

Dynamic Decade

Researchers uncover mutated genes involved in lung cancer; one affects nonsmokers (3/1/2005) UT Southwestern researchers show new drug [PD166326] may help treat certain forms of leukemia (5/2/2005) Antibody [3G4] combined with cancer drug shows promise against breast tumors (5/15/2005) UT Southwestern researchers discover master switch in cell death (6/30/2005) UT Southwestern gets NASA grant to study human cells' response to radiation (7/27/2005) Gene silencing technique offers new strategy for treating, curing disease (7/31/2005) Researchers find drug [GRN163L/imetelstat] that blocks spread of lung cancer in mice (9/1/2005) UT Southwestern researchers develop screening test for cells that activate immune system (9/6/2005) Hodgkin disease survivors face higher risk for stroke later in life (10/13/2005) Target identified for therapeutic drugs to fight adult brain cancer (1/15/2006) DNA end caps may lead to cancer treatments, UT Southwestern researchers report (2/2/2006) Mature muscle fibers can revert to become cancerous, researchers find (9/1/2006) Airborne metal particles from pollution may lead to lung cancer, UT Southwestern research team concludes (9/15/2006) Natural anti-viral enzyme [TBK-1] helps keep cancer cells alive, researchers find (10/5/2006) Study reveals mechanism for cancer-drug [hermiasterlin derivative] resistance (10/9/2006) Analysis of breast cancer gene role offers promising target for drugs to stop or slow progression of disease (10/30/2006) Survivors of childhood leukemia, brain tumors more at risk for strokes later in life (11/20/2006) Hair-growth drug artificially lowers PSA levels in prostate cancer screening, study finds (12/5/2006) Drug [bevacizumab] that chokes off tumor blood vessels offers new hope to lung cancer patients (12/13/2006) Profiling of cancer genes may lead to better and earlier detection of solid human cancers, study finds (12/26/2006) Tracing agent [microbubbles], ultrasound combo helps test [anti-VEGF] cancer therapy's effectiveness (1/8/2007) Novel laboratory technique nudges genes into activity (1/28/2007) New biomarker test could predict outcome for bladder cancer patients (2/1/2007) Sea creature's toxin [diazonamide] could lead to promising cancer treatment (2/5/2007) Massive gene screening points way to more effective chemotherapy (4/11/2007) Substance in tree bark [beta-lapachone] could lead to new lung cancer treatment (6/25/2007) Single-incision belly-button surgery to remove kidney performed first at UT Southwestern (8/23/2007) Radiation and drug [baviximab] combo helps boost efficacy of lung cancer treatment (9/1/2007) Radiation therapy technique reduces length of prostate cancer treatment (9/20/2007) New 'seed' therapy helps pinpoint breast tumors with more accuracy (10/11/2007) Synthetic compound [Smac mimetic] promotes death of lung cancer cells, tumors (11/12/2007) Hormonal dietary supplements might promote prostate cancer progression (1/15/2008) Pros, cons of drug proven to prevent prostate cancer should be considered, researchers recommend (1/21/2008) Arsenic aids tumor imaging when joined to cancer-homing drug (3/1/2008) Magnetic system could be key to surgery without scars (3/26/2007) Gene analysis might explain ethnic differences in sensitivity to chemotherapy in lung cancer (4/23/2007) Investigators uncover intriguing clues to why persistent acid reflux sometimes turns into cancer (8/9/2007) UT Southwestern offers Metroplex's only automated 3-D breast ultrasound machine (3/28/2008) Supplemental breast ultrasound boosts cancer detection, radiologist reports in national study (5/13/2008) Molecular "clock" could predict risk for developing breast cancer (5/14/2008) Fireflies' glow helps researchers track cancer drug's effectiveness (5/29/2008) New model predicts whether patients will be free of renal cancer 12 years after initial treatment (6/2/2008) UT Southwestern urologists identify seven biomarkers that may help pinpoint prostate cancer recurrence (6/15/2008) Nanotechnology, biomolecules and light unite to "cook" cancer cells (6/23/2008) Protein thought to promote cancer instead functions as a tumor suppressor, researchers report (7/7/2008) Digestive specialists freeze out esophagus cancer with new therapy (7/29/2008) Gene variant boosts risk of fatty liver disease, scientists discover (9/25/2008) Cancer requires support from immune system to develop, researchers report (10/30/2008) Researchers identify gene linked to inherited form of fatal lung disease (12/19/2008) Researchers disrupt biochemical system involved in cancer, degenerative disease (1/30/2009) Researchers find marker for severity in adult brain cancer (4/1/2009) New ultrasound-guided biopsy method allows improved diagnosis of endometrial disease (4/14/2009) Oxygen + MRI might help determine cancer therapy success (6/3/2009) Researchers investigate high-risk populations for bladder cancer screenings (7/16/2009) \$2 million grant aids study of lung cancer in people who never smoked (7/21/2009) Researchers launch study into search-and-destroy antigen for deadly skin cancer (8/10/2009) Researchers examine mechanisms that help cancer cells proliferate (9/1/2009) Certain cancers more common among HIV patients than non-HIV patients (9/25/2009) Researchers use drug [BEZ235]-radiation combo to eradicate lung cancer (10/29/2009) Stereotactic radiotherapy offers noninvasive, effective treatment for frail patients with early-stage lung cancer (11/2/2009) Childhood cancer survivor program celebrates 20 years (11/3/2009) Scientists identify possible therapy target [TGF-beta1] for aggressive cancer (12/1/2009) Minimally invasive surgery removes sinus tumor without facial disfiguration (12/14/2009) UT Southwestern scientists use DNA sequencing to attack lung cancer (12/16/2009) Fort Worth patient first in North Texas to undergo robot-assisted surgery for removal of lung tumor (12/21/2009) Experimental drug shows promise against brain, prostate cancers (1/4/2010) Loss of gene function makes some prostate cancer cells more aggressive, researchers find (2/2/2010) Single gene mutation induces endometrial cancer, researchers find (2/10/2010) UT Southwestern surgeons perform first robot-assisted cystectomy in Dallas/Fort Worth area (2/17/2010) UT Southwestern takes multidisciplinary approach to difficult head, neck cancers (2/22/2010) Fewer platelets could be used for some cancer and bone-marrow transplantation patients, helping alleviate shortages (3/10/2010) Precision radiation therapy may improve survival rates of patients with inoperable early-stage lung cancer, UT Southwestern physicians report (3/16/2010) Chemotherapy plus synthetic compound provides potent anti-tumor effect in pancreatic cancers, research shows (3/23/2010)

Surgeon experience trumps method of operation in patient outcomes for prostate surgery, UT Southwestern physician reports **(4/26/2010)** Heavy alcohol use, binge drinking might increase risk of pancreatic cancer **(5/19/2010)** Ablation proved as effective as traditional surgery in treating kidney cancer, surgeon reports **(6/4/2010)** Scientists uncover protein that thwarts tumor invasion **(6/7/2010)** UT Southwestern first in region to use newest generation of surgical robot **(6/14/2010)** Head and neck surgeons perform Dallas' first scarless robotic surgery for throat cancers **(6/17/2010)** Researchers discover how estrogen can prevent vascular disease without increasing cancer risk **(6/23/2010)** Simmons Comprehensive Cancer Center earns "gold standard" National Cancer Institute designation **(8/4/2010)** Lung cancer culprit could offer target for therapy, researchers report **(9/13/2010)** Gene information predicts survival time, possible new treatment options for lung cancer patients **(12/14/2010)** Dutasteride not a cost-effective way to prevent prostate cancer in some men **(2/8/2011)** Researchers develop synthetic compound that may lead to drugs to fight pancreatic, lung cancer **(3/10/2011)** UT Southwestern research advances fight against kidney cancer **(3/31/2011)** Anti-aging hormone Klotho inhibits renal fibrosis, cancer growth **(4/14/2011)** Gynecologic cancer expert helps pinpoint best treatment for fast-growing gestational tumors **(4/26/2011)** Researcher maps far-reaching effects of estrogen signaling in breast cancer cells **(5/5/2011)** UT Southwestern research reveals how cancer-driving enzyme works **(5/6/2011)** Researchers find protein that might be key to cutting cancer cells' blood supply **(5/12/2011)** Higher doses of radiation in fewer treatments are safe, effective for low-risk prostate cancer **(6/2/2011)** UT Southwestern research uncovers genetic link between emphysema, lung cancer **(6/9/2011)** Researchers find genetic changes in majority of advanced lung cancers **(6/16/2011)** Research reveals that significantly more genetic mutations lead to colon cancer **(7/18/2011)** Scientists discover new pathway to potential therapies for advanced prostate cancer **(7/25/2011)** Researchers find way to help donor adult blood stem cells overcome transplant rejection **(8/4/2011)** Program identifies families at high risk for colorectal cancer **(9/1/2011)** Researchers identify tumor-specific pathway; finding could lead to new cancer-stopping therapies **(11/22/2011)** Diagnostic brain tumor test could revolutionize care of patients with low-grade gliomas **(1/26/2012)** Researchers identify mechanism that maintains stem-cell readiness **(5/31/2012)** Study suggests new treatment target for deadly brain tumors **(8/1/2012)** Aspirin may help men with prostate cancer live longer, study suggests **(8/28/2012)** Spread of human melanoma cells in mice correlates with clinical outcomes in patients **(11/7/2012)** Study probes lung cancer detection by CT scanning **(12/26/2012)** Finding—and fighting—the fat that fuels cancer **(2/5/2013)** Scientists make mouse model of human cancer, demonstrate cure **(3/5/2013)** Researchers uncover a genetic vulnerability of lung cancer **(4/4/2013)** New potential target [alternative splicing] identified for cancer therapy **(4/22/2013)** Study: Bladder cancer could recur despite bladder removal **(5/7/2013)** Researchers identify novel class of drugs for prostate cancers **(5/28/2013)** Oxygen decelerates many cancer tumors when combined with radiation therapy **(7/23/2013)** Noninvasive test optimizes colon cancer screening rates **(8/5/2013)** Tumor measurements predict survival in advanced non-small cell lung cancer **(8/19/2013)** Interference with cellular recycling leads to cancer growth, chemotherapy resistance **(9/18/2013)** Cellular switch controls growth of brain tumor cells **(9/23/2013)** Less can be more when removing lymph nodes during breast cancer surgery **(10/1/2013)** Overexpressed protein the culprit in certain thyroid cancers **(10/14/2013)** Researchers discover new driver of breast cancer **(11/7/2013)** Study identifies potential therapeutic target for incurable, rare soft-tissue cancer **(12/26/2013)** Researchers identify target for shutting down growth of prostate cancer cells **(3/4/2014)** Inherited mutated gene raises lung cancer risk for women, those who never smoked **(3/21/2014)** Cancer biologists link tumor suppressor gene to stem cells **(3/26/2014)** Gene may predict if further cancer treatments are needed **(3/28/2014)** Physicians use CyberKnife to treat vocal cord cancer **(4/3/2014)** Blocking DNA repair mechanisms could improve radiation therapy for brain cancer **(4/7/2014)** NCI award supports access to national clinical trials **(4/9/2014)** Website information on colon cancer too complex, fails to address key concerns, researcher finds **(4/14/2014)** Liver cancer screening highly beneficial for people with cirrhosis **(5/5/2014)** Wound-healing role for microRNAs in colon offers new insight into inflammatory bowel diseases **(5/23/2014)** International collaboration highlights new mechanism explaining how cancer cells spread **(5/28/2014)** Cancer researchers identify irreversible inhibitor for KRAS gene mutation **(7/28/2014)** Ten UTSW researchers among 2014 World's Most Influential Scientific Minds **(7/28/2014)** Children's Research Institute scientists pinpoint gene likely to promote childhood cancers **(8/11/2014)** Researchers find new gene mutations for Wilms tumor **(9/5/2014)** UTSW one of two institutions to offer innovative four-flap microsurgery approach to breast reconstruction **(9/15/2014)** Cancer-fighting cocktail demonstrates promising results for advanced cervical cancer **(9/15/2014)** Many patients excluded from lung cancer trials due to prior cancer **(9/26/2014)** Researchers identify "Achilles heel" in metabolic pathway that could lead to new lung cancer treatments **(10/7/2014)** Study identifying cell of origin for nerve tumors lays groundwork for new therapies **(11/11/2014)** Scientists uncover mechanism that controls fitness of cells, impacting aging and disease **(11/15/2014)** Cancer researchers identify gene mutations and process for how kidney tumors develop **(11/17/2014)** Signaling mechanism could be target for survival, growth of tumor cells in brain cancer **(12/15/2014)** Neuro-oncologists discover cancer cells can burn acetate for fuel **(12/18/2014)** Researchers confirm whole-genome sequencing can successfully identify cancer-related mutations **(12/23/2014)** Stereotactic body radiation plus chemotherapy improves survival among stage 4 lung cancer patients **(12/30/2014)** Researchers target the cell's "biological clock" in promising new therapy to kill cancer cells, shrink tumor growth **(1/1/2015)** Study links deficiency of cellular housekeeping gene with aggressive forms of breast cancer **(1/30/2015)** Study finds no reason for cancer survivors to be excluded in advanced stage lung cancer trials **(2/9/2015)** UTSW receives key NCI funding to plan first U.S. Center for Heavy Ion Radiation Therapy Research **(2/10/2015)** MAGE genes provide insight into optimizing chemotherapy **(2/17/2015)** New cancer treatments could evolve from research showing that acetate supplements speed up cancer growth **(2/17/2015)** Mobile clinic brings expertise to doorstep of underserved cancer survivors **(2/18/2015)** New cyclotron facility expands research opportunities, imaging capabilities for detecting, tracking cancer **(3/18/2015)** Study reveals molecular genetic mechanisms driving breast cancer progression **(4/3/2015)** Physicians pioneer use of stereotactic body radiation for deadly kidney cancer complication **(4/7/2015)** Researchers lead collaborative charge to uncover genetic diversity of pancreatic cancer **(4/9/2015)** Scientists identify key receptors behind development of acute myeloid leukemia **(4/29/2015)** UTSW brings comprehensive clinical cancer services to Tarrant, surrounding counties at new Fort Worth facility **(5/4/2015)** Researchers discover molecule that accelerates tissue regeneration after bone marrow transplants **(6/11/2015)** National Cancer Institute awards top-tier comprehensive status to Simmons Comprehensive Cancer Center **(7/10/2015)** Cancer researchers first in Texas to use new prostate rectal spacer to minimize side effects of SABR treatments **(9/17/2015)** CRI scientists see through bones to uncover new details about blood-forming stem cells **(9/23/2015)** Immunotherapy superior to chemotherapy for lung cancer in international trial **(9/28/2015)** CRI identifies emergency response system for blood formation **(11/16/2015)**



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HAROLD C. SIMMONS COMPREHENSIVE CANCER CENTER

Setting the Stage. In 1988, a \$41 million gift from Dallas businessman Harold Simmons and his wife, Annette, provided seminal funds to transform cancer research and care at UT Southwestern. In 1991, the Harold C. Simmons Comprehensive Cancer Center was established.

Pioneering work by Drs. John Minna and Adi Gazdar opened the door in 1996 for Simmons Cancer Center to receive a flagship Specialized Program of Research Excellence grant—a highly competitive award in lung cancer that continues today.



In 2000, the 27,000-plus-square-foot Simmons Cancer Center Clinic was established in the Seay Biomedical Building, providing a central location for oncology services and related care.

Dr. James K.V. Willson was named Director in 2004. He launched a five-year plan to develop a “matrix” cancer center, building bridges among disciplines to ensure translation of cancer discoveries to patient care.

BUILDING MOMENTUM

2005

The continuing generosity of Mr. and Mrs. Simmons propels the Cancer Center forward, notably through a \$50 million commitment to ensure UT Southwestern’s eminence in care and research for all types of cancer.

Extramural funding for Simmons Cancer Research totals \$53 million.

The Cancer Center launches its Chemistry and Cancer, Development and Cancer, Cancer Cell Networks, and Molecular Pathogenesis and Therapeutic Targeting of Cancer scientific programs with institutional leadership from Drs. Melanie Cobb, Luis Parada, Steve McKnight, and John Minna to shed new light on factors that cause and promote cancer, and on the disease’s vulnerabilities and potential therapies. Cell biologist Dr. Michael White is named Associate Director for Basic Research. ▼



A \$9.8 million grant from NASA fuels research into the effects of radiation on astronauts, to better protect future space travelers and learn more about the risks of radiation exposure on Earth.

The Foundation for the Accreditation of Cellular Therapy (FACT) awards accreditation to UT Southwestern’s adult bone marrow transplant program, and the Myelodysplastic Syndromes Foundation recognizes UT Southwestern as a Center of Excellence in research, diagnosis, and treatment.

The Department of Radiation Oncology begins its residency training program, the first in the Dallas/Fort Worth area.

2006



◀ Noted lung cancer specialist Dr. Joan Schiller is appointed Deputy Director to lead the growth of Simmons Cancer Center’s Disease-Oriented Teams (DOTs).

A cooperative training program for oncology nursing students from Texas Christian University is created in Simmons Cancer Center Clinics.

