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DEPARTMENT of UROLOGY UPDATE

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DEPARTMENT *of* UROLOGY

UPDATE



A Comprehensive Effort to Combat Chronic Pelvic Pain

The Department of Urology is playing a leading role in the most ambitious effort to date to learn about the causes, risk factors and potential treatments for interstitial cystitis — also known as painful bladder syndrome — and other urologic chronic pelvic pain disorders.



Larissa V. Rodríguez, MD, co-leads the five-year interstitial cystitis study at UCLA.

The Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) represents a \$37.5 million, five-year effort funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH). UCLA is serving as one of the initiative's six research sites, with a multidisciplinary team led by co-principal investigators Larissa V. Rodríguez, MD, associate professor of urology, and Emeran Mayer, MD, professor of medicine, physiology, and psychiatry and biobehavioral sciences.

Interstitial cystitis (IC) is a chronic condition characterized by recurring pain or discomfort in the bladder and surrounding pelvic region.

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Frank Clark Urology Center

“We hope we will make progress that will ultimately lead to strategies that will enable us to intervene — both to improve treatment and to prevent the condition from becoming chronic.”

— Larissa V. Rodríguez, MD

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The symptoms depend on the individual, but can range from tenderness or pressure to intense pain, as well as an urgent and/or frequent need to urinate. The symptoms tend to come in cycles, flaring up for a period of time before diminishing, only to return at a later date. When patients are symptomatic, the impact on quality of life is significant. “People with IC are more likely to be depressed, to experience problems in their relationships and to miss significant time from work,” says Dr. Rodríguez, co-director of the Division of Female Urology, Reconstructive Surgery and Urodynamics and director of female urology research for the Department of Urology.

IC disproportionately affects women — more than 90 percent of the estimated 1.3 million Americans with IC are women, with symptoms usually beginning in their 30s and 40s — and is most common among people with a history of chronic urinary tract infections. But beyond that, little is known about IC or its causes; indeed, because of the widely varying symptoms and severity, most researchers now believe IC is not one but several diseases and have begun to use the term painful bladder syndrome

(PBS) to encompass all cases of urinary pain that can't be attributed to other causes, such as infection or urinary stones. Symptoms of IC/PBS often resemble those of a bacterial infection, but patients don't respond to antibiotic therapy, and no organism is found in their urine.

Given the lack of understanding, it's not surprising that there is no reliably effective treatment or cure for IC/PBS. But the MAPP study represents a major shift in strategy. “The NIH has put together a truly multidisciplinary group of investigators in an effort to think differently about this illness by looking for clues outside the bladder and prostate in a large-scale, coordinated effort,” Dr. Rodríguez explains.

Unlike previous organ-specific research, the MAPP initiative requires investigators to conduct highly collaborative studies of the most common urologic chronic pelvic pain syndromes from a broadened systemic perspective. The shift in focus is supported by recent epidemiological studies showing that IC/PBS and chronic prostatitis/chronic pelvic pain syndrome are frequently associated with other chronic pain disorders, such as fibromyalgia (chronic pain of unknown origin), chronic fatigue syndrome and irritable bowel



syndrome. These findings suggest the possibility of common underlying disease processes in these chronic disorders.

True to the multidisciplinary charge, the UCLA team led by Dr. Rodríguez and Dr. Mayer, a gastroenterologist who is director of the UCLA Center for the Neurobiology of Stress and Women's Health, includes investigators from a variety of fields. The UCLA site is playing a major role in two of the multi-center MAPP studies. An epidemiologic study conducted over the five-year period will attempt to learn more about potential causes and risk factors by comparing a large group of IC patients and controls. "We hope to better understand not only who gets the condition, but also who is most likely to experience what type of symptoms," Dr. Rodríguez says. Among the factors under investigation are genetics and the role of stress and traumatic life events. The researchers will also attempt to identify so-called biomarkers in the urine that could assist in diagnosis. In addition, the UCLA group is the lead site on a multi-center MAPP project that will use brain-imaging techniques to study the role of the central nervous system in IC/PBS. All of the study sites will also conduct basic laboratory research, with UCLA focusing on the relationship between stress and bladder function.

Dr. Rodríguez concludes: "We hope that by combining forces with other centers and taking this broad, multidisciplinary approach, we will make progress that will ultimately lead to strategies that will enable us to intervene — both to improve treatment and to prevent the condition from becoming chronic."



Alumni Spotlight

David F. Penson, MD, MPH

"My interest in health services research is 100 percent Mark Litwin's fault," quips David F. Penson, MD, MPH, when asked how he chose his line of work.

