From the Director
Dr. Melanie Cobb

Earlier this year, Dr. James Willson accepted a position as Chief Scientific Officer or the Cancer Prevention and Research Institute of Texas (CPRIT). I know the Friends of the Comprehensive Cancer Center join all of us at UT Southwestern in expressing our appreciation for Dr. Willson’s outstanding leadership over the past decade. We are grateful that his vision led to our recent designation by the National Cancer Institute (NCI) as one of just 45 Comprehensive Cancer Centers in the nation.

I am honored to announce that I will serve as Interim Director during the search process. At this juncture, we are in an enviable position to attract the best candidates for the next Director. UT Southwestern is engaged in the search for new leadership to continue the growth, collaboration, and commitment to outstanding science and clinical care that have distinguished the Harold C. Simmons Comprehensive Cancer Center among its peers.

The Simmons Cancer Center will benefit from the solid team-based leadership structure that is already in place and which has driven our current success. We are fortunate to have the continued leadership of directly related clinical departments to support our clinical and translational research programs. Key leaders include Dr. Michael Choti, Chair of Surgery; Dr. Hak Choy, Chair of Radiation Oncology; and Dr. David Johnson, Chair of Internal Medicine, among many others.

By any standard, the Simmons Cancer Center continues its rapid ascent. The numbers of patient visits and clinical trials have all doubled or more since 2010, and we have responded...continued on page 2

Tackling Pediatric Sarcomas as a Team

Dr. Stephen Skapek, Chief of the Division of Pediatric Hematology-Oncology and Professor of Pediatrics, leads a team of 24 faculty members, nine fellows, and more than 100 staff members who care for children with cancer and blood diseases. Members of his team are using a multidisciplinary approach to focus on sarcomas, which are among the most difficult tumors to treat in children.

Sarcomas are divided into two main groups: bone and soft issue sarcomas. Soft issue sarcoma can occur in the muscles, fat, blood vessels, tendons, fibrous tissues, and tissues around joints.

Many children with sarcomas are not cured of the disease, especially if the cancer is diagnosed at an advanced stage. The powerful chemotherapy currently used to treat these tumors can cause side effects that persist for years. To address these challenges, Dr. Skapek is leading a multi-investigator sarcoma research project funded by a 5-year, $7 million grant from the Cancer Prevention and Research Institute of Texas (CPRIT).

Imaging to Assist Biopsies

Osteosarcoma is the most common type of bone cancer in children and young adults and, despite years of research, 40 percent of patients still succumb to the disease. Knowing early on which patients are at high risk of poor outcomes would allow their therapy to be intensified. To address this challenge, Dr. Patrick Leavey, Professor of Pediatrics, has teamed up with investigators from the Departments of Pathology and Radiology and with experts in computerized image analysis from UT Dallas.

Supported by a multiyear grant from CPRIT, Dr. Leavey and...continued on page 4

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Clinical News

Studying a Novel Way to Minimize Radiation Side Effects

UT Southwestern cancer researchers – the first in Texas – are investigating whether an injectable, biodegradable gel can reduce potential side effects from extreme high-dose radiation treatments for prostate cancer.

In this trial, researchers are trying to determine whether a prostate rectal spacer works with the higher-dose radiation required by stereotactic ablative radiation (SABR). This type of radiation therapy better avoids organs at risk and thus leads to fewer side effects while achieving more disease control. However, early studies have shown that the powerful radiation doses delivered by SABR can be associated with an elevated risk of toxicity in certain circumstances. The treatment can damage the nearby rectum, potentially causing ulcers or injury to rectal wall tissue. Researchers are studying whether the gel can shift the rectum out of the radiation field and reduce these potential side effects.

“All we need are a few extra millimeters to separate the prostate and rectal wall, and the spacer will help us achieve that,” said Dr. Michael Folkert, Assistant Professor of Radiation Oncology and co-lead investigator of the trial. “SABR is very effective at treating prostate cancer, but we want to offer it with the fewest possible side effects. By working closely with our colleagues in Urology, we believe that we can significantly reduce the risk of long-term rectal toxicity.”

