Leading the Fight Against Kidney Cancer
Pioneering UCLA Program Offers New Hope

Each year in the United States, 12,000 people die of kidney cancer and more than 32,000 people are diagnosed with the deadly disease. For many years, treatment options after such a diagnosis were limited. But that has changed dramatically, thanks in no small part to the pioneering efforts of the UCLA Kidney Cancer Program.

Established in 1991, the UCLA Kidney Cancer Program is internationally recognized as a premier center for the comprehensive treatment of the disease in its many forms. The program’s physicians have lectured around the world, authored more than 350 journal articles and a major kidney cancer textbook, and trained physicians from more than 20 countries.

The program is distinguished by its comprehensive, multidisciplinary approach, bringing together the full spectrum of medical and surgical services into a coordinated consultation and treatment program that offers state-of-the-art care, along with access to the latest investigational treatments through enrollment in clinical trials. Patients – many of whom travel great distances from within California, from other states and from abroad – benefit from the convenience of evaluation by multiple experts in a single visit. Indeed, the program offers an everything-in-one-place clinic with specialists in urology, medical oncology, radiology, nephrology and endocrinology, all of whom consult regularly, bringing their special expertise to bear on each case. “Patients don’t need to go back and forth to specialists – we all come to them on the same visit, work together to develop a treatment plan, and schedule everything at that time,” says Dr Arie Belldegrun, the program’s surgical director. “It is truly a ‘one-stop shop’ for the kidney cancer patient.”

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Do You Want to Help?

Contributions to the Department of Urology support our research programs and help our faculty make the cutting-edge discoveries that can save lives. You can learn more about how to support the Department of Urology at www.uclaurology.com/gifts. Please feel free to call 310-825-5056 if you have questions about making a gift to UCLA Urology.

If you received multiple copies of this newsletter, please feel free to share with a friend or colleague.

Research that Makes a Difference Today:

Second of Two Parts

Part one of this series can be viewed at www.uclaurology.com.

The Fall 2006 issue of the Clark Urological Center newsletter detailed the new and conventional therapies offered at UCLA for men with early-stage prostate cancer. In addition to offering all available treatments – from robotically assisted minimally invasive nerve-sparing prostatectomy and nerve-sparing open radical prostatectomy to the full spectrum of non-surgical options – the UCLA Prostate Cancer Program is renowned for its basic and clinical research excellence. Benefits of UCLA’s research excellence to the patient are manifold: Research in the program’s laboratories is translated to better therapies and diagnostic methods; patients with high-risk tumors and metastatic disease are able to access cutting-edge treatment approaches through enrollment in clinical trials; and the results of established treatment approaches are monitored to assist future patients and their doctors in making better-informed decisions.

In this issue, we focus on how the UCLA Prostate Cancer Program’s research is improving the diagnosis and treatment of early-stage prostate cancer, offering new hope for patients with advanced forms of the disease, and identifying exciting new strategies for preventing prostate cancer and its recurrence.

SPORE Grant Supports Translation of Findings

The program’s strength has been recognized and rewarded by the National Cancer Institute, which in 2002 designated the UCLA Prostate Cancer Program as a Specialized Program of Research Excellence (SPORE), making it one of a few institutions nationwide tapped to improve prevention, detection and treatment of the disease. UCLA is the only SPORE site in Southern California and one of only three in the western United States. The designation came with an $11.5 million grant aimed at furthering the program’s ability to bring together laboratory and clinical researchers in a joint effort to improve the detection, treatment, and prevention of prostate cancer.

“What makes this program stand out, in addition to our offering the full spectrum of established and experimental treatments, is that we have so much research going on that can affect patient outcomes,” says Robert Reiter, MD, professor of urology and director of the UCLA Prostate Cancer Program. The research initiatives that are benefiting patients include the identification of molecular markers that can be used to predict prostate cancer aggressiveness; laboratory research to better understand the biology of the disease, which has led to new drugs and experimental treatments; the program’s involvement in making these clinical trials – including those in which the laboratory research did not take place at UCLA – available to patients; and its large database and ongoing research on patient outcomes to bring greater clarity to the often-difficult decisions about treatment course.

Molecular Markers, Targeted Therapies

One of the program’s major successes has been in identifying new molecular markers that can help to determine the risk level of a patient’s prostate cancer more accurately. “We are now able to test patients for different molecular abnormalities that can provide information about the risk of the cancer being outside of the prostate or recurring, and whether they should be on an experimental therapy early on,” explains Dr Reiter. “This research instructs us on how these cancers act and has led us to the development of new treatments.”

Cancer is caused by genetic changes, and every tumor has its own pattern of genes that are turned on or off, a so-called “gene signature,” Dr Reiter explains. By detecting the presence or absence of certain genes,
the UCLA program has learned more about the prognosis for patients' cancers. More recently, these molecular markers are being used to select the best treatment approach for individual patients. Dr Reiter's lab was the first to show a correlation between the absence of a certain gene, p27, and a poor prostate cancer prognosis; patients can now be tested for the presence or absence of p27. UCLA researchers were also instrumental in finding that when the gene PTEN is lost, it may also be an indicator of a high-risk cancer. That research led to a clinical trial that was recently completed at UCLA of the immunosuppressant drug CCI-779 in these patients, with encouraging results. CCI-779 was found in the UCLA laboratory of Dr Charles Sawyers to slow the growth of prostate cancer tumors that lost the PTEN gene.

