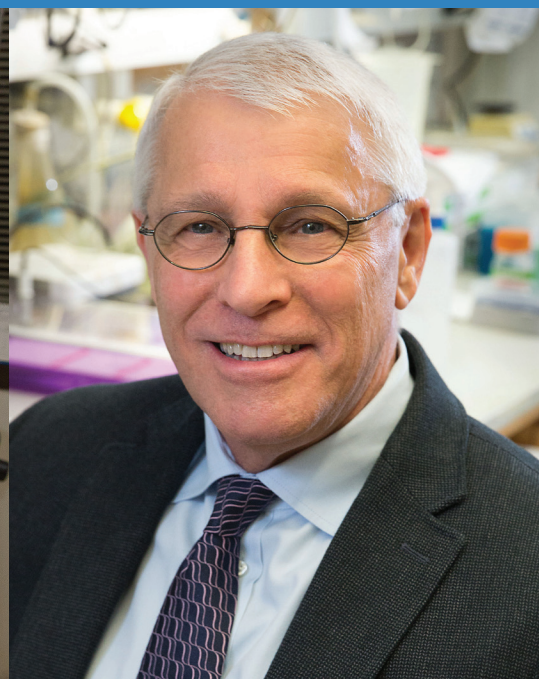
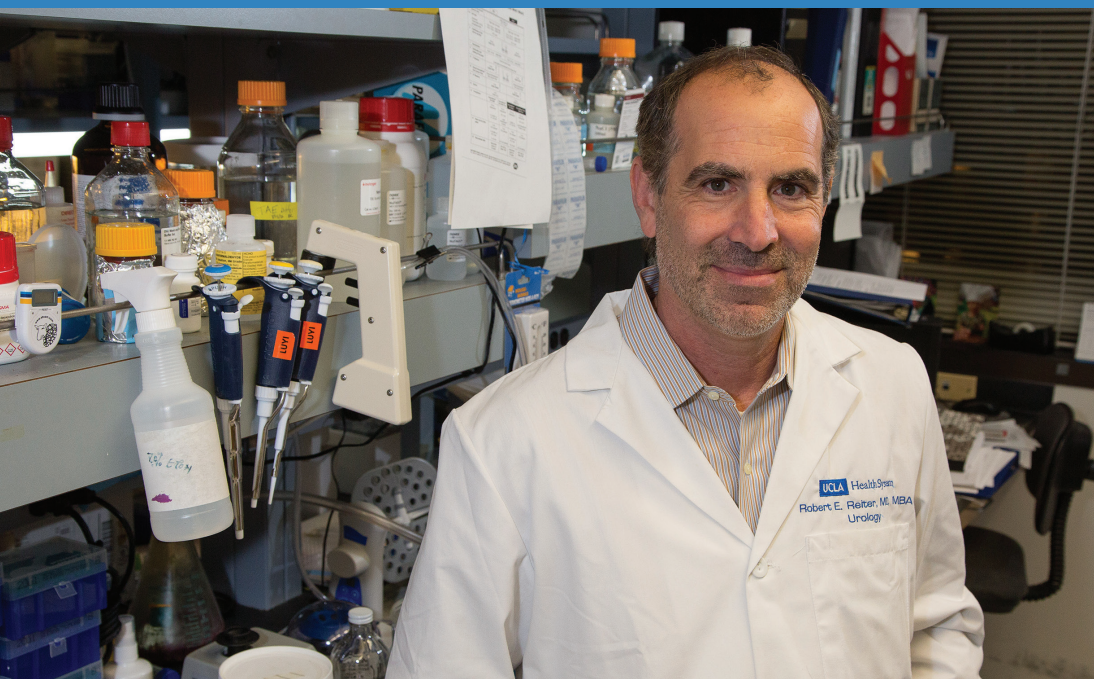




# UCLA UROLOGY

UPDATE



Dr. Robert Reiter (left), professor of urology and director of the UCLA Prostate Cancer Program, heads the UCLA Prostate Cancer Specialized Program of Research Excellence (SPORE). Dr. Owen Witte (right), founding director of the UCLA Broad Stem Cell Research Center, is working with City of Hope researchers on one of the key SPORE-funded projects.