The gel received approval from the Food and Drug Administration in 2015 for use in conventional radiation therapy for prostate cancer. In the trial leading to its acceptance, patients treated with the spacer in place experienced significant reductions in rectal radiation dose, rectal discomfort related to treatment, and severity of long-term side effects when compared with patients treated without the spacer.

The spacing gel is injected prior to radiation treatments during other required procedures, so it causes no additional inconvenience to patients. It is then absorbed over a three-month period.

“Placement of the prostate spacer is minimally invasive. The spacer can be placed at the same time that we place markers that help target the prostate during radiation therapy,” explained trial co-investigator Dr. Yair Lotan, Professor of Urology.

UT Southwestern, a pioneer in stereotactic ablative radiation, was the first medical center to test a high-dose, five-treatment radiotherapy regimen for prostate cancer.

Dr. Michael Folkert (left) and Dr. Yair Lotan are investigating whether an injectable, biodegradable gel can reduce potential side effects from extreme high-dose radiation treatments for prostate cancer.

From the Director

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Dr. Melanie Cobb

by both renovating existing spaces and building new spaces. Physical expansion is again underway, with new lab and clinical space expected to be completed this year.

Together, we will continue to strive for a future where cancer is no longer a threat to our community. To that end, I am pleased to share that the Simmons Cancer Center will directly benefit from the federal government’s “Moonshot” cancer initiative. The NCI has already received a 5 percent increase in its budget, which will mean more support for researchers and cancer centers nationwide. Specifically, our Center is anticipating increased support in its annual support grant from the NCI. As you know, the state of Texas has been a key supporter as well. As of this printing, UT Southwestern researchers have been awarded a cumulative total of more than $318 million from CPRIT since the organization’s inception in 2009.

This vital support from federal and state sources will enable us to heighten our efforts to find transformative solutions for fighting cancer, ultimately leading to improved methods of earlier detection and more effective treatments.

As we move into a new era of discovery in the cancer field, we are particularly fortunate to have dedicated members in the Friends of the Comprehensive Cancer Center who inspire us in our work every day. Thank you for your support as we continue to provide cancer care and pursue research at the highest levels in North Texas.

Dr. Choti holds the Hall and Mary Lucile Shannon Distinguished Chair in Surgery.

Dr. Choy holds The Nancy B. and Jake L. Hamon Distinguished Chair in Therapeutic Oncology Research.

Dr. Cobb holds the Jane and Bill Browning, Jr. Chair in Medical Science and is a member of the National Academy of Sciences.

Dr. Johnson holds the Donald W. Seldin Distinguished Chair in Internal Medicine.
Friends Tour Cancer Labs

In November, members of the Friends group gathered to enjoy lab tours and learn more about how researchers are finding new ways of fighting cancer. The following UTSW faculty members participated and spoke on these topics:

- Dr. James Kim, Assistant Professor of Internal Medicine and in the Hamon Center for Therapeutic Oncology Research, “Cell Signaling Pathways and their Impact on Lung Cancer.”
- Dr. Elisabeth Martinez, Assistant Professor of Pharmacology, “Novel Epigenetic Pathways and Potentially Therapeutic Small Molecules in Cancer.”
- Dr. Hao Zhu, Assistant Professor of Internal Medicine and Pediatrics and in the Children's Medical Center Research Institute at UT Southwestern, “Genetic and Cellular Factors Influencing Liver Regeneration and Cancer.”
- Dr. Xiankai Sun, Associate Professor of Radiology and in the Advanced Imaging Research Center, “Innovative Cancer Imaging using Cutting Edge Positron Emission Tomography (PET) Technologies Enabled by an Onsite Cyclotron Facility.” Dr. Sun holds the Dr. Jack Krohmer Professorship in Radiation Physics.

Friends Update

April 11, 2016: Annual Awards Reception and Program
Topic: Why We Need Research
Presenter: Dr. James Brugarolas, Associate Professor of Internal Medicine and leader of Kidney Cancer Program
Place: T. Boone Pickens Biomedical Building, 14th Floor
Time: 6 - 7:30 p.m.