Indeed, for patients diagnosed with very high-risk prostate cancer, the established therapies are not always enough. “Radiation or surgery alone might cure only 30-40 percent of these men, so we know that better treatments are needed,” says Dr Reiter. The UCLA Prostate Cancer Research Program is a leader in developing new therapies and in offering experimental treatments to high-risk patients through clinical trials, along with options ranging from dietary interventions to new combinations of chemotherapy for patients with recurrent and advanced disease. One current trial compares the use of chemotherapy and hormones to hormonal therapy alone in men with high-risk disease following radical prostatectomy. Other current studies include two trials of cancer vaccines in men with advanced prostate cancer; a late-stage trial of chemotherapy and Vitamin D, also in men with advanced disease; and a new focal therapy for men with early prostate cancer.

Perhaps the greatest testimony to the program’s strength is the translation, or application, of UCLA bench research to drug development. Research at UCLA by Dr Pinchas Cohen and colleagues on insulin growth factors has led to development of a new drug, insulin growth factor binding protein, that will soon be offered in a clinical trial. After identifying the prostate stem cell antigen (PSCA) as an important molecular marker for high-risk prostate cancer, researchers in Dr Reiter's lab developed a PSCA antibody that, they demonstrated, could slow the growth of prostate cancer in animal models. The drug was recently licensed from UCLA by Merck and is now being tested nationally.

A small study headed by Dr Allan Pantuck, assistant professor of urology, recently found that drinking an eight-ounce glass of pomegranate juice each day increases by nearly four-fold the period during which prostate-specific antigen (PSA) levels remain stable in men being treated for prostate cancer. Pomegranate juice is known to have anti-inflammatory effects and high levels of antioxidants, which are believed to protect the body from free-radical damage. “This is not a cure, but we may be able to change the way prostate cancer grows,” says Dr Pantuck. The results of the study were impressive enough to launch a large clinical trial, underway at UCLA and 10 other centers across the country.

Ongoing Outcomes Research Informs Decisions

One of the major strengths of the UCLA Prostate Cancer Program is that it not only offers the full spectrum of treatments, but also has long-term, ongoing studies of the quality-of-life outcomes of the major early-stage prostate cancer therapies to assist patients and their doctors in making better-informed decisions about their treatment course.

“Each of these treatments affects urinary, sexual and bowel functions differently,” says Dr Mark S. Litwin, professor of urology and public health. The quality-of-life measurements, developed by Dr Litwin, provide a more accurate measure than ever before of how patients are affected by the treatments, not only because of the use of patient-answered questionnaires rather than physician reports, but also because how patients felt before the treatment is incorporated in the findings.

Drs Reiter and Jean B. deKernion, chairman of the Department of Urology, have tracked the results of patients undergoing all of the major prostate cancer treatments over the last 15 years. Their database enables them to better understand which treatments are most effective for which patients, and to improve techniques based on the results.

“Sometimes it’s hard to see the tangible benefits of biomedical research,” concludes Dr Reiter. “That is not at all the case here. This is not a pie-in-the-sky type of research program; we are conducting research that improves our ability to take care of patients.”
Team of Experts Determines Best Treatment

Having the multidisciplinary team of experts together is an advantage to patients for reasons well beyond convenience. Every two weeks, kidney cancer cases are presented to a panel with representatives from urology, medical oncology, pathology, radiology, and radiation oncology. Together, the experts review the cases and discuss therapy. “It’s a forum for refinement and discussion of the most complicated cases,” says Dr. Belldegrun. Patients benefit from both this multidisciplinary meeting of the minds and the very fact that every conceivable treatment approach is offered, including a discussion of any clinical trials for which they are good candidates.

“A diagnosis of kidney cancer doesn’t mean the same thing for every patient,” says Dr. Fairooz Kabbinavar, the program’s medical director. “Because of our program’s 15-year experience and laboratory expertise, we are in a better position to tailor therapy to the patient’s cancer.”

The program offers the full range of surgical options for kidney cancer, from extensive and complicated surgical procedures for advanced cancer to minimally invasive treatments for early disease. These surgically demanding procedures include radical and partial nephrectomy, treating tumors invading the large blood vessels and adjacent organs, as well as laparoscopic, ablative and other minimally invasive approaches.

“We see patients with advanced disease who need complicated surgery and additional treatment from medical oncology,” explains Dr. Belldegrun. “But we also see patients whose tumors are small, and who don’t need aggressive therapy. For these patients, we also have good options.” UCLA surgeons have been leaders in offering these less invasive procedures, including laparoscopic and robotic surgery that removes cancerous growths with as little trauma to healthy tissue as possible; cryosurgery, which uses a small probe and ultrasound guidance to freeze the tumor, killing the cancer cells and preventing further growth; and partial nephrectomy, in which, following the model of the lumpectomy for breast cancer, part of the kidney is spared.

The program also offers all available medical therapies for primary, adjuvant or palliative care. In addition to standard chemotherapy and radiation therapy, the program’s physicians have extensive experience in the use of immunotherapy to treat patients whose kidney cancer has metastasized to other parts of the body, and have helped to pioneer the development and use of newer targeted therapies that are proving to be effective treatments for advanced kidney cancer with fewer side effects (see page 5).