The Advanced Imaging Research Center (AIRC) is established within the new Bill and Rita Clements Advanced Medical Imaging Building. The AIRC has become a leader in developing new magnetic resonance and other imaging technologies to shed light on cancer and other diseases.

The newly constructed T. Boone Pickens Biomedical Research Building opens on UT Southwestern’s North Campus, giving Simmons Cancer Center faculty more than 32,000 square feet of laboratory space.

2007

Moncrief Cancer Foundation commits \$20 million over 10 years to establish community outreach programs focused on cancer prevention and survivorship. Dr. Keith Argonbright is appointed Medical Director of UT Southwestern’s Moncrief Cancer Resources.

Texas voters approve a \$3 billion, 10-year initiative that establishes the Cancer Prevention and Research Institute of Texas, an agency whose mission is to secure the state’s position as a leader in innovative research, development of new treatments, and cancer prevention. ▼



Dr. Celette Sugg Skinner is recruited to lead Population Science and Cancer Control, a scientific program designed to partner with the community and local health systems to improve cancer prevention, screening, and other services, particularly in patients who lack ready access to a health care system. ▶



2008

UT Southwestern establishes a new biotech park, called BioCenter at Southwestern Medical District, to develop technologies and attract biotech companies to the region.



◀ The Annette Simmons Stereotactic Treatment Center at Zale Lipshy University Hospital is founded with support from Harold and Annette Simmons through UT Southwestern’s Innovations in Medicine capital campaign.

UT Southwestern’s bone marrow transplant program is accredited as a joint program with Children’s Medical Center Dallas.

2009

Zale Lipshy University Hospital receives the inaugural American College of Surgeons Commission on Cancer Outstanding Achievement Award. Fewer than 1 in 5 evaluated hospitals earn the award.

UT Southwestern’s Cancer Biology Graduate Program receives approval from the Texas Higher Education Coordinating Board; within five years, the program will have grown to include about 50 faculty trainers from more than 20 departments and about 60 full-time students. ▶



UT Southwestern is named a pilot center for the National Cancer Institute’s Cancer Target Discovery and Development Network, an initiative designed to translate masses of genomic data about cancers into strategies for treating patients.

GROWING IN DISTINCTION

2010
NCI-CC ◀ Simmons Cancer Center attains National Cancer Institute designation, placing it among an elite group of top-tier U.S. cancer centers. The recognition acknowledges Simmons Cancer Center for scientific leadership and its substantial resources devoted to finding new insights into, and better treatments for, cancer.

The state agency devoted to fighting cancer, the Cancer Prevention and Research Institute of Texas, funds its first research grants. By late 2015, the agency will have awarded more than \$1.47 billion in grants, including \$316 million to UT Southwestern, the most of any institution.

The Breast Screening and Patient Navigation program at Simmons Cancer Center, designed to overcome financial and geographical hurdles that keep women from getting mammograms and timely diagnostic services, begins outreach in five rural counties. ▼



Simmons Cancer Center is one of 14 medical sites selected to participate in the federally funded Lung Cancer Mutation Consortium, a clinical trial protocol that offers patients with advanced lung cancers free, extensive genetic testing of their tumors in an effort to find the best possible treatments.

2011
 A five-year, \$6.3 million National Cancer Institute grant establishes the Parkland Health & Hospital System-UT Southwestern PROSPR Center to promote colorectal cancer screening, a unique cancer prevention and detection effort that assists people who lack insurance or are underinsured. ▼



Dr. W. Phil Evans, Director of the UT Southwestern Center for Breast Care, is inducted as President of the American Cancer Society for 2011-12.

◀ Pediatric oncologist Dr. Stephen Skapek is recruited to lead the Division of Pediatric Hematology and Oncology and is named Director of what is now the Pauline Allen Gill Center for Cancer and Blood Disorders at Children's Medical Center Dallas.

Extramural cancer research funding at Simmons Cancer Center tops \$100 million for the first time.

Simmons Cancer Center launches the Experimental Therapeutics of Cancer scientific program to more closely focus on translating UT Southwestern's scientific discoveries into real-world cancer treatments.

2012
 Children's Medical Center Dallas, the primary pediatric teaching hospital for UT Southwestern, opens new inpatient and outpatient cancer treatment facilities.

◀ Children's Medical Center Research Institute at UT Southwestern is launched. Noted stem cell biologist Dr. Sean Morrison leads the \$150 million venture dedicated to transformative research on cancer, birth defects, and metabolic diseases.

The Cancer Prevention and Research Institute of Texas confers an additional five Multi-Investigator Research Awards, totaling more than \$33.5 million, to Simmons Cancer Center members, bringing to 12 the number awarded since 2010, with a cumulative value of more than \$78 million.

The Breast Screening and Patient Navigation program expands its mammography and breast cancer diagnosis support into 12 additional counties beyond Tarrant County, and plans an expansion targeting public housing residents in Dallas County through a partnership with the University of North Texas Health Science Center.

UT Southwestern begins offering low-dose CT screening for lung cancer after national trials show the technique saves lives by detecting tumors early in patients with a history of moderate to heavy smoking.

The new, \$22 million, 60,000-square-foot Moncrief Cancer Institute in Fort Worth is dedicated, offering genetic and nutritional counseling, mammography, telemedicine, and support services for cancer patients and survivors. ▼



2013
 Simmons Cancer Center establishes a Phase I Clinical Trials Unit to help speed testing of the latest potential treatments for cancer patients. ▼

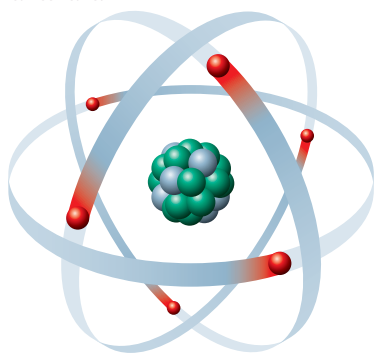
Please Ask Your Doctor About Our Clinical Trials

Clinical trials test new treatment options in people with cancer. The goal of this research is to find better ways to treat cancer and help cancer patients.

Simmons Cancer Center's external advisory board approves the Population Science and Cancer Control scientific program, led by Drs. Celette Skinner and Ethan Halm, to focus on early cancer detection.

The Cancer Answer Line (1-888-980-6050)—a Simmons Cancer Center service to help patients, family members, and others get answers to general questions about cancer and to better navigate care—makes its debut. In its first year, the Answer Line responds to more than 2,000 queries from the public.

2014
 UT Southwestern's Department of Radiation Oncology leads a consortium to plan for the first national heavy ion radiation therapy center, a major technological advance in cancer care. ▼



The American College of Surgeons Commission on Cancer awards UT Southwestern University Hospitals its highest level of accreditation—Three-Year with Commendation at the Gold Level. Additionally, the hospitals are among only about 15 percent of cancer programs nationwide to earn the Commission's Outstanding Achievement Award.

The state-of-the-art William P. Clements Jr. University Hospital opens its doors, with 64 beds—the entire 11th floor—devoted to cancer care. ▼



▲ UT Southwestern is among only 30 U.S. cancer research centers named a National Clinical Trials Network Lead Academic Participating Site, bolstering Simmons Cancer Center's clinical cancer research for adults and providing patients access to cancer trials sponsored by the National Cancer Institute.

The PROSPR Center mission expands its focus to cervical cancer prevention and detection, studying HPV vaccination and screening in under- and uninsured women.

A formal research affiliation with the Dallas Regional Campus of the University of Texas School of Public Health enhances Simmons Cancer Center's public health research expertise and faculty.

An anonymous donor provides \$10 million to establish the Eugene P. Frenkel Program for Endowed Scholars in Clinical Oncology to promote the recruitment and support of the next generation of clinical leaders in cancer care.

JOINING THE TOP TIER OF CANCER CENTERS

2015
 A new, 4,000-plus-square-foot cyclotron facility begins operations at Simmons Cancer Center, expanding scientists' ability to use positron emission tomography to see events inside the body as they occur, and to discern details of cancer and other diseases that may aid in the selection of more effective, individualized therapies.

Simmons Cancer Center's bone marrow transplant program, deemed a National Center of Excellence by major national insurance carriers, performs the 1,000th transplant in its 16-year history.

Parkland Memorial Hospital, UT Southwestern's primary teaching institution, opens its new 862-bed hospital, nearly doubling the size of its previous facility.

A \$4.8 million Cancer Prevention and Research Institute of Texas award to Moncrief Cancer Institute, the largest prevention grant the agency has awarded, funds the Colorectal Screening and Patient Navigation program. The program provides free colon cancer screening and assistance with follow-up care for patients in Tarrant and 20 surrounding rural counties.

UT Southwestern's Harold C. Simmons Comprehensive Cancer Center—Fort Worth, encompassing more than 22,500 square feet in Moncrief Cancer Institute, is dedicated, offering the latest in clinical care and access to clinical trials to residents of Tarrant and 10 other counties.



▲ Moncrief Cancer Institute and the Simmons Cancer Center roll out a \$1.1 million, custom-designed Mobile Cancer Survivor Clinic to deliver follow-up care and screening services in Tarrant and eight rural counties, focusing on underserved, uninsured cancer survivors.



◀ UT Southwestern earns recognition as one of the nation's top cancer hospitals by U.S. News and World Report magazine, earning high marks in areas including patient volume and survival, advanced technologies, nursing intensity, and accreditation for bone marrow and tissue transplantation.

Simmons Cancer Center is designated a "Comprehensive Cancer Center," the highest ranking awarded by the National Cancer Institute. The designation recognizes exceptional depth and breadth in cancer research, as well as innovative teamwork among scientists to better understand cancer and improve patient and community care. ▶



FROM FOUNDATIONS TO FULFILLMENT

For cancer care in North Texas, 2005–2015 has been a defining decade. Ten years ago, Simmons Comprehensive Cancer Center set the loftiest of goals—to meet the community’s many and varied cancer-related needs through 1) outstanding achievement in biomedical research; 2) exceptional patient care; 3) a rich training environment for the physicians and scientists of tomorrow; and 4) aggressive outreach to provide more North Texans with lifesaving prevention and early detection.

In just five years, Simmons Cancer Center earned National Cancer Institute (NCI) designation recognizing achievement in those areas, a milestone that also has opened some of the most advanced national clinical trials to local cancer patients. And now, after just another five years, Simmons has been awarded “comprehensive” designation from the NCI, becoming one of only three such top-tier institutions in the state and the only one in North Texas. The designation recognizes superior cancer care and prevention programs, along with pacesetting science and technology.

Those strides testify to the commitment of the Cancer Center’s 173 members—the people behind the ideas, inspiration, industry, and innovation that have propelled a decade of progress in the lab, the clinic, and the community. And this decade of achievement would not have been possible without a vanguard of visionaries who set in place the cornerstones upon which today’s Cancer Center has been built.

A VISION TAKES SHAPE

The center itself—designed with the goal of transforming cancer care and research at UT Southwestern—was established in 1991 through the generosity of local philanthropists Harold and Annette Simmons and shepherded with the commitment of UT Southwestern leadership. Around that time, Dr. John Minna began building a research framework focused on conveying basic-science discoveries to patients’ bedside care. And his work with longtime collaborator Dr. Adi Gazdar, probing the biology of lung cancer, brought the Cancer Center its flagship and long-running multi-investigator grant, a Specialized Program of Research Excellence (SPORE) award.

By the middle of the last decade, more support from the Simmonses, a five-year plan to build a “matrix” cancer center to foster scientific teamwork, and institutional dedication of resources and talent propelled the dynamic era that continues today. Scientific leadership by Drs. Steve McKnight, Melanie Cobb, Luis Parada, and Dr. Minna bridged departments and disciplines, bringing together investigators with a wide range of technical and medical expertise. These collaborations coalesced into scientific programs designed to tackle cancer’s complicated challenges and to deliver impactful science to patients and the public. Then, the Cancer Prevention and Research Institute of Texas (CPRIT), an agency set in motion by a 2007 statewide referendum, began fueling new discovery with its first research grants in 2010.

Since then, a new cadre of scientific leaders at the Cancer Center—such as Drs. Celette Sugg Skinner, David Boothman, Mike White, and Deputy Director Joan Schiller—has helped build novel translational research interactions. At the same time, a critical mass of UT Southwestern clinical leaders focused on cancer—including Drs. Hak Choy, David Johnson, Michael Choti, Stephen Skapek, and Jim Malter—are helping to create multidisciplinary patient-care teams that are bringing broad expertise to bedside care. These efforts not only promise to benefit patients and others at risk but are attracting scientific recognition, including an NCI National Clinical Trials Network Lead Academic Participating Site award, designed to promote large, leading-edge cancer clinical trials.

EXPLOSIVE GROWTH

Numbers also tell the story of the Cancer Center’s journey to NCI comprehensive status. For instance:

- Since 2005, the center’s peer-reviewed funding has more than doubled, and the number of multi-investigator projects has leapt from just three to 23;
- UT Southwestern has been awarded more research dollars from CPRIT—\$316 million in total—than any other institution in Texas;
- The Cancer Center fills more than seven times the physical space it did 10 years ago, and has a budget more than 14 times the size.

New facilities such as the cyclotron and the Cell and Nanoparticle GMP facility, and fresh talent—including 36 CPRIT Scholars recruited over the last half-decade—infuse extra energy into an already fast-moving engine of discovery. Meanwhile, in the past decade, the Cancer Biology Ph.D.-granting program has accelerated from zero to nearly 60. Under the leadership of Dr. Jerry Shay, the doctoral program, approved in 2009, has grown to include 58 full-time students as well as about 50 faculty trainers. Moreover, by traversing interdisciplinary bridges within the Cancer Center, the program provides a broad knowledge base upon which the next generation of cancer scientists can build their own careers and discoveries.

CLINIC AND COMMUNITY

Patient care programs also are flourishing. Multidisciplinary clinics and conferences are bringing together disease specialists to individualize patients' treatment and compare notes on their care. Advanced molecular testing is helping to ensure patients are more likely to receive the most effective therapies. A growing portfolio of clinical trials is available at all stages of disease, and since 2005, the number of patients enrolled in the Cancer Center's therapeutic clinical trials has increased an estimated twelvefold. Cutting-edge care and clinical trial access is available at the new William P. Clements Jr. University Hospital, in state-of-the-art Simmons Cancer Center facilities at Moncrief Cancer Institute in Fort Worth, and at UT Southwestern's partner sites, including Parkland and Children's Medical Center.

Over the past decade, the Cancer Center's patient care has earned important national recognition. The Foundation for the Accreditation of Cellular Therapy has accredited the adult bone marrow transplant program and, jointly with Children's, the pediatric bone marrow transplant program. Last year, University Hospitals received the highest level of accreditation, Three-Year with Commendation at the Gold Level, from the American College of Surgeons' Commission on Cancer. The hospitals were also among only about 15 percent of cancer programs reviewed nationwide to earn the commission's Outstanding Achievement Award.

Simmons is also breaking new ground in community outreach with novel, evidence-based programs aimed at cancer prevention and early detection among North Texans who lack easy access to medical care. Leading the way is the NCI-funded Parkland-UT Southwestern PROSPR Center, which is tapping the talents of a team of population science and health services researchers to ensure more efficient and effective screening for colon and cervical cancers.

The latest NCI recognition is an occasion to celebrate these and many more accomplishments of the past decade. It also represents a moment to look ahead. While important new achievements can be seen on the horizon—and other breakthroughs are yet to be conceived—the Cancer Center's objective remains the same: to generate innovative and impactful science, translated to ensure ever-better patient care, and disseminated to benefit all patients at risk.

James Willson

James K.V. Willson, M.D., Director
The Lisa K. Simmons Distinguished Chair
in Comprehensive Oncology



THE DECADE AHEAD

Important advances over the next decade will help Simmons Cancer Center realize the power and the promise of precision medicine for North Texas cancer patients. These key areas of progress include:

Delivery of Radiation Therapy. A full spectrum of radiation treatment technology will soon be consolidated under one roof in a new, three-story radiation oncology facility. And UT Southwestern researchers are leading an effort funded by the National Cancer Institute and state of Texas to plan research projects for the nation's first hospital-based Heavy Ion Radiation Therapy and Research Center.

