I would like to share with you some of the latest – and most promising – cancer research developments at the Harold C. Simmons Comprehensive Cancer Center.

In May, UT Southwestern announced the opening of a new $17 million cryo-electron microscope (cryo-EM) facility housing a unique collection of instruments that researchers can use to view 3-D images of objects as tiny as an atom all the way up to intact cells. The facility’s three cutting-edge instruments are expected to provide the technologies to accelerate UT Southwestern’s biomedical investigations on everything from cancer biology to drug discovery, and will run 24 hours a day, seven days a week.

Dr. Sandra Schmid, Chair of Cell Biology, and Dr. Michael Rosen, Chair of Biophysics, led a team that spent four years planning and building the facility, which will be a shared resource across the academic medical center. One of the first research projects to use the facility is led by Dr. Daniela Nicastro, Associate Professor of Cell Biology and Biophysics, who is studying mistakes in DNA repair that are believed to drive the development of cancer.

In June, UT Southwestern hosted two key events. The Simmons Cancer Center was honored to host a live stream broadcast of Vice President Joe Biden’s “Cancer Moonshot” announcement. Vice President Biden is challenging researchers and cancer program administrators to improve communication and collaboration amongst scientists and the public. Goals of the initiative include:

- Making clinical trials more accessible to cancer patients.
- Creating a new program to accelerate cancer product regulatory review.
- Establishing fast-track review for cancer treatment-related patents.

Bolstering its progress in addressing the rising threat of kidney cancer, the Kidney Cancer Program at UT Southwestern Medical Center’s Harold C. Simmons Comprehensive Cancer Center recently received $11 million in research funding from the National Cancer Institute (NCI). Kidney cancer currently has no method of early detection and is particularly challenging to treat.

The highly competitive Specialized Program of Research Excellence (SPORE) award from the NCI is the first for kidney cancer research earned by a single institution, and only the second in the nation.

“Receiving SPORE recognition for our Kidney Cancer Program is reflective of the collaborative, interdisciplinary environment that UT Southwestern has historically embraced. The early inroads that UT Southwestern researchers made in this arena serve as the ideal launching pad for future success against this devastating disease,” said Dr. J. Gregory Fitz, Executive Vice President for Academic Affairs, Provost and Dean of UT Southwestern Medical School, and Professor of Internal Medicine at UT Southwestern.

Nearly 400,000 Americans are currently living with kidney cancer, which is the fourth most commonly treated cancer at UT Southwestern. It is usually found indirectly, through a scan performed for a different reason, for example. More than 60,000 people in the U.S. are expected to be diagnosed with kidney cancer this year.

In a series of landmark findings over the past 20 years, UT Southwestern researchers have identified and characterized a key protein called HIF-2a involved in kidney cancer. These findings led to the development of a drug therapy now in clinical trials as part of...
Dr. David Gerber, Associate Professor of Internal Medicine, knows the importance of mentorship and its role in advancing cancer research. Through the years, he has mentored doctors-in-training who’ve won national awards and changed policy at hospitals where they worked, and others who beat out far more experienced physicians in national research competitions.

Now, a prestigious grant from the National Institutes of Health (NIH) will allow him to spend more time coaching young medical students, residents, and researchers as he conducts research to improve cancer treatment.

The NIH’s Midcareer Investigator Award in Patient-Oriented Research, K24 for short, is designed to give recipients more time to mentor promising clinical investigators. The five-year grant comes with salary support of up to $100,000 per year, plus benefits, up to $50,000 per year for research development support (supplies, equipment, travel, etc.), as well as additional funding for indirect costs.

“This grant will allow me to mentor more people, in greater depth, more intensively, and for longer periods of time,” said Dr. Gerber, who specializes in treating lung cancer and is also co-leader of the Experimental Therapeutics of Cancer Program in the Harold C. Simmons Comprehensive Cancer Center. The award also serves as evidence of UT Southwestern’s commitment to mentoring and training in clinical research, Dr. Gerber said.