## UCLA Prostate Cancer Program Earns Prestigious SPORE Grant Renewal

Substantial headway has been made against prostate cancer in the last 15-plus years, thanks in no small part to the UCLA Prostate Cancer Program, which has contributed to the development of effective new drugs for treating advanced forms of the disease; developed better imaging techniques for detecting it; and engendered a better understanding of risk, enabling many patients to avoid unnecessary treatment.

Last fall, in recognition of the program's impressive track record and, more importantly, its ability to take on the most significant challenges in what continues to be the second-leading cause of cancer-related death among U.S. men, the National Cancer Institute awarded the UCLA Prostate Cancer Program a prestigious Specialized Program of Research Excellence (SPORE) grant under the direction of Dr. Robert Reiter, professor of urology, director of

the UCLA Prostate Cancer Program and the grant's principal investigator.

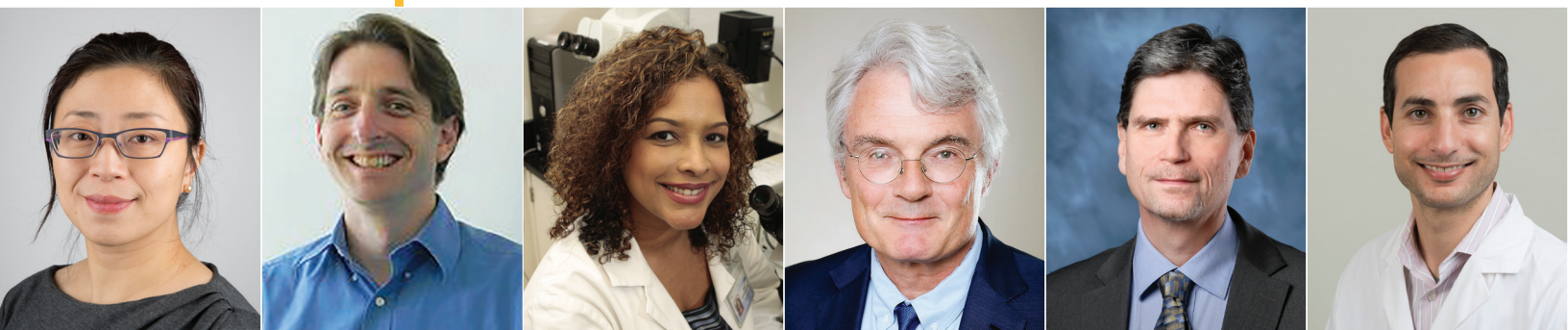
The \$8.7 million grant recognizes the UCLA Urology-led program as one of the nation's best and marks the fourth time it will receive the five-year cycle of funding. The UCLA Prostate Cancer SPORE — one of only eight currently funded in the country and the only one in California — is a multidisciplinary and translational research program in which

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Pictured across the top, left to right: UCLA prostate cancer SPORE researchers Drs. Huihui Ye, David Elashoff, Isla Garraway, Johannes Czernin, Michael Freeman (Cedars-Sinai), Andrew Goldstein, Paul Boutros, Saul Priceman (City of Hope), Tanya Dorff (City of Hope), Matthew Rettig, Stephen Forman (City of Hope), and Thomas Graeber. Opposite page, group photo: members of Dr. Owen Witte's laboratory at UCLA.

*continued from cover*

scientists and clinicians from diverse fields come together to develop new and innovative approaches to improving the diagnosis, prognosis and treatment of prostate cancer.