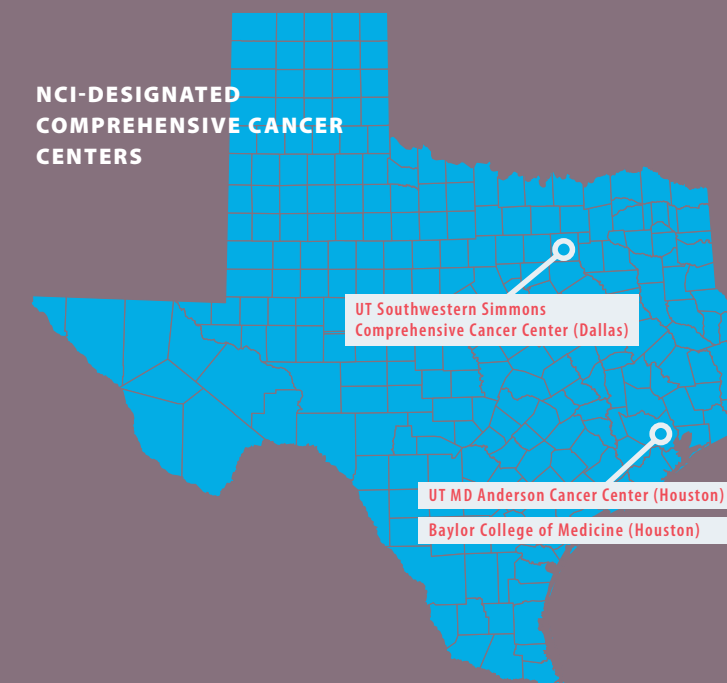
Clinical Trials Leadership. In its role as a National Clinical Trials Network Lead Academic Participating Site (LAPS), the Cancer Center is using cutting-edge genetic techniques to screen large numbers of cancer patients in clinical trials to identify those whose tumors have distinct molecular vulnerabilities targeted by specific therapies being investigated. This far-reaching strategy accords with a changing paradigm of cancer, in which emphasis is shifting from disease site to molecular traits of individual tumors.

Cross-Disciplinary Collaboration. Research at Simmons is moving out of departmental silos, enlisting a range of relevant disciplines to spark novel and clinically meaningful discoveries rooted in medicine's evolving understanding of cancer biology.

Drug Development. Expert biologists and medicinal chemists are engaged in a robust program to identify and improve lead compounds for new targeted treatments and hand them off for commercial development. Already, identification and characterization of the target HIF-2 α and development of the phosphatidylserine-targeting monoclonal antibody bavituximab have led to clinical trials of promising treatments, in collaboration with biotechnology industry partners.

Innovative Discovery. A novel technique called FUSION (Functional Signature Ontology), developed in an initiative led by Drs. Michael White and John MacMillan, is using cell-based screening and computational analysis to comprehensively identify both promising cancer-fighting chemicals derived from natural marine products and the proteins or biological processes they act on in cells. The technique uses libraries of small interfering RNAs and synthetic microRNAs, whose targets in cells are known, as a Rosetta stone, allowing researchers to match gene expression patterns from the library molecules with those of the

NCI-DESIGNATED COMPREHENSIVE CANCER CENTERS



marine-derived chemicals. From that, the scientists can infer whether and how promising chemicals exert anti-cancer effects.

Bioinformatics. Data management and integration capabilities are set to mushroom with establishment of the new Lyda Hill Department of Bioinformatics, along with a recent award of nearly \$5.6 million from the Cancer Prevention and Research Institute of Texas (CPRIT). Dr. Gaudenz Danuser, principal investigator for the CPRIT grant and a CPRIT Established Investigator Scholar, heads the new department. Meanwhile, Dr. Yang Xie, Director of the Cancer Center's Bioinformatics Shared Resource, is building bioinformatics and data integration expertise to facilitate cutting-edge cancer research.

UT Southwestern Genomic Panel. University pathologists are developing this next-generation sequencing tool capable of identifying dozens of disease-specific biomarkers that are relevant to cancer patients' care or are of interest otherwise to cancer researchers.

The Cancer Center will also impact cancer incidence, detection, and survival in other ways over the next 10 years through:

Liver and Kidney Cancer Initiatives. The renal and liver cancer programs are building on fundamental discoveries to pursue even more breakthrough science in the tradition of the highly successful lung cancer program, whose flagship Specialized Program of Research Excellence (SPORE) grant has fueled progress for nearly two decades. Rates of both kidney and liver cancer are high in the region the Cancer Center serves, with incidence of hepatocellular carcinoma growing the fastest among all cancers in Texas.

Recruitment. Support through the CPRIT Scholars program so far has attracted five Established and two Missing Link investigators, three Rising Star scientists, and 26 First-Time, Tenure-Track Faculty Members. Combined with the new Frenkel Program for Endowed Scholars in Clinical Oncology and other recruitment efforts, the Cancer Center's research and patient-care capabilities are being strategically broadened.

Clinical Capacity. Patient volume will continue to grow on the shoulders of Simmons' expanding multidisciplinary care teams, as pacesetter facilities, including the new Clements University and Parkland hospitals, herald a new era of care.

Clinical Trials Growth. North Texas patients will gain greater access to novel therapies than ever before, through extension of the clinical trials program to Moncrief Cancer Institute in Fort Worth and with the Cancer Center's Phase I Clinical Trials Unit and LAPS designation.

Early Detection. The third generation of the Breast Screening and Patient Navigation (BSPAN) program is expanding its reach to 21 counties and more than 180,000 medically underserved women, while the Colorectal Screening and Patient Navigation (CSPAN) program will encompass 20 counties and 165,000 people. Meanwhile, efforts at Parkland will continue to maximize delivery of prevention and early-detection services, such as HPV vaccination and liver cancer surveillance, to diverse and underserved populations of patients.

FACILITIES

Dallas' Medical District, about two miles west of downtown, is home to UT Southwestern Medical Center, including its Simmons Comprehensive Cancer Center and a number of facilities that support the Cancer Center's mission, as well as several key partners in community cancer care.

Parkland Memorial Hospital, a new 862-bed facility, is the primary teaching institution for UT Southwestern. Parkland Health & Hospital System is a vital partner in assessing health needs in a diverse community, investigating how best to deliver services and reaching out to improve cancer care and prevention throughout Dallas County.

Children's Medical Center, the primary pediatric teaching facility for UT Southwestern, recently opened new inpatient and outpatient cancer facilities and is the only academic medical center in North Texas that offers stem cell transplantation to children.

University of Texas School of Public Health Dallas Regional Campus broadens the reach and impact of local public health research focused on cancer through a formal research affiliation with Simmons Cancer Center.

William P. Clements Jr. University Hospital, opened in 2014, has an entire floor devoted to oncology, including a 32-bed, state-of-the-art bone marrow transplantation unit.

UT Southwestern's North Campus is home to the Simmons Cancer Center Clinics, Cancer Center administrative offices, the Children's Medical Center Research Institute, the Advanced Imaging Research Center, the Clinical Research Office, the Live Cell Imaging Resource, Biostatistics and Bioinformatics Resources, and many faculty research laboratories.



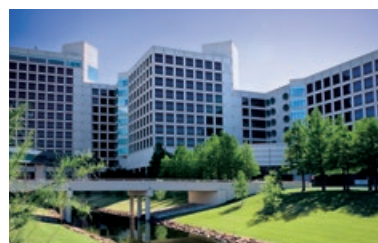
William P. Clements Jr. University Hospital



Moncrief Cancer Institute



Parkland Memorial Hospital



UTSW North Campus



Children's Medical Center

UT Southwestern's South Campus houses Cancer Center facilities such as Medicinal Chemistry and Mass Spectrometry Proteomics Cores, a Cell and Nanoparticle GMP facility, and High Throughput Screening, Tissue Management, and Small Animal Imaging Shared Resources, as well as the Health Promotion Intervention Shared Resource and other Population Science and Cancer Control research space.

Zale Lipshy University Hospital, a 152-bed facility, is known as a premier referral center for neurological care, including the treatment of brain and spinal malignancies. The hospital houses the Annette Simmons Stereotactic Treatment Center.

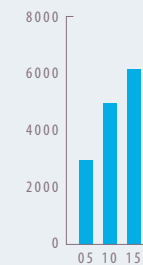
BioCenter at Southwestern Medical District, a 15.5-acre biotech park, was established by UT Southwestern to develop university technologies and to attract biotech companies to North Texas.

The Radiation Oncology Center, a 63,000-square-foot facility now under construction, will consolidate current programs and house the latest generation of cancer-fighting technology. The integrated complex will bring together many different modalities for the benefit of cancer patients and to further research. With seven treatment rooms, the center will be the largest radiation facility in North Texas.

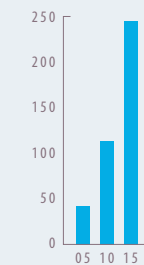
UT Southwestern Moncrief Cancer Institute, a 60,000-square-foot facility located in the Fort Worth Medical District, provides early cancer detection and survivorship services in Tarrant and surrounding rural counties. Moncrief also houses the brand-new, 20,000-plus-square-foot UT Southwestern Simmons Cancer Center – Fort Worth, which provides services including chemotherapy, cancer imaging, and access to clinical trials.

2005–2015: GROWTH BY THE NUMBERS

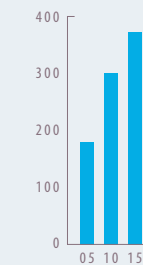
New Cancer Patients



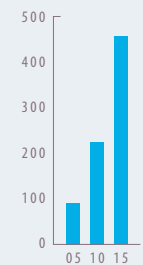
Total Open & Accruing Cancer Clinical Trials



Total Peer-Reviewed Funded Projects



Total Staff



Clinical Research	2005	2010	2015
Total patients accrued to clinical trials (excluding population science)	573	806	1,396
Total patients accrued to therapeutic clinical trials	57	391	687
Total participants in population science studies	0	230	191,680
Education	2005	2010	2015
Total cancer biology Ph.D. trainees	0	51	58
Research	2005	2010	2015
Total Cancer Center (full) members	107	121	173
Dollar amount of peer-reviewed funding	\$45.7M	\$75.8M	\$118.4M
Total multi-investigator awards	3	8	23
Number of Cancer Center members participating in one or more multi-investigator awards	13	21	46
Percent of intra-programmatic collaborative publications	n/a	23%	27%
Percent of inter-programmatic collaborative publications	n/a	14%	18%
Administrative	2005	2010	2015
Square feet of space assigned to the Cancer Center	28,593	94,420	207,283
Total operating budget	\$8.1M	\$41.0M	\$116.5M

Cancer Center chemists discover and develop a new approach that holds promise in treating kidney tumors.

BACKGROUND

Under normal conditions, hypoxia-inducible factors, or HIFs, allow the body's cells to thrive in low-oxygen environments, such as high altitudes. By responding to changes in oxygen levels, HIFs serve as master regulators, determining whether multiple genes that help healthy cells survive and reproduce are activated

downstream. But this mechanism also promotes growth and survival of cancer cells.

HIFs accumulate and drive these other genes when the von Hippel-Lindau (VHL) gene—normally a tumor suppressor that breaks HIFs down—is inactivated. This loss of VHL leads to the most common type of kidney cancer, renal clear cell carcinoma.

At UT Southwestern, fundamental studies into one type of HIF, called HIF-2, have blossomed into a promising potential treatment.

THE FOUNDATIONS

1997

UT Southwestern biochemist Dr. Steven McKnight and molecular geneticist Dr. David Russell lead research discovering and describing the protein encoded by the EPAS-1 gene, also known as HIF-2 α . Additional research at UT Southwestern sheds more light on the workings of the HIF family and related molecules, especially HIF-2 α .

2000–2009

Over the course of a decade, the laboratories of Drs. Richard Bruick and Kevin Gardner tease apart the structure of HIF-2. Biochemical analysis reveals how HIF-2 α docks with another protein to assemble into a functional HIF-2 complex, and how mutations that disrupt this binding halt HIF-2 activity. Finding drug-like chemicals that can likewise disrupt HIF binding holds the promise of impairing various downstream cancer-promoting targets, such as the VEGF receptor.

2009

The Bruick-Gardner research reveals a cavity within the HIF-2 α protein that is a potential “sweet spot” where disrupters may bind and shut down HIF-2 activity.

THE TRANSLATION

2007–2008

After gleaning insights from earlier, more focused screens, scientists deploying the Cancer Center’s High-Throughput Screening Shared Resource systematically test more than 200,000 drug-like molecules, one at a time, to see which ones might interfere with HIF-2. The effort identifies a slate of successful compounds.

2008–2013

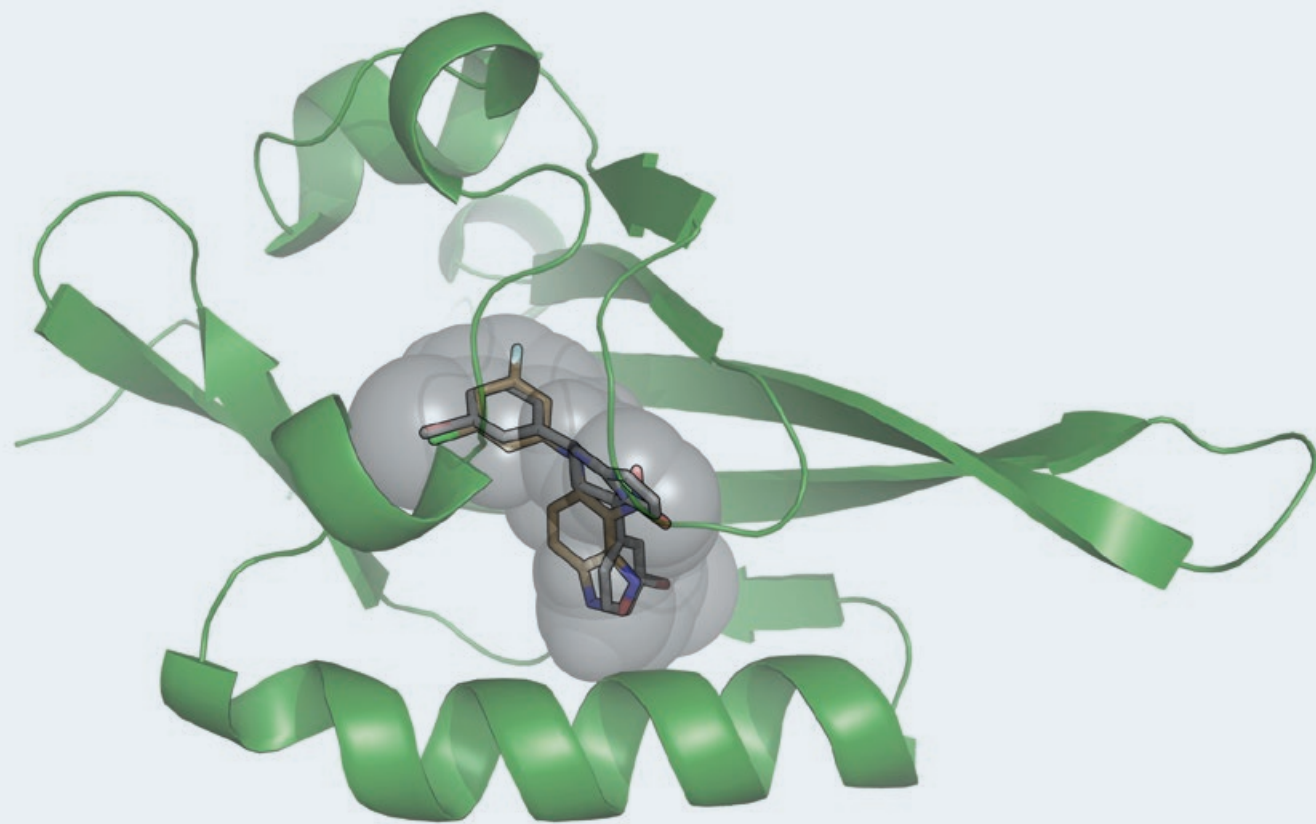
Medicinal chemists at Simmons Cancer Center study the HIF-2 disrupters, learning more about how they work and refining the most promising of these compounds to increase their potency and improve their safety profile.

2013

UT Southwestern scientists including Drs. Bruick, Gardner, John MacMillan, and Uttam Tambar detail how chemicals bind with the “sweet spot” cavity to disrupt HIF-2 function. The findings indicate that small molecules can feasibly regulate HIF-2 α , a type of molecule previously considered “undruggable.”

2013

Research shows that the newly discovered and refined compounds can block the assembly of the HIF-2 complex and disrupt its function in living cells originating from actual human tumors—rendering HIF-2 unable to turn on other cancer-related genes.



Tucked in the cavity found in a part of the HIF-2 molecule called the HIF-2 α PAS-B domain are two different small molecule disrupters of HIF-2 discovered by the UT Southwestern team. (Data from T.H. Scheuermann et al., *Nat. Chem. Biol.* 9[2013]: 271 and T.H. Scheuermann et al., *J. Med. Chem.* 58[2015]: 5930; image from Kevin Gardner)

THE IMPACT

2011

The most promising compounds are licensed to Peloton Therapeutics, a biotech firm co-founded by Dr. McKnight and based in new, state-of-the-art facilities on UT Southwestern’s BioCenter campus.

2014

The first HIF-2 inhibitor in clinical development, an oral drug known as PT2385, enters a phase I clinical trial for safety and dosing in patients with advanced or metastatic renal clear cell carcinoma. Dr. Kevin Courtney heads the trial at UT Southwestern, one of several sites across the U.S. testing the drug.

THE FUTURE

A mouse model of human renal clear cell carcinomas, developed and validated by UT Southwestern kidney cancer specialist Dr. James Brugarolas and colleagues, may provide insights into which patients are most likely to benefit from treatment with HIF-2 inhibitors.

HIF-2 also appears significant in other types of cancer, including deadly brain cancers called glioblastomas and non-small cell lung cancer, the most common type of lung malignancy.

