Family Hopes the Wait Will Soon Be Over

Sherry Ghassemlou has learned to recognize the signs indicating that her 7-year-old son Arya is experiencing a urinary tract infection (UTI). Unfortunately, that's because she has had lots of practice.

Arya was born with anal atresia – the absence of an opening at the bottom end of the intestinal tract. Among the complications he has suffered is lack of bladder control, which has caused frequent UTIs. “Arya has what is called a neurogenic bladder – his bladder doesn’t work well because messages from the spinal cord fail to get through,” says Dr Bernard Churchill, chief of pediatric urology at the Clark-Morrison Children's Urological Center at UCLA. Last year, Dr Churchill performed major reconstructive surgery that helped Arya become continent, but the boy continues to require catheterizations that make him prone to frequent infections.

continued on page 4
Each year, millions of people suffer from urinary tract infection (UTI), the most common urological disease in the United States. For decades, the approach to diagnosing and treating these infections has remained the same: Physicians who suspect a UTI take a urine specimen and send it to the laboratory for a testing process that takes at least two days to yield results.

In the meantime, the patient can either wait and continue to suffer, or be started on antibiotics that may or may not be necessary – and, even if they are indicated, may or may not be the right ones to kill the bacterial culprit.

Now, results of research on a new technology originally conceived by Drs Bernard Churchill, chief of pediatric urology at the Clark-Morrison Children’s Urological Center at UCLA, and Joseph Liao, a former resident in Dr Churchill’s lab, suggest that in the future, UTI diagnosis could be reduced from days to minutes – with greater accuracy.

In addition to reducing patient suffering, this “urosensor” could substantially decrease health care costs.

The new technology, developed by Drs Churchill and Liao in collaboration with Drs. David Haake and Yang Li, researchers in UCLA’s engineering school, the VA Medical Center and GeneFluidics, is a chip embedded with ultra-sensitive electrochemical sensors. In a study reported in the February issue of the peer-reviewed Journal of Clinical Microbiology, the urosensor correctly identified the infection-causing gram-negative bacteria species in 98 percent of the clinical UTI samples that were tested. The results represent the first-ever species-specific detection of bacteria in human clinical fluid samples using a microfabricated electrochemical sensor array. Equally important, these results were produced in 45 minutes, compared to the two days required for conventional testing methods.

“By coupling UCLA’s robust probes with GeneFluidics’ ultra-sensitive biosensor system, we were able to identify urinary tract infection pathogens in a time frame that would enable physicians to make dramatically superior clinical decisions,” Dr Churchill explains.

Modern Science for an Old Problem

UTIs account for more than 7 million office visits and more than 1 million hospital admissions per year in the United States. In the hospital, catheter-associated UTI accounts for 40 percent of all in-hospital acquired infections – more than 1 million cases each year. The total cost of UTIs to the U.S. health care system in 2000 was approximately $3.5 billion.

In current laboratory practice, contaminating pathogens in urine specimens are grown in culture dishes until they can be visually identified. The major drawback of this century-old technique is the two-day time lag between specimen collection and bacteria identification. As a result, physicians must decide whether to prescribe antibiotic therapy and, if so, which type of bacteria to treat – all without knowing the cause of the infection, if any.

“It really puts the physician in the dark,” says Dr Liao. “As doctors we can use our clinical judgment to start patients on certain antibiotics while the testing is taking place, but sometimes we’re wrong, and it takes time to get that information to the patient – who, meanwhile isn’t getting any better.”

Adds Dr Churchill: “For a UTI, the three important questions are whether there are significant bacteria in the urine, what kind of bacteria are there, and what antibiotics those bacteria are susceptible to. With the current testing method, we have to make decisions about treatment based on...
clinical history, physical examination and some rudimentary supportive tests before the lab information comes back to tell us whether we were right.”

In contrast, the new biosensor technology would allow physicians to prescribe targeted treatment without the wait, based on a molecular diagnosis. “UTI is a microbiological problem that has been treated as a macrobiological problem – growing the bacteria on a Petri dish for analysis,” says Dr Churchill. “With this new technology, we are applying molecular biological techniques and microbiological analysis to these bacteria, and eliminating that step of growing them.”

