Baylor
College of
Medicine

DAN L DUNCAN COMPREHENSIVE CANCER CENTER

Annual Report 2019

PEER-REVIEWED FUNDING

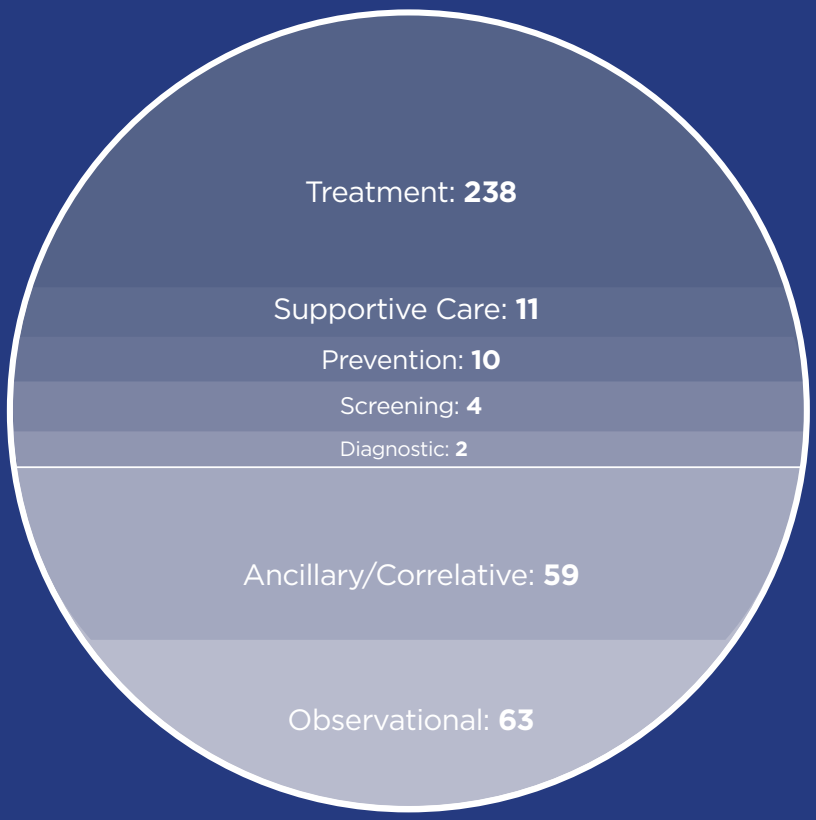
SPECIFIC FUNDING SOURCE	PROJECT DIRECT COST	PROJECT TOTAL COSTS	TOTAL NUMBER OF PROJECTS
NCI Peer-Reviewed Research Projects	$33,900,404	$49,010,729	140
Other NIH Peer-Reviewed Research Projects	$32,035,745	$46,954,513.50	136
CPRIT Research Projects	$28,445,736	$29,770,175	65
Other Peer-Reviewed Research Projects	$13,466,290	$17,701,921	87
Non-Peer-Reviewed Research Projects	$29,518,031	$37,482,343	173
Grand Total (All Projects)	$137,366,206	$180,919,681	601

NUMBER OF TRIALS IN 2017 & 2018

Total trials
387

Interventional
265

Non-Interventional
122



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GET TO KNOW THE DAN L DUNCAN

The Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine has grown and matured over the 11 years since its original designation as a Cancer Center by the National Cancer Institute, which was followed by an NCI Comprehensive Cancer Center designation in 2015. Our clinical operations have expanded with new faculty and programs, and we moved into our new clinical space on the McNair campus in January 2019. Our research portfolio has grown dramatically to more than $180 million in annual cancer relevant research funding today from less than $100 million in 2007. These amazing accomplishments were made possible by the transformational gift in 2006 from Dan L Duncan and his family, who we owe a great debt of gratitude, and by our outstanding faculty and staff.