Clinical Trials Offer New Hope

For patients in whom surgery alone or in combination with one of the established medication regimens is not curative, enrolling in a clinical trial can offer new hope by providing access to cutting-edge treatments. The UCLA Kidney Cancer Program either originates or actively participates in virtually all significant clinical studies of promising new kidney cancer treatments. The program’s physicians can evaluate patients to determine if they are suitable candidates to participate in one or more of the ongoing trials. Current studies that are producing encouraging results include a vaccine therapy, molecular therapies, and newly discovered monoclonal antibodies against kidney cancer.

“We have seen patients who had been told they had no treatment options and have enrolled them in a clinical trial with positive results,” says Nazy Zomorodian, MSN, CUNP, the program’s clinical trials director. “Offering so many innovative clinical trials based on the different stages of disease provides major benefits to our patients.”

Beyond its impact on the patients seen at UCLA, the program helps to advance kidney cancer care throughout the world through its training of many of those who have gone on to leadership roles in major programs in the United States and abroad; through its numerous publications and presentations; and through its pioneering research efforts.

“Kidney cancer research and clinical care is all our group does, and patients really benefit from that experience,” says Dr. Allan Pantuck, the UCLA Kidney Cancer Program’s director of translation research. “It is a big advantage for them to be seen by a multidisciplinary team of experts who can develop a treatment plan based on the most up-to-date knowledge, with access to so many different established and investigational treatment options.”

New Urology Board of Advisors Meets

In December 2006, the new Board of Advisors of the UCLA Department of Urology held its first meeting in the department’s Belt Library. The purpose of the Board of Advisors is to provide assistance to the department in the areas of fundraising, donor development, advocacy, and public relations.

Members will participate in quarterly meetings where various faculty members present reports on their latest research projects. Frank W. Clark, Jr., a longtime donor and friend of the department, is serving as an honorary member. Other members include:

- Sheldon Appel
- Gunnar Bjorg
- James J. Carroll III
- Roy Doumani
- Amid Kheir
- John Lyddon
- Kenneth Ruby
- Steve Wallace
- Robert L. Winston
- David M. Zarem
Dramatic strides are being made in the treatment of metastatic kidney cancer as UCLA Kidney Cancer Program and other researchers develop targeted therapies – drugs that, unlike the more toxic chemotherapy, aim specifically at killing cancer cells without harming normal cells.

These new drugs have been facilitated by the great progress that has been achieved over the last decade by kidney cancer scientists – led by those at UCLA – in understanding the molecular mechanisms involved in the disease, which has, in turn, made kidney cancer a popular subject of pharmaceutical research. “Now that we have a better idea of the chain of events that are occurring in kidney cancer, we can use drugs that break one of the links in the chain,” says Dr Arie Belldegrun, surgical director of the UCLA Kidney Cancer Program. “That’s what is happening now, and it’s translating to improved survival for patients.”

In late 2005 and early 2006, two targeted drugs were approved by the U.S. Food and Drug Administration for treating advanced kidney cancer: Sutent and Nexavar. A third, CCI-779, has shown great promise in clinical trials at UCLA, and a fourth, Avastin, which is approved for treating colorectal and lung cancers, is also being tested in kidney cancer. All of these drugs target biological and molecular mechanisms that researchers at UCLA and elsewhere have found to be involved in the growth and progression of kidney cancer, including proteins such as Vascular Endothelial Growth Factor (VEGF), Platelet Derived Growth Factor (PDGF) and Tumor Growth Factor Alpha (TGF-α).

Sutent and Nexavar were the first two drugs to be approved for the treatment of kidney cancer since 1992, when the FDA approved Interleukin-2 based on pioneering research by Dr Belldegrun and colleagues at UCLA showing that it was effective, in combination with surgery, in treating some kidney cancer patients. In the ensuing years, considerable progress was made in treating metastatic kidney cancer thanks largely to strategies to stimulate the immune response to tumor antigens. So-called immunotherapy using Interferon alpha (Inf-α) and Interleukin-2 (IL-2) is expected to continue to play an important role in kidney cancer treatment, perhaps in combination with emerging targeted therapies – a strategy that is among those currently being tested in UCLA Kidney Cancer Program clinical trials.

The UCLA program was also at the forefront in the clinical trials that led to the approval of Sutent, which has become first-line therapy for metastatic kidney cancer patients. The first patients put on Sutent were at UCLA, and a large study that was instrumental in the drug’s approval involved UCLA patients. Dr Fairooz Kabbinavar, the UCLA Kidney Cancer Program’s medical director, has played an instrumental role in the development of Avastin and other anti-VEGF drugs, which block the tumor’s blood supply.

“The previous drugs we were using to treat metastatic kidney cancer were fairly toxic, and only a handful of patients responded to those treatments,” says Dr Kabbinavar. “These new targeted drugs are taken orally, have much more manageable side effects, and have shown significant benefit in many patients. This has provided us with additional, potentially effective treatment options.”

With the emerging FDA-approved and experimental targeted therapies – which are typically given in combination with surgery – the UCLA Kidney Cancer Program is better able to designate metastatic patients for drug treatments based on the molecular profile of their tumor and how, as a result of that profile, they are expected to respond to a given approach. Taking advantage of its vast database of patients treated over a 15-year period, the program has developed measures for determining patients’ prognosis and deciding who requires the most aggressive therapy (see the accompanying article on page 9). “Kidney cancer is actually multiple diseases that we need to treat differently,” explains Dr Kabbinavar. “Using various combinations of these new drugs with surgery and chemotherapy, we are moving toward an era of personalized kidney cancer therapy.”