**Chip Transmits DNA Sequence Information**

In the study, funded by the National Institutes of Health, individual sensors on GeneFluidics’ 16-sensor chips were coated with UCLA-designed species-specific genetic probes. Clinical urine samples were directly applied to the chips and the electrochemical signal was subsequently measured by GeneFluidics’ multi-channel reader instrument. The UTI pathogens were identified by examining which signals on the sensor chip were elevated. “Just as the telephone turns sound into an electrical signal, our sensor turns DNA sequence information into an electrical signal, which is then read on a computer,” Dr Churchill explains.

The collaboration between UCLA, the VA and GeneFluidics began in 2001, thanks to initial funding from Frank W. Clark Jr., and the Wendy and Ken Ruby Fund for Excellence in Pediatric Urology Research. Subsequently, the work has been supported by a $5.6 million Bioengineering Research Partnership grant from the NIH’s National Institute of Biomedical Imaging and Bioengineering.

Ongoing work at UCLA and the VA Medical Center is now focused on developing even better detection methods. At GeneFluidics, engineers are integrating the biosensors into microfluidic cartridges and building a new instrument for faster and completely automated experimentation. Says Dr Churchill: “This technology might reach the point where it is feasible for high-risk patients to do the tests in their own homes.”

**KUDOS:**

**Isla Garraway, MD, PhD**

assistant professor of urology, received a National Institutes of Health supplemental award of $151,000 for her project titled “Animal Models of Human Cancers” and a Department of Defense grant of $347,550 for her project titled “Development of a Mouse Model for Prostate Cancer Imaging and Study of Disease Progression.”

**Robert Reiter, MD**

professor of urology and microbiology, was awarded a $579,375 Department of Defense grant for “Mechanism of Action of Prostate Stem Cell Antigen Targeted Antibody Therapy and its Relevance to Clinical Application in Prostate Cancer.”

**Lily Wu, MD, PhD**

was awarded a postdoctoral fellowship by the American Cancer Society for $44,000 for his project titled “Unwarranted Surgical Variation for Early-Stage Kidney Cancer” and $60,000 from the Ruth L. Kirschstein National Research Service Award Fellowship for his project, “Variation in Surgical Care for Early-Stage Kidney Cancer.” Mark S. Litwin, MD, MPH, professor of urology in the David Geffen School of Medicine at UCLA and professor of health services in the School of Public Health, will serve as the mentor for both of these projects. Dr Miller was also awarded a $30,000 AUA Research Scholar Award for “Unwarranted Variation in Surgical Treatment of Patients with Early-Stage Kidney Cancer.” Dr Miller will start a one-year health services research fellowship with Dr Litwin on July 1.

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**Gang Zeng, PhD**

visiting assistant professor of urology, received a Department of Defense grant for $347,552 for his project titled “Isolation and Characterization of Prostate Cancer Stem Cells Following Androgen Ablation.”

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Although the Ghassemlous have gotten better at recognizing when their son has the symptoms of a UTI, they must contend with a problem common to the millions of people who suffer from these infections each year. “By the time you make an appointment, go in, give the urine sample, wait for the results, and then go back in to get them, it can be a week or more,” says Ms Ghassemlou. “In the meantime, you can be prescribed an antibiotic but it takes a couple of days to know whether it’s the right one…and if it’s not, you have to start with something else and the situation has gotten worse.”

The time it takes to reach a definitive diagnosis and the discomfort she sees in her son during that delay explain why Sherry Ghassemlou is excited about research being conducted by Dr Churchill and colleagues at the Clark-Morrison Children’s Urological Center at UCLA, the Los Angeles VA and the biotech company GeneFluidics (see the article on page 2). The research group, headed by Dr Churchill, recently reported promising results on their urosensor, which could one day provide immediate, definitive results while patients like Arya Ghassemlou wait in the doctor’s office – or, perhaps, could be used at home. “To have access to a simple test that we could take at home whenever Arya experiences these symptoms would make an enormous difference in our lives,” says Ms Ghassemlou.

A bill introduced in the California Legislature by Sen Deborah Ortiz (D-Sacramento), which was approved and signed by the governor last fall, makes IMPACT (Improving Access, Counseling and Treatment for Californians with Prostate Cancer) – led by UCLA Department of Urology professors Mark S. Litwin, MD, MPH, and James R. Orecklin, MD, MPH – a permanent entity within the California Department of Health Services. Adoption of this legislation put the program back on track, enabling enrollment to resume and services to continue. In April, UCLA was once again awarded the IMPACT administration contract in a new three-year, $9.7 million agreement.