SIGNIFICANT PUBLICATIONS

Tian, H. et al. Endothelial PAS domain protein 1 (EPAS1), a transcription factor selectively expressed in endothelial cells. *Genes Dev* 11, 72-82 (1997).

Erbel, P. J. et al. Structural basis for PAS domain heterodimerization in the basic helix-loop-helix-PAS transcription factor hypoxia-inducible factor. *Proc Natl Acad Sci USA* 100, 15504-09 (2003).

Yang, J. et al. Functions of the Per/ARNT/Sim domains of the hypoxia-inducible factor. *J Biol Chem* 280, 36047-54 (2005).

Scheuermann, T.H. et al. Artificial ligand binding within the HIF2 α PAS-B domain of the HIF2 transcription factor. *Proc Natl Acad Sci USA* 106, 450-55 (2009).

Scheuermann, T.H. et al. Allosteric inhibition of hypoxia inducible factor-2 with small molecules. *Nat Chem Biol* 9, 271-76 (2013).

Rogers, J.L. et al. Development of inhibitors of the PAS-B domain of the HIF-2 α transcription factor. *J Med Chem* 56, 1739-47 (2013).

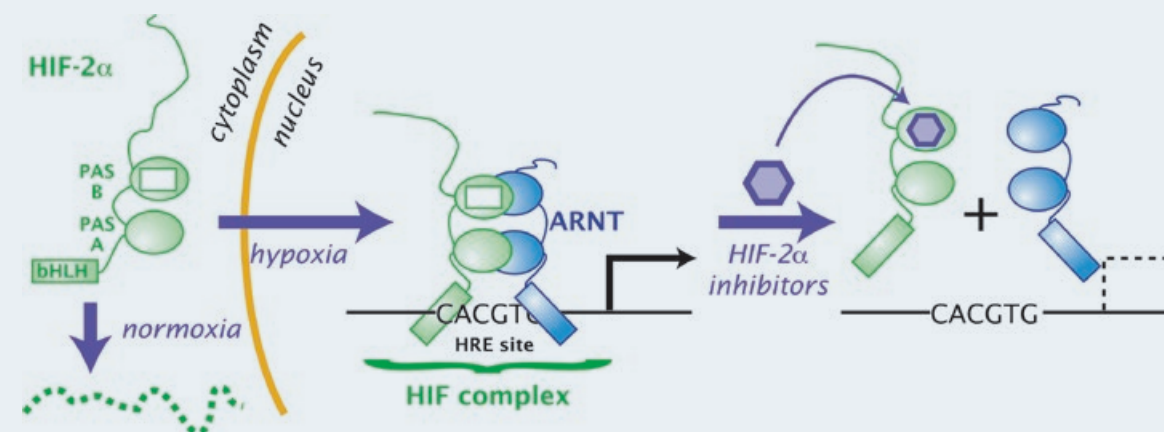
Scheuermann, T.H. et al. Isoform-selective and stereoselective inhibition of hypoxia inducible factor-2. *J Med Chem* 58, 5930-41 (2015).



Dr. Richard Bruick



Dr. Kevin Gardner



Human cells respond to low oxygen levels (hypoxia) using the hypoxia inducible factor, or HIF, complex (near center of diagram) assembled from two proteins: HIF α and ARNT. When oxygen levels fall, the HIF α subunit can accumulate in the cell nucleus, where it binds to ARNT, forming HIF complexes. These complexes control transcription (depicted at right) of more than 100 genes affecting the cell’s ability to adapt and respond to hypoxia. Small molecules developed at UT Southwestern can bind to the HIF-2 α subunit to disrupt its activity in cancer cells (also depicted at right). (Illustration by Gardner/Bruick)



Dr. Thomas Froehlich, Medical Director of the Simmons Cancer Center's cancer clinics

COMPREHENSIVE CANCER CARE: THE PATIENT EXPERIENCE

Surgery. Cancer patients requiring surgery benefit from Simmons Cancer Center's:

- Highly skilled surgical oncologists who specialize in treating cancers in specific locations in the body;
- Broad and deep expertise in minimally invasive procedures; and
- Access to leading-edge technology in advanced surgical suites in the new Clements University Hospital.

Blood and Marrow Transplantation (BMT).

Patients undergoing blood or marrow transplantation are cared for in Clements University Hospital's state-of-the-art, 32-bed BMT unit. The nationally accredited program is recognized as a Center of Excellence by major insurance carriers, and it:

- Offers the latest therapies, some of which are not available in every hospital's program;

- Leads in North Texas for one-year survival rates in transplants involving donor cells; and

- Provides blood or marrow transplants for children at a 12-bed pediatric unit at Children's Medical Center.

Radiation Therapy. Patients undergoing radiation therapy at the Cancer Center have access to specialists providing therapies not widely offered elsewhere. Care includes:

- Stereotactic ablative radiotherapy, in which tumors are bombarded by radiation from multiple directions—concentrating the radiation on the tumor, minimizing dose to surrounding tissue, and adjusting for motion such as breathing in the body (see page 20);
- Stereotactic radiosurgery/stereotactic radiotherapy for brain tumors, which similarly applies high doses of radiation to the cancer while minimizing dose to adjacent tissue;
- Brachytherapy, or placement of a radiation source in direct contact with a tumor or treatment area;
- Intensity-modulated radiation therapy, which “sculpts” the radiation field so it conforms to a tumor's shape;

Cutting-Edge

Richard, diagnosed with kidney cancer at age 40 in 2008, was running out of treatment options. After enrolling in a clinical trial at Simmons Comprehensive Cancer Center, he was the first patient in Texas to receive a new, promising medication that he credits with saving his life. “I truly believe that if I had not come to UT Southwestern, I would not be here.”

- Four-dimensional radiation treatment planning, using a CT scanner that simulates tumor dimensions, location, and movement for each patient, ensuring extreme accuracy;
- Vision RT video monitoring to help protect the heart during whole-breast radiation to the left breast; and
- Pediatric care, including an anesthesiologist to help treat very young patients.

EXCEPTIONAL FACILITIES

Clements University Hospital. In their own individual rooms, patients at Clements University Hospital can:

- Control the lights, temperature, and window shades, and even order a snack, from their bed;
- Access Wi-Fi;
- Review with their cancer-care providers personal test results and scans on a large-screen TV monitor or watch an educational video with loved ones; and
- Rest and recover quietly, away from the clamor of high-traffic locations in the hospital.

Family members can:

- Stay overnight on custom sleeper sofas;
- Discuss patient care in private conference rooms; and
- Learn more about medical conditions and clinical trials in a staffed, interactive Patient and Family Resource Center.

Moncrief Cancer Institute. At UT Southwestern's Moncrief Cancer Institute, patients in or near Fort Worth benefit from:

- Brand-new facilities, including exam rooms and private chemotherapy infusion rooms;
- The latest imaging technologies;
- On-site laboratory and pharmacy services;
- Preventive care and cancer screening;
- Programs to promote health in cancer survivors, including nutritional counseling and cooking classes; and
- Secure telemedicine consultation with specialists at UT Southwestern in Dallas.

Children's Health. Children and teens with cancer are treated by UT Southwestern physicians at the Gill Center for Cancer and Blood Disorders at Children's Medical Center, which:

- Treats the full range of pediatric cancers, including leukemia and lymphoma, brain and other nervous system tumors, Wilms tumor, musculoskeletal tumors, and sarcoma;
- Provides long-term monitoring for children, adolescents, and young adult survivors of childhood cancer through its ACE (After the Cancer Experience) program;
- Offers early-phase clinical trials, bringing promising new treatment options to fight some of the most challenging childhood cancers; and
- Treats one in five children in Texas diagnosed with cancer.

Parkland Health & Hospital System. Cancer patients at Parkland Health & Hospital System, Dallas County's safety net system for patients who cannot easily access health care, likewise receive care from Simmons Cancer Center experts and other UT Southwestern physicians.

Simmons Cancer Center. Throughout the Cancer Center, patients have the benefit of:

- Expert physicians and other providers who treat each patient's disease and coordinate other aspects of care;
- Clinical trials providing access to the latest therapies—and new possibilities for patients who have exhausted standard treatment options;
- Advanced genetics screening and counseling based on personal and family history of cancer;

Comprehensive

The paternal side of Denise's family had a history of cancer. Genetic testing in 2014 at the Simmons Cancer Center revealed that the 50-year-old had a mutation in the BRCA1 gene, meaning she had a higher risk for breast and ovarian cancer. When she underwent surgery to prevent cancer from developing, two small but aggressive tumors were found in her fallopian tubes. Of her cancer journey at UT Southwestern, she says, “Everything I needed was right here.”

- Support from psychologists, chaplains, social workers, dietitians, and others;
- An electronic medical record that encompasses all care patients have received at UT Southwestern, giving physicians instant access to patient information and test results across hospitals, clinics, and disciplines—and allowing patients to view test results and communicate with care providers through the university's MyChart portal; and
- Excellence in research, prevention, and patient care that is the hallmark of a National Cancer Institute-designated Comprehensive Cancer Center.

In patient rooms at Clements University Hospital, large-screen TV monitors allow videoconferencing with loved ones or with health care providers.



Compassionate

Eight-year-old Shadiamond told her mother she was having “painful, painful headaches” that led to the discovery of her brain cancer in 2014. After treatment, she’s looking forward to growing up and becoming a lawyer. One aspect of her medical care that she found very important was “just to know you always have somebody near you.”

- Recognition as a Lead Academic Participating Site for the National Cancer Institute’s National Clinical Trials Network, which means Cancer Center patients have access to the most cutting-edge drugs that are undergoing testing;
- More than twice the number of patients than a decade ago enrolling in trials to test new cancer therapies, with participants including a substantial representation of racial and ethnic minorities; and
- More than 200 patients a year participating in national cooperative group trials.

CLINICAL RESEARCH OFFICE

Simmons Cancer Center’s Clinical Research Office provides research infrastructure for cancer-related clinical trials at UT Southwestern. Besides managing numerous details related to each trial and its patients, the office coordinates with partner facilities including Parkland, other participating institutions, and cooperative groups.

The office’s research nurses, coordinators, and other staff collaborate with the Cancer Center’s disease-oriented teams to provide specialized care and expertise based on the site or sites of cancers that are targeted in each study. The office has a staff of more than 80, nearly 30 percent of whom speak another language in addition to English—including Spanish, Mandarin, Vietnamese, French, Italian, Arabic, Urdu, Romanian, Russian, Ukrainian, Yoruba, Punjabi, Tamil, Malayalam, Hindi, Japanese, and Korean.

CLINICAL TRIALS

With partner health systems in Dallas and Fort Worth, Simmons Comprehensive Cancer Center is able to offer North Texas cancer patients access to many of the latest therapies available in clinical trials. Simmons Cancer Center has a thriving and nationally recognized clinical trials program with achievements including:

- The launch of a new Phase I Clinical Trials Unit, which helps speed the translation of scientific discoveries made at UT Southwestern for potential patient benefit;

Clinical Research	2005	2010	2015
Number of cancer clinical trials open and accruing	42	113	245
Number of patients accrued to all SCC clinical trials (excl. pop sci)	573	806	1,396
Number of patients accrued to therapeutic clinical trials	57	391	687
Number of participants in population science studies	0	230	191,680



Clinical research coordinator Jenny Chang and Kidney Cancer Program leader Dr. James Brugarolas work with patient Diane Greckel in a clinical trial of an experimental therapy for renal cell carcinoma. The phase I trial, led at UT Southwestern by genitourinary cancer specialist Dr. Kevin Courtney, tests a drug called PT2385, which was developed after groundbreaking research by Simmons Cancer Center biochemists (see page 12).

UT Southwestern is helping redefine lung cancer care through innovations in stereotactic body radiation therapy.

BACKGROUND

Stereotactic radiotherapy, originally piloted for treating tumors situated in important functional parts of the brain, operates on a converging-beam principle in which dozens of highly focused yet relatively weak radiation beams from different directions travel through normal tissues on their way to a

tumor target deep within the body. The intentionally weak beams cause little entry damage, but at the point of convergence, they add up to deliver a very potent tumor treatment.

For decades, its use was confined to the cranium. Precise but also extremely powerful, stereotactic radiotherapy was not possible elsewhere in the body, where breathing and other functions could cause the target to move, potentially resulting in disastrous side effects.

However, recognition that new image-guidance technology could address that challenge has fueled development of stereotactic body radiation therapy (SBRT), also known as stereotactic ablative radiotherapy (SABR). For the past decade, UT Southwestern has been on the leading edge of SABR innovations.

THE FOUNDATIONS

2003

Dr. Hak Choy is named Chairman of Radiation Oncology at UT Southwestern, with the goal of developing a department that deploys the most promising technologies against cancer.

2003

At a national meeting of radiation oncologists, Dr. Robert Timmerman, then a faculty member at Indiana University and a renowned expert in stereotactic radiosurgery, is met with skepticism when he presents early results of a clinical trial indicating that SABR appears effective in patients with early-stage, non-small cell lung cancer (NSCLC).

2004

Dr. Timmerman is recruited to join the radiation oncology faculty at UT Southwestern in a practice focused on stereotactic radiation. The lung—the most mobile and difficult site to work with—is the subject of the first wave of SABR research because proof-of-principle in that location would translate readily to cancers in other locations.

2011

UT Southwestern becomes the first North American institution to install Vero SBRT, an advanced system for imaging tumors and delivering treatment. Vero joins Simmons Cancer Center's formidable arsenal of stereotactic radiotherapy technology, including cutting-edge Gamma Knife, CyberKnife, Agility, and TrueBeam technology.

THE TRANSLATION

2010

In a study of 55 early-stage lung cancer patients too frail to withstand traditional surgery, Drs. Timmerman, Choy, and colleagues report SABR has achieved control of 98 percent of the primary tumors, a rate comparable with surgical resection. Previously, for early-stage patients unable to withstand surgery, standard radiation had achieved only a 30 to 40 percent rate of tumor control. The publication changes the standard of care for so-called medically inoperable patients.

2011

A \$3.5 million grant from the Cancer Prevention and Research Institute of Texas (CPRIT) funds a five-year multi-institution effort to develop advanced radiotherapy technology for lung cancer with the aim of also reducing toxicity. The program is led by Dr. Choy and includes Cancer Center members Dr. Timmerman, Dr. Chul Ahn, and Dr. Puneeth Iyengar.

2012

Cancer Center scientists receive a \$4.1 million multi-investigator research award from CPRIT to explore in lung cancer how best to exploit the radiobiological effects of SABR, whose cancer-killing properties at the cellular level appear different than standard radiation. Dr. Timmerman heads the project, which also involves Cancer Center members Drs. Ralph Mason, Rolf Brekken, Chul Ahn, Debu Saha, and others, along with the work of Dr. Phil Thorpe.

2014

Cancer Center researchers led by Drs. Timmerman and Choy potentially extend the use of SABR to patients with stage 4 limited metastatic NSCLC. In a phase II, multi-institution trial combining lowered doses of SABR with the drug erlotinib, the treatment is well-tolerated and patients markedly surpass the time periods they otherwise would be expected to survive without disease progression. Tissue analyses suggest the SABR is primarily responsible for the benefit.

THE IMPACT

2008–2015

As stereotactic radiotherapy research flourishes, new studies indicate its effectiveness on various cancers that have spread to a limited number of sites within organs such as the liver and lungs. SABR also appears promising in classically “radio-resistant” tumors such as renal cancer and melanoma.

2009

UT Southwestern's Department of Radiation Oncology begins hosting quarterly, hands-on courses to train peers interested in implementing SABR in their clinical practice. To date, more than 300 practitioners from all over the world have been trained through the initiative.

2014

A team led by Dr. Timmerman reports on five-year follow-up results among the patients, too frail for surgery, who received SABR for early-stage lung cancer. The rate of recurrence at primary tumor sites is low, and the powerful therapy is not associated with any surge of late ill effects—demonstrating SABR's long-term efficacy and safety in early lung cancer.

2015

Investigation of SABR continues at UT Southwestern for cancers in sites including the prostate, breast, and larynx, and a range of clinical trials of the therapy is open at Simmons Cancer Center.

THE FUTURE

Drs. Timmerman, Choy, and Ahn are leading an ambitious phase III study that encompasses more than two dozen sites, directly comparing the benefits of surgery versus SABR in lung cancer patients healthy enough to choose surgery. The trial aims to collect evidence from 258 patients with high-risk stage 1 NSCLC.

UT Southwestern scientists continue to reveal other possible uses for SABR—for instance, treating inferior vena cava tumor thrombus, an often deadly kidney cancer complication—while medical physicists are advancing imaging techniques to more precisely predict motion, further improving treatment safety and accuracy.

Simmons researchers also aim to develop SABR using heavy particles instead of photons—lowering radiation dose to healthy tissues. And with a \$1 million planning grant from the National Cancer Institute, as well as state funding, UT Southwestern is leading a Texas consortium to plan for the first national Heavy Ion Radiation Therapy and Research Center, with the goal of researching and providing innovative cancer treatments that leverage the potency and precision of heavy particles.

SIGNIFICANT PUBLICATIONS

Timmerman, R. et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA* 303, 1070-76 (2010).