“We are moving toward and era of personalized kidney cancer therapy.”
-Dr Fairooz Kabbinavar
Jean-Jacques Patard is one of many visiting researchers who have traveled long distances to take part in the world-renowned UCLA Kidney Cancer Program. Dr Patard is professor of urology at Rennes University Hospital in France, where he is director of the Angiogenesis and Tumour Invasion Group. He received his medical degree in 1993 from the Paris XII University and subsequently completed his fellowship at the Mondor University Hospital in Paris, earning his PhD at the Paris V University in 1996. He is a member of several professional associations and committees, including the French Urological Association, the French Oncology Committee for Kidney Cancer, the French National Cancer Institute for Kidney Cancer Research, the European Association of Urology, the EAU Guidelines Group for renal cell carcinoma and the American Urological Association. Dr Patard has tallied more than 140 publications in his main areas of interest, which include urological oncology, renal cancer, nephron-sparing surgery, prognostic factors, adjuvant treatments and angiogenesis inhibitors.

When Daniel Vesneski died in 2004 after a 10-month struggle with kidney cancer, his daughter Sara decided to raise money in support of kidney cancer research. She was also determined to keep her father’s memory alive. So Sara Vesneski, a student at California State University, Long Beach, started Pony on a Boat Kidney Cancer Foundation, drawing the name from her father’s favorite song, Lyle Lovett’s “If I Had a Boat.”

In March 2006, Pony on a Boat held its first fundraiser, the Daniel Vesneski Memorial Golf Tournament, in Temecula, Calif. The event succeeded beyond Sara’s expectations. Nearly 100 golfers from all over Southern California turned out in support. “I even got contacted by people who had worked for my dad 15 years ago, and hadn’t seen me since I was 5,” she says. Revenues from the event were donated to the UCLA Kidney Cancer Program (where Daniel Vesneski was treated after being diagnosed with Stage 4 disease in September 2003) and its research toward better treatments and the ultimate goal of a cure. The second annual golf tournament was held this year in March, and Sara hopes to add other fundraising events in the future.

“I didn’t know anything about kidney cancer until my dad was diagnosed with it,” Sara explains. “As I learned more about it, I realized there aren’t that many treatment options. Starting a nonprofit foundation to help move the research forward seemed like the right thing to do, and it has also helped my family and me deal with the death of my father, to keep his name out there. I will always remember my dad as the most wonderful man I have ever met. I don’t want anyone to forget him.”

For more information about Pony on a Boat Kidney Cancer Foundation, call (951) 317-5572 or email swsc@yahoo.com.

A Long Way from Home

Dr Jean-Jacques Patard is one of many visiting researchers who have traveled long distances to take part in the world-renowned UCLA Kidney Cancer Program. Dr Patard is professor of urology at Rennes University Hospital in France, where he is director of the Angiogenesis and Tumour Invasion Group. He received his medical degree in 1993 from the Paris XII University and subsequently completed his fellowship at the Mondor University Hospital in Paris, earning his PhD at the Paris V University in 1996. He is a member of several professional associations and committees, including the French Urological Association, the French Oncology Committee for Kidney Cancer, the French National Cancer Institute for Kidney Cancer Research, the European Association of Urology, the EAU Guidelines Group for renal cell carcinoma and the American Urological Association. Dr Patard has tallied more than 140 publications in his main areas of interest, which include urological oncology, renal cancer, nephron-sparing surgery, prognostic factors, adjuvant treatments and angiogenesis inhibitors.
IRA Contributions to Charities Allowed Through 2007

Between now and the end of 2007, individuals who are 70½ years of age and older who have either a traditional IRA or Roth IRA will be able to contribute at least part of their IRA to charity without paying the income tax. Individuals who qualify can donate up to $100,000 per year – regardless of income. There will be no income tax charitable deduction – but neither does one pay income tax on the withdrawal.

What steps need to be taken? One must notify the institution where the IRA is managed and administered well before the December 31 deadline. The individual should request a “charitable IRA rollover” to transfer a specific amount directly to the charity of choice. The check should not be made to the owner of the account, but rather, directly to the charity.

These transfers must be made as current gifts. Under the Pension Protection Act of 2006, transfers cannot be made to establish a life income arrangement such as a gift annuity, charitable remainder unitrust, or pooled income fund.

For more information about ways to take advantage of these new giving opportunities, please call the UCLA Office of Gift Planning at (800) 737-UCLA. As always, we encourage you to consult with your advisers as to the specific implications of such a gift in your particular situation.

Donor Notes:

Bert and Doris Ladd Make an Impact on UCLA Urology

Doris and Bert Ladd believe there are many good causes that need support. Yet, instead of scattering seeds, they prefer to focus their giving on a small number of organizations where they can have the greatest impact. The Ladds, who live in Los Angeles, have been very impressed with the UCLA Healthcare system and have chosen the Department of Urology to be one of their important charitable causes.

Raised in the Kansas and Oklahoma oil fields, Mr Ladd had always been very healthy. He served as a pilot in the Army Air Force during World War II and is a graduate petroleum engineer from the University of Kansas. He established a long and successful career in the energy business and is still very much involved with his roles in several companies. About 10 years ago, he was diagnosed with prostate cancer. “That gets your attention. It’s an important event,” he says. “I was very impressed with Arie (Arie Belldegrun, MD, professor in the department) and everyone else over there. Choosing a cause that’s dear to your heart is not hard to do when you’re dealing with the outstanding UCLA Department of Urology.”