June 9, 2016: Spring/Summer Luncheon
Topic: Precision Medicine: Individualized Drug Regimens by Genetic Profil
Presenter: Dr. David Gerber, Associate Professor of Internal Medicine, Co-Director of the Lung Cancer Disease Oriented Team, and co-leader of the Experimental Therapeutics Program
Place: T. Boone Pickens Biomedical Building, Conference Room C
Time: 11:45 a.m. - 1 p.m.
his team are using cutting-edge image reconstruction techniques to more precisely evaluate how well tumors are responding to treatment. They are using whole-slide imaging, which allows virtual pathology evaluation of a tumor sample. Computer-based systems are now in development that will automate the identification of subtle changes in the tumor. The images can be merged with results from high-resolution magnetic resonance imaging (MRI), ultimately allowing the MRI scan to serve as a virtual “tumor biopsy.”

Accurate and early identification of tumor characteristics will allow greater detail in biopsies and help predict which patients are at highest risk of poor outcomes.

Heat Aids Treatment

Dr. Ted Laetsch, Assistant Professor of Pediatrics, is working with Dr. Rajiv Chopra, Associate Professor of Radiology and in the Advanced Imaging Research Center, to develop a novel technology called MR-HIFU for the treatment of sarcomas and other relapsed pediatric solid tumors.

This technology uses a high-intensity, focused ultrasound transducer built into the table of an MRI scanner to selectively heat tumors without damaging surrounding tissue. This heating can be used to target liposomes carrying chemotherapy to tumors. The liposomes are heat-sensitive, so they melt when they encounter the heated tumors.

Researchers hope they will deliver the chemotherapy more effectively, while sparing adjacent tissue.

One of these temperature-sensitive drugs, ThermoDox, is in clinical trials for adult cancers, but has never been studied in pediatric cancers. ThermoDox selectively delivers a chemotherapy drug called doxorubicin to tumors. Doxorubicin is known to be effective against most pediatric solid tumors, but it can cause serious long-term side effects if not precisely targeted to the tumor.

Dr. Laetsch is leading a clinical trial to determine the ability of MR-HIFU to safely heat tumors in pediatric patients and to evaluate the safety of combining this treatment with liposomal doxorubicin. Dr. Laetsch plans to open larger clinical trials of MR-HIFU treatment for pediatric patients as part of a growing collaboration of major pediatric cancer centers across the country.

Ewing's Sarcoma Project

Dr. James Amatruda, Associate Professor of Pediatrics, Internal Medicine, and Molecular Biology, is leading a multidisciplinary group of investigators whose goal is to build innovative collaborations for more effective treatment of Ewing’s sarcoma. The Ewing’s sarcoma project has been generously supported with a $250,000 grant from the 1 Million 4 Anna Foundation. Researchers collaborating on this project include:

- Dr. Ralph DeBerardinis, Chief of the Division of Pediatric Genetics and Metabolism, who studies how the metabolism and energy usage of Ewing’s sarcoma cells can be targeted for new cancer therapies.
- Dr. Ralf Kittler, Assistant Professor of Pharmacology and in both the Eugene McDermott Center for Human Growth and Development and the Simmons Cancer Center, who dissects the complex transcription factor networks driving the growth of Ewing’s sarcoma.
- Dr. David McFadden, Assistant Professor of Internal Medicine and Biochemistry, who uses genetic engineering and chemical screens to discover new treatments for Ewing’s sarcoma.
- Dr. Angelique Whitehurst, Assistant Professor in the Simmons Cancer Center and of Pharmacology, who has discovered that Ewing’s sarcoma tumors express cancer-testis antigens (a group of proteins), which are promising targets for immunotherapy.
- Dr. Amatruda, a pioneer in the development of zebrafish genetic models of Ewing’s sarcoma, who is using these models to study how a normal cell becomes a Ewing’s sarcoma cell and to identify new drugs for treatment of the disease. This work also was supported by a CPRIT grant to Dr. Amatruda.

Together, these researchers collaborate to drive progress as rapidly as possible for pediatric sarcoma patients at UT Southwestern.

