



UCLA UROLOGY

UPDATE



A multidisciplinary trial headed by UCLA Urology's Dr. Jeffrey Veale (above left) aims to bring "transplant tolerance" to kidney recipients so that they no longer require immunosuppressive medications. Above right: Dr. Veale (center) with donor Tom Macias (left) and recipient Andrew Macias (right), the first well-matched sibling pair on the research protocol. (Photos taken at the celebration on pages 1 and 2 are by Harry Bugarin of HP Photography.)

Transplant 'Tolerance' Eliminates Need for Immunosuppression

It's commonly known as "the gift of life," and it's one of the most remarkable and heartwarming procedures in modern medicine – the transfer of a healthy organ from one individual into someone who desperately needs it to stay alive.

The UCLA Urology-led Kidney Transplant Program is among the nation's busiest and most successful, transforming the lives of hundreds of patients each year who receive kidneys through the generosity of either deceased or living, biologically compatible donors.

But the transformation comes at a price: the powerful medications required to prevent transplant recipients from rejecting their new organ. "To accept a kidney from another person, you need to take immunosuppression drugs," explains Jeffrey Veale, MD, UCLA Urology

clinical professor and director of the UCLA Kidney Exchange Transplantation Program. "Otherwise, your body sees the new organ as a foreign invader and the immune system attacks it." A lifetime regimen of anti-rejection drugs helps to tamp down this natural response, but the suppressed immune system leaves patients more susceptible to complications for which they are closely monitored, including increased risk of heart disease, hypertension, diabetes, certain cancers, and infections. Moreover, Dr. Veale

continued on page 2

Winter 2022

VOL. 33 | NO. 1

A Brother's Present	p3
Donor Spotlight	p4
Healthy at Every Age	p4
Letter from the Chair	p5
Kudos	p6
Alumni Profile	p7
Thank You for Your Support	p7
The Men's Clinic at UCLA	p8

continued from cover



From left to right: Integral members of the transplant tolerance team include Neil Kogut, MD, a bone marrow transplant specialist; and Erik Lum, MD, a transplant nephrologist. A celebration was held to commemorate the first successful tolerance trial transplant.

notes, some of the medications cause narrowing of the blood vessels of the small arteries in the kidney, essentially choking out the organ, or graft, they are meant to sustain. At UCLA, the average graft survival for kidneys transplanted from living donors is 20 years; for kidneys from deceased donors, the average is about 10 years.

Now, the UCLA program has embarked on a multidisciplinary undertaking to achieve what professionals in the field have long viewed as the Holy Grail: a way for organ recipients to reach a level of “transplant tolerance” so that the body’s immune system doesn’t recognize the organ as foreign and it lasts indefinitely, without the need for immunosuppressive medications. The protocol, which builds on research that has been evolving for decades at several institutions, was used in the first two patients at UCLA in early 2021 – both of them involving well-matched sibling donors – with encouraging results.

The approach involves blending the donor’s and recipient’s immune systems through an infusion into the recipient of the donor’s hematopoietic progenitor stem cells – cells capable of differentiating into the full range of blood and immune cells in the body – shortly after the transplant. This process leads to what is known as “mixed chimerism,” in which the donor and recipient cells coexist, overcoming the need for immunosuppression approximately a year after the transplant. “The recipient’s immune system recognizes that kidney as self,” says Dr. Veale, who was instrumental in developing the new

“The recipient’s immune system recognizes that kidney as self.”

tolerance protocol at UCLA and is the study’s principal investigator.

Potentially, Dr. Veale notes, transplant tolerance could eliminate the current shelf life of transplanted kidneys, allowing recipients to keep the same graft for life. “We need long-term results before we can make that claim, but that’s the hope,” Dr. Veale says. “And since approximately 20% of the people on the kidney transplant waiting list require a second or third transplant, this could significantly decrease the waiting time by removing the need for those individuals to be on the list.”