In the ensuing years, Mr Ladd has maintained an active business and family life, and he and Mrs Ladd continue to generously support prostate cancer research programs at UCLA. The Department of Urology wishes to extend the gratitude of the entire faculty and staff to Doris and Bert Ladd for their ongoing friendship and partnership and for the significant contributions they have made to cancer research.
Robert E. Reiter, MD, professor of urology, received a three-year grant from Takeda Pharmaceuticals for his laboratory’s project “Targets of Epithelial to Mesenchymal Transition (EMT) in Urological Cancers.” The goal of the project is to study the role of EMT in urologic cancers.

William Aronson, MD, professor of urology, and Susanne Henning, PhD, RD, researcher and director of the Clinical Nutrition Research Unit’s Nutritional Biomarker Laboratory in UCLA’s Center for Human Nutrition, recently received a five-year RO1 grant from the National Cancer Institute. The goal of their project, titled “Tea Polyphenols for Chemoprevention of Prostate Cancer,” is to determine the chemopreventive potential – the ability of chemicals to slow or prevent cancer – and bioactive metabolites of green and black tea antioxidants through a prospective randomized trial comparing these agents in men with prostate cancer. Dr Aronson was also awarded a five-year Veterans Administration Clinical Merit Grant for his project “Obesity, Weight Loss, and Prostate Cancer.” Through a prospective randomized trial, this project will evaluate the role of weight loss on the insulin-like growth factor axis and on tissue biomarker changes in men with prostate cancer.

Jeremy Burton, MS, pre-doctoral graduate student, was the recipient of the Prostate Cancer Research Program Pre-doctoral Training Award from the U.S. Department of Defense. His project, titled “The Role of Lymphangiogenesis in Orthotopic Prostatic Tumor Environment on Regional Lymph Node and Systemic Metastasis,” will receive two years of funding. The goal of the research is to determine the extent to which lymphatics play a role in the metastasis of prostate cancer and whether inhibiting lymphangiogenesis is feasible for controlling systemic dissemination.

Lily Wu, MD, PhD, associate professor of urology, received a one-year research award from the Prostate Cancer Foundation for her project titled “Multimodal Imaging to Track and Detect Prostate Nodal Metastasis,” which aims to build better prostate models that will enable precise monitoring in order to decipher the connection between lymphatic and systemic metastasis and to advance a non-invasive “prostate sentinel lymph node” diagnostic imaging that could prove very helpful toward improving the management of metastatic prostate cancer.

Allan Pantuck, MD, MS, FACS, associate professor of urology, was recently awarded a research grant by The Sence Foundation for his project, “Evaluation of the Mechanisms of Pomegranate Polyphenol-Mediated Suppression of Nuclear Factor kappa B (NF-kB) Activity.” This one-year award will support Dr Pantuck’s research investigating the effects of pomegranate juice on prostate cancer growth. This grant was made in conjunction with additional funding from Pom Wonderful, LLC.

Sally L. Maliski, PhD, RN, and co-recipient Mark S. Litwin, MD, MPH, were recently granted a two-year award by the National Institutes of Health for their project investigating the associations between health literacy and self-efficacy for communicating with physicians on health-related quality of life among low-income, uninsured men treated for prostate cancer in the IMPACT program. The study will include both English and Spanish speakers.

In Other News: In a time of shrinking health care resources, California is providing access to life-saving prostate cancer treatment free of charge to low-income, uninsured men through the IMPACT Program (Improving Access, Counseling and Treatment for Californians with Prostate Cancer). This innovative program, created and led by UCLA Department of Urology professors Mark S. Litwin, MD, MPH, and James R. Orecklin, MD, MPH, strives to improve the health of underserved men in California who develop prostate cancer. In addition to offering all of the standard treatments for prostate cancer treatment – surgery, radiation therapy, hormone therapy, watchful waiting, and chemotherapy – IMPACT covers all medical expenses directly related to a man’s prostate cancer treatment. The program also provides nursing case management, education interventions, counseling and nutritional support.

For more information about this program, to refer a patient, or to find out if you are eligible to receive services from the program, please call (800) 409-8252 or visit the IMPACT website at www.california-impact.org.
**UCLA Kidney Cancer Program: Research Charts a Promising Path**

The dramatic gains in kidney cancer therapy are a cause for great optimism, but at the UCLA Kidney Cancer Program, which has been a leader in the fight against the deadly disease, there is a sense that the recent progress is just the beginning.

Targeted therapies such as the recently FDA-approved drugs Sutent and Nexavar represent a major advance with the potential to revolutionize the treatment of metastatic kidney cancer, but there are still many questions regarding the optimal use of these and other new drugs. Questions include whether targeted therapy combinations can be more effective than individual therapies alone, and whether there are ways to predict, based on patients’ molecular profiles, who will respond best to which treatment approaches.

“These new drugs are improving patient response rates, disease control, and length of survival, but they are not curative,” says Dr. Fairooz Kabbinavar, the UCLA Kidney Cancer Program’s medical director. “Thus, the focus of our research continues to be on finding better targeted therapies and better combinations of therapies.” The program’s active clinical trials effort includes testing new compounds that are in the same class as the recently approved drugs, as well as using these compounds with the existing drugs. Among the most promising approaches are angiogenic inhibitors, which target the blood supply that tumors need to thrive; and mammalian target of Rapamycin (mTOR) inhibitors, which target one of the significant intermediate steps in kidney cancer, as the cancer signal moves from the surface of the cell to the nucleus.