Dr. Amatruda holds the Nearburg Family Professorship in Pediatric Oncology Research. Dr. DeBerardinis holds the Joel B. Steinberg, M.D. Chair in Pediatrics. Dr. Kittler is a John L. Roach Scholar in Biomedical Research. Dr. Skapek holds the Distinguished Chair in Pediatric Oncology Research.
An international team of cancer researchers that included UT Southwestern physicians announced "game-changing results" using the immunotherapy drug nivolumab to treat certain lung cancers that failed to respond to first-line therapies.

"The idea behind immunotherapy is to kick-start the body’s natural immune response to a cancer. Cancer develops and grows in part because it has put the brakes on the immune response. These drugs take the foot off the brake, allowing the immune system to accelerate and attack the cancer," said Dr. David Gerber, Associate Professor of Internal Medicine and a contributing author to this study published last fall in the New England Journal of Medicine. Dr. Gerber also is Associate Director for Clinical Research in the Harold C. Simmons Comprehensive Cancer Center.

Researchers compared an immunotherapy and a chemotherapy drug in patients with non-squamous, non-small cell lung cancer (NSCLC) whose disease continued to progress after first-line chemotherapy. They found that nivolumab improved overall survival and was generally well tolerated. The results are significant because options for patients whose lung cancer progresses after initial treatment are limited.

"This clinical trial shows that people with lung cancer not only live longer when treated with the immunotherapy drug nivolumab, but their quality of life is better and toxicities are fewer and less severe," said Dr. Gerber, Co-Director of the Lung Cancer Disease Oriented Team and co-leader of the Experimental Therapeutics Program at UT Southwestern.

According to the National Cancer Institute, lung cancer is the second most common cancer for both men and women, and the top cause of cancer death. While it affects more than 221,000 Americans each year, 5-year overall survival is only 17 percent, and the survival rate is far lower for metastatic lung cancer.

The Food and Drug Administration (FDA) approved the use of nivolumab for squamous non-small cell lung cancer in March 2015 and previously had approved the drug to treat patients with treatment-resistant metastatic melanoma and melanoma that can’t be removed via surgery.

Nivolumab is an immunotherapy drug that works by inhibiting the cellular pathway known as PD-1 protein on cells that block the body’s immune system from attacking cancerous cells. The study compared nivolumab to the chemotherapy drug docetaxel, one of the most commonly used FDA-approved second-line treatments for advanced NSCLC.

Donna Fernandez of Rockwall, Texas, said nivolumab has improved her quality of life. A smoker for 40 years, Mrs. Fernandez was diagnosed with NSCLC several years after quitting smoking in 2007. She’s been fighting stage 4 lung cancer for the past three years and needed another option after her initial round of chemotherapy wasn’t successful. She decided to join the trial at UT Southwestern.

"No one thought I’d still be alive. I’m not just alive – I’m living life to the fullest," said Mrs. Fernandez, who receives treatment every two weeks, and except for a little fatigue the next day, she said she is able to continue with her normal activities, including agility training with her dogs. Mrs. Fernandez retired from her career as an educational grant writer but has found a new role as an advocate for cancer research funding and greater cancer awareness.

In addition to studying safety and efficacy, the clinical trial examined the protein biomarker PD-L1, which may play a role in suppressing the immune system. The study results suggest that patients with a higher level of PD-L1 in their cancers may experience the greatest benefit from nivolumab. Using a biomarker helps oncologists predict which patients will do best on which treatment, and plan their treatment accordingly.

UT Southwestern has taken part in a number of nivolumab trials, including the squamous NSCLC trial and a phase 1 study examining nivolumab combinations with chemotherapy, targeted therapies, and other immunotherapies. Other types of cancer also have shown benefit from nivolumab and other immunotherapies.

“We have seen promising effects against some lymphomas, colon cancer, ovarian cancer, bladder cancer, and other malignancies,” said Dr. Gerber.