It is now my pleasure to highlight several of these accomplishments and review the exceptional clinical, research, educational and community outreach initiatives undertaken by our talented members. Excellence in these areas culminated in our "Comprehensive" designation from the NCI, placing us among the other 49 Comprehensive Centers, including only two in Houston and three in all of Texas, as the top cancer centers in the country. Because of the Duncan Cancer Center's affiliation with the Harris Health System and Ben Taub Hospital, the Michael E. DeBakey Veterans Affairs Medical Center, Texas Children's Hospital and Texas Children's Cancer Center, and Baylor St. Luke's Medical Center, we can accurately be called "the Cancer Center for all Houstonians."

In this report, we will read about the exceptional research conducted in our seven research programs: Breast Cancer, Cancer Biology, Cancer Evolvability, Cancer Prevention and Population Sciences, Nuclear Receptor, Cancer Cell and Gene Therapy and Pediatric Cancer. Other working groups focus their state-of-the-art research and patient care in specific cancer types or in other areas such as Precision Cancer Medicine, Clinical/Translational Research, or Cancer Survivorship and Integrative Medicine. We continue to recruit new faculty, several internationally known for their work. Dr. Chris Amos, associate director for quantitative science, is an expert in epidemiology of lung and other cancers and he also directs the Institute for Clinical and Translational Research at Baylor. Dr. Cheryl Walker, is the new co-leader of the Nuclear Receptor Program and director of the Center for Precision and Environmental Health. She is internationally known for her expertise in the interaction between genetics and the environment and its role in causing cancer. Dr. Alastair Thompson, an internationally recognized surgeon and translational researcher, was recruited to be the director of breast surgery, while Dr. Taylor Ripley, now directs our Mesothelioma Treatment Center. Two new centers at Baylor College of Medicine will enhance our cancer

drug development capabilities. The Center for Drug Discovery (CDD) provides expertise in drug screening and early drug development and the Therapeutic Innovation Center (THINC) focuses on developing new therapies targeting proteins involved in gene regulation.

Recognizing serious health problems in our own community such as the rapidly rising incidence of certain cancers, we established a new working group in obesity and cancer. This team cuts across many disciplines and is focusing on liver, esophageal and triple negative breast cancers, as well as other cancers related to the obesity epidemic, a major problem in Texas and across the county. Liver cancer is the most rapidly rising cancer in the nation due to what is known as fatty liver disease, which is increasingly common in people with obesity and metabolic syndrome. Esophageal cancer is the most rapidly rising cancer in middle-aged white males because of abdominal obesity and chronic gastric acid reflux. It's clear that successfully addressing the obesity problem will be crucial to ensuring further reductions in cancer morbidity and mortality that have been observed in this country in the past two decades.

Comprehensive designation also requires significant accomplishments in career enhancement (education of future doctors and scientists) and community outreach to reduce health disparities and improve survival from cancer, especially in underserved populations. The associate directors for education in the Cancer Center, Drs. Suzanne Fuqua and Jason Yustein, played major roles in the development of Baylor's new graduate program in cancer biology and are creating new educational programs in the Center. Our Office of Outreach and Health Disparities (OOHD) has had a major impact on increasing screening services in our underserved communities and in education of our patients through a series of innovative educational materials. Dr. Maria Jibaja-Weiss, director of the OOHD, created and leads the Community Network for Cancer Prevention that includes most of the academic institutions in the Texas Medical Center, Harris Health and other agencies in the city and county in order to reach as many underserved patients in the community as possible.

Achievement of comprehensive designation would not have been possible without the generous support of the Houston community. In addition to the transformative gift from the Duncan family, additional philanthropic support and hard work in collaboration with our Houston partners has had a profound effect on the growth and maturation of the Duncan Cancer Center. A large group of our supporters, donors and cancer survivors, collectively known as the Cancer Center Advocacy Council, recently was created to continue our relationships and expand them in the community. Perhaps the most exciting new venture is the recently completed the Duncan Cancer Center's Clinical location on the McNair Campus. This new facility was designed as a patient-centered, multidisciplinary, comprehensive clinical care center, bringing together our faculty, staff and their patients in one location to improve patient care. Our vision is to provide services through the continuum of cancer care from risk assessment, including genetic testing and counseling, screening, prevention, diagnosis, treatment, and survivorship, to end-of-life care and support services for the patient and their family. The creation of integrated practice units where the patient visits one clinic site to see all of the physicians and support staff involved in the care of that particular cancer is key to this vision. Optimal care of the cancer patient today requires collaboration and close communication between many different types of physicians: surgical oncologists, medical oncologists, radiation oncologists, radiologists and pathologists as well as physicians and staff from many other disciplines. It is imperative that these doctors practice side by side in the same location in order to provide optimal patient care today. The new clinical venue accomplishes our dream.