"For the past 15 years, the SPORE grant has played a pivotal role in bringing a sense of cohesiveness to our program," says Dr. Reiter. "It funds projects that include researchers and scientists from diverse disciplines and backgrounds all around campus — such as chemistry, nanotechnology, radiology, pathology and stem cell biology — to help accelerate our goal of combating prostate cancer."

Dr. Reiter notes that the UCLA Prostate Cancer SPORE has evolved in ways that reflect the evolution of knowledge about the disease. It began in 2004 with a small nucleus of basic and clinical investigators at a time when there was relatively little prostate cancer research, and has steadily grown as the science became more fruitful. The most notable early success emerged from the work of Dr. Michael Jung, a UCLA distinguished professor of chemistry and biochemistry, and Dr. Charles Sawyers, a former professor of medicine and molecular pharmacology at UCLA, in developing the drugs enzalutamide and apalutamide — testosterone-blocking treatments that have extended the lives of thousands of men with advanced prostate cancer that no longer responds to hormone and chemotherapies.

In the last decade, the UCLA SPORE has been a leader in developing new ways of detecting, assessing and managing prostate cancer through imaging — first with MRI, and most recently using prostate-specific membrane antigen (PSMA) PET/CT. The program has also pioneered research leading to the recognition that many prostate

cancers can be observed rather than treated, and in identifying biomarkers that better clarify patients' risk, along with the improved imaging techniques that have made "active surveillance" a viable option for many patients. The SPORE also supported the important work of the group headed by UCLA Urology's Dr. William Aronson on the impact of diet in prostate cancer.

Along the way, UCLA's SPORE has leveraged the breadth of expertise on the UCLA campus to bring in researchers from wide-ranging disciplines. And with the recent grant renewal, the program has expanded beyond the UCLA campus to include citywide expertise through the inclusion of collaborators from institutions such as Cedars-Sinai and City of Hope.

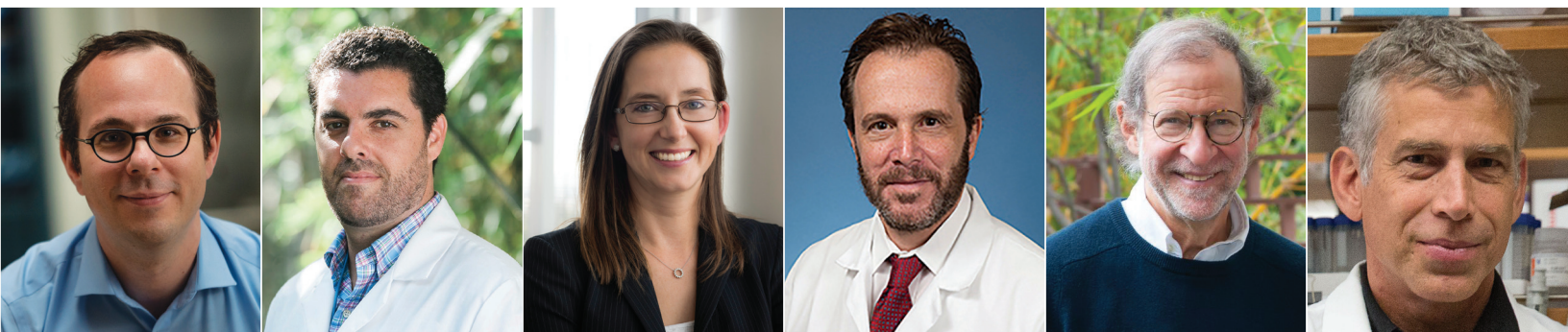
As it moves into its fourth funding cycle, Dr. Reiter notes, the UCLA SPORE is taking on the major current challenges confronting the prostate

*"The SPORE grant has played a pivotal role in bringing a sense of cohesiveness to our program."*

cancer field, including the need to continue improving on the classification of which patients require no treatment as opposed to those who should receive standard or more aggressive treatment; applying metastatic prostate cancer treatments at earlier stages in the disease; and, for patients who reach

the end stage, overcoming the resistance to currently available drugs. In addition, with the recruitments of a renowned bioinformatician and pathologist — Drs. Paul Boutros and Huihui Ye, respectively — UCLA's SPORE is accelerating efforts at understanding and exploiting knowledge of prostate cancer genomics and histopathology to better manage men with prostate cancer. Dr. Andrew Goldstein, an assistant professor of urology and molecular, cell and developmental biology, leads the career development program — a key facet of the SPORE that helps bring new





junior and senior faculty into the prostate cancer research field.