Born and raised in Long Island, New York, Dr. Penson completed his undergraduate work at the University of Pennsylvania and received his medical degree from Boston University School of Medicine. When a friend moved to Los Angeles for a job in the entertainment industry, Dr. Penson decided to look into residency programs on the West Coast. "UCLA had the best program in the country, and I was smart enough to apply and lucky enough to be accepted," he says. From 1991 to 1997, Dr. Penson served as a resident in both surgery and urology at UCLA; he cites Dr. Jean deKernion (chair of the Department of Urology), Dr. Jacob Rajfer (professor of urology) and Dr. Litwin (professor of urology and health services) as physician-scientists who influenced his career.

Dr. Litwin, in particular, served as a mentor to Dr. Penson and exposed him to the impact health services research can have on a patient's life. "I am able to do studies that influence practices and care," Dr. Penson says. "This type of research can affect policy that changes patient care for the better." While his studies focus on clinical epidemiology and health services research for all urologic diseases,

Dr. Penson's specific interests include the impact of prostate cancer and erectile dysfunction on patients' quality of life. He also maintains a strong interest in health policy and quality improvement initiatives.

In August of last year, Dr. Penson joined the faculty at Vanderbilt University as professor of urologic surgery and director of the Center for Surgical Quality and Outcomes Research at the Vanderbilt Institute for Medicine and Public Health. He maintains a clinical practice in urologic oncology at Vanderbilt University Medical Center. Dr. Penson says he enjoys his role at Vanderbilt because "it is four or five different jobs in one, which keep me engaged and on my toes."

He looks forward to spending more time working with fellows and residents in his current position and building on the lessons imparted by Dr. Litwin and others at UCLA. "The importance of building human capital is something I learned at UCLA," Dr. Penson says. "Knowing that I am passing on what I have learned to the next generation of urologists brings me great satisfaction."

Donor Spotlight

One of the most important missions of the UCLA Department of Urology is to educate and train the next generation of leading physicians and scientists. It is a cause that **Dr. Jean deKernion**, department chair, considers essential for all leading medical institutions. The department, Dr. deKernion explains, has an obligation to bring the "best and brightest" into its laboratories and patient settings, where they can work under the mentorship of some of the country's top investigators and practitioners. This experience gives these young men and women the insight and enthusiasm to pursue exceptional careers. Once they have acquired their knowledge and skills and are operating laboratories and

departments of their own, they too will build upon their strengths, make new discoveries and pass that vital information on to others.

Following are brief sketches of donors and their gifts that have supported rising stars in the department. Their commitment has helped trainees with their education at UCLA, as well as enhanced the service capacity of the clinical program, enriched research projects and exponentially increased the number of urologists across the globe who will become the doctors for our children and grandchildren.

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Simple “Sling” Improves Male Incontinence



Jennifer T. Anger, MD, MPH, performs the procedure for men who experience mild to moderate post-prostatectomy incontinence.

“The AdVance transobturator sling has become increasingly popular among men who are experiencing leakage after their prostate surgery.”

— Jennifer T. Anger, MD

An effective, minimally invasive surgical alternative to the artificial urinary sphincter has emerged for men who experience mild to moderate urinary incontinence after a radical prostatectomy.

“The AdVance transobturator sling has become increasingly popular among men who are experiencing leakage after their prostate surgery,” according to Jennifer T. Anger, MD, MPH, assistant professor in the UCLA Department of Urology, who performs the procedure. “Many men, even if they don’t expect a cure from the sling, prefer to have an improvement in their symptoms that doesn’t involve having to pump an artificial device,” Dr. Anger explains.

The incidence of post-prostatectomy incontinence has declined in recent years with advances in surgical techniques; however, even in the hands of the best surgeons, a small percentage of men will develop urinary incontinence after prostatectomy, Dr. Anger notes.

The artificial urinary sphincter is still considered the “gold standard” for treating post-prostatectomy incontinence: An implanted device keeps the urethra closed to eliminate leakage, and a small pump placed in the scrotum is controlled by the patient to void. The device restores continence in the majority of men, who typically require only one pad per day — if they even need that.

Nonetheless, Dr. Anger says, “Although most men adapt very quickly to this device, many choose not to have it because they don’t want to have to pump anything mechanical in order to void.” In addition, she notes, the artificial sphincter tends to break down over time, usually within 10-15 years after it is placed.