Mentors will assist Dr. Gerber in one or more of his five federally funded research projects aimed at improving cancer treatment. That research includes:
- Examining whether cancer patients previously treated for cancer have a worse prognosis – a concern that has led most cancer trials to exclude such patients.
- Testing whether the antifungal drug trastuzumab, used to treat nontubular brain, might be an effective and more affordable inhibitor of a signaling pathway involved in cancer.
- Determining if survival rates improve in patients with locally advanced lung cancer who get immunotherapy after standard chemotherapy and radiation treatments.
- Analyzing whether survival rates improve for a group of cancer surgery patients assigned to targeted, personalized treatments. The test group, derived from a National Cancer Institute effort involving molecular testing on 8,000 cancer surgery patients, includes those whose tumors had specific aberrations. Dr. Gerber is leading the NCIC study.
- Testing whether beta-lapachone, a drug derived from the South American lapacho tree, might inhibit cancer growth in patients with advanced, nonresponsive tumors. Other Simmons Cancer Center investigators participating in the research and mentoring supported by Dr. Gerber’s grant include: Dr. Rolf Brekken, Professor of Surgery and Pharmacology; Dr. Kathy O’Donnell-Mendell, Assistant Professor of Molecular Biology; and Dr. Jasmin Tins, Associate Professor of Clinical Sciences.

Texas University Health Sciences Center. Dr. Gerber is the first UTSW researcher honored with a K24 grant in about a decade.

He said he is looking forward to “the opportunity to share with trainees what I think is an incredibly satisfying and exciting career. Being a clinical investigator has its challenges, but it’s creative, it’s impactful. Right now, I’m approached by considerably more potential mentees than I have the ability to take on.”

The grant will allow him to expand his mentoring efforts. And, looking to the future, he pointed out, “Those mentees become others’ mentors.”

Dr. Boothman holds the Robert B. and Virginia Payne Professorship in Oncology. Dr. Brekken is an Effie Marie Cain Research Scholar. Dr. Halm holds the Walter Family Distinguished Chair in Internal Medicine in Honor of Albert D. Roberts, M.D.

From the Directorcontinued from page 1

Oct. 17: 2016: Fall Reception and Lab Tours

Presenters: Dr. Rolf Brekken, Professor of Surgery and Pharmacology; Dr. Jenna Jewell, Assistant Professor of Molecular Biology; Dr. Kathy O’Donnell-Mendell, Assistant Professor of Molecular Biology; and Dr. Jasmin Tins, Associate Professor of Clinical Sciences.

Place: T. Boone Pickens Biomedical Building, 14th Floor.

Time: 5:30 – 7:30 p.m.

Invitations to follow. For more information, call 214-648-2344 or email giving@utsouthwestern.edu.

Additional events to be added to the fall schedule.

Friends of the Comprehensive Cancer Center Event

Dr. Melanie Cobb

Dr. Melanie Cobb, Interim Director of the Simmons Cancer Center and Professor of Pharmacology, said the extraordinary new treatment approaches. August brought a long-anticipated achievement when UT Southwestern’s Kidney Cancer Program was recognized by the NCI with the prestigious Specialized Program of Research Excellence (SPORE) award. This extraordinary award from the NCI supports the extensive kidney cancer research program led by Dr. James Brugarolas, program leader of the Kidney Cancer Program, and built by our faculty over the past several years. I’d also like to thank Dr. Michael White for his tremendous service to the Simmons Cancer Center. As Adjunct Professor of Cell Biology and former Associate Director for Basic Research, Dr. White has been instrumental in the growth of the Simmons Cancer Center and cancer research at UT Southwestern. I am thrilled to welcome Dr. Lawrence Lum, Associate Professor of Cell Biology, to the senior leadership team as the new Associate Director for Basic Research, Dr. Lum’s research focuses on cancerrelevant signal transduction with the use of highthroughput screening methodology as the starting point for uncovering uncharted areas in anti-cancer intervention. He holds two NCI grants and a Cancer Prevention and Research Institute of Texas grant.