Advocates for the program are extremely pleased that UCLA will continue to direct IMPACT because they see the university’s uninterrupted leadership as providing stability and continuity of care for the men participating. “We are very happy to be awarded the contract to continue administering the IMPACT program,” says Dr Litwin. “Our goal with IMPACT has always been to improve the health of underserved men in California who develop prostate cancer. We look forward to continuing our efforts to address not only patients’ acute treatment needs, but also their longer term needs to help them return to healthy, fulfilling lives after prostate cancer.”

IMPACT statewide enrollment now exceeds 700 men. Without the program, low-income, uninsured men would have been forced to let their cancer progress untreated until they became disabled and eligible for Medi-Cal (at a much higher public cost). “IMPACT is the program of last resort for hundreds of men who are diagnosed with prostate cancer, but have limited access to public health programs,” says Sen Ortiz, author of the legislation establishing and continuing the program. “I’m thrilled that this important medical care program will continue under the leadership of UCLA, and that these men will continue to receive quality care without interruption.”
Department Is Seeking Volunteers for Trials

The Department of Urology is committed to ongoing research in a quest to develop new treatments and cures for all urologic conditions. It is our goal to focus on basic and population-based research with the hopes that we can rapidly translate the findings into clinical trials and community applications. Below is a list of our trials. For additional program information, please contact the Clinical Trials Office at (310) 825-5538.

Kidney Cancer:

A Phase II Study of Bortezomib (Velcade) Administered as a Single Agent in Metastatic Non-Clear Cell Renal Cell Carcinoma Patients. The management options for papillary renal cell carcinoma (RCC) are limited, as patients in this subtype of RCC, which represents about 15% of all RCC cases, are not responsive to immunotherapy and have not been well-studied in recent trials of some of the novel small molecule inhibitors. In this trial, Velcade (bortezomib) is being administered as a single agent in patients with papillary RCC. The trial is open to patients with metastatic papillary RCC and measurable disease. Patients will be treated with the FDA-approved dose and schedule of Velcade. The primary endpoint of this study is objective response rate. (PI: Robert Figlin, Co-PI: Allan Pantuck)

A Phase II Open-Label Study of Volociximab (M200) Patients with Metastatic Renal Cell Carcinoma. Volociximab is a high-affinity chimeric monoclonal antibody that binds α5ß1 integrin. This receptor plays a pivotal role in angiogenesis and is necessary for the proliferation migration and survival of activated endothelial cells. Inhibition of α5ß1 prevents endothelial cell migration, induces apoptosis of endothelial cells, and inhibits angiogenesis. Renal cell is a highly vascular tumor and appears to display α5ß1 on its vasculature. Because this molecule has shown to prevent tumor angiogenesis, volociximab may arrest or prevent tumor growth. (PI: Robert Figlin, Co-PI: Allan Pantuck)

A Randomized Double Blind Phase III Study to Evaluate Adjuvant G250 Treatment Versus Placebo in Patients with Clear Cell RCC and High Risk of Recurrence. (PI: Arie Belldegrun, MD)

A Randomized Phase III Study of the Efficacy and Safety of Sunitinib Malate Alone or in Combination with Interferon Alfa-2B as First-Line Therapy for Metastatic Renal Cell Cancer (PI: Robert Figlin, Co-PI: Allan Pantuck)

Phase II Study Designed to Estimate the Efficacy of Combination Therapy of Standard High Dose Bevacizumab and Aldesleukin in Patients with Metastatic Renal Cell Carcinoma (PI: Robert Figlin, Co-PI: Allan Pantuck)

Dendritic Cell Vaccine as Cancer Immunotherapy in Patients with Metastatic Renal Cell Cancer (PI: Robert Figlin, Co-PI: Allan Pantuck)

Prostate Cancer:

Multicenter, Open-Label, Randomized, Phase III Trial Comparing Immediate Adjuvant Hormonal Therapy (ELIGARD - leuprolide acetate) in Combination with TAXOTERE (docetaxel) Administered Every Three Weeks Versus Hormonal Therapy Alone

Versus Deferred Therapy Followed by the Same Therapeutic Options in Patients with Prostate Cancer at High Risk of Relapse After Radical Prostatectomy (PI: Robert Reiter, MD)