“Stem-cell transplants and solid-organ transplants are usually conducted very independently of each other,” says Neil Kogut, MD, a bone-marrow transplant specialist who has worked closely with Dr. Veale on the protocol. “This is a synergy of these two fields in which we’re essentially giving the recipient both the donor’s kidney and the immune system. We think this has tremendous potential for changing the field of transplant medicine.”

The protocol, made possible by funding from the OneLegacy Foundation, brings together a broad range of specialties, including nephrology, urology, hematology, radiation oncology, and others, for a series of treatments that prime the transplant recipient’s body to accept the new organ. Aside from Drs. Veale and Kogut, key members of the team include Erik Lum, MD, a transplant nephrologist who brought his

A Brother's Christmas Present: Life



It's a large family, but everyone at the annual Macias Christmas gathering exchanges gifts, no matter how small. So when Andrew Macias was handed a gift-wrapped box by his brother Tom, nothing seemed out of the ordinary.

The 58-year-old general contractor had been on dialysis for 18 months, and he was deteriorating. More than 20 friends and family members had tested to see if they were compatible kidney donors, but an appropriate candidate had yet to be identified. Unbeknownst to Macias, though, his brother had quietly gotten tested and learned he was a perfect match.

Macias still becomes emotional when he recalls what came next. "Inside the box was a letter," he says. "Tom basically stated, 'I got tested. I'm a perfect match. My gift to you is life.'"

When the brothers met with the UCLA kidney transplant team, they discovered they were ideal candidates to be the first sibling pair enrolled in the Tolerance Trial, a groundbreaking research protocol (see the cover story) in which an infusion of stem cells from Tom after the transplant would allow Andrew's immune system to recognize the new kidney as its own, potentially averting the need for lifelong immunosuppressive therapy and the rejection that eventually occurs. "I said, if my brother is willing to do it, let's do it," Andrew Macias says.

As an MRI technician, Tom Macias understands the importance of research. "And I knew that anti-rejection medications are what kill the kidney, then Andy would have to go through this whole process again," he says. From his everyday work routine, he was also all too familiar with "that look" — of patients who weren't likely to survive much longer. When he saw his brother just before the transplant, he recognized that frailty and knew he was doing the right thing.

Nearly seven months post-transplant, Tom Macias was running 6-8 miles a day, and his brother Andrew was on the road to recovery — exercising on the treadmill, doing yard work and remaining active in his business as he was gradually tapered off of his immunosuppression-drug regimen, with the goal of being completely free of the anti-rejection drugs by early 2022.

Andrew Macias is grateful for the new life he can have with his wife — who met him when he was already sick, and has been by his side through the trying times. And he's glad his mother got to experience the beautiful act that transpired between two of her sons. "I'm feeling good, and the future is exciting because of this new technique," he says. "I'm just happy to be a husband, a father and a grandpa...and a brother."

expertise in tolerance research from Stanford University, where he participated in a study on which the UCLA protocol is based; Monica Mead, MD, the hematologist-oncologist who oversees clinical management of the stem cell transplant; and radiation oncologist Ann Raldow, MD, MPH, who leads a post-transplant effort known as "total lymphoid irradiation" that helps to prevent so-called graft-versus-host disease prior to the stem cell infusion, minimizing the need for immunosuppressive drugs.

UCLA Health is one of only five medical centers in the world capable of the groundbreaking approach, and is the only center in the United States currently running an active tolerance protocol for well-matched siblings. "It requires a lot of interplay between different disciplines," Dr. Lum says. "This really demonstrates the strength of a place like UCLA. You can't do this just anywhere."

At Stanford, where Dr. Lum began working on the protocol as a trainee, in transplants involving well-matched siblings approximately 80% of recipients have been able to come off of anti-rejection medications, with the protocol's earliest patients now having had their new kidneys survive without immunosuppressive drugs for 15 years. Both UCLA patients who received kidneys from their well-matched siblings in the first half of 2021 have achieved mixed chimerism and are now tapering off of the immunosuppression regimens. "We're optimistic that after one year we can stop the anti-rejection medications entirely," Dr. Kogut says. Two additional transplants have been scheduled under the tolerance protocol.

