schwarzenegger to the board of the California State Summer School for the Arts, where she served as chair of the Board of Trustees for more than 20 years. Their lives are filled with family and rewarding work; however, two years ago, Jonathan Dolgen suffered a cerebral hemorrhage. He was taken to Ronald Reagan UCLA Medical Center, where Dr. Neil A. Martin, chair of the Department of Neurosurgery and W. Eugene Stern Chair in Neurosurgery, performed emergency surgery and saved his life. With courage and determination, Susan and Jonathan Dolgen committed themselves to Jonathan’s intensive rehabilitation, and he continues to improve.

Elizabeth Goldhirsh-Yellin — Visionary Leadership Award
Elizabeth Goldhirsh-Yellin comes to her role as president of the newly formed Goldhirsh-Yellin Foundation after serving as director of the Goldhirsh Foundation since 2003. In this new position, she remains dedicated to furthering the legacy of her late parents, sharing their passion for funding medical research, promoting education from early childhood through college and supporting Jewish causes centered on a commitment to the State of Israel and the preservation of its heritage and history. Her parents’ illnesses and deaths are a driving force in her philanthropic vision. Her father Bernard Goldhirsh battled brain cancer, and her mother Wendy passed away from stage-four stomach cancer. Mrs. Goldhirsh-Yellin will always be committed to supporting research in both these cancers, funding scientists in the United States and in Israel.

Kelsey Grammer — Rodney Respect Award
Kelsey Grammer has excelled at the highest level in theater, television and film as an actor, producer and director. As the recipient of five Emmy Awards, three Golden Globe Awards and a Screen Actors Guild Award, it was his role as Dr. Frasier Crane on Cheers that developed into the cornerstone of the Juilliard-trained actor’s career. He played the celebrated character over a span of 20 years, tying the record for the longest-running television character. His Gramnet NH Productions produced such hit series as Medium, and he was most recently seen in the films X-Men: Days of Future Past, The Expendables 3 and Think Like a Man Too. Grammer generously shares his time and talents with a number of worthy causes, including the Center for Autism and Related Disorders, the Los Angeles Police Memorial Foundation and the Andre Agassi Foundation for Education.

A reception to celebrate the new location of the UCLA Institute of Urologic Oncology (IUO) was held on November 10, 2014. The IUO, on the third floor of the new Edie & Lew Wasserman Building at UCLA, provides a “one-stop shop” for patients with urologic cancers. The new space also supports the IUO’s clinical trials, which allow scientists and researchers to translate laboratory findings from bench to bedside more rapidly and effectively. More than 90 guests and faculty members attended the reception, which featured remarks by Dr. Mark S. Litwin (FEL ’93), chair of the Department of Urology and The Fran and Ray Stark Foundation Chair in Urology; Dr. Arie Belldegrun, director of the IUO and the Roy and Carol Doumani Chair in Urological Oncology; Dr. Stuart Holden, associate director of the IUO and the Roy and Carol Doumani Chair in Urological Oncology; Dr. Stuart Holden, associate director of the IUO; and Wasserman building architect Michael Palladino of Richard Meier & Partners Architects, LLP.

For more information, contact Leti McNeill Light at: (310) 267-9475

For more information, contact Alex Ashworth at: (310) 794-8290
RX for Graceful Aging

The Dr. S. Jerome and Judith Tamkin Auditorium at Ronald Reagan UCLA Medical Center was the setting for the UCLA Health Board Meeting on November 13, 2014. A prestigious panel of UCLA physicians and scientists presented some of the latest findings about aging, turning the table on previous beliefs and sharing tips to ensure healthy aging.

Following opening remarks by board chairman Henry Gluck, moderator Dr. John C. Mazziotta (RES ’81, FEL ’83), vice chancellor of UCLA Health Sciences, dean of the David Geffen School of Medicine at UCLA and CEO of UCLA Health, introduced the panel of experts on aging. The panel included Dr. Dale E. Bredesen, director of the UCLA Mary S. Easton Center for Alzheimer’s Disease Research; Dr. David S. Eisenberg, Paul D. Boyer Professor of Biochemistry and Molecular Biology; Dr. Brandon Koretz (RES ’99, FEL ’00), co-chief of the Division of Geriatric Medicine; and Dr. Gary Small (FEL ’83), Parlow-Solomon Professor on Aging and director of the Division of Geriatric Psychiatry and the UCLA Longevity Center in the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA.