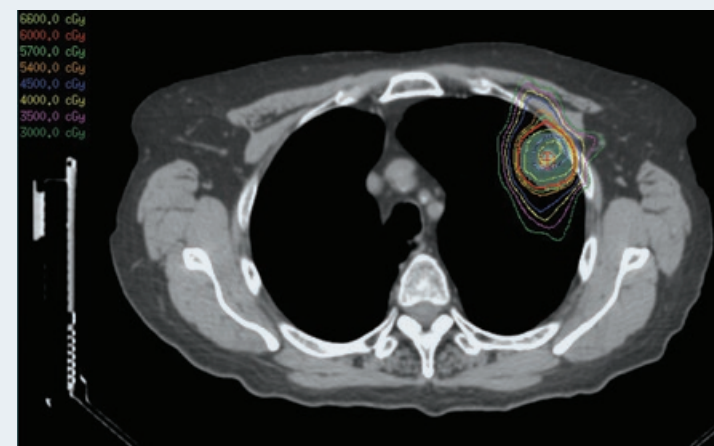
Iyengar, P. et al. Phase II trial of stereotactic body radiation therapy combined with erlotinib for patients with limited but progressive metastatic non-small cell lung cancer. *J Clin Oncol* 32, 3824-30 (2014).

Timmerman, R.D. et al. Emergence of stereotactic body radiation therapy and its impact on current and future clinical practice. *J Clin Oncol* 32, 2847-54 (2014).

Westover, K.D. et al. SABR for aggressive local therapy of metastatic cancer: A new paradigm for metastatic non-small cell lung cancer. *Lung Cancer* 89, 87-93 (2015).



Dr. Robert Timmerman



SABR plan for a lung cancer

Current Department of Radiation Oncology facilities include the 30,000-square-foot W.A. Monty & Tex Moncrief Radiation Oncology Building; the Annette Simmons Stereotactic Treatment Center, which houses the Gamma Knife (1) and CyberKnife (2) for cranial and extracranial stereotactic radiosurgery; and the newly added 16,000-square-foot Radiation Oncology Building housing technologies such as the Vero SBRT (3).



Simmons Comprehensive Cancer Center serves urban, suburban, and rural populations throughout the 12 counties that make up the nearly 7 million-resident Dallas/Fort Worth metropolitan area. As partner sites, the Dallas County and Tarrant County public hospital systems, Parkland and JPS Health Network, are invaluable proving grounds for new, more impactful ways of delivering cancer services, especially to people who lack financial resources for care.

In a region in which nearly one in five people are uninsured and where urban centers quickly transition to rural communities, the Cancer Center's outreach programs target populations that have greater financial, geographical, or other challenges in accessing care. These programs focus on prevention, screening and early detection (along with health care navigation), genetics, patient and family education, and cancer survivorship.

UT Southwestern's Moncrief Cancer Institute in Fort Worth is an essential link to Tarrant County's JPS network, as well as the hub for the Cancer Center's rural network in western counties outside the metropolitan area. Through telemedicine, a mobile clinic, and extensive collaborations with local health care providers, Simmons Cancer Center and Moncrief deliver services to a wide swath of rural counties across North Texas.

CANCER PREVENTION

Cervical Cancer. UT Southwestern cancer researchers at Parkland Health & Hospital System clinics are improving delivery of vaccination for HPV, the virus that causes cervical cancer.

Lung Cancer. Research by Cancer Center members is addressing challenges that make it hard for homeless individuals to quit smoking, including inadequate no-smoking areas at shelters and difficulty accessing nicotine-replacement therapy.

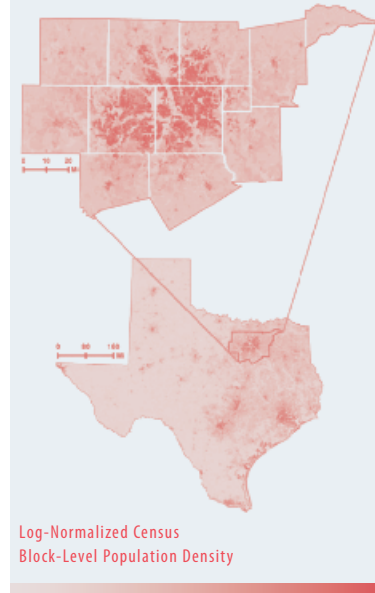
SCREENING & EARLY DETECTION

Breast Cancer. Simmons Cancer Center's Breast Screening and Patient Navigation (BSPAN3) program, based at Moncrief, strengthens community care resources and connects low-income and uninsured women in rural and underserved counties to local health care providers for screening, diagnostic, and follow-up services. The program, now in 17 counties, will expand to 21, reaching more than 180,000 women who are eligible for screening and connecting about 14,000 with services.

Colorectal Cancer. Simmons Cancer Center investigators have been building a coordinated, evidence-based strategy to increase colon cancer screening rates in the Parkland and JPS Health systems (see page 40). The center's research on multiple aspects of colorectal screening resulted in establishment of the Parkland-UT Southwestern Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) Center, to expand the research and help export lessons learned in order to benefit patients across the U.S., especially those who are medically underserved. (The center's mission has since been expanded to include cervical cancer.)

Like the BSPAN3 breast cancer program, the Cancer Center's Colorectal Screening and Patient Navigation (CSPAN) initiative, also based at Moncrief, develops and fosters local partnerships across North Texas to improve screening rates among uninsured, underserved people and to help guide them to needed care. Building on previous Cancer Center research, CSPAN targets 20 local counties and 165,000 individuals due for screening, using test kits mailed to patients.

Simmons Comprehensive Cancer Center serves urban, suburban, and rural populations throughout the 12 counties that make up the nearly 7 million-resident Dallas/Fort Worth metropolitan area.



Liver Cancer. Cancer Center scientists, focusing their efforts at Parkland, are testing ways to overcome systemic obstacles that prevent patients at highest risk of hepatocellular carcinoma, the most common type of liver cancer, from receiving ongoing monitoring to catch the disease early.

GENETICS/PATIENT & FAMILY EDUCATION

Hereditary Cancer Risk. Working at UT Southwestern, Moncrief, and 15 sites throughout the Dallas/Fort Worth area, nine certified genetic counselors advise individuals about their personal risk of breast, colon, and other cancers; discuss the role of lifestyle and other risk factors in the disease; and guide

patients through any recommended testing for genes that could increase their cancer vulnerability. Patients who test positive for a genetic predisposition to cancer work with their genetic counselor and physicians to obtain follow-up care, and counselors empower the patients to reach out to their family members who might likewise be at risk. The Cancer Center's genetics team serves patients in rural areas by providing counseling at satellite sites and through telemedicine.

Cancer Answer Line. About 200 calls a month are fielded by Simmons Cancer Center's Cancer Answer Line (1-888-980-6050), which allows callers to ask for information about treatment, clinical trials, cancer care referrals, quitting smoking, and more. Questions also are submitted through the Cancer Center's website, at utswmedicine.org/cancer/community-outreach/cancer-info.html.

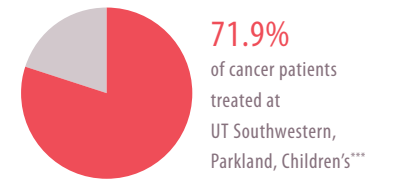
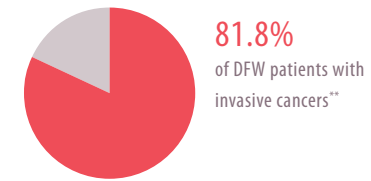
CANCER SURVIVORSHIP

Moncrief Cancer Institute. Moncrief offers a robust range of services for cancer survivors, including exercise instruction, nutritional guidance, smoking cessation, genetics counseling, planning and coordination of follow-up cancer care, emotional support and stress management, and assistance with accessing community resources.

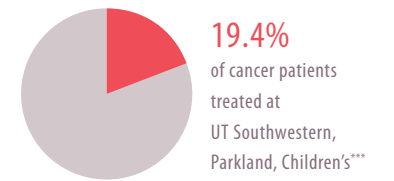
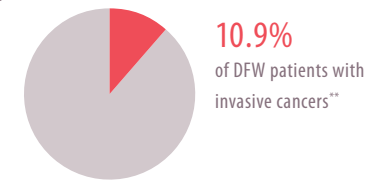
On-The-Road Outreach. Moncrief's Mobile Cancer Survivor Clinic, a custom-designed 18-wheeler, travels twice a month to locations in nine North Texas counties, where more than half the population is considered medically underserved and where one-third of cancer survivors are at risk of not receiving adequate follow-up care due to factors such as lack of facilities or transportation. The mobile clinic provides bilingual services including mammography and colon cancer screening in addition to physical and psychosocial assessments, one-on-one exercise training, nutrition education, and telemedicine links to experts at Moncrief and Simmons Cancer Center.

POPULATION OVERVIEW

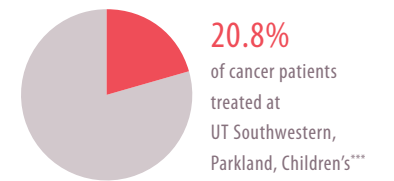
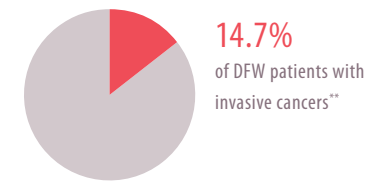
CAUCASIANS **75.4%** of DFW population*



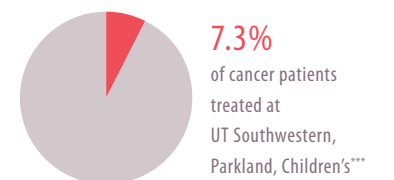
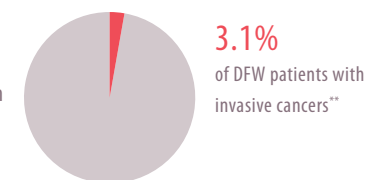
HISPANICS **28%** of DFW population*



AFRICAN-AMERICANS **15.7%** of DFW population*



ALL OTHERS **8.9%** of DFW population*



*2012 data for DFW Metropolitan Statistical Area (MSA), U.S. Census Bureau;
2011 data for DFW MSA, Texas Cancer Registry; *2012 data

Imaging innovations developed by UT Southwestern scientists are being deployed to improve brain cancer care.

BACKGROUND

Nearly one-third of brain tumors are gliomas. These tumors can lie dormant for months or years, then suddenly start growing rapidly in a deadly form called glioblastoma.

Gliomas traditionally have been diagnosed via surgical biopsy, an invasive procedure that is especially risky when tumors are near sensitive sites in the brain. Detecting precisely when gliomas become glioblastomas is a challenge, and the transformation requires aggressive treatment. Doctors would also like more information about how tumors respond to treatment and which treatments best target traits specific to individual tumors.

Building on fundamental imaging and metabolism research at UT Southwestern, Cancer Center scientists and physicians have developed innovative approaches to address these challenges.

THE FOUNDATIONS

1980s

Ongoing work at UT Southwestern, spearheaded by Drs. Dean Sherry and Craig Malloy, focuses on development of tracer molecules that can be used with magnetic resonance (MR) technology to measure changes in metabolism that occur with disease.

2007

The two researchers hone the use of carbon-13 (¹³C), a stable natural isotope, in a hyperpolarized state—activating its nuclei so they create a signal powerful enough to track in the body. Enriching substances such as glucose with ¹³C allows the researchers to better detect details of the substances' metabolism than does current technology.

THE TRANSLATION

2009

Research elsewhere links cancer-associated mutations in the gene IDH1 to high levels of a metabolite called 2-hydroxyglutarate (2HG) and finds elevated 2HG in surgical samples of

malignant gliomas. UT Southwestern physicist Dr. Changho Choi and neuro-oncologist Dr. Elizabeth Maher, already working on MR spectroscopy of glioblastoma to find tumor biomarkers, focus their work on developing an approach to noninvasively detect 2HG.

2010–2012

UT Southwestern researchers, including Dr. Ralph DeBerardinis, Dr. Maher, Dr. Malloy, Dr. Robert Bachoo, and neurosurgeon Dr. Bruce Mickey, pioneer the presurgery infusion of ¹³C-labeled glucose to directly study metabolic flux in patients with brain tumors. Once the tumors are removed, researchers use MR spectroscopy to provide a “snapshot” of the tumor cells' metabolic processing of the glucose. The team finds that glioma cells—and metastatic lung and breast cancer cells in the brain—metabolize glucose much more rapidly than does the rest of the brain, using the energy to survive and to help perpetuate growth of new tumor cells.

2012

A team led by Drs. Choi and Maher finds 2HG is detectable with MR technology using a technique called point-resolved spectroscopy, or PRESS. Accumulation of 2HG is associated with mutations in *IDH1* and *2*, a hallmark of about 70 percent of gliomas. Thus, 2HG can be used as a biomarker to identify gliomas with-

out need for surgical biopsy; the biomarker also can provide information on patient prognosis and has the potential to help track tumor progression and drug response.

2014

Infusing mouse models of human gliomas with ¹³C-labeled glucose and ¹³C-labeled acetate, a team led by Dr. Bachoo demonstrates that cancer cells can use acetate to fuel growth. The study, along with research led by Cancer Center biochemists, pinpoints ACS2, an enzyme that metabolizes acetate, as a potential treatment target.

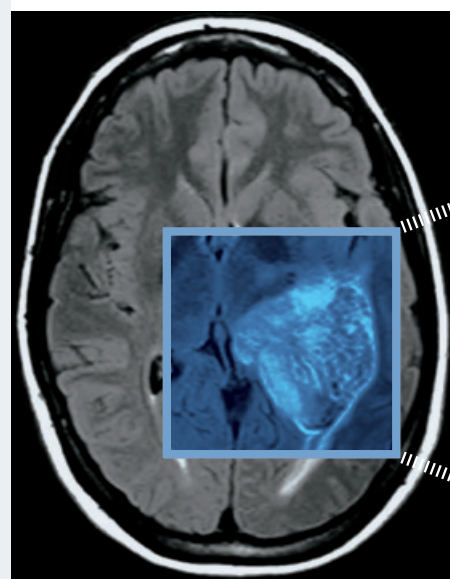
THE IMPACT

2014–2015

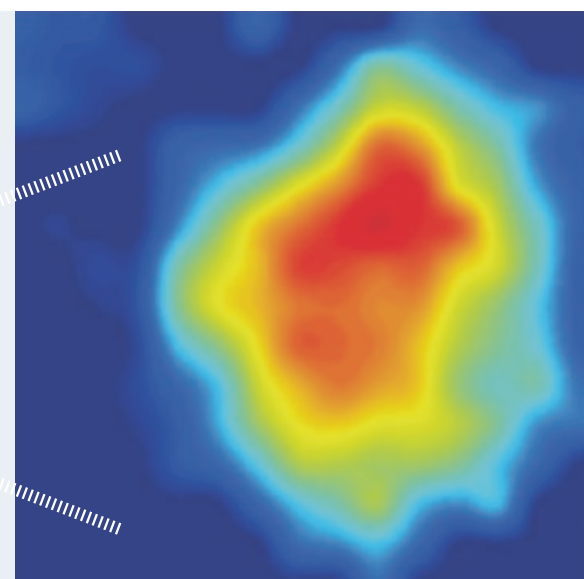
Researchers launch a prospective phase I/II clinical trial, led by Dr. Maher and conducted at Clements University Hospital, testing the IDH2 inhibitor AG-221 (Agiros Pharmaceuticals), the first drug of its type, in patients with tumors including gliomas. Researchers deploy

IDH1-Mutated Astrocytoma

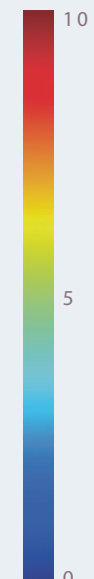
T2w-FLAIR



2-Hydroxyglutarate



mM



Proton magnetic resonance spectroscopy provides noninvasive evaluation of 2-hydroxyglutarate in IDH1-mutated gliomas.

their approach to noninvasively measure levels of 2HG (the metabolite associated with the *IDH1/2* mutation) in gliomas, providing a way to monitor drug penetration into the tumor and ability to inhibit the target.

THE FUTURE

Building on the finding that acetate can fuel cancer growth, Cancer Center scientists are revealing more about the role of ACS2, which is expressed in a variety of human tumors, as a potential vulnerability that may be exploited therapeutically.

Based on the insights made in studying tumor metabolism in brain cancer patients at the time of surgery, several other areas of focus have emerged. Dr. DeBerardinis and colleagues are pursuing similar studies in lung cancer, and Drs. Maher and Bachoo are studying early-stage breast cancer in collaboration with Dr. Roshni Rao. They are also working with pediatric neurosurgery and neuro-oncology teams to address many of the same metabolic questions in childhood brain cancers.

Dr. Choi and colleagues are working to bring their MR technique for measuring 2HG in the brain—developed in research scanners at a magnetic field strength of 3 Tesla—to 3T clinical scanners, as well as to achieve 2HG detection using lower-powered (1.5T) scanners.