This is an exciting time for cancer treatment and research. Technology allows us to interrogate the cancer cell down to the very genes that cause it, thereby providing new treatment targets and new markers of the tumor's aggressiveness. From a genomic standpoint, every tumor has its own fingerprint which then demands individualized and personalized care. Combining compassionate care of the patient and family with expertise in precision cancer medicine and research is the challenge in which the Duncan Cancer Center excels, and we look forward to the future where cancer is no longer a public health problem.

Best regards,

C. Kent Osborne

C. Kent Osborne, M.D.
Director, Dan L Duncan Comprehensive Cancer Center

BREAST CANCER PROGRAM

The side effects many patients experience when they go through chemotherapy treatment are often the most distressing part of their cancer journey, but for certain forms of breast cancer, there may be strategies to deescalate chemotherapy. Researchers in the Breast Center Program in the Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine have uncovered breakthroughs in treating metastatic or locally advanced HER2-positive breast cancer with a combination therapy consisting of less aggressive chemotherapy paired with an aromatase inhibitor and therapies targeting HER2.

"Previous data and research suggest that in breast cancer, the interaction between HER2 and certain estrogen receptor signaling pathways contributes to treatment resistance for these patients," said Dr. Mothaffar Rimawi, co-leader of the Breast Cancer Program and associate professor in the Lester and Sue Breast Center at Baylor. "It was also found that progression-free survival and overall survival rates were higher when HER2-positive metastatic breast cancer patients were treated with first-line pertuzumab, trastuzumab and docetaxel. We are expanding this research to determine effect of adding an aromatase inhibitor during the chemotherapy rather than after, or elliminiating chemotherapy all together."

The primary data from the Phase 2 PERTAIN clinical trial, published in the *Journal of Clinical Oncology*, showed that the combination of pertuzumab, trastuzumab and an aromatase inhibitor is effective and well-tolerated and may offer a novel first-line treatment option for patients with HER2-positive, hormone receptor-positive locally advanced or metastatic breast cancer.

"This was the first study looking at this particular combination, with or without chemotherapy, for the treatment of HER2-positive disease. The results of the phase 2 trial are encouraging because chemotherapy is not always well tolerated by patients, so this allows us to introduce another less toxic agent into treatment and still see positive results as well as improved quality of life for patients," said Rimawi, who also is the medical director of the Lester and Sue Smith Breast Center. "This is an ongoing trial, so we look forward to collecting additional data and moving this therapy forward."

Bringing new alternatives to chemotherapy and improving quality of life for patients undergoing treatment for breast cancer are primary focuses of the Breast Cancer Program. The team works with scientists and physicians across cancer disciplines to develop the most effective and state-of-the-art treatment plans for each patient, which sometimes can include a clinical trial.

"Clinical trials are major focus across all areas of the Dan L Duncan Comprehensive Cancer Center. Conducting cutting edge, multidisciplinary research helps us bring new therapies to the clinic, and clinical trials are a crucial step in moving those therapies into practice," said Dr. Kent Osborne, director of the Dan L Duncan Comprehensive Cancer Center.

Bringing new alternatives to chemotherapy and improving quality of life for patients undergoing treatment for breast cancer are primary focuses of the Breast Cancer Program.

BREAST CANCER PROGRAM

LEADER
Jeffrey Rosen, Ph.D.

CO-LEADER
Mothaffar Rimawi, M.D.