Responding to questions from the moderator and the audience, panel members indicated that researchers and clinicians now focus on preventing signs of aging and identifying problems early rather than trying to repair damage. A key myth debunked by the experts was that cognitive decline is primarily genetic. These researchers have shown that regular exercise, a healthy diet, adequate sleep and stress reduction contribute more to overall health than a person’s genes. A recent UCLA study was highlighted, suggesting that memory loss in patients with Alzheimer’s disease may be reversed — and improvement sustained — by using a complex therapeutic program that affects brain chemistry. Panelists also discussed the varied UCLA programs available to the public that support successful aging.

Dr. Leonard Rome, UCLA professor of biological chemistry and associate director of the California NanoSystems Institute, followed the panel discussion with a presentation on cancer research. The event concluded with a reception and music by the Jamie Rosenn Trio.

For more information, contact Kathryn Carrico at:
(310) 825-2558
New Kidney Transplant Center Enhances Patient Experience

Friends and family of Connie Frank and her husband Evan Thompson, along with UCLA faculty and guests of the UCLA Kidney Transplant Program, celebrated the dedication of the Connie Frank Kidney Transplant Center at UCLA on January 24, 2015. The event marked the fulfillment of Ms. Frank’s vision to create a transformative, new healing facility that will improve the clinical experience for UCLA kidney-transplant patients. Housed in the Peter Morton Medical Building in UCLA Medical Plaza, the new transplant center is three times larger than the former clinic. The redesigned space has 14 exam rooms, four infusion rooms and a dedicated conference room. With the expanded square footage, the center will function as a hub of vital services for patients.

Highlighting the event were a ribbon-cutting ceremony and remarks by UCLA Chancellor Gene D. Block; Dr. David T. Feinberg (RES ’92, FEL ’94), then-president of UCLA Health and associate vice chancellor of UCLA Health Sciences; Dr. Gabriel Danovitch, medical director of the UCLA Kidney Transplant Program and John J. Kuiper Chair in Nephrology and Renal Transplantation; Dr. H. Albin Gritsch (RES ’91), surgical director of the UCLA Kidney Transplant Program; Dr. Jeffrey Veale (FEL ’06), director of the UCLA Kidney Transplant Exchange Program; and Connie Frank.

The new state-of-the-art facility will significantly enhance UCLA’s Kidney Transplant Program, which is recognized as one of the most successful in the country.

For more information, contact Kathleen Lago at:
(310) 206-3079
Preparing Tomorrow’s Leaders

The most recent UCLA Leaders of Tomorrow Scholars (Class of 2018) gathered on December 11, 2014, for a luncheon with Dr. Clarence H. Braddock, vice dean for education, chief medical education officer and the Maxine and Eugene Rosenfeld Endowed Chair in Medical Education; and Dr. Eric Esrailian (FEL ’06), associate clinical professor, co-chief of digestive diseases/gastroenterology and The Lincy Foundation Chair in Clinical Gastroenterology.

Since 2012, when an anonymous donor established the merit-based full-tuition awards, 37 students have benefited from the UCLA Leaders of Tomorrow Scholarships. Recipients have cited such benefits as an enhanced ability to pursue nontraditional paths, research and careers consistent with their passions. A rise in scholarship support in recent years has contributed to a 20-percent increase in applications to the David Geffen School of Medicine at UCLA and nearly doubled the school’s success in recruiting from among the nation’s most competitive candidates.