Developing drug inhibitors for men with metastatic castration-resistant prostate cancer is among the translational research projects included in the new round of SPORE funding. Dr. Jung, part of the group whose research led to enzalutamide and apalutamide, is teaming with UCLA Urology's Dr. Matthew Rettig to develop a drug inhibitor targeting the androgen receptor in an effort to address tumor-escape mechanisms associated with current androgen receptor-targeted therapies. The goal is to minimize resistance, prolong life expectancy, and improve quality of life for the castration-resistant form of the disease, which currently accounts for virtually all prostate cancer-specific deaths.

The SPORE is also funding a collaboration between a City of Hope research group led by Drs. Stephen Forman and Saul Priceman and a UCLA team headed by Dr. Owen Witte, founding director of the UCLA Broad Stem Cell Research Center, that is testing a new immunotherapy approach using CAR T cells to target the prostate stem cell antigen (PSCA) in metastatic castration-resistant patients in a phase 1 clinical trial at City of Hope. The therapy has shown promise in laboratory models of prostate cancer. "We know CAR T cells can be effective against certain blood cancers, but there is an emerging body of knowledge to try this technology in solid tumors," Dr. Witte explains. "The City of Hope group has great expertise in developing such reagents for clinical trials, and we are bringing our expertise in prostate cancer pathogenesis and target identification to the collaboration."

Dr. Priceman notes that the City of Hope research team has had an established CAR T cell program in multiple disease settings, including a phase 1 clinical trial treating prostate cancer patients, which is built on the groundbreaking work of Dr. Reiter's lab in discovering and developing antibodies to PSCA. "The biggest drawback we have encountered is the heterogeneity of metastatic prostate cancer in advanced stages, in which it has a mixed phenotype: both adenocarcinoma and neuroendocrine disease," Dr. Priceman says. "Dr. Witte's group is helping us establish a novel combination approach that targets both disease types. We're excited to work with UCLA to develop these platforms."

The SPORE is also funding a collaboration between a research group headed by Dr. Michael Freeman of Cedars-Sinai and UCLA Urology's Dr. Isla Garraway. Dr. Freeman's lab discovered a protein, ONECUT2, that is a driver of prostate cancer metastasis and drug-resistant disease, and showed that where the protein is depleted, the metastasis is suppressed. His lab then developed a drug-like small molecule that targets the protein

and found that it suppresses human drug-resistant prostate cancer cell metastasis in mice. The project with Dr. Garraway, which also includes Dr. Jung, will test whether ONECUT2 can be a therapeutic target in a subset of aggressive prostate cancers in which the protein is highly active.

"As a clinician-scientist, Dr. Garraway brings a whole range of technical capabilities as well as deep knowledge of the clinical disease that is complementary to the work our lab does," Dr. Freeman says. "We are very happy to be working with her and to be part of the UCLA Prostate Cancer SPORE for the first time."

Dr. Garraway says the SPORE serves to elevate the work of all of its members. "It's so beneficial in the way it brings together investigators from different fields," she says. "Having this network of researchers where you can meet and engage in discussions, get access to different reagents and technologies, and learn about new ways to approach the disease that you wouldn't necessarily consider leads to a synergy that raises the bar for everyone."