MEMBERSHIP
24 Research members
5 Clinical members
4 Adjunct members

AIMS
Mechanisms of resistance to therapy; Stem cells in normal mammary gland development and breast cancer progression; Estrogen receptor and other signaling pathways in development, prevention and progression of breast cancer; Development of new preclinical metastasis models

RESEARCH FUNDING
NCI: $4.2M
NIH: $0.3M
Peer-Reviewed: $9.2M
Non-Peer Reviewed: $1.8M
Total: $15.7M

THE LESTER AND SUE SMITH BREAST CENTER

The Lester and Sue Smith Breast Center strives to improve prevention, diagnosis and treatment of breast disease while providing top-tier education for future physicians and researchers. Clinically, the center offers comprehensive, compassionate care for women with breast disease and cancer. Clinical research is an integral component of the center, which offers nationwide and regional clinical studies in all aspects of breast health. Currently this group is one of only six recipients nationally of the NIH Specialized Program of Research Excellence (SPORE) Grant in Breast Cancer. Training of physicians, fellows, medical students and other healthcare providers is also an integral function of the Smith Breast Center. Dr. Matthew Ellis, an international leader in breast cancer genomics, was recruited to Baylor in September 2014 to serve as director of the center.

CANCER BIOLOGY PROGRAM

The Cancer Biology Program at the Dan L Duncan Comprehensive Cancer Center focuses its research on understanding the complex genetic and biological pathways that control cancer cells. Its researchers use a variety of sophisticated techniques to study the tumor's DNA, RNA and proteins together with a variety of model systems in the laboratory to clarify the cancer "drivers" and then develop new drugs targeting those pathways.

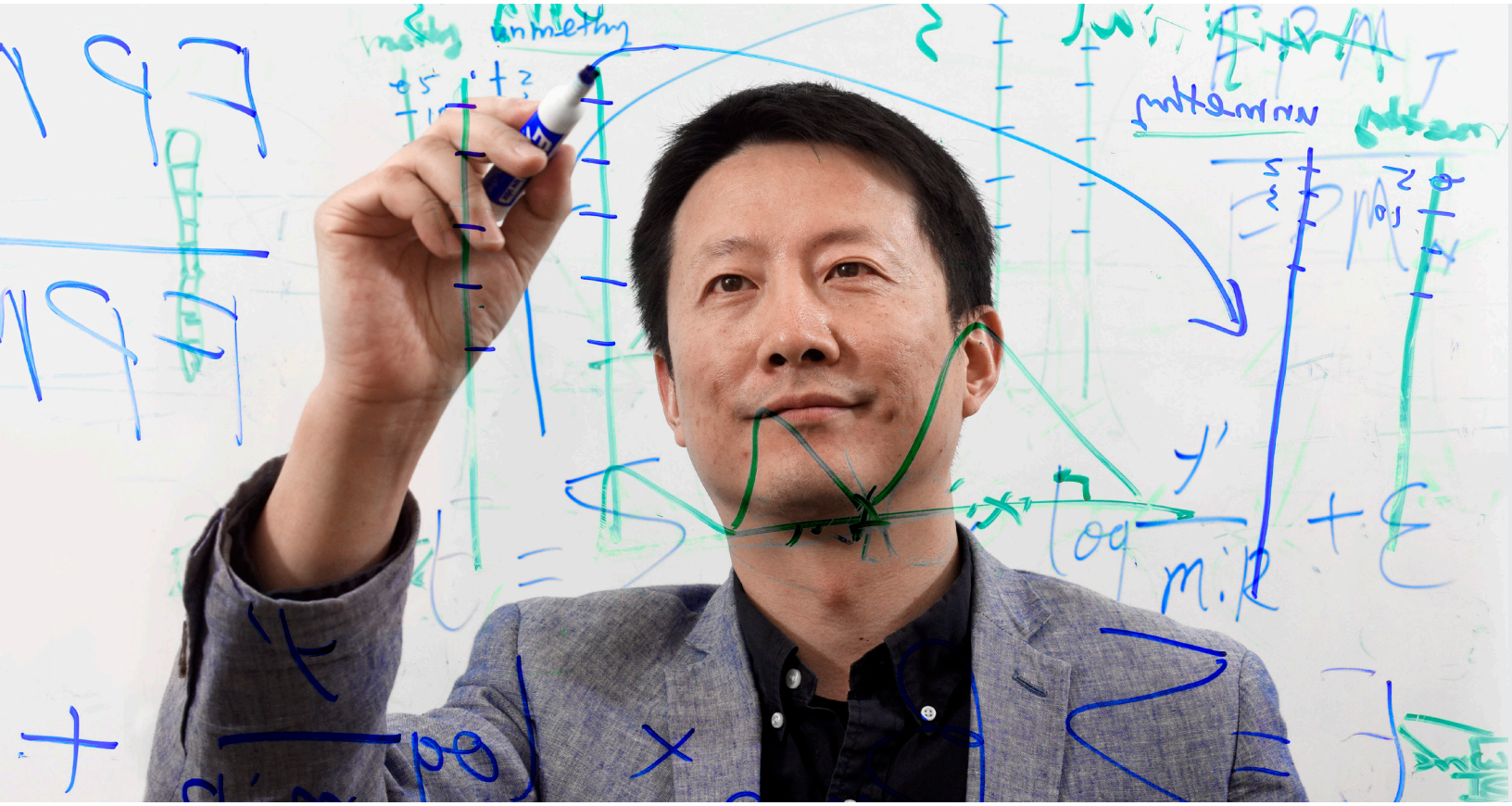
Through his work, Duncan Scholar Dr. Wei Li, professor in the Dan L Duncan Comprehensive Cancer Center at Baylor and an expert in bioinformatics, has contributed an out-of-the-box research approach that is revolutionizing the way researchers believe tumors develop.