“Kidney cancer was once seen as a single disease, but now we know that it is multiple tumors that histologically are different,” says Dr. Arie Belldegrun, the program’s surgical director. “Using genetics, we have been isolating the different subtypes of tumors and identifying molecular markers. As we learn more about the chain of molecular events that take place in these tumors, we are able to devise ways to cut a link in the chain in an effort to halt the cancer.”

The program’s research strength is derived in part from the numerous dedicated international fellows who have conducted significant clinical, translational, and basic research over the years, contributing to its evolution and expansion as a world-renowned program. The program’s excellence continues to draw top people from all over the world; currently, fellows are here from Germany and Italy.

**New Prognostic Method Developed**

Dr. Belldegrun and colleagues are summarizing the program’s 15-year experience treating more than 2,500 kidney cancer patients in order to learn more about the disease and its treatment. With such an extensive database – more than 250 variables covering various aspects of each patient’s genetics, lifestyle factors, characteristics of the tumor, the treatment that was given, and the patient’s response to it – the UCLA Kidney Cancer Program is developing methods to predict the impact of different treatment options for individual patients as a way of moving toward more personalized kidney cancer therapy. Already, the program has validated a widely heralded prognostic method, the UCLA Integrated Staging System, that divides patients into six categories based on risk, helping to determine which patients need the most aggressive treatments.

In addition, the program has embarked on an ambitious new path of “fingerprinting” kidney cancer in collaboration with Dr. Dennis Slamon. The approach follows the model that has proved so successful in Dr. Slamon’s breast cancer research, which led to the drug Herceptin. “In the past, cancer therapy has been a one-size-fits-all approach,” explains Dr. Slamon. “What we have learned is that we are dealing with a heterogeneous group of diseases, even when they come from the same organ. We have begun to learn how to characterize and classify those diseases and then tailor our therapy appropriately. This has changed the face of oncology.”

More than in most sites, that changing face is on display at the UCLA Kidney Cancer Program, which is renowned for its multidisciplinary approach and integration of laboratory and clinical research efforts. Those efforts are now heavily focused not only on developing new targeted therapies – those that go after a particular defect in kidney cancer – but in determining which targeted treatments work best in which subgroups of patients.

**UCLA-Discovered Vaccine to Be Tested**

The laboratory efforts of Dr. Belldegrun and colleagues have also led to the discovery of a new genetic vaccine for kidney cancer patients. The National Cancer Institute (NCI) recognized the unique features and importance of this vaccine and is now producing it for the program at its National Institutes of Health facility; upon completion of this complex process, the UCLA Kidney Cancer Program’s urological oncology team will start the first-ever clinical trial for such a vaccine, most likely by the end of this year, as part of the NCI’s Rapid Access to Intervention Development (RAID) program.

In addition to the National Cancer Institute’s RAID grant for translational research, the UCLA Kidney Cancer Program receives generous private funding. The program is grateful for the support of Nancy and Richard Bloch, Doris and Bert Ladd, Nancy and Howard Marks, Carrie and Alvin Meinhardt, and Judith and Robert Winston: Contributions from these individuals are playing an important role in finding solutions, cures, and treatments for patients at UCLA and beyond.

“The concept here is that as we make important observations in the course of taking care of patients, we go back to the laboratory and learn more about what we’re seeing in the clinic, then we take those findings and apply them to the patient’s benefit,” explains Dr. Allan Pantuck, UCLA Kidney Cancer Program director of translation research. “Very few kidney cancer programs have such a strong connection between the laboratory and the clinic.”
Clinical Trials in Urology
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 prostate hyperplasia) treatments
- Kidney cancer and transplantation
- Male infertility and sexual dysfunction
- Pelvic medicine, incontinence and reconstructive surgery

What sets the UCLA Department of Urology apart from others nationwide is the close collaboration and partnership of research scientists with faculty members — internationally renowned physician specialists in their fields — in advancing the field of urology. Many of these relationships also include involvement with researchers and physicians in UCLA’s Jonsson Comprehensive Cancer Center. This unique collaboration makes UCLA a leader in new treatments and cures for urology patients nationwide.

If you would like to find out if you’re eligible to participate in a UCLA Urology Clinical Trial, contact Nazy Zomorodian, MSN, CUNP, at (310) 794-7704 or go to www.uclaurology.com and click on the “Research & Clinical Trials” link for more information. Most of the trials listed below are open and accepting applicants.

BLADDER CANCER AND DISORDERS

- Female Urology – Interstitial Cystitis, PI: Larissa Rodriguez, MD – A study to evaluate the effectiveness of acupuncture on symptoms of interstitial cystitis.
- Uropathogen Detection, PI: Bernard M. Churchill, MD – Using DNA biosensors, this study investigates a detection system that would identify uropathogens quickly and enable point-of-care diagnosis and treatment of urinary tract infections.