Ultimately, the UCLA team members hope to expand the pool of tolerance participants beyond well-matched sibling donor-recipient pairs. They recently received approval from the U.S. Food and Drug Administration for a tolerance protocol involving mismatched living donors; if they show success with that group, the next step, in collaboration with OneLegacy, would be to include deceased donors, who accounted for more than 77% of the 22,800 kidney transplants performed in the U.S. in 2020.

"What's really driving this is the desire to get this transplant tolerance approach to work not just in the relatively infrequent situation of a well-matched sibling transplant," Dr. Kogut says. "If we can get this to work with less well-matched donor-recipient pairs, we think it can work in deceased donors — and that would open the door to using this approach for other types of organs, like hearts, livers and lungs."

Whether or not that goal comes to fruition, the transplant tolerance team members believe the work they are doing is certain to have a major impact. "Even if we can't get everyone off of anti-rejection medicines for life, this can help us learn more about immunosuppression in ways that we can minimize it, which is itself a lofty goal," Dr. Lum says. "Of course we hope for the Holy Grail, but short of that we can still make people's lives much better."

Linda and Frank Damon



For Linda and Frank Damon, supporting UCLA and its Department of Urology represents payback for all that the university has given them.

Both are devoted Bruin alumni. Frank, a retired insurance regulatory attorney, graduated with his BA in Political Science from UCLA in 1965. Linda, a clinical psychologist, earned her PhD in Psychology from UCLA in 1971 — the same year the two got married, after being introduced by a mutual UCLA friend.

In September, the Damons celebrated their 50th wedding anniversary, a milestone Frank is convinced they would never have seen but for the care he received at UCLA. As a student in 1964, he suffered a serious illness that left him hospitalized for five weeks and ultimately resulted in the removal of one of his kidneys. “UCLA saved my life,” Frank Damon says. “And we didn’t have much money in my family, but Student Health covered the entire bill. I’ve always been grateful for that.”

Over the years, the Damons became more involved in UCLA activities. Frank became a certified memory trainer for the UCLA Longevity Center, and joined the Scholarship Council for UCLA’s Academic Advancement Program (AAP); Linda taught and volunteered as a psychology clinic supervisor. The couple established an endowment that provides scholarships to two deserving students each year through the AAP.

Several years ago, when redoing their wills, the Damons decided they wanted to support UCLA in other ways, and UCLA Urology was a natural beneficiary. The couple met Dr. Jeffrey Veale, director of the UCLA Kidney Exchange Transplantation Program, and were drawn to his efforts to expand the number of individuals who could benefit from life-saving kidney transplants through innovations that include exchanges between incompatible donor-recipient pairs, and vouchers that enable the living-donor procedure to be uncoupled in time from the recipient’s transplantation. Recently, the Damons began to support the multidisciplinary “transparent tolerance” research program led by Dr. Veale, which aims to eliminate the need for immunosuppression drugs and eventual organ rejection by blending the donor’s and recipient’s immune systems through an infusion of the donor’s stem cells shortly after the kidney transplant (see this issue’s cover story).

“UCLA is such a special place that provided the avenue for lifelong friendships and the life that Linda and I have had together,” Frank Damon says. “And Dr. Veale is a visionary who is setting a new standard for what can be done in kidney transplantation. We’re not capable of doing the things that Dr. Veale does, but we’re fortunate that we can provide the financial support to help make it possible.”

Peyronie’s Disease

Peyronie’s disease is a condition in which scar tissue called plaque develops on the inside of the penis. This can cause pain for some men, and can manifest as a deformity of the penis. The most common deformity is a curvature or angulation of the erect penis, but there can be indentations, an “hourglass” appearance, and hinging of the penis with sexual intercourse. Many times, men can feel a firm lesion or mass in the penis — often this is described as a “knot” or a “marble.”