Scientists for years have conducted translational research by studying the cancer by means of basic science. By studying cultured cells in test tubes, animals or even fruit flies they've been able to make basic discoveries that can then be translated to human cancer patients to improve their outcome. Sometimes the laboratory model, however, doesn't translate to a human outcome, as our biology can be different from that of a cultured cancer cell or a laboratory mouse, for instance.

Li uses novel bioinformatics algorithms to analyze existing genomic data, called "Big Data," from patients. He and his team hypothesized that by applying bioinformatics algorithms to patients' genomic sequencing data, results would offer a more accurate understanding of the biology of cancer cells. They termed this strategy "reverse translational research."

Li and his colleagues focused on identifying mechanisms that could disrupt the normal regulation of gene expression and the proteins that carry out the genes' instructions. The researchers began looking at RNA data from human tumors and found a huge loss of mRNA at the three-prime untranslated region, or 3'UTR, which is a section of mRNA that can alter gene expression into proteins.

"The entire cancer community has never paid attention to this huge genetic loss of this segment of RNA," Li said. "Traditionally, much attention has been focused on studying mutations in these genes that can either promote or suppress cancer development, but this approach has not been sufficient to explain



all cancers. We took a different approach."

That is when Li teamed up with the University of Texas Medical Branch in Galveston to develop a mouse model experiment to validate what they found from patient "Big Data."

"We used both a computational biology approach to analyze large amounts of genetic data along with classical molecular experiments in the laboratory," said first author Dr. Hyun Jung Park, who was a postdoctoral associate in the Li lab during the development of this project and currently is an assistant professor of human genetics at the University of Pittsburgh. "Our statistical model accurately predicted gene expression changes mediated by mRNA 3'UTR shortening in human breast cancer, particularly the repression of the expression of tumor suppressor genes."

The laboratory studies provided a functional validation of these predictions, confirming 3'UTR shortening plays a major role in leading to the repression of tumor suppressor genes; genes that normally suppress development of cancer but when lost or repressed allow cancers to form.

"A big focus of the Cancer Biology Program is to facilitate communication among scientists that leads to research collaborations, which will hopefully then lead to new discoveries more rapidly and eventually to new diagnostics and therapeutics," said Dr. David Rowley, professor of cellular and molecular biology and leader of the Cancer Biology Program. "This research illustrates successful collaborations with other institutions, as well as within the Dan L Duncan Comprehensive Cancer Center itself."

"We think that our findings can lead to new treatment or prevention strategies to overcome the effects of the 3'UTR shortening mechanism, and thus restore the expression of tumor suppressor genes involved in breast and other cancers," Li said.

CANCER BIOLOGY PROGRAM

LEADER
David Rowley, Ph.D.

CO-LEADERS
Michael Ittmann, M.D., Ph.D.
Cheryl Walker, Ph.D.