Chairs of Distinction

The UCLA Department of Urology has received a commitment of $2 million from a small group of donors to establish the Jean B. deKernion, M.D., Chair in Urology. The chair was established to pay tribute to and carry forward the legacy of Dr. deKernion, who, after more than 25 years as chair of the UCLA Department of Urology, retired in 2011. Dr. deKernion’s research included important advances in the treatment of patients with bladder, kidney and prostate cancer. To this day, the study and development of immune-based therapies pioneered by Dr. deKernion remain at the forefront of cancer research and reinforce the importance of his contributions. Dr. deKernion also worked tirelessly to build the department by recruiting and nurturing excellent faculty and educating students at all levels. Dr. Leonard Marks, (RES ’73, ’78), professor of urology, was selected as the inaugural deKernion chair holder, which was announced at the celebratory reception in the Frank Clark Urology Center, Westwood, on January 29, 2015. Vital to the future of higher education, endowments sustain the university even through tumultuous economic climates. Endowed chairs provide long-term teaching and research support for distinguished faculty, enabling them to pursue innovative investigations.

For more information, contact Laura Pescatore at: (310) 825-1288

For more information, contact Alex Ashworth at: (310) 794-8290

(From left) Dr. Mark S. Litwin (FEL ’93), professor of urology and health policy and management and The Fran and Ray Stark Foundation Chair in Urology; Dr. Leonard Marks, the newly appointed Jean B. deKernion, M.D., Chair in Urology; and Dr. Jean B. deKernion, professor and chair emeritus of urology.

Photo: Vince Bucci
Gifts

The California Community Foundation’s Centinela Valley Medical Funds has awarded the UCLA Department of Neurology a $600,000 grant for the stroke-prevention, care-coordination and delivery program called SUCCEED. Led by Dr. Barbara Vickrey (FEL ’90), professor of neurology, SUCCEED is culturally adapted for African-American, Hispanic, Chinese and Korean populations and, in partnership with the Watts Labor Community Action Committee and the Worker Education and Resource Center, addresses unmet medical needs of and barriers to post-stroke risk-factor control.

Through this program, Centinela Valley residents who are hospitalized at either Ronald Reagan UCLA Medical Center or Cedars-Sinai Medical Center will be offered a team-care approach over a 12-month time frame after a stroke or transient ischemic attack.

Alumni and longtime friends and supporters of UCLA Carol and James Collins have pledged $1 million to support the Alzheimer’s Risk Reduction Initiative in the UCLA Longevity Center under the direction of Dr. Gary Small (FEL ’83). The initiative is a research project that examines lifestyle modifications and their potential to delay Alzheimer’s symptoms. This gift from the Collins family will continue their legacy of advancing medical discoveries and will ensure UCLA’s role as a leader in reducing Alzheimer’s and dementia suffering, while accelerating research that benefits people globally.

Singer and actor Steve Lawrence made a lead gift to the Institute of Urologic Oncology (IUO) to honor his late wife and performance partner Eydie Gormé, who died in August 2013. The gift will establish the Steve Lawrence and Eydie Gormé Patient Center within the IUO. The patient center on the third floor of the new Edie & Lew Wasserman Building is designed to be a space of healing while offering added privacy for IUO patients. It features artwork provided by the Los Angeles County Museum of Art and a large monitor that presents educational information to visitors.

The Della Martin Foundation has made a $1-million pledge to establish the Della Martin Educational Endowment in Developmental Neurobiology in the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA. This endowment will facilitate the education and research development of postdoctoral fellows and junior faculty in the Semel Institute (the Della Martin Scholars) who are seeking a career in developmental neuroscience.

In 1981, UCLA physicians reported the world’s first AIDS cases. The McCarthy Family Foundation — one of the most steadfast supporters of the UCLA AIDS Institute — has made a new gift of $500,000 with the intent to help the institute and the disease in the very place it was discovered.

The funds will serve as a catalyst for the HIV Extinction Project, which brings together a team of researchers with expertise in stem-cell and anti-retroviral therapies, immune function, genetics, vaccines and new technologies and will advance their most innovative and original ideas. The contribution will help the institute, led by internationally respected virologist Dr. Irvin S.Y. Chen, accelerate the pace of pilot work that has already shown great promise and enhance UCLA’s ability to leverage early results into significant breakthroughs in the search for a cure.