## Geoffrey Sonn, MD



As a urologic oncologist at Stanford University, Dr. Geoffrey Sonn devotes half of his time to clinical work focusing predominantly on the diagnosis and treatment of prostate cancer. When he's not seeing patients, he conducts research aiming to develop more accurate and less invasive diagnostic and treatment techniques for

prostate cancer, drawing on the training he received as a UCLA urologic oncology fellow.

"Traditionally, men with a high PSA blood test are subjected to an uncomfortable and invasive prostate biopsy involving blind sampling of the prostate," Dr. Sonn says. "This approach finds many small, non-aggressive cancers that don't require treatment. Our goal is to be more selective about who needs a biopsy and more accurate when biopsy is performed. That's where imaging comes in. Ideally, if your blood test is abnormal and you get a normal imaging test, it's safe to avoid biopsy. If it's abnormal, we target that specific area and find only aggressive cancers that require treatment."

Dr. Sonn's efforts to improve prostate cancer imaging focus on ultrasound, MRI and PET scans as well as newer investigational approaches such as photoacoustic imaging — a technique with the potential to offer real-time cancer-specific molecular imaging in the clinic. His laboratory, in collaboration with engineers, computer scientists, and radiologists at Stanford, focuses extensively on using artificial intelligence to standardize interpretation of prostate MRI.

Improved prostate cancer imaging also enables a fundamentally different approach to treatment called focal therapy, a minimally invasive way of killing locally confined prostate cancers while minimizing side effects and preserving non-cancerous areas. Dr. Sonn currently heads the first clinical trial in Northern California to use MRI-guided focused ultrasound to treat prostate cancer.

After completing his urology residency at Stanford, Dr. Sonn came to UCLA in 2011 for a urologic oncology fellowship, which included a clinical year followed by a year dedicated to research. He studied prostate cancer molecular imaging in the laboratory of Dr. Robert Reiter, director of the UCLA Prostate Cancer Program, and worked with Dr. Leonard S. Marks, a pioneer in the use of MRI/ultrasound fusion for prostate biopsy and focal therapy to treat prostate cancer, with whom Dr. Sonn continues to collaborate nearly a decade later.

"What I have been able to do at Stanford was a direct result of the outstanding training I received at UCLA," Dr. Sonn says. "I built a targeted biopsy and focal therapy program at Stanford following the blueprint that I learned from UCLA Urology."

## Howard Klein



In nearly a decade as a loyal and consistent supporter of the research of Dr. Robert Reiter, director of the UCLA Prostate Cancer Program, and Dr. William Aronson, chief of urology at Olive View UCLA Medical Center and chief of urologic oncology at the Greater Los Angeles VA Medical Center, Howard Klein has gotten to know both UCLA Urology professors well, and his admiration has only grown.

"Their dedication to their work has really impressed me," Mr. Klein says. "People always joke, 'It's not like you're curing cancer.' Well, these guys actually are."

In addition to being a major Downtown Los Angeles real estate developer, Mr. Klein is a partner in Seattle-based Ocean Beauty Seafoods, a primary producer of salmon and other seafood from Alaska. That has given him a special interest in the work of Dr. Aronson, a leading researcher on the role of diet and lifestyle factors for prostate cancer prevention and treatment.

Mr. Klein and his wife, Deborah, are currently supporting a study led by Dr. Aronson that will determine whether a fish-based diet with fish-oil supplementation has the potential to delay prostate cancer progression in men who have been diagnosed and are being monitored through active surveillance. The study has nearly reached its target enrollment of 100 patients.

"This important work would not be possible without the generous support of Mr. and Mrs. Klein," Dr. Aronson says.

To show his appreciation for the work of Drs. Reiter and Aronson and lend context to the research, Mr. Klein has taken both on a tour of Alaska and his company's factories during the salmon season. "Anyone who has gotten to know these two individuals the way I have would appreciate that they are brilliant, compassionate physician-scientists who are deeply committed to research that will make a difference in the fight against prostate cancer," Mr. Klein says. "It gives us great satisfaction to know we're able to support them in that effort."