MEMBERSHIP
53 Research members
22 Clinical members
7 Adjunct members

AIMS
New discovery; Actionable targets; Translation

RESEARCH FUNDING
NCI: $4.8M
NIH: $4.1M
Peer-Reviewed: $8.9M
Non-Peer Reviewed: $2.8M
Total: $20.7M

CANCER CELL AND GENE THERAPY PROGRAM

The goal of the Cancer Cell and Gene Therapy Program in the Dan L Duncan Comprehensive Cancer Center is to rapidly but safely move basic research into clinical translational studies and to share its core scientific expertise in cell and gene therapies with other centers. The program is organized into three major themes: normal and malignant stem cell biology, adoptive cellular immunotherapy of cancer, and improving the outcome of hematopoietic stem cell transplantation.

Clinical trials are an important way to blend the program's basic research and clinical translational studies. One such study underway in Phase 1 is already giving hope for improved treatment for Hodgkin's lymphoma, including to one trial participant, David Cross.

For 10 months in 2015, Cross battled progressive excruciating pain at his home in Florida. He was passed from local general physicians to internists to rheumatologists and had numerous scans and several biopsies before finally being told he had stage IV Hodgkin's lymphoma.

Cross was diagnosed on a Friday in 2016. He saw his oncologist the following Monday. By that Thursday, one of his metastasized tumors had grown so quickly that it pressed on his spinal cord, causing paralysis less than a week after diagnosis. The next Monday, he began a standard treatment of chemotherapy. The chemotherapy allowed the tumor by his spine to shrink enough so he could regain his mobility, but did little else to slow or stop his cancer. Determined to continue fighting, Cross tried a checkpoint inhibitor immunotherapy called Nivolumab. While Cross had positive results with Nivolumab, his regular scans were never stable and his cancer was slowly progressing. That is when Cross started searching for another option.

After searching clinical trials on the internet, Cross found Dr. Carlos Ramos, physician and associate professor at the Center for Cell and Gene Therapy (CAGT). Dr. Ramos is conducting a Phase 1 Clinical Trial targeting CD30, a cell membrane protein expressed in most Hodgkin's lymphomas.

Ramos and his team have engineered T cells, which are instrumental in the body's immune response and ordinarily kill cells infected by pathogens to prevent their spread. These engineered T cells express a new protein called a chimeric antigen receptor, or CAR. The CAR in the T cells acts like Velcro and binds together the T cells with the CD30 in the tumor cells. Once the two cells are bound together, the CAR-T cells become activated and attack and kill the cancer.

After speaking with Ramos by phone, Cross boarded a plane in June 2017 to participate in the CD30 Clinical Trial. He gave 24 vials of blood, providing Ramos' team plenty of blood to engineer his CD30 CAR-T cell immunotherapy, before flying back to his home in Florida.

It took Ramos' team two months to grow Cross' therapy in the Good Manufacturing Practice (GMP) laboratory, a cell and vector production shared resource of the Duncan Cancer Center, and complete all the safety and activity testing. He was scheduled to fly back for his treatment at the end of August 2017, when Hurricane Harvey landed on Houston, dropping more than 50 inches of rain in a matter of days. The storm flooded one-third of Houston, making travel in and out of the city virtually impossible. However, the Texas Medical Center had installed safety measures, learning from catastrophic damage done in the 2001 flooding of Tropical Storm Allison, protecting most research and infrastructure from future flooding. Because of those measures, Cross' CD30 CAR-T cell immunotherapy was only

> "I feel really good. My energy level is good. I've gained about 15 pounds back. I'm moving forward and doing things like learning to fly a plane."
>
> **-DAVID CROSS**

delayed a week.

In September 2017, Cross received 41 million CAR-T cells in a single treatment. Ramos observed him for two weeks for any negative reactions to the therapy before Cross flew home. Cross is now in remission, after that single treatment.

“I feel really good. My energy level is good. I’ve gained about 15 pounds back,” Cross said. “I’m moving forward and doing things like learning to fly a plane.”

“Six out of nine patients had positive results, that is complete responses, in this clinical trial,” Ramos said. “It’s remarkable because Phase 1 trials usually only have at most a 10 percent positive response rate or so. We still don’t know if this approach can cure patients with this type of cancer, but the results are very encouraging. A Phase 2 trial would help determine that.”