In some men, Peyronie’s disease is genetic, but it can be associated with a history of penile trauma — for example, from an injury sustained during sexual intercourse. In many men, there is no obvious cause identified. Peyronie’s disease is reported to affect 2%-10% of men, but this may be an underestimate, since men don’t always come to the doctor for mild changes in the penis.

Early in the course of Peyronie’s disease, men may experience pain or uncomfortable tightness or a “pulling” sensation with erections. When the deformity or the pain first starts, this is considered the “acute phase” of the condition, and there are certain medications that can reverse or stop the penile changes. Penile traction (stretching) devices have been shown in clinical trials to help in reducing the severity of deformity or penile length loss.

Once the deformity stabilizes, this is considered the chronic phase of the condition. In men who have a bothersome curvature or other deformity, procedures or penile injections can be used to treat the plaque and the deformity. Before choosing a treatment, an ultrasound is done to take measurements of the plaque and evaluate the penile blood flow.

For many decades, surgery was the most effective treatment and it is still an important option for many men. However, in the last decade, an effective non-surgical treatment called collagenase (Xiaflex) has emerged. This is the first FDA-approved medication for Peyronie’s disease and is given as a series of injections into the plaque to cause the plaque to dissolve. The Men’s Clinic at UCLA is one of the highest-volume centers in the country to offer Xiaflex injections.

For more information, visit www.uclaurology.com. To make an appointment, call (310) 794-7700.



Letter from the Chair



As academic urologists, a significant portion of our work is quantitative. In arriving at a diagnosis or determining the best course of treatment, we rely on such measurements as blood levels of certain proteins or how many flights of stairs a patient can climb before becoming short of breath, and we look at objective markers to interpret imaging or biopsy results. Yet, as important as this data-driven aspect of our work may be, we also derive great benefit from many faculty members in our department who bring a quality to their work that's immeasurable.

We derive great benefit from faculty members in our department who bring a quality to their work that's immeasurable.

Our cover story this issue highlights the exciting new transplant tolerance trial headed by one such faculty member, Dr. Jeffrey Veale. This potentially game-changing research seeks to allow kidney transplant recipients to avoid eventual rejection of their organ without the need to take powerful immunosuppressive medications. It's cutting-edge work — propelled forward by an individual whose passion for advancing the field of kidney transplantation is impossible to quantify, but fosters an environment that inspires and motivates those of us fortunate enough to serve as his colleagues.

In any profession, as we get older it becomes easy to get bogged down in the minutiae of our daily routines and forget the ideals that originally fueled us. Dr. Veale's upbeat, can-do approach reminds us that the world is not yet complete, and that we can all contribute to making it more just and compassionate. In a divided time, he points out to anyone who will listen that all kidneys are pink. And for those fortunate enough to be a part of it, that climactic moment during the transplant — when the artery and vein of a healthy transplant kidney are connected to the patient's artery and vein and the urine begins spurting out, literally infusing life into a desperately ill human being — it's an extraordinary feeling that transcends whatever stressors we might otherwise feel in our lives.

At UCLA Urology we're incredibly blessed to be in a position to make such contributions to healing the world, whether it's through patient care, research, training, or our work in communities. We're also fortunate to have people like Dr. Veale, who embrace that opportunity, commit to making the most of it, and bring an incalculable energy and optimism that lifts the spirits of everyone around them.