A Randomized, Double-Blind, Placebo-Controlled Study of the Pomegranate Juice, or Extract, or Placebo in PSA Rising Prostate Cancer Patients Following the Failure of Primary Treatment (PI: Allan Pantuck, MD)

A Randomized, Double Blind, Placebo Controlled Phase 3 Trial of Immunotherapy with Autologous Antigen Presenting Cells Loaded with PA2024 (Provenge, APC8015) in Men with Metastatic, Androgen Independent Prostatic Adenocarcinomas (PI: Allan Pantuck, MD)

A Phase 3 Randomized, Open-Label Study of Docetaxel in Combination with CG1940 and CG8711 Versus Docetaxel and Prednisone in Taxane-Naive Patients with Metastatic Hormone-Refractory Prostate Cancer with Pain (PI: Allan Pantuck, MD)

A Phase 3, Randomized, Open-label Study Evaluating DN-101 (Vitamin D Analog) in Combination with Docetaxel in Androgen-Independent Prostate Cancer (PI: Allan Pantuck, MD)

Quality Assessment of the Roei Loop Resectoscope for Transurethral Resection of Bladder Neoplasm and BPH (PI: Arie Belldegrun, MD)

Pelvic Medicine, Incontinence and Reconstructive Surgery:

Acral Root Neuromodulation for Pelvic Pain and Overactive Bladder (PI: Larissa Rodriguez, MD, Co-PI: Shlomo Raz, MD)

Evaluation of Family History and Genetic Predisposition for Development of Vaginal Prolapse (PI: Larissa Rodriguez, MD, Co-PI: Eric Vilain, MD)

Evaluation of General Stress Response in Patients with Interstitial Cystitis (PI: Bruce Naliboff, MD, Co-PI: Larissa Rodriguez, MD)
Judith and Robert Winston completed a gift to UCLA’s Clark Urological Center that will fund the distinguished Judith and Robert Winston Chair in Pediatric Urology and also support Urologic Oncology. The Winsters included an additional contribution to be used for general research purposes within the Department. The Department appreciates the Winsters’ continued generosity. “Clark Urology is a valuable resource to the field of medicine,” Mr Winston explains. “Funding endowed chairs and research programs at UCLA ensures that we will have the best people in place performing cutting-edge research far into the future.”

Wendy and Ken Ruby’s Support Launched Urosensor Research

Donors Dedicate Gifts to New Research

Just over five years ago, Wendy and Ken Ruby wanted to show their support for UCLA’s leadership in medical research and express their gratitude for the lifesaving treatment that Mrs Ruby had received from Dr Jean B. deKernion, chair of the Department of Urology. While discussing their goals with Dr deKernion, the Rubys learned of the tremendous needs in pediatric medicine. They responded with a major contribution that provided start-up funding for the urosensor project, led by Drs Bernard Churchill and Joseph Liao. The Rubys’ gift made it possible for Drs Churchill and Liao and their team of researchers to gather the data necessary to apply successfully for multimillion-dollar funding from the National Institutes of Health (NIH). The broader research performed under the NIH grant resulted in the successful automation of the urosensor device.

When Dr deKernion emphasized the significance of funding children’s medicine in that initial meeting, “We couldn’t have agreed with him more,” Mr Ruby says. The Rubys believe that support for pediatrics is especially critical because when young children are saved, entire lifetimes are transformed. Through several meetings with some of Dr Churchill’s young patients and their mothers, the Rubys witnessed firsthand how a child’s severe illness can create a complicated scenario for the entire family. “The mother, father, and siblings are all affected in a major way. Healing the child heals the whole family,” Mrs Ruby says.

Mr and Mrs Ruby continue to be actively involved with the Department of Urology as well as with other areas within the David Geffen School of Medicine at UCLA, including the Jonsson Cancer Center Foundation and the Department of Orthopaedic Surgery. Keeping in the spirit of providing seed and start-up moneys, they recently established the Wendy & Ken Ruby Urology Research Fund to support the investigations of Drs Isla Garraway and Larissa Rodriguez. These young Department of Urology faculty researchers are making strides in models for bladder and prostate cancer (Dr Garraway) and bladder tissue engineering from a patient’s own stem cells (Dr Rodríguez).