Dan L Duncan Chair Dr. Helen Heslop, associate director of clinical research and leader of the Cancer Cell and Gene Therapy Program, said, “This trial is an example of an approach that was developed in the CAGT laboratories, translated to the clinic with the help of Bambi Grilley and the regulatory group and Adrian Gee, Zhuyong Mei and the GMP facility and is now showing very promising results in patients.”

“Dr. Ramos really cares about his patients. All of his staff were great. I went there expecting to be a lab rat, but I never felt that way,” Cross said. “Without the CD30 immunotherapy, I would be dead or on Nivolumab every two weeks forever.”

David Cross at Aviation School

CANCER CELL AND GENE THERAPY PROGRAM

LEADER
Helen Heslop, M.D.

CO-LEADER
Margaret Goodell, Ph.D.

MEMBERSHIP
21 Research members
9 Clinical members
1 Adjunct members

AIMS
Normal and malignant stem cells;
Adoptive immunotherapy of cancer;
Improving outcomes of stem cell transplantation for cancer

RESEARCH FUNDING
NCI: $2.3M
NIH: $5.4M
Peer-Reviewed: $5.3M
Non-Peer Reviewed: $8.9M
Total: $22M

CENTER FOR CELL AND GENE THERAPY

As a collaborative initiative between Baylor, Texas Children’s Hospital and Houston Methodist Hospital, the Center for Cell and Gene Therapy brings together the resources of all three institutions. Established in 1998, the center has expanded to employ more than 40 clinical and research faculty members and 300 staff members. Patient facilities include the adult stem cell transplant unit at Houston Methodist Hospital and the pediatric stem cell transplant unit at Texas Children’s Hospital. The center is a major component of the translational Cancer Cell and Gene Therapy Program in Baylor’s Duncan Cancer Center.

CANCER EVOLVABILITY PROGRAM

The charge of the Cancer Evolvability Program in the Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine is to understand processes that generate variation among cells that enables them to evolve by variation and selection, including evolution of cancers and resistance to therapeutics. Understanding mechanisms that propel evolution may lead to new therapies to slow cancer evolution and provide new ways to diagnose cancers early and identify at-risk individuals.

In new research published in the journal *Cell*, a team of researchers led by Cancer Evolvability Program labs at Baylor College of Medicine and the University of Texas at Austin applied an unconventional approach that used bacteria to discover human proteins that can promote cancer.

"We discovered a new major class of cancer-promoting genes, by showing that many normal proteins made by our cells can act like carcinogens—they damage DNA and cause mutations," said Dr. Susan M. Rosenberg, leader of the Cancer Evolvability Program, Ben F. Love Chair in Cancer Research and professor of molecular and human genetics, of molecular virology and microbiology and of biochemistry and molecular biology at Baylor. "Cancer is a disease of mutations. A normal cell that has accumulated several mutations in particular genes becomes likely to turn into a cancer cell."

Mutations that cause cancer can be the result of DNA damage. External factors such as tobacco smoke and sunlight can damage DNA, but most DNA damage seems to result from events that occur within cells and is mediated by cellular components, including proteins.

"Overproduction of one or another protein is a frequent cellular event," said Rosenberg. "In this project, we set out to uncover proteins that, when overproduced by the cell, cause damage to DNA in ways that can lead to cancer."

To uncover proteins that promote DNA damage in human cells, the researchers searched first for proteins that can cause DNA damage in the bacterium E. coli.

"Although bacteria and people are different, their basic biological processes are similar, so with this approach we thought we might find common mechanisms of DNA damage that could be relevant to cancer," Rosenberg said. "This was a wild idea."

By genetically modifying bacteria to glow red when DNA was damaged, then overexpressing each of the 4,000 genes that make up E. coli individually, the researchers could determine which genes made the bacteria glow when overexpressed.

"We uncovered an extensive and varied network of proteins that can lead to DNA damage," Rosenberg said. "Some of these proteins are, as expected, involved in DNA processing or repair, but, surprisingly, most are not directly connected to DNA."