KIDNEY CANCER

- Kidney Cancer, PI: Fairooz Kabbinavar, MD – A Phase II study of M200 (anti-a 5f1 integrin monoclonal antibody) in patients with metastatic renal cell carcinoma. This study uses a form of immunotherapy treatment for patients whose disease has stopped responding to other therapy. This drug is designed for a specific form of kidney cancer that is verified by pathology.
  - Kidney Cancer – Adjuvant Trial, Non-Metastatic Disease, PI: Arie Belldegrun, MD – The purpose of this trial is to evaluate the efficacy and safety of adjuvant cG250 treatment versus placebo in patients post-nephrectomy (no more than six weeks) with surgically completely resected clear-cell renal cell carcinoma at high risk of recurrence. This study is for newly diagnosed, high-risk kidney cancer patients who will undergo removal of their diseased kidney (nephrectomy). This form of immunotherapy works on specific kidney cancer biomarkers.
  - Kidney Cancer – Relapsed Renal Cancer, PI: Arie Belldegrun, MD – A multicenter, open-label, single-agent, two-stage Phase II study to evaluate the safety and efficacy of AMG 102 in subjects with relapsed renal cancer. This study uses the new molecule pathway to block tumor cells from growing in patients with kidney cancer (all kinds of pathology) that spreads to other organs and has stopped responding to other treatments.
  - Kidney Cancer – Newly Diagnosed Stage IV Renal Cell Carcinoma, PI: Allan Pantuck, MD, MS, FACS – A Phase Ila study testing the biological activity and safety of autologous renal cell carcinoma total mRNA and huCD40L mRNA co-transfected dendritic cell vaccine in patients with newly diagnosed stage IV renal cell carcinoma. This study is for patients with newly diagnosed cancer where the patient’s own blood cells are boosted to make vaccine. The vaccine is a form of gene therapy that teaches cells a new genetic code to fight the cancer.
  - Kidney Cancer – Metastatic Papillary Renal Cell Carcinoma, PI: Matthew Rettig, MD – A Phase II study of Velcade administered as a single agent in metastatic papillary renal cell carcinoma. This study is cell alteration therapy for patients whose disease has spread to other organs and is not responding to other therapy. This drug is designed for a specific form of kidney cancer.
  - Kidney Cancer – Metastatic Renal Cell Carcinoma, PI: Allan Pantuck, MD, MS, FACS – A trial designed to prospectively validate predictive models of response to high-dose IL-2 treatment in patients with metastatic renal cell carcinoma. This study uses a form of immunotherapy treatment for patients whose disease has spread to other sites.

KIDNEY TRANSPLANTATION

- Kidney Transplantation, Co-PI: H. Albin Gritsch, MD – A study comparing a new immunosuppressive medication to standard immunosuppression. The new immunosuppressive medication allows the patients to be steroid-free (many patients don’t like to be on steroids), but inhibits healing, promotes delayed graft function and elevates cholesterol.
- Kidney Transplantation, Co-PI: H. Albin Gritsch, MD – The purpose of this study is to test two different combinations of medications to see if they are effective in preventing kidney transplant rejection and also to see if these combinations create fewer side effects than standard kidney transplant treatment.
- Kidney Transplantation – Reducing the Rate of Heart and Blood Vessel Disease in Stable Kidney Transplant Subjects, Co-PI: H. Albin Gritsch, MD – This study compares the effects of two separate vitamin regimens on the cardiovascular health of kidney transplant recipients over a period of five years.
- Kidney Transplantation – The Effects of Switching Kidney Transplant Patients with Diabetes from Prograf to Neoral, Co-PI: H. Albin Gritsch, MD – This study seeks to discover the effects on blood sugar levels of switching patients who are currently taking Prograf and who have developed diabetes after receiving a kidney transplant, to Neoral.
- 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.
**CLINICAL TRIALS PHASES**

- **Phase I:** These trials are the first studies on humans following the animal studies and use a limited number of patients, testing for safety and MTID (maximum tolerated dose).
- **Phase II:** These trials take place after Phase I, involve more patients, and check for safety and efficacy.
- **Phase III:** This phase involves hundreds of patients, and tests for safety and efficacy, primarily by means of randomized trials with a placebo control group. Phase III trials are usually multi-center and often international in scale.

**PROSTATE CANCER AND DISORDERS**

- **Prostate Cancer, PI: Robert Reiter, MD – Four-arm study of adjuvant treatment after prostatectomy for high-risk patients with either hormonal and chemotherapy or hormone alone administered as either immediate or deferred therapy. (Pharmaceutical company: Sanofi)**
- **Prostate Cancer, PI: Arie Belldegrun, MD – Targeted therapy and surgery for locally advanced prostate cancer. (Pharmaceutical company: Pfizer)**
- **Prostate Cancer, PI: Allan Pantuck, MD, MS, FACS – A Phase III study of the effects of patient-derived tumor vaccine in patients with hormone refractory prostate cancer. (Pharmaceutical company: Roll)**
- **Prostate Cancer, PI: Allan Pantuck, MD, MS, FACS – Chemotherapy with or without vaccine in patients with hormone refractory metastatic disease. (Pharmaceutical company: Cell Genesys)**
- **Prostate Cancer, PI: Allan Pantuck, MD, MS, FACS – Evaluating DN-101 (high-dose calcitrol) with or without chemotherapy in metastatic hormone-independent prostate cancer. (Pharmaceutical company: Novacea)**
- **Prostate Cancer, PI: William Aronson, MD – Patients who are scheduled to undergo radical prostatectomy (localized disease), who have more than minimal disease, are being recruited for a trial in which they are randomized to a balanced Western diet or a low-fat diet with fish oil capsules, to study serum and tissue biomarkers.**
- **Chronic Prostatitis/Chronic Pelvic Pain Syndrome, PI: Mark S. Litwin, MD, MPH – A randomized, placebo-controlled, multi-center clinical trial to evaluate the efficacy and safety of pregabalin; the study investigates the efficacy and safety/tolerability of pregabalin (brand name: Lyrica) in treating patients with CP/CPPS.**
- **Chronic Prostatitis: Pain, Marital and Sexual Functioning Among Men with Chronic Prostatitis/Chronic Pelvic Pain Syndrome, PI: Mark S. Litwin, MD, MPH – Examines the pain, disability, adjustment and marital and sexual relationships experienced by patients with CP/CPPS and their partners/spouses.**