Thank you for your continued support, which helps us launch new and exciting directions for cancer research.

Dr. Brugarolas, also Associate Professor of Internal Medicine, is a Virginia Marchion Linthicum Scholar in Medical 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. Lum is a Virginia Marchion Linthicum Scholar in Medical Research. Dr. Rosati holds the Mar Nell and E. Andrew Bell Distinguished Chair in Biochemistry. Dr. Schond holds the Cecil H. Green Distinguished Chair in Cellular and Molecular Biology.

Kidney Cancer Research

the Kidney Cancer Program.

The UT Southwestern SPORE program involves four innovative disease and clinical research teams targeting adult and pediatric kidney cancer, as well as a patient advocate group, development of new cancer research, and core facilities to support these efforts through data analysis, imaging technology, and a tissue repository.

The four research teams:
- Search for biomarkers to identify kidney cancer tumors most likely to respond to a HIF-2α inhibitor, as well as to anticipate those in which these tumors may evade the drug’s impact.
- Investigate the function of a gene that identifies a cluster of particularly aggressive tumors associated with clear cell renal cell carcinoma, in hopes of identifying vulnerabilities that can be targeted with drugs.
- Examine kidney cancer metabolism to distinguish aggressive and relatively inactive tumors potentially yielding a tailored treatment approach.
- Test novel treatments for childhood kidney cancer by researching the implications of a Wilms tumor subtype. “These funds will support a variety of new and ongoing activities, including the development of a new drug, studies of kidney cancer subtypes in adults and children, and a novel approach to determine which small tumors may be eligible for treatment,” said Principal Investigator Dr. James Brugarolas, Associate Professor of Internal Medicine and program leader of UT Southwestern’s Kidney Cancer Program.

Dr. Melanie Cobb, Interim Director of the Simmons Cancer Center and Professor of Pharmacology, said the extraordinary award from the NCI supports the extensive kidney cancer research built by UT Southwestern faculty over the years. “Sixteen distinguished research leaders – each nationally recognized in his or her field of expertise – will lead the team of more than 40 scientists that will focus on developing new approaches toward disease, which is particularly deadly,” Dr. Cobb said.

This award marks the second SPORE grant for UT Southwestern, which for 20 years has led a multiinstitutional SPORE program in lung cancer that is the largest thoracic oncology effort in the U.S.

Dr. Fitz holds the Nadine and Tom Crockdick Distinguished Chair in Medical Science, and the Atticus James Gill, M.D. Chair in Medical Science.
ATRX is lost in nearly all ALT-positive tumors, and recent studies at UT Southwestern demonstrate an important role for ATRX in normal telomere biology. However, the mechanism behind the loss of ATRX in ALT tumors remains unknown.

Telomeres are structures that cap chromosomes to protect the ends from deterioration. These structures naturally shorten with age, resulting in reduced cell growth. Telomeres play a crucial role in maintaining genomic stability by preventing the fusion of chromosomes. If telomeres become too short, the cell enters a state called replicative senescence, which prevents cell division and arrests the cell cycle. This process is thought to be a mechanism that helps prevent the development of cancer, as cells that escape senescence and continue to divide can become cancerous.

Epigenetics relates to external modifications to DNA that turn genes “on” or “off” without changes in the underlying DNA sequence. Epigenetic regulation includes DNA methylation, histone modifications, and non-coding RNA interactions. These modifications can affect gene expression and are thought to play a role in the development of cancer. For example, alterations in epigenetic marks have been observed in many cancer types, including changes in DNA methylation and histone modifications. These changes can lead to the activation or silencing of genes that are involved in cell growth, apoptosis, and other cellular processes.