# Letter from the Chair



*Our Prostate Cancer Program is emblematic of the way we leverage our strengths as a department within a world-class health system and university.*

As one of the nation's leading academic urology departments, UCLA Urology conducts research, patient care, and training efforts across the full spectrum of urologic conditions. But no condition draws more attention in our work than prostate cancer — whether it's in the laboratory or the clinic, in our teaching, or in our engagement with the community. The attention is certainly warranted given the number of people affected: One in nine men will be diagnosed in his lifetime, and although most will not die from the disease, prostate cancer remains the second-leading cause of cancer death among U.S. men. Thus, it should come as no surprise that caring for patients with prostate cancer — and their families — is foundational to our training as urologists.

In our determination to improve the way patients with prostate cancer are diagnosed and treated (or, when appropriate, not treated), our Prostate Cancer Program, the subject of this issue's cover story, is emblematic of the way we leverage our strengths as a department within a world-class health system and university in our battle against a disease. Now beginning its fourth consecutive five-year cycle as a prestigious National Cancer Institute-funded Specialized Program of Research Excellence (SPORE), the program has contributed seminal advances by bringing together laboratory and clinical scientists to address the most pressing problems we see in patients with prostate cancer.

What we refer to as translational science — bringing clinical observations to the lab and laboratory discoveries to the clinic — is possible only in a program with a wealth of basic and clinical researchers and a strong culture of collaboration among them. Under the leadership of Dr. Robert Reiter, the UCLA Prostate Cancer Program SPORE has cast an even wider net, recruiting investigators from a variety of disciplines to ensure that all relevant expertise is brought to bear in ways that will advance the science. This multidisciplinary, translational work is what we strive for in all of our research programs, for it is the most effective way to meet our ultimate goal of improving the lives of the patients we see and the broader community we serve.

❖ **Mark S. Litwin, MD, MPH**

*Professor and Chair, UCLA Urology*

# Kudos

Incoming UCLA Urology fellow **Denise Asafu-Adjei, MD, MPH**, currently chief resident in urology at Columbia/New York-Presbyterian Hospital, is the recipient of a Research Scholar Award from the Urology Care Foundation and American Urological Association to study disparities in access to care for men with sexual dysfunction. She will join UCLA Urology in July as an andrology fellow and undertake this project under the mentorship of UCLA Urology faculty **Dr. Jesse Mills, Dr. Sriram Eleswarapu, Dr. Stanley Frencher, and Dr. Mark S. Litwin**.

**Paul Boutros, PhD**, UCLA Urology professor and member of the Institute of Urologic Oncology, led an international team of researchers that created a way to accurately estimate how fast an individual cancer is evolving using open-source software, which makes big data sets easily accessible to the public. A paper detailing the group's method was published in the journal *Nature Biotechnology*. This approach can now be used to develop a series of new tools and biomarkers for any type of cancer, and could help improve patient outcomes. *OncLive* also reported on research from Dr. Boutros suggesting that predicting how a person's cancer will evolve may lie in their inherited DNA.

**Richard Boxer, MD**, a UCLA urologist at West Los Angeles VA Medical Center, was elected to the prestigious American Society of Clinical Oncology Foundation (Conquer Cancer) Board.

**Jeremie Calais, MD, MSc**, a member of the Institute of Urologic Oncology, has been awarded \$105,000 from the Society of Nuclear Medicine and Molecular Imaging. The two-year grant will help fund a new UCLA-led study that aims to advance the method of locating cancer by detecting tumor stroma, the connective tissue and blood vessels in the tumor environment that are necessary for cancer growth.

**Matthew Dunn, MD**, UCLA Urology associate clinical professor, received a grant from Boston Scientific in support of the UCLA Urology Endourology fellowship.

**Katherine Fero, MD**, UCLA Urology resident, received a \$25,000 grant from the HH Lee Foundation for her proposal, "Development and Validation of a Symptom-Based Questionnaire for Patients with Non-Muscle Invasive Bladder Cancer Undergoing Intravesical Therapy." Her mentor is **Dr. Karim Chamie**.