Drs. DeBerardinis, Malloy, Sherry, and others are working to develop imaging of hyperpolarized pyruvate and acetate to study metabolism of cancers in the body. One important goal is to understand energy production in cancers, which identifies possible vulnerabilities and the opportunity for drug targeting.

A new hyperpolarizing technology called SPINlab—funded through an award from the National Institutes of Health, along with support from UT Southwestern—will enable metabolic analyses at the cellular level in patients. By improving sensitivity of nuclear MR by a factor of 10,000 or more, hyperpolarization could help physicians determine cancer severity, identify recurrence or metastasis, gauge the impact of treatment, and better predict disease outcomes. The technique might also help guide novel therapy choices for patients, based on their tumors' individual metabolism.

SIGNIFICANT PUBLICATIONS

Merritt, M.E. et al. Hyperpolarized ¹³C allows a direct measure of flux through a single enzyme-catalyzed step by NMR. *Proc Natl Acad Sci USA* 104, 19773-77 (2007).

Choi, C. et al. 2-hydroxyglutarate detection by magnetic resonance spectroscopy in IDH-mutated patients with gliomas. *Nat Med* 18, 624-29 (2012).

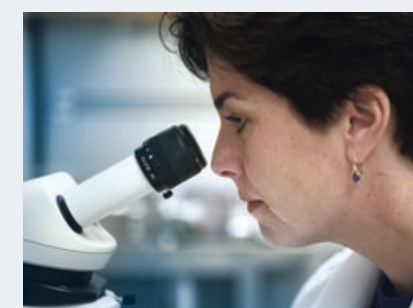
Marin-Valencia, I. et al. Analysis of tumor metabolism reveals mitochondrial glucose oxidation in genetically diverse human glioblastomas in the mouse brain in vivo. *Cell Metab* 15, 827-37 (2012).

Maher, E.A. et al. Metabolism of ¹³C glucose in human brain tumors in vivo. *NMR Biomed* 25, 1234-44 (2012).

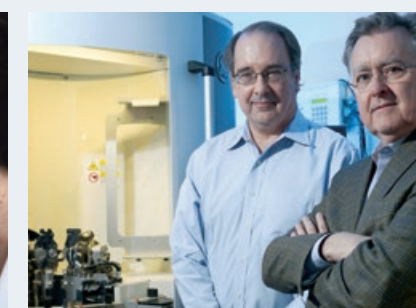
Sagiyama, K. et al. In vivo chemical exchange saturation transfer imaging allows early detection of a therapeutic response in glioblastoma. *Proc Natl Acad Sci USA*, 111, 4542-47 (2014).

Mashimo, T. et al. Acetate is a bioenergetic substrate for human glioblastoma and brain metastases. *Cell* 159, 1603-14 (2014).

Burgess, S.C. et al. Limitations of detection of anaplerosis and pyruvate cycling from metabolism of [1-¹³C] acetate. *Nat Med* 21, 108-9 (2015).



Dr. Elizabeth Maher



Drs. Craig Malloy (left) and Dean Sherry



Dr. Changho Choi

DEVELOPMENT & CANCER

MISSION

To conduct studies at the intersection of developmental biology and cancer biology in living animals.

OVERVIEW

The Development and Cancer Program explores the role of aberrant development in the genesis of cancer. The program includes both laboratory researchers and physician-scientists and features 40 members from 17 departments, including scientists from the fields of cancer, stem cell, and developmental biology. Program members investigate the developmentally and evolutionarily conserved ancestral themes that are fundamental to cell and organism growth, development, and physiology, and how these factors influence cancer biology.

THEMES

- Tumor-stroma interactions
- Cancer cell programming
- Epigenetics and cell fate
- Stem cell biology

PEER-REVIEWED FUNDING

2015 total – \$33.3 million

LEADERSHIP



Stephen X. Skapek, M.D.
Professor, Pediatrics



Joshua Mendell, M.D., Ph.D.
Professor, Molecular Biology

OF NOTE A \$6.9 million grant from the Cancer Prevention and Research Institute of Texas (CPRIT) is fueling a multi-investigator, multi-institution research project to conduct molecular genetics and functional genomics studies in soft-tissue and Ewing sarcoma. The project aims to uncover unknown drivers of soft-tissue sarcoma, with the goal of developing molecularly targeted therapies. The effort includes a biospecimen banking initiative encompassing patients at cancer centers across Texas, and builds upon UT Southwestern research developing unique, non-mammalian models of human cancer, including a *Drosophila* (fruit fly) model of rhabdomyosarcoma, and zebrafish models of malignant germ cell tumor and Ewing sarcoma.

SIGNIFICANT PUBLICATIONS

1. Asterholm, I.W. et al. Altered mitochondrial function and metabolic inflexibility associated with loss of caveolin-1. *Cell Metab* 15, 171-185 (2012).
2. Baek, G. et al. MCT4 defines a glycolytic subtype of pancreatic cancer with poor prognosis and unique metabolic dependencies. *Cell Rep* 9, 2233-2249 (2014).
3. Buszczak, M. et al. Cellular differences in protein synthesis regulate tissue homeostasis. *Cell* 159, 242-251 (2014).
4. Chen, J. et al. A restricted cell population propagates glioblastoma growth after chemotherapy. *Nature* 488, 522-526 (2012).
5. Chen, Z. et al. Cells of origin in the embryonic nerve roots for NF1-associated plexiform neurofibroma. *Cancer Cell* 26, 695-706 (2014).
6. Chivukula, R.R. et al. An essential mesenchymal function for miR-143/145 in intestinal epithelial regeneration. *Cell* 157, 1104-1116 (2014).
7. Choi, C. et al. 2-hydroxyglutarate detection by magnetic resonance spectroscopy in IDH-mutated patients with gliomas. *Nat Med* 18, 624-629 (2012).
8. Hatley, M.E. et al. A mouse model of rhabdomyosarcoma originating from the adipocyte lineage. *Cancer Cell* 22, 536-546 (2012).
9. Krzeszinski, J.Y. et al. miR-34a blocks osteoporosis and bone metastasis by inhibiting osteoclastogenesis and Tgif2. *Nature* 512, 431-435 (2014).
10. Magee, J.A. et al. Temporal changes in PTEN and mTORC2 regulation of hematopoietic stem cell self-renewal and leukemia suppression. *Cell Stem Cell* 11, 415-428 (2012).
11. Mahajan, P. et al. PAX genes in childhood oncogenesis: developmental biology gone awry? *Oncogene* 34, 2681-2689 (2015).
12. Marin-Valencia, I. et al. Analysis of tumor metabolism reveals mitochondrial glucose oxidation in genetically diverse human glioblastomas in the mouse brain in vivo. *Cell Metab* 15, 827-837 (2012).
13. Mashimo, T. et al. Acetate is a bioenergetic substrate for human glioblastoma and brain metastases. *Cell* 159, 1603-1614 (2014).
14. Mo, W. et al. CXCR4/CXCL12 mediate autocrine cell-cycle progression in NF1-associated malignant peripheral nerve sheath tumors. *Cell* 152, 1077-1090 (2013).
15. Mullen, A.R. et al. Reductive carboxylation supports growth in tumour cells with defective mitochondria. *Nature* 481, 385-388 (2011).
16. Nguyen, L.H. et al. Lin28b is sufficient to drive liver cancer and necessary for its maintenance in murine models. *Cancer Cell* 26, 248-261 (2014).
17. Park, J. et al. Neuregulin 1-HER axis as a key mediator of hyperglycemic memory effects in breast cancer. *Proc Natl Acad Sci USA* 109, 21058-21063 (2012).
18. Park, J., Scherer, P.E. Adipocyte-derived endotrophin promotes malignant tumor progression. *J Clin Invest* 122, 4243-4256 (2012).
19. Patel, A.J. et al. BET bromodomain inhibition triggers apoptosis of NF1-associated malignant peripheral nerve sheath tumors through Bim induction. *Cell Rep* 6, 81-92 (2014).
20. Pozo, K. et al. The role of Cdk5 in neuroendocrine thyroid cancer. *Cancer Cell* 24, 499-511 (2013).
21. Rakheja, D. et al. Somatic mutations in DROSHA and DICER1 impair microRNA biogenesis through distinct mechanisms in Wilms tumours. *Nat Commun* 2, 4802 (2014).
22. Shi, Q. et al. Hedgehog-induced phosphorylation by CK1 sustains the activity of Ci/Gli activator. *Proc Natl Acad Sci USA* 111, E5651-E5660 (2014).
23. Signer, R.A. et al. Haematopoietic stem cells require a highly regulated protein synthesis rate. *Nature* 509, 49-54 (2014).
24. Wu, Q. et al. 27-Hydroxycholesterol promotes cell-autonomous, ER-positive breast cancer growth. *Cell Rep* 5, 637-645 (2013).
25. Yang, C. et al. Glutamine oxidation maintains the TCA cycle and cell survival during impaired mitochondrial pyruvate transport. *Mol Cell* 56, 414-424 (2014).
26. Yue, T. et al. The cell adhesion molecule echinoid functions as a tumor suppressor and upstream regulator of the Hippo signaling pathway. *Dev Cell* 22, 255-267 (2012).
27. Zeitels, L.R. et al. Tumor suppression by miR-26 overrides potential oncogenic activity in intestinal tumorigenesis. *Genes Dev* 28, 2585-2590 (2014).
28. Zheng, J. et al. Inhibitory receptors bind ANGPTLs and support blood stem cells and leukaemia development. *Nature* 485, 656-660 (2012).
29. Zheng, J. et al. Ex vivo expanded hematopoietic stem cells overcome the MHC barrier in allogeneic transplantation. *Cell Stem Cell* 9, 119-130 (2011).

CANCER CELL NETWORKS

MISSION

To promote research that will contribute to an understanding of the mechanisms at work in aberrant cell regulatory networks that support cancer initiation and growth.

PEER-REVIEWED FUNDING

2015 total – \$37.2 million

LEADERSHIP

OVERVIEW

The Cancer Cell Networks Program facilitates investigations that shed light on the mechanisms by which aberrant cell regulatory networks support the initiation of cancers. Program members' approaches range from structural biology to animal models.

Cancer Cell Networks has 45 members representing 14 departments and centers. Key goals of the program are to define mechanisms and pathways that integrate external and internal regulatory cues at the cell-autonomous level; to determine how aberrant cell regulation contributes to the transformation of normal cells to cancer cells; and to engage translational and clinical scientists in investigating whether modulating specific aspects of cell regulation has therapeutic potential against cancer.



Melanie Cobb, Ph.D.
Professor, Pharmacology



Pier Paolo Scaglioni, M.D.
Associate Professor,
Internal Medicine

OF NOTE Supported by new CPRIT funding of more than \$889,000, Dr. Zhijian “James” Chen and colleagues are shedding light on innate immune responses to DNA and RNA. The researchers previously discovered a new enzyme, cyclic GMP-AMP synthase (cGAS), that acts as a sensor of innate immunity. The work also has described a novel cell signaling pathway: When cGAS detects foreign DNA or even host DNA that is in the cell’s cytoplasm, the enzyme binds to the DNA, catalyzing formation of a chemical called cyclic GMP-AMP, or cGAMP. Then cGAMP binds to the protein STING, activating a signaling cascade that produces interferons and pro-inflammatory cytokines. The work also has revealed a potential new avenue for enhancing anti-tumor immunity and developing cancer vaccines.

THEMES

- Chromatin regulation
- Autophagy
- G protein signaling
- Organelle communication
- Stem cells
- RNA processing
- Inflammation
- Metabolism

SIGNIFICANT PUBLICATIONS

1. Augustyn, A. et al. ASCL1 is a lineage oncogene providing therapeutic targets for high-grade neuroendocrine lung cancers. *Proc Natl Acad Sci USA* 111, 14788-14793 (2014).
2. Avirneni-Vadlamudi, U. et al. Drosophila and mammalian models uncover a role for the myoblast fusion gene TANC1 in rhabdomyosarcoma. *J Clin Invest* 122, 403-407 (2012).
3. Bodemann, B.O. et al. RalB and the exocyst mediate the cellular starvation response by direct activation of autophagosome assembly. *Cell* 144, 253-267 (2011).
4. Brugarolas, J. Molecular genetics of clear-cell renal cell carcinoma. *J Clin Oncol* 32, 1968-1976 (2014).
5. Chen, B. et al. The WAVE regulatory complex links diverse receptors to the actin cytoskeleton. *Cell* 156, 195-207 (2014).
6. Eliazer, S. et al. Lsd1 restricts the number of germline stem cells by regulating multiple targets in escort cells. *PLoS Genet* 10, e1004200 (2014).
7. Gagnon, K.T. et al. RNAi factors are present and active in human cell nuclei. *Cell Rep* 6, 211-221 (2014).
8. Gao, D. et al. Cyclic GMP-AMP synthase is an innate immune sensor of HIV and other retroviruses. *Science* 341, 903-906 (2013).
9. Hao, Y.H. et al. Regulation of WASH-dependent actin polymerization and protein trafficking by ubiquitination. *Cell* 152, 1051-1064 (2013).
10. He, C. et al. Beclin 2 functions in autophagy, degradation of G protein-coupled receptors, and metabolism. *Cell* 154, 1085-1099 (2013).
11. He, C. et al. Exercise-induced BCL2-regulated autophagy is required for muscle glucose homeostasis. *Nature* 481, 511-515 (2012).
12. Hou, F. et al. MAVS forms functional prion-like aggregates to activate and propagate antiviral innate immune response. *Cell* 146, 448-461 (2011).
13. Kim, H.S. et al. Systematic identification of molecular subtype-selective vulnerabilities in non-small-cell lung cancer. *Cell* 155, 552-566 (2013).
14. Konstantinidou, G. et al. RHOA-FAK is a required signaling axis for the maintenance of KRAS-driven lung adenocarcinomas. *Cancer Discov* 3, 444-57 (2013).
15. Li, X.D. et al. Pivotal roles of cGAS-cGAMP signaling in antiviral defense and immune adjuvant effects. *Science* 341, 1390-1394 (2013).
16. Mender, I. et al. Induction of telomere dysfunction mediated by the telomerase substrate precursor 6-thio-2'-deoxyguanosine. *Cancer Discov* 5, 82-95 (2015).
17. Osborne, J.K. et al. NeuroD1 mediates nicotine-induced migration and invasion via regulation of the nicotinic acetylcholine receptor subunits in a subset of neural and neuroendocrine carcinomas. *Mol Biol Cell* 25, 1782-1792 (2014).
18. Ou, Y.H. et al. TBK1 directly engages Akt/PKB survival signaling to support oncogenic transformation. *Mol Cell* 41, 458-470 (2011).
19. Pavia-Jimenez, A. et al. Establishing a human renal cell carcinoma tumorgraft platform for preclinical drug testing. *Nat Protoc* 9, 1848-1859 (2014).
20. Pena-Llopis, S. et al. BAP1 loss defines a new class of renal cell carcinoma. *Nat Genet* 44, 751-759 (2012).
21. Ram, R.R. et al. RASSF1A inactivation unleashes a tumor suppressor/oncogene cascade with context-dependent consequences on cell cycle progression. *Mol Cell Biol* 34, 2350-2358 (2014).
22. Schuster, K. et al. Nullifying the CDKN2A locus promotes mutant K-ras lung tumorigenesis. *Mol Cancer Res* 12, 912-923 (2014).
23. Shoji-Kawata, S. et al. Identification of a candidate therapeutic autophagy-inducing peptide. *Nature* 494, 201-206 (2013).
24. Sivanand, S. et al. A validated tumorgraft model reveals activity of dovitinib against renal cell carcinoma. *Sci Transl Med* 4, 137ra75 (2012).
25. Srivastava, N. et al. Inhibition of cancer cell proliferation by PPARgamma is mediated by a metabolic switch that increases reactive oxygen species levels. *Cell Metab* 20, 650-661 (2014).
26. Tang, Z. et al. Autophagy promotes primary ciliogenesis by removing OFD1 from centriolar satellites. *Nature* 502, 254-257 (2013).
27. Wang, R.C. et al. Akt-mediated regulation of autophagy and tumorigenesis through Beclin 1 phosphorylation. *Science* 338, 956-959 (2012).
28. Wang, S. et al. Ablation of the oncogenic transcription factor ERG by deubiquitination inhibition in prostate cancer. *Proc Natl Acad Sci USA* 111, 4251-4256 (2014).
29. Wei, Y. et al. EGFR-mediated Beclin 1 phosphorylation in autophagy suppression, tumor progression, and tumor chemoresistance. *Cell* 154, 1269-1284 (2013).
30. Wong, M.S. et al. Regulation of human telomerase splicing by RNA:RNA pairing. *Nat Commun* 5, 3306 (2014).

CHEMISTRY & CANCER

MISSION

To discover drug-like chemicals that impede (or enhance) biological processes related to the development (or inhibition) of cancer.

OVERVIEW

The Chemistry and Cancer Program combines the expertise of synthetic and medicinal chemists, molecular biologists, biochemists, structural biologists, and clinician-scientists to discover, design, and optimize drug-like small molecules that regulate biological pathways deregulated in cancer. The program engages 19 members drawn from six departments on campus.