“We continue to support new research programs in order to get projects started that would otherwise not get off the ground,” Mrs Ruby says of the couple’s desire to contribute initial funding. “We know that private support helps the researchers get to the point where they can apply for major public funding that will help them make important scientific discoveries.”
March Conference Draws Record Attendance; Prominent Guest Speakers Tackle Current Challenges for Practicing Urologists

The 21st annual UCLA State-of-the-Art Urology Conference was held March 9-12 at the Ritz-Carlton Hotel in Marina del Rey. This ongoing conference, offered by the Department of Urology in conjunction with UCLA’s Continuing Medical Education office, is specifically designed for practicing urologists and the challenges they face in practice management.

The conference explores the most challenging management problems facing the practicing urologist. This year’s conference drew a record attendance of physicians participating in the three-day meeting, which featured lectures by departmental speakers along with several prestigious visiting professors, including Anthony V. D’Amico, MD (Harvard Medical School), Peter T. Scardina, MD, FACS, (Memorial-Sloan Kettering Cancer Center), and Joseph A. Smith, MD (Vanderbilt University Medical Center), acclaimed authorities on prostate cancer. Other visiting lecturers included Fergus V. Coakley, MD (UC San Francisco School of Medicine), Philip Kantoff, MD (Dana Farber Cancer Institute an Harvard Medical School), Steven A. Kaplan, MD (Columbia University), Randall B. Meacham, MD (University of Colorado School of Medicine), and Margaret S. Pearle, MD, PhD (University of Texas Southwestern Medical Center).

The Department wishes to thank the 2006 Course Chair, William J. Aronson, MD, and Conference Coordinator, Rain Burch, for their efforts in making State-of-the-Art 2006 such a success.

Dr. David F. Penson, one of a handful of fellowship-trained outcomes researchers in urology, was honored in 2006 with the American Urological Association’s Gold Cystoscope, the highest award given to a urologist within 10 years of completing residency.

After graduating cum laude from the University of Pennsylvania and earning his medical degree from Boston University, Dr. Penson completed his urology residency at UCLA in 1997, and was simultaneously awarded an American Foundation in Urologic Disease Health Services Research Scholarship and a Robert Wood Johnson Clinical Scholars Fellowship. As a fellow, he studied clinical epidemiology and health services research at Yale University, obtaining a Master’s in Public Health. Upon completion of his fellowship, Dr. Penson joined the faculty of the University of Washington School of Medicine. In 2004, he was recruited to the Keck School of Medicine at the University of Southern California, where he is now a tenured associate professor of urology and preventive medicine.

Dr. Penson’s academic work in the field of health-related quality of life (HRQOL) assessment in urologic disease has been extensive: He has published numerous articles on quality-of-life outcomes in both prostate cancer and erectile dysfunction. He is the co-developer of the Psychological Impact of Erectile Dysfunction (PIED) scale, a validated and reliable instrument designed to capture the effect of erectile dysfunction on the psychosocial aspects of HRQOL in the general population of men.

Since his move to USC, Dr. Penson has maintained an appointment as affiliate investigator at the Fred Hutchinson Cancer Research Center in Seattle, where he serves as principal investigator on an NIH-funded, population-based study designed to assess long-term HRQOL outcomes in younger men with prostate cancer. He recently received funding from the Centers for Disease Control and Prevention and the National Cancer Institute to study decision-making and HRQOL in men with localized prostate cancer. In addition to his research expertise in clinical epidemiology and health services research, Dr. Penson maintains important clinical perspective through his practice in urologic oncology at the USC/Norris Cancer Center and the Los Angeles County/USC Medical Center. Dr. Penson is the epitome of what the UCLA Urology Program strives to produce.
# Department of Urology Faculty

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<tr>
<th>Name</th>
<th>Position</th>
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<td>Urologic Oncology</td>
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<tr>
<td>William Aronson, MD</td>
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<td>Arne Beldregen, MD</td>
<td>Professor of Urology</td>
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<td>Carol Bennett, MD</td>
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<td>Robert A. Figlin, MD</td>
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<td>H. Albin Gritzsch, MD</td>
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<td>Christina Jamieson, PhD</td>
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<td>Mark S. Litwin, MD, MPH</td>
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<td>Urologic Oncology, Prostate Diseases</td>
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<td>Jacob Rajfer, MD</td>
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<td>Shlomo Raz, MD</td>
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<td>Robert E. Reiter, MD</td>
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<td>Larissa V. Rodríguez, MD</td>
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For appointments and referrals: Urology Appointment Line 310-794-7700

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