The AdVance male sling improves or eliminates incontinence symptoms without

the need for more extensive surgery or the implantation of a mechanical device that requires pumping to void. A small piece of polypropylene mesh is used to restore the anatomy. “After a radical prostatectomy, the urethra can prolapse out of the pelvis,” Dr. Anger explains. “The sling allows the patient’s own sphincter to properly function by elevating the urethra back to its original position.”

The procedure involves a single incision made in the perineum (the area just under the testicles) and two small incisions where the sling is placed in the groin area. The surgery takes less than an hour and patients are able to go home on the same day, with minimal recovery time.

“Even mild incontinence can have a significant impact on quality of life.”

Ideal candidates for the AdVance male sling are patients with mild incontinence after prostatectomy — requiring between one and three pads per day — who have a functional external sphincter (the ability to voluntarily start and stop their urinary stream). Men who have had radiation therapy or brachytherapy for their prostate cancer may be less likely to benefit from the sling, but are often able to experience significant improvement with the artificial sphincter device, Dr. Anger notes.

“Even mild incontinence can have a significant impact on quality of life,” Dr. Anger says. “Wearing pads can be a major nuisance, affecting everything from exercise to sexual intimacy. Having an effective, minimally invasive alternative to the artificial sphincter device represents a major step forward.”

Donor Spotlight

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The **Jean Perkins Foundation** has been involved in many projects within the Department of Urology, as well as other fields of medicine at UCLA. Within the last several years, the foundation has funded new faculty members and young researchers; propelled innovative, early stage research projects to the next level; and been instrumental in helping advance the treatment of a number of urologic diseases and disorders. Its most recent gift established the Jean Perkins Foundation Research Scholars Program, which supports two residents during their research year.

Over several years, **Donald de Brier's** contributions have made a significant impact on the department's bladder cancer research and the Laparoscopic Urology and Endourology Fellowship Program. Mr. de Brier's educational funding, along with employee matching gifts through Occidental Petroleum Corporation, gives fellows the opportunity to hone their minimally invasive surgical techniques and lay the groundwork for future innovations and achievements.

Because of their interaction with Dr. Shlomo Raz and his team, **Anna and David Grotenhuis** decided to create the Anna and David Grotenhuis Fellowship in Female Urology, Reconstructive Surgery and Urodynamics in late 2009. Under Dr. Raz's direction, each trainee completes a two-year fellowship with time in the clinic treating patients and furthering this division's cutting-edge laboratory research. The current trainee wishes to specialize in female pelvic floor disorders and male voiding dysfunction, and the couple's generosity will enable her to continue the pursuit of her goals.

Long-time UCLA supporters **Wendy and Kenneth Ruby** give across campus and to several areas within the medical sciences. The couple has remained engaged with the department through its Board of Advisors and by providing seed and start-up moneys for Pediatric Urology and young faculty research projects. Most recently, the Rubys funded two residents during their research year, both focused in the area of prostate cancer. Such generosity was invaluable to the residents' investigations and careers.

Kudos

In a major development for the Department of Urology, four faculty members have been named as holders of endowed chairs: **Peter Schulam, MD**, is the holder of the Henry E. Singleton Chair in Urology; **Shlomo Raz, MD**, is the holder of the Shlomo Raz, MD, Chair in Urology; **Robert Reiter, MD, MBA**, is the holder of the Bing Professorship of Urologic Research; and **Fairooz Kabbinavar, MD**, is the holder of the Henry Alvin and Carrie L. Meinhardt Chair for Kidney Cancer Research. Appointment to an endowed chair is a special honor for a faculty member and recognition of his or her achievement as a distinguished scholar and teacher.

Jennifer Anger, MD, MPH, assistant professor of urology, was awarded a highly competitive Challenge Grant through the National Institutes of Health (NIH) for her "Abdominal Colpopexy: Comparison of Endoscopic Surgical Strategies (ACCESS)" proposal. Her team will compare the efficacy of robotic versus laparoscopic surgery for vaginal vault prolapse with respect to costs of care and patient convalescence. For this project, Dr. Anger built a collaborative team that includes faculty from UCLA's departments of urology and obstetrics & gynecology, along with colleagues from the UCLA School of Public Health and the departments of urology and obstetrics & gynecology at the Loyola University Health System in Chicago. It is Dr. Anger's fourth NIH grant.

Arnold I. Chin, MD, PhD, assistant professor of urology, is the recipient of the 2009 STOP CANCER Research Career Development Award. It provides funding over three years and is matched with in-kind funding through UCLA's Jonsson Comprehensive Cancer Center. It is given to young scientists at the National Cancer Institute-designated UCLA's Jonsson, USC's Norris and City of Hope comprehensive cancer centers. Awardees are selected yearly based on nominations of each center's internal peer-reviewed recommendations.