**Stuart Holden, MD**, co-director of the Institute of Urologic Oncology and the Spielberg Family Chair in Urologic Oncology, received a testamentary gift of \$1 million to support research into prostate cancer. The funds are to support the Institute of Urologic Oncology.

**Raj Jayadevan, MD**, UCLA Urology resident, published "Infrapubic approach for placement of inflatable penile prosthesis: Contemporary review of technique and implications." Co-authors were UCLA Urology faculty **Dr. Sriram Eleswarapu** and **Dr. Jesse Mills**.

**Amar Kishan, MD**, assistant professor of radiation oncology and urology and a member of the Institute of Urologic Oncology, received the 2019 ASTRO – PCF Career Development Award to End Prostate Cancer. Dr. Kishan aims to develop biomarkers that can better select the most appropriate treatment regimens for patients with localized high-grade prostate cancer.

UCLA Urology faculty **Dr. Jesse Mills** and **Dr. Sriram Eleswarapu** were editors of the February 2020 special issue of *World Journal of Urology*, which focused on Peyronie's disease in contemporary urological practice. The issue includes

a paper authored by UCLA fourth-year medical student **Arash Amighi**. Arash is also first author on a paper entitled "Safety of collagenase Clostridium histolyticum injection therapy for Peyronie's disease in patients continuing antiplatelet or anticoagulant therapy," to be published in *Journal of Sexual Medicine*; co-authors include UCLA Urology physician assistant **Keith Regets**, former andrology fellow **Dr. Justin Nork**, and UCLA Urology resident **Dr. Neil Mendhiratta**. Dr. Eleswarapu and Dr. Mills served as senior authors and faculty mentors for both projects.

**Leonard S. Marks, MD**, UCLA Urology professor, had his manuscript "MRI-guided biopsy to evaluate prostate cancer severity in African-American men" published in the journal *Urology Practice*. His co-authors included **Dr. Jorge Ballon, Dr. Adam Kinnaird, Dr. Rajiv Jayadevan, Steve R. Zhou, Danielle E. Barsa**, and **Lorna Kwan**.

**Victor Nitti, MD**, UCLA Urology professor, professor of obstetrics and gynecology and chief of Female Pelvic Medicine and Reconstructive Surgery, received a Lifetime Achievement Award from the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction.

**Vadim Osadchiy**, fourth-year UCLA medical student and incoming UCLA Urology resident, is a recipient of the Viola G. Hyde Travel Award, which will fund him to present his research at a national meeting. Vadim is author of a paper accepted for publication in *Journal of Medical Internet Research (JMIR)*: "Understanding patient anxieties in the social media era: Qualitative analysis and natural language processing of an online male infertility community," co-authored by faculty mentors **Dr. Jesse Mills** and **Dr. Sriram Eleswarapu**.

**Dyvon Walker**, UCLA medical student, has published an article entitled “Management of the acute phase of Peyronie’s disease: a contemporary review” in *Current Sexual Health Reports*. His co-authors are medical student **Arash Amighi**, UCLA Urology resident **Dr. Steven Mills**, and UCLA Urology faculty **Dr. Sriram Eleswarapu** and **Dr. Jesse Mills**.

To make an appointment, call (310) 794-7700.







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No. 1 in Los Angeles,  
No. 1 in California and  
No. 6 in the nation in the 2019-20  
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UCLA Urology: #10 in the Nation  
Highest Ranked in Los Angeles



# The Men's Clinic at UCLA

## DID YOU KNOW?

Forty percent of men with low fertility have varicoceles, a usually painless swelling of veins in the scrotum. Surgeons at the Men's Clinic at UCLA perform more than 200 varicocele repairs a year using state-of-the-art microsurgical techniques to help men improve their fertility potential.

*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.*



### UPDATE

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