❖ **Mark S. Litwin, MD, MPH**

Professor and Chair, UCLA Urology

Kudos

A. Lenore Ackerman, MD, PhD, assistant professor of urology and director of research in the Division of Female Pelvic Medicine and Reconstructive Surgery, received the 2021 Rising Stars in Urology Research Award from the American Urological Association (AUA) and the Urology Care Foundation. The Rising Stars in Urology Research Award program was established in 2005 to encourage recipients to contribute to urology as both surgical specialists and scientists investigating causes, prevention, treatment, and cures that will improve patients' lives. The award program provides up to five years of supplemental support to urologists who have successfully competed for career development awards from the National Institutes of Health or other major funding organizations. Focusing on the roles urinary microbes (the "urobiome") play in the lower urinary tract, Dr. Ackerman will examine urinary bacterial and fungal communities in different types of voiding dysfunction to identify patterns in the urobiome associated with specific lower urinary tract symptoms. She is mentored by **David M. Underhill, PhD**, and **Jennifer T. Anger, MD, MPH**.

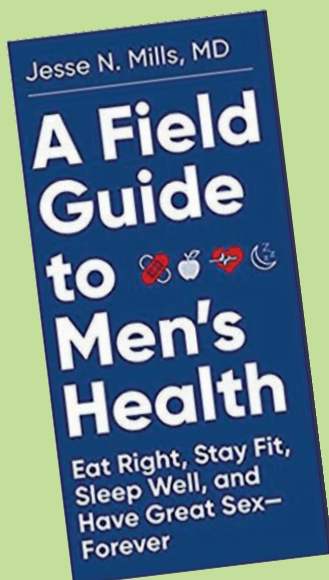
Nima Nassiri, MD, UCLA Urology kidney transplant fellow, received a \$100,000 grant from OneLegacy Foundation for his study, "Understanding drivers of participation in tolerance protocols, impact on quality of life, and the induction of sustained mixed chimerism after combined hematopoietic stem cell and kidney transplantation in HLA-mismatched donor and recipient pairs." His faculty mentor is **Dr. Jeffrey Veale**.

Alvaro Santamaria, MD, UCLA Urology resident, received an \$18,500 grant from ENDO Pharmaceuticals to study atypical complications of collagenase injections and a Traveling Scholars Award from the Society for Male Reproductive Urology to support the presentation of his research at the American Society of Reproductive Medicine at its annual conference in Baltimore.

Kymora Scotland, MD, PhD, UCLA Urology assistant professor, received a 2021-22 Faculty Career Development Award from the UCLA Office of Equity, Diversity and Inclusion to support her efforts to develop a shared decision-making tool for patients with kidney stones.

Former David Geffen School of Medicine at UCLA student **Dr. Dyvon Walker**, current student **Tommy Jiang**, and UCLA Urology residents **Dr. Alvaro Santamaria** and **Dr. Vadim Osadchiy** are co-authors of the manuscript, "3D printed phantoms to quantify accuracy and variability of goniometric and volumetric assessment of Peyronie's disease deformities," accepted for publication in the *International Journal of Impotence Research*. Senior authors were UCLA Urology faculty **Drs. Sriram Eleswarapu** and **Jesse Mills**.

UCLA Urology's Andrology Research Group had seven abstracts presented at the recent AUA annual meeting. Presenters included UCLA Urology residents **Dr. Alvaro Santamaria** and **Dr. James Weinberger**, former UCLA Urology fellow **Dr. Denise Asafu-Adjei**, and medical students **Tommy Jiang** and **Christopher Yang**. Several members of the group also presented at the Sexual Medicine Society of North America meeting. The team is supervised by **Drs. Sriram Eleswarapu** and **Jesse Mills**.



Jesse N. Mills, MD, UCLA Urology associate clinical professor, authored the newly published book, *A Field Guide to Men's Health: Eat Right, Stay Fit, Sleep Well, and Have Great Sex – Forever*, which demystifies men's health and empowers men to take control of their health by learning the fundamentals of nutrition, exercise, and sleep medicine and establishing a good relationship with physicians. The book will be available December 7, 2021, across multiple platforms.



Alberto Breda, MD



When Dr. Alberto Breda performed Europe's first robotic-assisted kidney transplantation in 2015, it brought together the two elements of his UCLA Urology fellowship training.