In loving memory of their beloved daughter Robyn Faye Weinstein, Susan Pondfield and Bill Mentlik have established and endowed the Robyn Faye Weinstein Memorial Fund for Liver Transplantation. The fund will serve as a lasting tribute to Ms. Weinstein, who passed away at Ronald Reagan UCLA Medical Center on April 8, 2014, and to her unending desire to help others. Ms. Weinstein’s sister, Dr. Stacey Weinstein (RES ’14), who now is pursuing the Kennamer Fellowship in General Internal Medicine at UCLA, has been involved in the fund’s establishment.

The Jean Perkins Foundation continues its commitment to the UCLA Health Sciences through several recent major gifts. The Department of Urology received funding for the groundbreaking bladder-cancer research of Dr. Arnold Chin (MD ‘03, RES ‘09), and for the focal-therapy and targeted-biopsy work of Dr. Leonard Marks (RES ’73, ’78). Jean B. de Kernion, M.D., Chair in Urology.

In addition, the foundation directed the contribution to the bone-growth research of Dr. Justine Lee (FEL ’13), in the Division of Plastic and Reconstructive Surgery; to the newly created Restorative Transplantation Research Collaborative, spearheaded by Dr. Kodi Azari (FEL ’04), which focuses on the immunological and nerve-regeneration challenges of vascularized composite allotransplantation; and to the Center for Advanced Surgical and Interventional Technology to support the surgical simulator program under the direction of Dr. E. Carmack Holmes. In addition, the UCLA Department of Molecular and Medical Pharmacology benefited from this philanthropy.

The UCLA Division of General Surgery received a $250,000 contribution from multiple donors, including comedian Garry Shandling, to establish a new endowed lectureship in pancreatic diseases.

The lectureship will honor the accomplishments and legacy of Dr. Howard A. Reber, distinguished professor emeritus of surgery and former director of the Section of Gastrointestinal and Pancreatic Surgery. The speaker series will foster collaboration and promote education by enabling UCLA to welcome experts from around the world to visit and share their knowledge.

Three complementary patient programs centered on compassionate care at UCLA will benefit from a gift from the Samuel Steinberg donor-advised fund at the California Community Foundation to improve the quality of life for patients and their families. The gift will support the Palliative Care Clinical Research Program, the establishment of a Geriatric Inpatient Care Companion Program and the Children’s Pain and Comfort Care Program.

These programs will advance the palliative-care research and education work of Dr. Thomas Strouse (RES ’91), Maddie Katz Endowed Chair in Palliative Care Research and Education; geriatric inpatient care in UCLA Medical Center, Santa Monica; and pediatric pain and palliative-care service at Mattel Children’s Hospital UCLA.

For more information, contact Health Sciences Development at: (310) 267-1845

In Memoriam

Florence Brawer Cohen, MA ’62, EdD ’67, passed away on September 5, 2014, at the age of 91. She received both her master’s degree and doctorate from the UCLA Graduate School of Education and Information Studies and, along with her husband, UCLA Professor Emeritus Arthur M. Cohen, PhD, was a generous benefactor of UCLA and the health sciences. The couple has been especially dedicated to supporting scholarships and fellowships and established the Arthur M. Cohen and Florence Brawer Cohen Scholarship at the David Geffen School of Medicine at UCLA to benefit medical students with financial need, particularly those in their fourth year of studies interested in pursuing careers in primary care.
As I approached my 70th birthday, I made a decision to write a brand new and altogether different chapter for my life. Never could I have imagined the story that would then unfold.

My daughter Natasha had for some time been considering the possibility of donating a kidney altruistically — giving one of her organs to a complete stranger. She became interested in the idea after hearing of someone who had donated a kidney to a relative, and the seed of an idea that had been planted years before began to grow.