H. Albin Gritsch, MD, associate professor of urology and surgical director of the Kidney Transplantation Program, received a grant from

the Research Services Research Fund (RSRF) for his proposal "Patterns of Messenger RNA and Micro RNA Expression in Renal Allograft Rejection." RSRF is a collaboration between UCLA's Department of Pathology & Laboratory Medicine and the David Geffen School of Medicine (DGSOM) at UCLA to provide support for DGSOM faculty-initiated research, with a particular emphasis on translational research projects that utilize the Department of Pathology Clinical Microarray Core Laboratory.

Since 2001, **Mark S. Litwin, MD, MPH**, professor of urology and public health, and his team have managed the state IMPACT (Improving Access, Counseling and Treatment) for Californians with Prostate Cancer program for low-income, uninsured men with prostate cancer. This important and productive program has served thousands of indigent men throughout California. Dr. Litwin was notified that the state will renew funding for the program at more than \$3 million for 2010-11 — a notable achievement in this time of fiscal austerity.

The National Association for Continence awarded **Shlomo Raz, MD**, professor of urology and co-director of the Division of Female Urology, Reconstructive Surgery and Urodynamics, with the Rodney Appell Continence Care Champion Award. The honor was presented by Eric Rovner, MD, one of Dr. Raz's former fellows, at the Society for Urodynamics & Female Urology annual meeting in St. Petersburg, Florida, last winter.

Gang Zeng, PhD, associate professor of urologic oncology and member of UCLA's Jonsson Comprehensive Cancer Center, received an NIH grant as part of the American Recovery Reinvestment Act for his project "Autologous Antibody Plus PSA Assay for Prostate Cancer Patients," which aims to develop a novel technology for prostate cancer detection and diagnosis. **David Nguyen, PhD**, who works in Dr. Zeng's lab, has received a postdoctoral fellowship as part of UCLA's Tumor Immunology NIH Training Grant. His project is designed to find prostate cancer-derived ligands that interact with the human innate immune system.



Clinical Trials Update

Discovering New Ways to Care



The UCLA Department of Urology is committed to ongoing research in a quest to develop new treatments and cures for all urologic conditions. Our team has been instrumental in making major breakthroughs in the areas of:

- Prostate cancer, prostatitis and BPH (benign prostatic hyperplasia) treatments
- Kidney cancer and transplantation
- Male infertility and sexual dysfunction
- Pelvic medicine, incontinence and reconstructive surgery

FEATURED CLINICAL TRIAL: SUNITINIB (SU011248) VERSUS PLACEBO IN PATIENTS WITH ADVANCED UROTHELIAL CARCINOMA

• **Bladder Cancer**, PI: **Arie Beldegrun, MD**; co-PI: **Arnold I. Chin, MD, PhD** — a study examining the use of sunitinib (SU011248), a small molecule that targets the growth factors and inhibits the blood supply to tumors, in the treatment of patients with advanced bladder cancer. To be eligible for this trial, patients must have achieved at least stable disease following combination chemotherapy. Few alternatives are available to bladder cancer patients after chemotherapy. SU011248 has been investigated and used extensively in kidney cancer; this investigation will be the first in bladder cancer.

KIDNEY CANCER

- **Kidney Cancer**, PI: **Fairooz Kabbinar, MD** — a study to evaluate the safety and effectiveness of sunitinib when given in a neoadjuvant setting prior to radical nephrectomy (surgical removal of the kidney).
- **Kidney Cancer**, PI: **Allan Pantuck, MD, MS, FACS** — a study of post-surgery therapy for

patients with high-risk recurrence of kidney cancer. (*Pharmaceutical company: Pfizer*)

- **Kidney Cancer**, PI: **Fairooz Kabbinar, MD** — a study of two combination therapies for patients with advanced kidney cancer. Study aims to discover if RAD001, in combination with bevacizumab, can slow progression of cancer when compared to bevacizumab combined with interferon alfa-2a. (*Pharmaceutical company: Novartis*)
- **Kidney Cancer**, PI: **Fairooz Kabbinar, MD** — a study to learn whether Torisel and Nexavar (taken as single treatments) are safe and useful in treating advanced kidney cancer when given after failure with Sutent treatment. (*Pharmaceutical company: Wyeth*)

KIDNEY TRANSPLANTATION

- **Kidney Transplantation**, PI: **H. Albin Gritsch, MD** — A study to evaluate new methods of monitoring the immune system in patients following renal transplantation. The goal is to detect rejection at an early stage, before the new kidney is severely injured. These new techniques may reduce the need for biopsy of the kidney and may allow for less immunosuppression in some patients.