The program's discovery process takes one of two approaches. For a chemistry-to-biology approach, discovery starts by identifying natural or unnatural small molecules that are selectively lethal to human cancer cell lines, then determining exactly how the small molecules have their effect. In a biology-to-chemistry approach, hypotheses regarding the "drugability" and cancer relevance of specific biological pathways investigated by Cancer Center scientists can be tested with drug-like chemicals.

THEMES

- Molecular targets of cancer cell-specific small-molecule toxins
- Novel, cancer cell-specific pathways
- Proof-of-concept preclinical development of cancer cell-specific small-molecule toxins
- The hypoxia response pathway

PEER-REVIEWED FUNDING

2015 total – \$10.9 million

LEADERSHIP



Steven McKnight, Ph.D.
Chair, Biochemistry



Jef De Brabander, Ph.D.
Professor, Biochemistry



John MacMillan, Ph.D.
Associate Professor,
Biochemistry

OF NOTE Supported by nearly \$1.5 million from the National Institutes of Health, Simmons Cancer Center investigators (with collaborators at Simon Fraser University) are developing an innovative research paradigm to characterize mechanisms of action of natural products and botanicals more quickly and precisely. The approach of the new Center for High-Throughput Functional Annotation of Natural Products (HiFAN) incorporates natural products chemistry, biological screening, data analytics, and bioinformatics, combining two high-throughput platforms (cytological profiling and a technique called FUSION, developed at UT Southwestern) to discern in greater detail the impact on cells of both complex chemical mixtures and pure natural compounds.

SIGNIFICANT PUBLICATIONS

1. Chau, V. et al. Preclinical therapeutic efficacy of a novel pharmacologic inducer of apoptosis in malignant peripheral nerve sheath tumors. *Cancer Res* 74, 586-597 (2014).
2. Comerford, S.A. et al. Acetate dependence of tumors. *Cell* 159, 1591-1602 (2014).
3. Fang, M. et al. The ER UDPase ENTPD5 promotes protein N-glycosylation, the Warburg effect, and proliferation in the PTEN pathway. *Cell* 143, 711-724 (2010).
4. Fu, P. et al. Carpatamides A-C, cytotoxic arylamine derivatives from a marine-derived *Streptomyces* sp. *J Nat Prod* 77, 1245-1248 (2014).
5. Guo, Y. et al. Regulating the ARNT/TACC3 axis: multiple approaches to manipulating protein/protein interactions with small molecules. *ACS Chem Biol* 8, 626-635 (2013).
6. Hu, Y. et al. Discoipyrroles A-D: isolation, structure determination, and synthesis of potent migration inhibitors from *Bacillus hunanensis*. *J Am Chem Soc* 135, 13387-13392 (2013).
7. Hunter, J.C. et al. In situ selectivity profiling and crystal structure of SML-8-73-1, an active site inhibitor of oncogenic K-Ras G12C. *Proc Natl Acad Sci USA* 111, 8895-8900 (2014).
8. Jat, J.L. et al. Direct stereospecific synthesis of unprotected N-H and N-Me aziridines from olefins. *Science* 343, 61-65 (2014).
9. Kilgore, J.A. et al. Identification of DNMT1 selective antagonists using a novel scintillation proximity assay. *J Biol Chem* 288, 19673-19684 (2013).
10. Kim, H.S. et al. Systematic identification of molecular subtype-selective vulnerabilities in non-small-cell lung cancer. *Cell* 155, 552-566 (2013).
11. Kwon, I. et al. Phosphorylation-regulated binding of RNA polymerase II to fibrous polymers of low-complexity domains. *Cell* 155, 1049-1060 (2013).
12. Laxman, S. et al. Npr2 inhibits TORC1 to prevent inappropriate utilization of glutamine for biosynthesis of nitrogen-containing metabolites. *Sci Signal* 7, ra120 (2014).
13. Li, N. et al. Poly-ADP ribosylation of PTEN by tankyrases promotes PTEN degradation and tumor growth. *Genes Dev* 29, 157-170 (2015).
14. Orvedahl, A. et al. Image-based genome-wide siRNA screen identifies selective autophagy factors. *Nature* 480, 113-117 (2011).
15. Partch, C.L., Gardner, K.H. Coactivators necessary for transcriptional output of the hypoxia inducible factor, HIF, are directly recruited by ARNT PAS-B. *Proc Natl Acad Sci USA* 108, 7739-7744 (2011).
16. Petersen, S.L. et al. Overcoming cancer cell resistance to Smac mimetic induced apoptosis by modulating cIAP-2 expression. *Proc Natl Acad Sci USA* 107, 11936-11941 (2010).
17. Potts, M.B. et al. Using functional signature ontology (FUSION) to identify mechanisms of action for natural products. *Sci Signal* 6, ra90 (2013).
18. Rogers, J.L. et al. Development of inhibitors of the PAS-B domain of the HIF-2alpha transcription factor. *J Med Chem* 56, 1739-1747 (2013).
19. Scheuermann, T.H. et al. Allosteric inhibition of hypoxia inducible factor-2 with small molecules. *Nat Chem Biol* 9, 271-276 (2013).
20. Sengupta, S. et al. Regulation of OSR1 and the sodium, potassium, two chloride cotransporter by convergent signals. *Proc Natl Acad Sci USA* 110, 18826-18831 (2013).
21. Skrypnik, N. et al. PPARalpha activation can help prevent and treat non-small cell lung cancer. *Cancer Res* 74, 621-631 (2014).
22. Sun, Q. et al. Nuclear export inhibition through covalent conjugation and hydrolysis of Leptomycin B by CRM1. *Proc Natl Acad Sci USA* 110, 1303-1308 (2013).
23. Wang, Z. et al. Orexin/hypocretin activates mTOR complex 1 (mTORC1) via an Erk/Akt-independent and calcium-stimulated lysosome v-ATPase pathway. *J Biol Chem* 289, 31950-31959 (2014).
24. Zhang, Y. et al. Inhibition of the prostaglandin-degrading enzyme 15-PGDH potentiates tissue regeneration. *Science* 348 (6240), aaa2340 (2015).

EXPERIMENTAL THERAPEUTICS OF CANCER

MISSION

To identify and validate novel targets, pathways, and therapies for selective tumor targeting; to establish biomarkers that can predict tumor response; and to test the efficacy of resulting potential medicines in clinical trials.

OVERVIEW

The Experimental Therapeutics Program supports development of novel therapeutic strategies for cancer. The program provides a science-based infrastructure for translating discoveries from the Cancer Center's scientific programs to preclinical models and then to evaluation through investigator-initiated clinical trials.

Program leaders and members interact extensively with the Cancer Center's disease-oriented teams to focus specific therapeutics on select cancers based on laboratory research that indicates optimal targets and relevant biomarkers.

The program represents key oncology disciplines and has 44 members, comprising 12 basic science investigators and 32 clinical investigators from 15 departments or centers. It is also home to the Cancer Center's Specialized Program of Research Excellence (SPORE) in lung cancer.

THEMES

- Molecular therapeutic sensitizers
- Tumor microenvironment and protein therapy
- Imaging and drug delivery
- Cancer vulnerabilities

PEER-REVIEWED FUNDING

2015 total – \$27 million

LEADERSHIP



John Minna, M.D.
Professor, Internal Medicine
and Pharmacology



David Boothman, Ph.D.
Professor, Simmons
Cancer Center



David Gerber, M.D.
Associate Professor,
Internal Medicine

OF NOTE Research by the lab of Dr. David A. Boothman on the anti-cancer effects of the natural substance beta-lapachone has led to two multidisciplinary projects—funded through PanCAN and totaling \$1.3 million—testing the substance against pancreatic ductal adenocarcinoma (PDA) and non-small cell lung cancer (NSCLC). The first project is pursuing lab studies and a phase IB clinical trial involving chemotherapy plus a formulation of beta-lapachone called ARQ761 (from the biotechnology firms NQ Oncology and ArQule). The other project is exploring the efficacy of combining ARQ761 with PARP inhibitors to treat PDA, NSCLC, and other NQO1 over-expressed malignancies. The combination has proved effective against pancreatic, breast, and non-small cell lung cancer cells in vitro, and NSCLC in mouse xenografts.

SIGNIFICANT PUBLICATIONS

1. Bey, E.A. et al. Catalase abrogates beta-lapachone-induced PARP1 hyperactivation-directed programmed necrosis in NQO1-positive breast cancers. *Mol Cancer Ther* 12, 2110-2120 (2013).
2. Chang, K.H. et al. A gain-of-function mutation in DHT synthesis in castration-resistant prostate cancer. *Cell* 154, 1074-1084 (2013).
3. Chang, K.H. et al. Dihydrotestosterone synthesis bypasses testosterone to drive castration-resistant prostate cancer. *Proc Natl Acad Sci USA* 108, 13728-13733 (2011).
4. Chung, J.S. et al. The DC-HIL/syndecan-4 pathway regulates autoimmune responses through myeloid-derived suppressor cells. *J Immunol* 192, 2576-2584 (2014).
5. Frankel, A.E. et al. Activity of SL-401, a targeted therapy directed to interleukin-3 receptor, in blastic plasmacytoid dendritic cell neoplasm patients. *Blood* 124, 385-92 (2014).
6. Gerber, D.E. et al. Phase I safety and pharmacokinetic study of bavituximab, a chimeric phosphatidylserine-targeting monoclonal antibody, in patients with advanced solid tumors. *Clin Cancer Res* 17, 6888-6896 (2011).
7. Gil del Alcazar, C.R. et al. Inhibition of DNA double-strand break repair by the dual PI3K/mTOR inhibitor NVP-BE235 as a strategy for radiosensitization of glioblastoma. *Clin Cancer Res* 20, 1235-1248 (2014).
8. Huang, X. et al. An NQO1 substrate with potent antitumor activity that selectively kills by PARP1-induced programmed necrosis. *Cancer Res* 72, 3038-3047 (2012).
9. Iyengar, P. et al. Phase II trial of stereotactic body radiation therapy combined with erlotinib for patients with limited but progressive metastatic non-small-cell lung cancer. *J Clin Oncol* 32, 3824-3830 (2014).
10. Jeong, Y. et al. Nuclear receptor expression defines a set of prognostic biomarkers for lung cancer. *PLoS Med* 7, e1000378 (2010).
11. Li, L.S. et al. Modulating endogenous NQO1 levels identifies key regulatory mechanisms of action of beta-lapachone for pancreatic cancer therapy. *Clin Cancer Res* 17, 275-285 (2011).
12. Li, X. et al. Aiolos promotes anchorage independence by silencing p66Shc transcription in cancer cells. *Cancer Cell* 25, 575-589 (2014).
13. Ma, X. et al. Ultra-pH-sensitive nanoprobe library with broad pH tunability and fluorescence emissions. *J Am Chem Soc* 136, 11085-11092 (2014).
14. Shao, C. et al. Essential role of aldehyde dehydrogenase 1A3 for the maintenance of non-small cell lung cancer stem cells is associated with the STAT3 pathway. *Clin Cancer Res* 20, 4154-4166 (2014).
15. Singel, S.M. et al. A targeted RNAi screen of the breast cancer genome identifies KIF14 and TLN1 as genes that modulate docetaxel chemosensitivity in triple-negative breast cancer. *Clin Cancer Res* 19, 2061-2070 (2013).
16. Tang, H. et al. A 12-gene set predicts survival benefits from adjuvant chemotherapy in non-small cell lung cancer patients. *Clin Cancer Res* 19, 1577-1586 (2013).
17. Tomimatsu, N. et al. Phosphorylation of EXO1 by CDKs 1 and 2 regulates DNA end resection and repair pathway choice. *Nat Commun* 5, 3561 (2014).
18. Wang, L. et al. A small molecule modulates Jumonji histone demethylase activity and selectively inhibits cancer growth. *Nat Commun* 4, 2035 (2013).
19. Wang, Y. et al. A nanoparticle-based strategy for the imaging of a broad range of tumours by nonlinear amplification of microenvironment signals. *Nat Mater* 13, 204-212 (2014).
20. Yun, E.J. et al. DAB2IP regulates cancer stem cell phenotypes through modulating stem cell factor receptor and ZEB1. *Oncogene* 34, 2741-2752 (2015).

POPULATION SCIENCE & CANCER CONTROL

MISSION

To understand and impact factors associated with cancer risk in clinical, safety-net, and community settings among diverse populations.

OVERVIEW

Drawing from the large and diverse population that Simmons Cancer Center serves, the Population Science and Cancer Control Program has a special focus on uninsured residents served by local public health systems. Studies are centered on cancer disparities among subpopulations of individuals who traditionally are medically underserved.

Research focuses on processes of care with the goal of translating findings into improved cancer care in local health systems. The 25 members of the Population Science Program are based in five departments and at the University of Texas School of Public Health's Dallas campus.

THEMES

- Cancer prevention (including the study of biomarkers for colon and liver cancers and risk prevention behaviors)
- Screening for early detection of colon, liver, and esophageal cancers
- Cancer survivorship

PEER-REVIEWED FUNDING

2015 total – \$6.1 million

LEADERSHIP



Ethan Halm, M.D., M.P.H.
Professor, Internal Medicine



Jasmin Tiro, Ph.D., M.P.H.
Associate Professor,
Clinical Sciences

OF NOTE A thriving research effort is evaluating strategies to improve screening effectiveness and ensure that more people at high risk for hepatocellular carcinoma (HCC), the most common form of liver cancer, receive appropriate testing so tumors can be detected earlier and treated more effectively. Population Science program members are key investigators for the multi-institution Texas HCC Consortium, a \$9.7 million initiative funded by the Cancer Prevention and Research Institute of Texas. Consortium projects include characterizing factors that predict liver cancer in a diverse group of patients with cirrhosis, evaluating novel biomarkers to increase sensitivity for early tumor detection, and a trial comparing interventions to boost screening rates in at-risk patients.

SIGNIFICANT PUBLICATIONS

- Anhang Price, R. et al. Knowledge and intention to participate in cervical cancer screening after the human papillomavirus vaccine. *Vaccine* 29, 4238-4243 (2011).
- Baldwin, A.S. et al. Understanding how mothers of adolescent girls obtain information about the HPV vaccine: associations between mothers' health beliefs, information seeking, and vaccination intentions in an ethnically diverse sample. *J Health Psychol* 18, 926-938 (2013).
- Brown, E.R. et al. States' use of local population health data: comparing the Behavioral Risk Factor Surveillance System and independent state health surveys. *J Public Health Manag Pract* 19, 444-450 (2013).
- Businelle, M.S. et al. Comparing homeless smokers to economically disadvantaged domiciled smokers. *Am J Public Health* 103, S218-S220 (2013).
- Chien, L.C. et al. The modifying effect of patient location on stage-specific survival following colorectal cancer using geosurvival models. *Cancer Causes Control* 24, 473-484 (2013).
- Garey, L. et al. Subjective social status and readiness to quit among homeless smokers. *Am J Health Behav* 39, 157-166 (2015).
- Gerber, D.E. et al. Impact of prior cancer on eligibility for lung cancer clinical trials. *J Natl Cancer Inst* 106, dju302 (2014).
- Gierisch, J.M. et al. Finding the minimal intervention necessary for sustained mammography adherence. *Am J Prev Med* 30, 334-344 (2010).
- Guda, K. et al. Novel recurrently mutated genes in African American colon cancers. *Proc Natl Acad Sci USA* 112, 1149-1154 (2015).
- Gupta, S. et al. Comparative effectiveness of fecal immunochemical test outreach, colonoscopy outreach, and usual care for boosting colorectal cancer screening among the underserved: a randomized trial. *JAMA Intern Med* 173, 1725-1732 (2013).
- Gupta, S. et al. Measurement of colorectal cancer test use with medical claims data in a safety-net health system. *Am J Med Sci* 345, 99-103 (2013).
- Kendzor, D.E. et al. Financial incentives for abstinence among socioeconomically disadvantaged individuals in smoking cessation treatment. *Am J Public Health* 105, 1198-205 (2015).
- Kozlitina, J. et al. Exome-wide association study identifies a TM6SF2 variant that confers susceptibility to nonalcoholic fatty liver disease. *Nat Genet* 46, 352-356 (2014).
- Li, J.Z. et al. Chronic overexpression of PNPLA3/148M in mouse liver causes hepatic steatosis. *J Clin Invest* 122, 4130-4144 (2012).
- Murphy, C. et al. Competitive testing of health behavior theories: how do benefits, barriers, subjective norm, and intention influence mammography behavior? *Ann Behav Med* 47, 120-129 (2014).
- Pruitt, S.L. et al. Residential racial segregation and mortality among black, white, and Hispanic urban breast cancer patients in Texas, 1995-2009. *Cancer* 121, 1845-1855 (2015).
- Pruitt, S.L. et al. Physicians, clinics, and neighborhoods: multiple levels of influence on colorectal cancer screening. *Cancer Epidemiol Biomarkers Prev* 23, 1346-1355 (2014).
- Reitzel, L.R. et al. Subjective social status predicts quit day abstinence among homeless smokers. *Am J Health Promot* 29, 43-45 (2014).
- Singal, A.G. et al. Effectiveness of hepatocellular carcinoma surveillance in patients with cirrhosis. *Cancer Epidemiol Biomarkers Prev* 21, 793-799 (2012).
- Singal, A.G. et al. Racial, social, and clinical determinants of hepatocellular carcinoma surveillance. *Am J Med* 128, 90.e1-7 (2015).
- Singal, A.G. et al. The effect of PNPLA3 on fibrosis progression and development of hepatocellular carcinoma: a meta-analysis. *Am J Gastroenterol* 109, 325-334 (2014).
- Singal, A.G. et al. Early detection, curative treatment and survival rates for HCC surveillance in patients with cirrhosis: a meta-analysis. *PLoS Med* 11, e10011624 (2014).
- Singal, A.G. et al. Therapeutic delays lead to worse survival among patients with hepatocellular carcinoma. *J Natl Comp Canc Netw* 11, 1101-1108 (2013).
- Singal, A.G. et al. Failure rates in the hepatocellular carcinoma surveillance process. *Cancer Prev Res (Phila)* 5, 1124-1130 (2012).
- Spechler, S.J., Souza, R.F. Barrett's esophagus. *N Engl J Med* 37, 836-845 (2014).
- Tiro, J.A. et al. The CRC screening process in community settings: a conceptual model for the Population-based Research Optimizing Screening through Personalized Regimens consortium. *Cancer Epidemiol Biomarkers Prev* 23, 1147-1158 (2014).
- Tiro, J.A. et al. Multilevel correlates for human papillomavirus vaccination of adolescent girls attending safety net clinics. *Vaccine* 30, 2368-2375 (2012).
- Wang, D.H. et al. Hedgehog signaling regulates FOXA2 in esophageal embryogenesis and Barrett's metaplasia. *J Clin Invest* 124, 3767-3780 (2014).
- Yopp, A.C. et al. Establishment of a multidisciplinary hepatocellular carcinoma clinic is associated with improved clinical outcome. *Ann Surg Oncol* 21, 1287-1295 (2014).