I had never heard of such a thing. As Natasha went through the protocol to become a donor, reaching out to UCLA and learning about the kidney-exchange program and starting a chain of donations, she shared her wish to make this gift with her family and close friends. Some were, understandably, concerned for her well-being, but all were supportive of her decision to go forward. Her desire and commitment to help a total stranger in this way was incredible, and I was intrigued.
Once she was put into the exchange-program system, a match was found relatively quickly, and the surgery was scheduled for a day in June 2012. I bought a plane ticket to come to Los Angeles to help her during her recovery. Though her first match fell through — we were spending time together on Catalina a few days before the scheduled surgery when she received a call that the recipient had fallen ill — a second match was made in short order.

As I sat in the waiting room at UCLA on the day of the operation, a remarkable thing happened. I overheard a family talking about kidneys. I asked if they had someone having kidney surgery. Yes, they responded, their 26-year-old son was receiving a kidney from a 39-year-old female angel. When I told them my daughter was donating a kidney, we all jumped up and hugged and cried. I was so moved by the power of my own daughter making this remarkable gift and by the joy and gratitude of this family upon receiving such a life-giving blessing that I decided then and there to join Natasha and to also become a living donor.

In January of 2013, I began the process at Saint Barnabas Medical Center in New Jersey. By this time, I was completely committed to donating one of my kidneys. Now came the tests to determine whether or not I was healthy enough to do so. Waiting for the results from each test felt like torture, but a few months later, I was deemed healthy, and I was placed on the National Kidney Registry.

On May 13, 2013 — at the age of 70 years old — my left kidney was successfully removed. Immediately, it was packed in ice and taken to a waiting plane. After a flight of some 3,000 miles, my kidney arrived, and was transplanted into a 64-year-old man — at UCLA! Natasha's kidney had been scheduled to go to another hospital, but it also went to UCLA. Amazing.

My recovery has been uneventful. Since my surgery, I have gone paintballing with my grandchildren and skydiving, just to mention a couple activities in which I have been an eager and active participant. But I felt there was something incomplete in my connection with organ donations. So I began to attend training to become a volunteer with the New Jersey Sharing Network, which is dedicated to educating the public about the need for organ donation. Sharing my story and speaking about the need for organ donations are my way of helping to possibly save a life. If Natasha hadn't done her research and shared it with me, I never would have known about the dire need for organ donations. It just takes one voice to bring awareness.

Many have asked me why I donated a kidney at 70 years of age to a stranger. My life has been full with family, my five children and grandchildren, careers, school and travel, I tell them. I've enjoyed good health and keen awareness. My answer when asked why I donated is, “Why not!”

Throughout my life, I’ve been given many opportunities to connect with people in ways I never could have imagined. The heartfelt connections in each case have been unexpected gifts. In December of 2014, I received another such gift: I met my recipient. About 15 months after the transplant, I wrote a note to him via Saint Barnabas and UCLA, mentioned I would be in California to walk with the Donate Life float in the Rose Parade, and I included my phone number in case he felt comfortable enough to contact me. He called on a Sunday afternoon several weeks later. Our conversation was one of the most overwhelming few minutes of my life; I was talking to a man on the other side of the country who had one of my kidneys. Unbelievable.

We met a few days before the parade in Pasadena. His family is beautiful and so gracious. It was a wonderful time. To see the joy in his smile and among the gathering of 15 family and friends was a profound reminder that one life is precious to so many.

And on New Year’s Day, Natasha and I had the privilege of walking in the Rose Parade. As I walked, and occasionally jogged, down Colorado Boulevard, I listened to the words of the theme song for our float, “I Was Here,” by Beyoncé. It was a constant reminder of this moment I was living and of our connection with the thousands of people who lined the parade route. What a celebration of life.

I intend to keep sharing this message wherever I can. To borrow from the theme of the Donate Life float: This is my never-ending story.
Pediatric allergist Dr. Maria I. Garcia-Lloret (RES ‘00, FEL ’98, ’03) (seated right) and nurse Stacey Skura Zedeck (standing) talk with a parent and child about asthma treatment in the UCLA Breathmobile, which travels to inner-city schools to provide medical care to children whose families cannot otherwise afford it. The Breathmobile was a winner in the recent Helping U Help the Community competition.