ATRX is a protein involved in epigenetic regulation and is known to be important for maintaining telomere integrity. However, the mechanism by which ATRX is lost in ALT tumors is not fully understood.

Dr. Banaszynski is a Virginia Murchison Linthicum Scholar in Medical Research at UT Southwestern Medical Center. Dr. Banaszynski is also a member of the Cecil H. and Ida Green Center for Reproductive Biology Sciences and with the Children’s Medical Center Research Institute at UT Southwestern, will study the epigenetic regulation of genome stability in human cancers.

Work in Dr. Banaszynski’s lab has included projects to identify unique aspects in tumor metabolism of patients with clear cell renal cell carcinoma – the most common type of kidney cancer – and prostate cancer. By analyzing tumor metabolism of acetate and glucose, Dr. Banaszynski hopes to understand how different tumors use these molecules. This research may lead to the development of novel therapeutic targets. One of these targets is 11C-acetate PET imaging, which seeks to determine if radiolabeled acetate can be used to effectively detect metastasis, or spread, of clear cell renal cell carcinoma and response to treatment. “Hopefully, this will lead to an improved ability to noninvasively monitor patients for treatment response and cancer progression,” Dr. Banaszynski said.

Dr. Banaszynski is a Virginia Murchison Linthicum Scholar in Medical Research at UT Southwestern Medical Center.
Research News

Research Shows 98% Cure Rate for Prostate Cancer Using High-Dose Radiation Therapy

Five years of patient follow-up by UT Southwestern researchers has shown that using stereotactic body radiation therapy (SBRT) to treat prostate cancer appears to offer a higher cure rate than more traditional approaches.

“The conventional form of radiation is 44 treatments given over nine weeks. SBRT is both more convenient and has increased potency,” said Dr. Robert Timmerman, Director of the Annette Simmons Stereotactic Treatment Center at UT Southwestern, Professor and Vice Chairman of Radiation Oncology, and Professor of Neurological Surgery. “UT Southwestern served as the lead site for the multi-institutional clinical trial, which involved first-time prostate cancer patients diagnosed with stage I or stage II (low and intermediate risk) prostate cancer. A total of 91 patients were treated and followed for five years, with only one patient experiencing a recurrence of his cancer. The findings were published in the European Journal of Cancer.

Terry Martin of McKinney, Texas, said a compelling advantage was a reduction in the number of treatment sessions when he was evaluating his options. “I gave 45 minutes away from UT Southwestern. The difference between being treated five times versus four times is enormous,” said Mr. Martin, a retired airline pilot. “I felt that I was back to normal just 10 days after finishing treatment.” Researchers found that side effects were not necessarily different compared with other forms of prostate cancer treatment that require more time. In the short term, the side effects of SBRT can include urinary issues (urgency, frequency, and burning) and rectal irritation, which are often temporary and reverse within four weeks of treatment. Researchers found a small increase in the risk of longer-term urinary and rectal complications, which is comparable to conventional treatments. Decrease in erectile function was seen in only 25 percent of patients, which is less than with conventional radiation or surgery, Dr. Hannan said.

To reduce the side effects associated with SBRT, current clinical trials at UT Southwestern are using a biodegradable rectal spacer gel to protect the rectum. UT Southwestern currently is the only accredited site in Texas at which this spacer gel can be used. The increased potency of the SBRT treatments is expected to partially offset the impact high-risk (stage III) prostate cancer patients for whom the cure rate is dismal, says Dr. Hannan, principal investigator of the high-risk prostate SBRT trial at UT Southwestern.

The SBRT study for prostate cancer was supported by a grant from the U.S. Department of Defense. Additional UTSW researchers involved in the study include Dr. Yair Lotan, Professor of Urology, and Dr. Xian-Jin Xie, Professor of Clinical Sciences.

Dr. Timmerman holds the Effie Marie Cain Distinguished Chair in Cancer Therapy Research.

Dr. Lotan holds the Helen J. and Robert S. Strauss Professorship in Urology.