The Cancer Center tackles the complex challenge of boosting colon cancer screening among minorities and underserved populations.

BACKGROUND

Colorectal cancer screening—generally advised for people age 50 and older—saves lives. Yet only about 15 percent of those who lack insurance receive screening, research has indicated, compared with 50 percent of insured people. And rates

for African-Americans and Hispanics lag substantially behind those for whites.

Thus a key challenge in reducing colon cancer deaths is delivery of early detection and follow-up services to people who are inadequately insured and to minorities. Partnering with the community and local health systems, Simmons Cancer Center

researchers are addressing that challenge and are setting an agenda nationally for colorectal cancer detection in the neediest of populations.

THE FOUNDATIONS

2009

Parkland Health & Hospital System, Dallas County's sole "safety-net" health care provider for more than 1 million underinsured or uninsured people, adopts an electronic medical record, integrating data from its hospital, clinics, and health centers. The massive data pool provides a unique opportunity to investigate how to improve health care delivery in a highly diverse, low-income population.

2009

Cancer Center members Dr. Chul Ahn, Dr. Keith Argenbright, and Dr. Celette Sugg Skinner study colon cancer screening among more than 20,000 patients ages 50–75 in the JPS Health Network, Tarrant County's medical safety net. The findings indicate a need to simplify access to screening, laying the groundwork for a project testing different methods to encourage more people to get screened.

2011

A five-year, \$6.3 million National Cancer Institute grant led by Drs. Skinner and Ethan Halm establishes the Parkland-UT Southwestern PROSPR Center to more efficiently target and deliver screening for colorectal cancer. (PROSPR stands for Population-based Research Optimizing Screening through Personalized Regimens.) The center is one of just three nationwide focused on colorectal screening, and the only one targeting a population that lacks health care resources. The PROSPR Center begins studying all aspects of colon cancer screening among a racially and ethnically diverse group of some 70,000 Parkland primary-care patients to identify opportunities to improve screening rates, follow-up, and other care.

THE TRANSLATION

2009–2013

Cancer Center members lead a project involving about 5,900 people in Tarrant County that compares three means of engaging primary-care patients in screening: usual care, a direct invitation to receive a free colonoscopy, or a free fecal immunochemical test kit mailed directly to them. Participation

rates rise to about 41 percent for people sent a test kit and 25 percent among those invited for colonoscopy, compared with just 12 percent for those receiving usual care. The findings have implications for public health policy-making.

2014

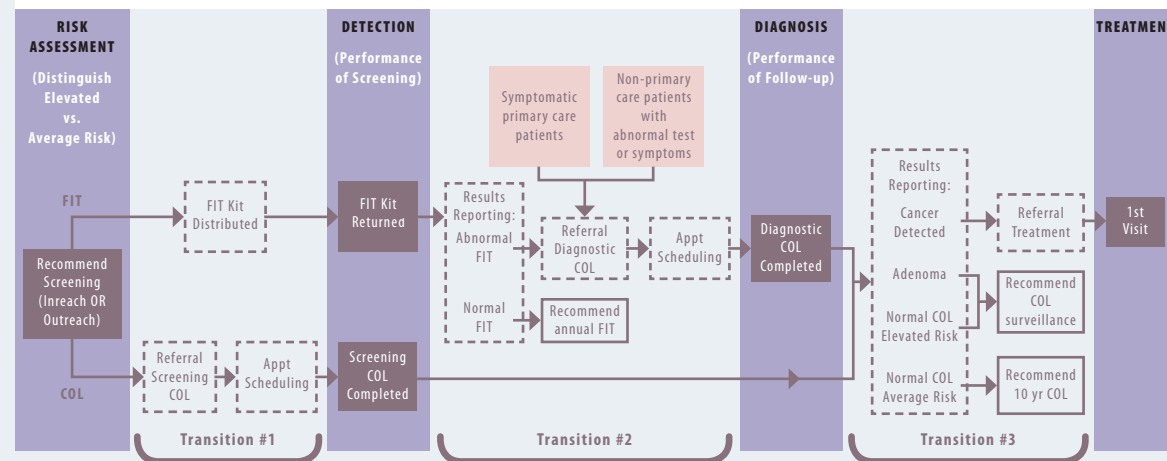
Led by Dr. Sandi Pruitt, a statistical analysis of patients in the Tarrant County study who received usual care indicates that factors related not just to patients but to their physicians, neighborhoods, and clinics are relevant in screening decisions. The work highlights potentially important avenues to boost screening rates, such as reminders built into clinic systems or neighborhood campaigns.

THE IMPACT

2011

In a PROSPR project, two Parkland Community-Oriented Primary Care clinics in Dallas begin deploying the Cancer Risk Intake

Cancer Center scientists and colleagues have developed a model conceptualizing the colon cancer screening process. The model has been adopted by all PROSPR colon cancer sites to help guide future screening research (from J.A. Tiro et al., *Cancer Epidemiol Biomarkers Prev* 23[2014]).



■ Type of Care: care delivered to accomplish a specific goal, such as detection, diagnosis, and treatment

⤵ Transition: set of steps and interfaces necessary to go from one type of care to another

□ Step: medical encounters or actions within a type or transition in care

⌌ Interface: interactions that link steps and involve transferring information and/or responsibility among patients, providers, and clinic staff

System, a bilingual touch-screen computer application that asks patients about personal risk factors and family history of colon cancer, using responses to generate personalized screening recommendations. As of May 2015, about 2,700 patients had used the program.

2013

The PROSPR Center implements a program, embedded in Parkland's electronic medical record, that matches colonoscopic findings with follow-up care guidelines for surveillance and rescreening. The program ensures that subsequent care is provided based on the individually determined risk of colon cancer in each patient.

2014

The PROSPR Center's mission expands to include cervical cancer screening, an effort led by Dr. Jasmin Tiro and Dr. Skinner. Additional funding supports initiatives such as a project to follow some 178,000 screening-eligible women in the Parkland system (24 percent of them African-American, and 61 percent Hispanic). Rates of cervical cancer in Hispanic women are about 60 percent higher than in non-Hispanic Caucasian women.

THE FUTURE

Investigators are studying whether higher colorectal cancer screening participation rates found among patients mailed test kits will carry over into repeat screening and follow-up

when needed. Also, a large CPRIT-funded initiative called CSPAN (colorectal cancer screening and patient navigation) is partnering with agencies and institutions in 20 local counties to expand the test-kit mailing program to 165,000 underserved suburban and rural residents and to ensure access to needed follow-up care.

Building on infrastructure and insights developed through colorectal screening research, Simmons Cancer Center scientists are improving delivery of screening and preventive care in other malignancies, including liver and cervical cancers.

Meanwhile, new insights into the genetics of colon cancers may someday better guide screening and follow-up care among African-Americans, who face higher risk of the disease and are more likely to die from it. Work by a team of investigators including Simmons Cancer Center Director Dr. James Willson has identified a set of previously unrecognized mutations in colorectal cancers among African-Americans, shedding light on biological differences in the disease that may help explain that group's elevated risk.

SIGNIFICANT PUBLICATIONS

Gupta, S. et al. Screening for colorectal cancer in a safety-net health care system: access to care is critical and has implications for screening policy. *Cancer Epidemiol Biomarkers Prev* 18, 2373-79 (2009).

Tiro, J.A. et al. Multilevel correlates for human papillomavirus vaccination of adolescent girls attending safety net clinics. *Vaccine* 30, 2368-75 (2012).

Singal, A.G. et al. Screening process failures for hepatocellular carcinoma. *J Natl Compr Canc Netw* 12, 375-82 (2014).

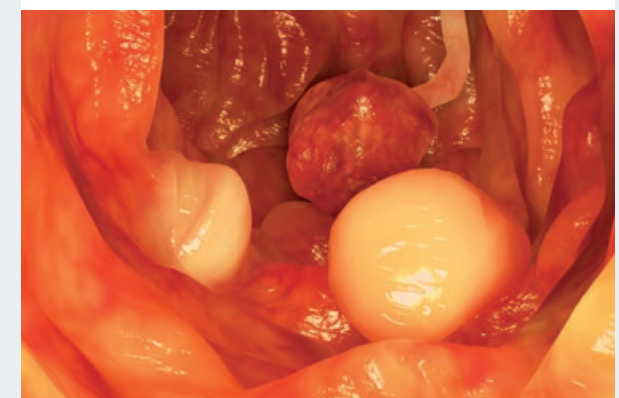
Tiro, J.A. et al. The CRC screening process in community settings: a conceptual model for the Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) Consortium. *Cancer Epidemiol Biomarkers Prev* 23, 1147-58 (2014).

Skinner, C.S. et al. Development of the Parkland-UT Southwestern Colonoscopy Reporting System (CoRS) for evidence-based colon cancer surveillance recommendations. *J Am Med Inform Assoc* (2015).

Skinner, C.S. et al. Impact of risk assessment and tailored versus nontailored risk information on colorectal cancer testing in primary care: a randomized controlled trial. *Cancer Epidemiol Biomarkers Prev* 24, 1523-1530 (2015).

Singal, A.G. et al. Outreach invitations for FIT and colonoscopy improve colorectal cancer screening rates: a randomized controlled trial in a safety-net health system. *Cancer* 122, 456-63 (2016).

Colonoscopy reveals a polyp



**SIMMONS CANCER CENTER
LEADERS, 2015**



James K.V. Willson, M.D. — Director; Associate Dean for Oncology Programs; Professor of Internal Medicine; The Lisa K. Simmons Distinguished Chair in Comprehensive Oncology



David Boothman, Ph.D. — Associate Director for Translational Research; Professor of Simmons Cancer Center; Robert B. and Virginia Payne Professorship in Oncology



Jerry Shay, Ph.D. — Associate Director for Training and Education; Professor of Cell Biology; Southland Financial Corporation Distinguished Chair in Geriatrics



Michael White, Ph.D. — Associate Director for Basic Science; Professor of Cell Biology; Sherry Wigley Crow Cancer Research Endowed Chair, in Honor of Robert Lewis Kirby, M.D.; Grant A. Dove Chair for Research in Oncology



Joan Schiller, M.D. — Deputy Director; Chief of Hematology/Oncology; Professor of Internal Medicine; Andrea L. Simmons Distinguished Chair in Cancer Research



Hak Choy, M.D. — Associate Director for Radiation Oncology; Professor and Chair of Radiation Oncology; Nancy B. and Jake L. Hamon Distinguished Chair in Therapeutic Oncology Research



Stephen X. Skapek, M.D. — Director of Pediatric Hematology/Oncology; Professor of Pediatrics; Children's Cancer Fund Distinguished Professorship in Pediatric Oncology Research



Stephanie Clayton Hobbs, M.H.S.M. — Associate Vice President for Cancer Programs



Chul Ahn, Ph.D. — Associate Director for Biostatistics and Bioinformatics; Professor of Clinical Sciences



David Gerber, M.D. — Associate Director for Clinical Research; Associate Professor of Internal Medicine



Celette Sugg Skinner, Ph.D. — Associate Director for Cancer Control and Population Science; Professor of Clinical Sciences; Chief of the Division of Behavioral and Communications Sciences; Parkland Community Medicine Professorship



Tim Strawderman, Ph.D. — Associate Director for Research Administration

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Associate Professor, Radiation Oncology

Larry Anderson, M.D., Ph.D. (Heme)

Assistant Professor, Internal Medicine–Hematology/Oncology

Victor Aquino, M.D. (Pediatrics)

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Yull Arriaga, M.D. (GI)

Associate Professor, Internal Medicine

Glen Balch, M.D. (GI)

Associate Professor, Surgery

Muhammad Beg, M.D. (GI)

Assistant Professor, Internal Medicine

Daniel Bowers, M.D. (Pediatrics)

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Jeffrey Cadeddu, M.D. (GU)

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Ralph C. Smith, M.D. Distinguished Chair in Minimally Invasive Urologic Surgery*

Hsienchang (Thomas) Chiu, M.D. (Lung)

Associate Professor, Internal Medicine

Robert Collins, M.D. (BMT)

*Professor, Internal Medicine
Sydney and J.L. Huffines Distinguished Chair in Cancer Research in Honor of Eugene Frenkel, M.D.;
H. Lloyd and Willye V. Skaggs Professorship in Medical Research*

Kevin Courtney, M.D., Ph.D. (GU)

Assistant Professor, Internal Medicine–Hematology/Oncology

Jonathan Dowell, M.D. (Lung)

Associate Professor, Internal Medicine–Hematology/Oncology

W. Phil Evans, M.D. (Breast)

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*Professor, Internal Medicine
Elaine Dewey Sammons Distinguished Chair in Cancer Research, in Honor of Eugene P. Frenkel, M.D.;
A. Kenneth Pye Professorship in Cancer Research;
Raymond D. and Patsy R. Nasher Distinguished Chair in Cancer Research, in Honor of Eugene P. Frenkel, M.D.*

Barbara Haley, M.D. (Breast)

*Professor, Internal Medicine
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Raquibul Hannan, M.D., Ph.D. (GU)

Assistant Professor, Radiation Oncology

Randall Hughes, M.D. (Head & Neck)

Associate Professor, Internal Medicine

James Huth, M.D. (Melanoma)

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Professor, Pathology

Theodore Laetsch, M.D. (Pediatrics)

Assistant Professor, Pediatrics

Patrick Leavey, M.D. (Pediatrics)

Professor, Pediatrics

A. Marilyn Leitch, M.D. (Breast)

*Professor, Surgery
S.T. Harris Family Distinguished Chair in Breast Surgery, in Honor of A. Marilyn Leitch, M.D.*

Hsiao-Ching (Jenny) Li, M.D. (Breast)

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Helen J. and Robert S. Strauss Professorship in Urology*

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Bruce Mickey, M.D. (NeuroOnc)

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William Kemp Clark Chair of Neurological Surgery*

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*Professor, Obstetrics and Gynecology
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Lucien Nedzi, M.D. (Head & Neck)

Associate Professor, Radiation Oncology

Edward Pan, M.D. (NeuroOnc)

Assistant Professor, Neurology & Neurotherapeutics

David Pistenmaa, M.D., Ph.D. (GU)

*Professor, Radiation Oncology
David Bruton Jr. Professorship in Clinical Cancer Research*

Claus Roehrborn, M.D. (GU)

*Professor and Chairman, Urology
S.T. Harris Family Chair in Medical Science, in Honor of John D. McConnell, M.D.; E.E. Fogelson and Greer Garson Fogelson Distinguished Chair in Urology*

Zora Rogers, M.D. (Pediatrics)

Professor, Pediatrics

Cynthia Rutherford, M.D. (Heme)

*Professor, Internal Medicine
Barrett Family Professorship in Cancer Research*

Arthur Sagalowsky, M.D. (GU)

*Professor, Urology
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Professor, Pathology

Rohit Sharma, M.D. (Melanoma)

Assistant Professor, Surgery

Ann Spangler, M.D. (Breast)

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Masaya Takahashi, Ph.D. (Lung)

Associate Professor, Advanced Imaging Research Center

Stan Taylor, M.D. (Melanoma)

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Associate Professor, Internal Medicine

Madhuri Vusirikala, M.D. (Heme)

Associate Professor, Internal Medicine

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