This study was funded by Bristol-Myers Squibb, which worked jointly with investigators to collect and analyze the study results. Dr. Gerber reported nonfinancial support from Bristol-Meyers Squibb outside of the submitted work.
Bringing Kidney Cancer to the Forefront

Researchers and clinicians at UT Southwestern are working hard to better understand a cancer that is not well-known or well-understood by the public—kidney cancer. Texas has the highest incidence of this deadly disease in the U.S.

“It is unknown what causes this higher incidence of kidney cancer in Texas,” said Dr. James Brugarolas, Associate Professor of Internal Medicine, and program leader of UT Southwestern’s Kidney Cancer Program. “What is clear is that the incidence rates have been rising, and we have no screening methods for early detection. We need to find new ways to combat this cancer through research and discovery.”

The National Cancer Institute (NCI) estimated 61,560 cases would be diagnosed in 2015, and 14,080 deaths would occur. The average age of a kidney cancer patient is 64; the cancer strikes all ethnicities and both genders. The young also are affected: Wilms tumor, a type of kidney cancer in children, is the third most common type of solid tumor in children.

To meet this need, UT Southwestern formalized its commitment to the care of kidney cancer patients and research on kidney cancer by officially founding a Kidney Cancer Program. The program was inaugurated by Dallas Mayor Mike Rawlings in 2013. It includes more than 20 physicians specialized in kidney cancer, many of whom are renowned international leaders in their fields of urology, oncology, radiation oncology, radiology, and pathology. In addition, more than 40 basic scientists and their research laboratories contribute to the effort. The UT Southwestern Kidney Cancer Program is one of the largest such programs in the world.

Current treatments, divided into immunotherapy and molecularly targeted therapies, have achieved modest results. New treatments are sorely needed and will be investigated through an ambitious initiative, pending funding from the NCI.

Two years after its founding, the Kidney Cancer Program is in the running for a prestigious Specialized Program of Research Excellence (SPORE) grant from the NCI. Launched in 1992, the SPORE program has 50 active grants nationwide of about $12 million each. Each is 5 years in duration. UT Southwestern currently holds one SPORE grant in lung cancer research, in partnership with MD Anderson Cancer Center. The grant is led by Dr. John Minna, Director of the Nancy B. and Jake L. Hamon Center for Therapeutic Oncology Research, the W.A. “Tex” and Deborah Moncrief Jr. Center for Cancer Genetics, and Co-Director of the Experimental Therapeutics Program at the Simmons Cancer Center.

To date, only one SPORE grant has been awarded for kidney cancer, to the Harvard Cancer Center. UT Southwestern’s application received an exceptionally high score, improving its odds to receive a SPORE award during 2016.

“We are translating seminal discoveries and technological innovation at UT Southwestern to develop new treatments and to improve treatment selection for both adult and pediatric Wilms tumor patients,” said Dr. Brugarolas. “We will examine how tumors develop resistance to treatment, how we can determine if a weak tumor will become aggressive, and how to classify our patients based on their genetic mutations, thus providing opportunities for more targeted treatments.”

The work outlined in the grant application builds upon groundbreaking discoveries by UTSW researchers over the past two decades and comprises four research projects, four core facilities, a developmental research program, and a career enhancement program.

An essential aspect of the grant and the Kidney Cancer Program is the involvement of patients, some of whom participate in an advocacy group. A Patient Council has been launched to provide support, advocate for increased funding, raise awareness, and communicate advances to the broader community.

Tony Towler, a 4-year kidney cancer survivor and Patient Council member, sees reasons for hope. “During the past four years, treatments have diversified. One type of treatment cuts off the blood supply to the tumor, and another uses the immune system to fight the cancer,” Mr. Towler said. “What’s next in line? As a patient, I’m hoping to hang around long enough so that when one drug stops working, there’s a new one to try.” Other current members of the Patient Council include Carole Baas, Merlinda Chelette, Sophia Moschos, and Victoria Towler. Council members actively volunteer in UT Southwestern cancer clinics, visiting newly diagnosed patients to share their experiences.

For more information on UT Southwestern’s Kidney Cancer Program, visit utsouthwestern.edu/kidneycancer.