Dr. Breda, who currently heads the Oncology-Urology Unit and Kidney Transplant Surgical Team at Fundació Puigvert in Barcelona, Spain, was a

third-year urology resident in his native Italy when he came to UCLA in 2003 to complete his residency. He then stayed on for a three-year clinical fellowship in urology, minimally invasive surgery, and kidney transplantation, learning about robotic and other minimally invasive techniques from Dr. Peter Schulam and kidney transplantation under the mentorship of Drs. H. Albin Gritsch and Jeffrey Veale.

"The majority of things I'm doing now resulted from my experience at UCLA," Dr. Breda says. "I arrived as a young resident and left as a fully formed urologist, having made great contacts and having learned so much about leadership, teamwork, and surgical skills."

After completing his fellowship, Dr. Breda stayed on as a UCLA Urology clinical instructor and assistant professor before returning to Europe in 2009 to start a program as chief of the kidney transplantation division at Fundació Puigvert. In 2017, two years after the milestone robotic-assisted kidney transplant, he

assumed leadership of the Oncology Urology Unit, where he has continued to promote the advancement of robotic-assisted surgery — a technique that was new when Dr. Breda began performing it at UCLA in 2004, and was later to take hold in Europe. Over the last several years, Dr. Breda has trained surgeons in 10 European centers to perform robotic-assisted kidney transplantation, and established a registry to track the cases for research purposes. More than 400 have now been performed, and the approach has led to fewer complications compared to open surgery.

Last July, Dr. Breda became chair of the European Association of Urology's Robotic Urology Section (ERUS). In that role, he is responsible for organizing an annual conference and managing facilities throughout Europe, aimed at training more surgeons in robotic urologic procedures so that more patients can benefit from the less-invasive approach. Dr. Breda notes that in organizing meetings for ERUS, which involve leaders from around the world, he has invited many top surgeons from UCLA and elsewhere in the U.S. whom he met through his training.

"In the end, you can have all the titles in the world, but the real reward comes from saving the lives of patients and contributing to research that offers hope we can provide even better care in the future," Dr. Breda says. "When I was at UCLA, that was the feeling that everyone had — this extreme expertise and, at the same time, humility about our purpose. It was inspiring, and it set the stage for my career success."

Thank You for Your Support

As we approach the season of giving, UCLA Urology would like to thank you for your support of the department and share additional ways to make an impact through philanthropy.

Philanthropy drives creativity, innovation, and progress, and we are immensely grateful for philanthropic support that is spurring new ways to detect, diagnose, and treat urologic diseases.

There are opportunities to support current needs with projects in research and training the next generation of scientists, as well as larger endowment opportunities to support the priorities of UCLA Urology chair Dr. Mark S. Litwin and the department. Endowments are invaluable in supporting the mission of the David Geffen School of Medicine at UCLA, and offer an extraordinary opportunity to invest in scholarly and scientific achievement. They provide a reliable source of funds, with the income/payout from each endowed fund applied to underwrite the purpose established by the donor.

Your investment has the potential to move the needle significantly in accelerating research to advance new interventions, clinical trials, late-stage research, drug development, and advanced training for the next generation of physician-scientists, resulting in outstanding patient care and treatments.

For more information, please contact:

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UCLA Urology: #8 in the Nation
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The Men's Clinic at UCLA

DID YOU KNOW?

Direct-to-consumer internet marketing of erectile dysfunction (ED) pills is at an all-time high, but these companies omit crucial evaluation of the medical causes of ED. Researchers at The Men's Clinic at UCLA recently found that conditions such as high cholesterol, high blood pressure, diabetes, low testosterone, and varicoceles are missed by internet "pill mills." Learn more by scheduling a consultation.

The Men's Clinic at UCLA is a comprehensive, multidisciplinary health and wellness center located in Santa Monica, now with locations in Burbank and Santa Clarita. For more information or to make an appointment, call (310) 794-7700.



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