**Why Would a Patient Be Interested in a Clinical Trial?**

Patients take part in clinical trials for many reasons. Most commonly, they hope for benefits for themselves. They may hope for a cure of disease, a longer time to live, or to feel better. Often they want to contribute to a research effort that may help others.

Based on what researchers learn from laboratory studies, and sometimes earlier clinical studies and standard treatments as well, they design a trial to see if a new treatment will improve on current therapies. The hope is that it will. Often researchers use standard treatments as the building blocks to try to design better remedies.

Although there is always a chance that a new treatment will be disappointing, the researchers involved in a study have reason to believe that it will be as good as, or better than, current options.

The patients in a clinical trial are among the first to receive new research treatments before they are widely available. How a treatment will work for a patient in a trial can’t be known ahead of time. Even standard treatments, although effective in many patients, do not carry sure benefits for everyone. But patients can choose if they want to take part in a study or not only after they understand both the possible risks and benefits.

The patients who take part in clinical trial procedures that do improve on existing treatments have the first opportunity to benefit.

All patients in clinical trials are carefully monitored during a trial and receive follow-up after the trial concludes. They become part of a network of clinical trials carried out around the country. In this network, doctors and researchers pool their ideas and experience to design and monitor clinical studies. Knowledge is shared from many specialties about cancer treatment and care. Patients in these studies receive the advantage of their expertise. At cancer centers, patients receive care from a special research team. Through new programs, community hospitals and doctors are also entering into the research network.

Nazy Zomorodian, MSN, CUNP
Director of the General Urology Clinical Trials Office

Do you want to read more FAQs (frequently asked questions)? Go to www.uclaurology.com and click on the “Research & Clinical Trials” link.
Jean B. deKernion, MD
Professor and Chairman of Urology
Specialty: Urologic Oncology

Jennifer Anger, MD
Assistant Professor of Urology
Specialty: Female Urology

William Aronson, MD
Associate Clinical Professor of Urology
Specialty: Urology

Arie Belldegrun, MD
Professor of Urology
Specialty: Urologic Oncology, Biologic Therapy

Carol Bennett, MD
Associate Professor of Urology
Specialty: Male Infertility

Bernard M. Churchill, MD
Professor of Urology
Specialty: Pediatric Urology

Nand Datta, MD
Adjunct Associate Professor of Urology
Specialty: General Urology, Pediatric Urology

Isa Garraway, MD, PhD
Assistant Professor of Urology
Specialty: Urologic Oncology

Nestor Gonzalez-Cadavid, PhD
Adjunct Professor of Urology
Specialty: Biochemistry, Andrology Research

H. Albin Grutsch, MD
Associate Professor of Urology
Specialty: Renal Transplantation

Christina Jamieson, PhD
Assistant Professor of Urology and Human Genetics
Specialty: Urologic Research

David A. Leff, MD
Assistant Clinical Professor of Urology
Specialty: BPH, Sexual Dysfunction, General Urology

Steven E. Lerman, MD
Assistant Professor of Urology
Specialty: Pediatric Urology

Mark S. Litwin, MD, MPH
Professor of Urology and Public Health
Specialty: Urologic Oncology, Prostate Diseases

James R. Orecklin, MD, MPH
Associate Clinical Professor of Urology
Specialty: BPH, Urology, General Urology

Allan J. Pantuck, MD, MS, FACS
Assistant Professor of Urology
Specialty: Urologic Oncology

Jacob Raff, MD
Professor of Urology
Specialty: Male Infertility, Sexual Dysfunction

Shlomo Raz, MD
Professor of Urology
Specialty: Urodynamics, Female Urology

Robert E. Reiter, MD
Professor of Urology
Specialty: Urologic Oncology, Prostate Diseases

Larissa V. Rodríguez, MD
Assistant Professor of Urology
Specialty: Urodynamics, Female Urology

J. Thomas Rosenthal, MD
Professor of Urology
Specialty: Renal Transplantation

Jonathan Said, MD
Professor of Pathology and Urology
Specialty: Pathology

Christopher Saigal, MD, MPH
Associate Professor of Urology
Specialty: Health Services Research

Peter G. Schulam, MD, PhD
Associate Professor of Urology
Specialty: Urology, Endoscopic Procedures

Jennifer S. Singer, MD
Assistant Professor of Urology
Specialty: Pediatric Urology, Urologic Oncology

Robert B. Smith, MD
Professor of Urology
Specialty: Urologic Oncology, General Urologic Surgery

Eric Vilain, MD, PhD
Assistant Professor of Urology
Specialty: Human Genetics and Pediatrics

Lily Wu, MD, PhD
Assistant Professor of Urology
Specialty: Molecular Biology, Cancer Research

Gang Zeng, PhD
Assistant Professor of Urology
Specialty: Tumor Immunology, Cancer Vaccine