Clinical News

Engineered Stem Cell Transplant Abates Leukemia

At age 62, Texan Chuck Dandridge thought he was healthy – he felt good and exercised regularly – until a routine checkup revealed leukemia. Today, he is cancer-free thanks to his son, Jon. In 2015, Mr. Dandridge became the first adult in the U.S. to receive a newly modified stem cell transplant that uses genetically engineered blood cells from a family member. His physician, Dr. Madhuri Vusirikala, Professor of Internal Medicine and a bone marrow transplant specialist at UT Southwestern’s Harold C. Simmons Comprehensive Cancer Center, directed the treatment.

The transformational journey began in 2015, when Mr. Dandridge visited his doctor for a routine check of his cholesterol levels. Laboratory tests detected low blood counts. Mr. Dandridge was diagnosed with myelodysplastic syndrome, sometimes called pre-leukemia, or MDS. By 2014, his disease had progressed to acute myeloid leukemia (AML), which affects about 20,000 Americans annually, according to the National Cancer Institute. He was referred to the Simmons Cancer Center, where his disease was tested for genetic mutations.

“We found a mutation called IDH2, which causes the body to produce an abnormal protein that promotes excessive cell growth. If you can target that mutation and stop that abnormal protein from being produced, you can get the cells to start behaving normally,” Dr. Vusirikala said. “But the risk of graft-versus-host-disease (GvHD) following a transplant would be at least a half match. Using a same-sex donor is preferred because it reduces the risk of complications, so his son Jon emerged as the best choice,” Dr. Vusirikala said.

Once again, Mr. Dandridge enrolled in a UT Southwestern clinical trial evaluating a therapy called AG-221. He took four pills each morning for the next eight months.

“He did not go into complete remission, but he had an excellent response,” said Dr. Vusirikala. “He was referred to UT Southwestern’s National Marrow Donor Program.”

That success made him eligible for a full match. “The best chance of finding a full match is usually a full sibling, however, Chuck had no full siblings,” Dr. Vusirikala said. Additionally, minorities are underrepresented in the National Marrow Donor Program’s registry, with about 70 percent of donors being Caucasian. Mr. Dandridge is African-American, so the search for an unrelated donor proved unsuccessful.

“We knew his daughter and his son would be at least a half match. Using a same-sex donor is preferred because it reduces the risk of complications, so his son Jon emerged as the best choice,” Dr. Vusirikala said.

Once again, Mr. Dandridge volunteered for a clinical trial, known as BP-001, which processed the stem cells used in the transplant to reduce the risk of graft rejection and GvHD. In July 2015, the genetically engineered blood cells were transplanted from Mr. Dandridge’s 51-year-old son at UT Southwestern’s William P. Clements Jr. University Hospital. Mr. Dandridge’s leukemia is now in remission.

“Giving my dad the same gift of life that he gave me when he brought me into this world was the most amazing feeling a son could have,” Jon Dandridge said.

“At the beginning,” Mr. Dandridge said, “I always wondered how I could give something back to my parents, who have given me so much.”

The bond is mutual. “I have my son Jon’s DNA in my bloodstream, bone marrow, and immune system,” said Mr. Dandridge, now 65. “My skin is my own DNA, but inside I’m all Jon.”
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:

- Prostate cancer
- Bladder cancer
- Anal cancer
- Oral, and head & neck cancer
- BMT family bereavement
- Life after bone marrow/stem cell transplant
- Husbands and partners of women with cancer
- Women with early-stage breast cancer
- Survivorship – Life after treatment for cancer

As part of the ongoing effort to help educate the Dallas-Fort Worth community on today’s important medical and health care topics, the Simmons Cancer Center has developed an exciting Speakers Bureau program available to you or your organization. Topics pertain to cancer research, cervical cancer, genetics and cancer, HPV vaccines, recommended screenings, mammography and dense breast tissue, among others.

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