PROSTATE CANCER AND DISORDERS

- *Prostate Cancer*, PI: **Matthew Rettig, MD** — a study examining use of TOK-001 in chemotherapy naïve castration-resistant prostate cancer patients to determine the safest dose and discover how TOK-001 moves through the body, how effective it is at treating prostate cancer, and to learn if it is safe. (Pharmaceutical company: Tokai)
- *Prostate Cancer*, PI: **Sven de Vos, MD** — a safety study to determine the maximum tolerated dose of SGI-1776, a PIM kinase inhibitor, in patients with hormone- and docetaxel-refractory prostate cancer and relapsed/refractory non-Hodgkin's lymphoma. (Pharmaceutical company: SuperGen, Inc.)
- *Benign Prostate Hyperplasia*, PI: **Leonard S. Marks, MD** — an investigational therapy study for the treatment of symptoms of benign prostate hyperplasia (BPH) by testing the safety and effectiveness of Litx in treating patients with lower urinary tract symptoms (LUTS) due to BPH. (Pharmaceutical company: Light Sciences Oncology)
- *Prostate Cancer*, PI: **Matthew Rettig, MD** — a study to evaluate the use of a cancer drug (ZD4054) versus a placebo in nonmetastatic hormone-resistant prostate cancer patients. (Pharmaceutical company: Astra Zeneca)

PELVIC MEDICINE

- *Pelvic Medicine*, PI: **Larissa Rodríguez, MD** — a study for those suffering from chronic pelvic pain, interstitial cystitis, chronic prostatitis or painful bladder syndrome. The purpose is to better understand how pain is originated and maintained in people with chronic pain.

For more information about eligibility requirements and participation in these or other UCLA Urology clinical trials, please contact Nazy Zomorodian, MSN, CUNP, at (310) 794-3550, or go to www.urology.ucla.edu and click on the "Clinical Trials" link.

Comings & Goings

The UCLA Department of Urology is proud to introduce the newest members of its faculty:



Salley Stewart, RN, NP, was recruited in October as nurse practitioner in the Department of Urology after an extensive search. She is a graduate of the Harbor-UCLA Medical Center nurse practitioner training program and has 12 years of experience as a nurse practitioner with a focus on women's health and gynecology. In her new role, she will be supporting the Division of Female Urology, Reconstructive Surgery and Urodynamics.



Ala Wheelock, RN, MSN, joined the Department of Urology in January as the nursing administrator for all three of the UCLA Urology clinics (Frank Clark Urology Center, Westwood; Frank Clark Urology Center, Santa Monica; and Clark-Morrison Children's Urological Center). She also will be instrumental in leading program development and patient satisfaction initiatives. Ms. Wheelock is a recent graduate of the UCLA Master of Science in Nursing program, with an emphasis in nursing administration, and has worked as a charge nurse at the UCLA emergency department since 2004. Her past positions include critical care nurse and flight nurse with a paramedic helicopter team.

Institute of Urologic Oncology Launched at UCLA

UCLA has launched the Institute of Urologic Oncology, bringing together a multidisciplinary team of scientists and physicians to develop leading-edge therapies for the treatment of prostate, kidney, bladder and testicular cancers. Disciplines represented in the institute include urologic oncology, medical oncology, diagnostic and interventional radiology, pathology and nursing, with expertise in both basic sciences and clinical trials.

Patients will benefit from the institute's top diagnostic tools, expertise in robotic and minimally invasive surgery, and the combined experience of the experts, who often treat the most complicated urologic cancer cases. In addition, a joint, multidisciplinary board representing all genitourinary specialties meets at the institute to prioritize and implement collaborative research,

as well as to discuss complicated and challenging cancer cases referred to UCLA.

"Our mission is to offer patients outstanding, individualized surgical and medical care and access to the latest and most innovative clinical trials, with the overall goal to cure urologic cancers," adds urologist Arie Belldegrun, MD, the institute's director, professor of urology, Roy and Carol Doumani Chair in Urologic Oncology, and a researcher at UCLA's Jonsson Comprehensive Cancer Center.

"With this approach, we are able to get leading-edge therapies to patients faster, taking the findings out of the lab and into practice in much less time," adds Jean deKernion, MD, chair of the UCLA Department of Urology.