Dr. Brugarolas is a Virginia Murchison Linthicum Scholar in Medical Research. Dr. Minna holds the Max L. Thomas Distinguished Chair in Molecular Pulmonary Oncology, and the Sarah M. and Charles E. Seay Distinguished Chair in Cancer Research.
Despite decades of lung cancer diagnosis and treatment, early detection methods have remained elusive. Finally, researchers have an opportunity to detect lung cancer early with low-dose computed tomography (CT) scans, and it all began just four years ago.

In 2012, results were published from the National Lung Cancer Screening Trial involving 53,000 patients who were at high risk for lung cancer. Researchers found that the use of low-dose CT scans resulted in a 20 percent reduction of mortality.

Thanks to these encouraging results, Medicare and Medicaid began to cover lung cancer screening in 2015. Many health insurance providers also provide full or partial coverage for those who qualify for the test.

“Currently, more than two-thirds of lung cancer patients at the Harold C. Simmons Comprehensive Cancer Center are diagnosed at an advanced cancer stage, making treatment very difficult. If researchers can flip that to diagnosing most of the patients at an early stage, that will have a tremendous impact on lung cancer outcomes,” said Dr. Muhanned Abu-Hijleh, Associate Professor of Internal Medicine and lead for the CT scan initiative at UT Southwestern. “Prevention, risk reduction including nicotine cessation, and early detection will combine to help improve both survival rates and quality of life.”

Annual low-dose CT scans for lung cancer are covered by Medicare and Medicaid, and many health insurance providers, if the patient meets the following criteria:

• Age 55 to 77.
• Smoked 30 pack-years (that is, a pack a day for 30 years, or two packs a day for 15 years, or the equivalent).
• Stopped smoking within the past 15 years, or currently smokes.
• Has a written order from a physician asking for the CT scan.

There are other risk factors in addition to tobacco use, such as personal or family history of cancer and exposure to chemicals, radon gas, or second-hand smoke. Patients are encouraged to discuss the benefits and risks of the screening with their physician.

Some of the possible risks with low-dose CT scans include anxiety, false-positive results – which may lead to unnecessary procedures such as frequent scans and lung biopsies – and radiation exposure. As with any CT scan, there is some radiation exposure. Compared with conventional CT scans, however, low-dose CT scans are a much lower risk.

Experts Share Insight at Patient Event

In August, the Kidney Cancer Program held its annual educational event for patients and their families at UT Southwestern. A panel of experts discussed the latest news in kidney cancer treatment, and members of the Patient Council shared their insights.

Panelists included (from left) Jeffrey Gahan, Assistant Professor of Urology; Dr. Payal Kapur, Associate Professor of Pathology and Urology; Dr. Ivan Pedrosa, Associate Professor of Radiology and in the Advanced Imaging Research Center, Dr. Pedrosa hold the Jack Reynolds, M.D. Chair in Radiology.
Join Us

Join the Friends of the Comprehensive Cancer Center

The Harold C. Simmons Comprehensive Cancer Center is working diligently toward its mission to reduce the burden of cancer. A gift to join the Friends of the Comprehensive Cancer Center will support innovative and highly promising projects that directly impact cancer research and care. In addition to supporting the Simmons Cancer Center, members will enjoy educational benefits throughout the year. Annual memberships start at $500 for individuals or couples, and at $250 for Younger Friends up to age 40. We also welcome gifts of larger amounts, which will accelerate our goals.

Membership at the $250 level and above is recognized in UT Southwestern’s Southwestern Medicine Annual Review. For more information, please call the Development Office at 214-648-2344.

Patient and Community Outreach Programs Available

Support groups are available at the Harold C. Simmons Comprehensive Cancer Center, led by licensed social workers. Meetings are scheduled regularly for:

- Ovarian cancer
- Thoracic/lung cancer
- Husbands and partners of women with cancer
- Prostate cancer
- Breast cancer
- Brain cancer

For more information about patient-care services at the Simmons Cancer Center, please call 214-645-HOPE (214-645-4673) or toll-free, 866-460-HOPE (866-460-4673).

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