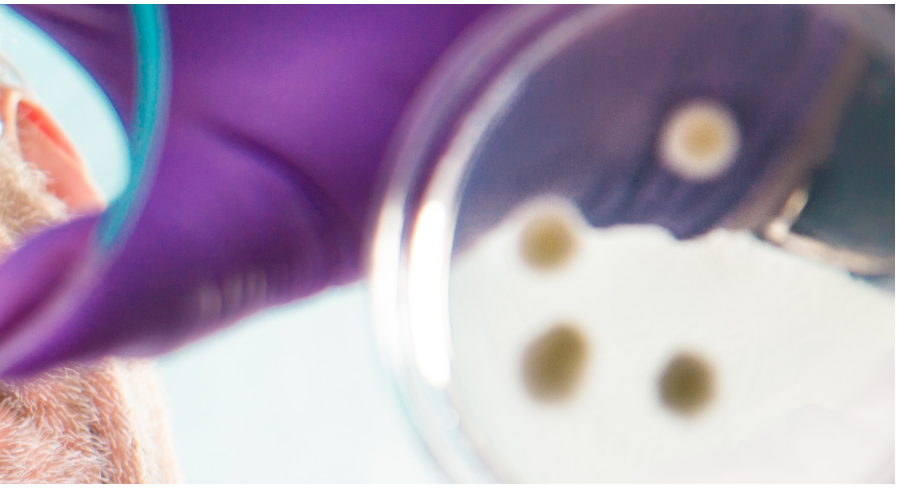
Further investigations uncovered 284 human protein relatives of the DNA "damage-up" proteins the researchers had found in bacteria. These human proteins are linked to cancer more often than random sets of proteins. Also, when overproduced in human cells in the lab, half of the proteins triggered DNA damage and mutation.

"E. coli can help identify DNA damage-up proteins and mechanisms of action in human cells quickly and inexpensively," said Dr. Christophe Herman, professor of molecular and human genetics and molecular virology and microbiology at Baylor, co-corresponding author and member of the Cancer Evolvability Program in the Dan L Duncan Comprehensive Cancer Center.

"I think it is extraordinary to identify so many ways DNA can be damaged. This study is opening up new avenues for discoveries of novel mechanisms that protect our genomes and how their dysfunction can alter the integrity of our DNA and cause cancer," said Cancer Evolvability Program member and co-corresponding author Dr. Kyle M. Miller. Other Cancer Evolvability Program members who participated include Dr. David Bates, associate professor of molecular and human genetics, and Dr. Philip Hastings, professor of molecular and human genetics.

"In the future, this finding may lead to new ways to identify people who are likely to develop cancer so that strategies to prevent it, slow it down or catch it early can be used," Rosenberg said. "This work reflects the central goal driving the Cancer Evolvability Program: to identify novel understandings of the evolution of tumors, which supports their growth."

This out-of-the-box approach was made possible by funding from two sources aimed at supporting high-risk strategies that, if successful, would have high impact: a National Institutes of Health Director's Pioneer Award and a gift from the W.M. Keck Foundation, among many other grants to the 16-lab team.



CANCER EVOLVABILITY PROGRAM

LEADER
Susan M. Rosenberg, Ph.D.

CO-LEADER
Elizabeth Yu Chiao, M.D., M.P.H.

MEMBERSHIP
30 Research members
1 Clinical members
1 Adjunct member

AIMS
Intrinsic: Genome and Phenotypic Plasticity (mutation, genome rearrangement, recombination, epigenetic and stochastic protein and RNA variation); Extrinsic: Infectious Oncogenesis and Microbiome, in which introduction of foreign genes, proteins, RNAs, and other molecules and genetic programs by infectious agents (viruses, microbes, microbiome) promote (or prevent) oncogenesis

RESEARCH FUNDING
NCI: $1.1M
NIH: $11.9M
Peer-Reviewed: $1.1K
Non-Peer Reviewed: $0.5M
Total: $14.8M

CANCER PREVENTION AND POPULATION SCIENCES PROGRAM

The mission of the Cancer Prevention and Population Sciences Program (CPPS) is to conduct transdisciplinary research focusing on vulnerable populations, especially children and young adults, high-risk families, the medically underserved and cancer survivors. The goal is to reduce cancer incidence and mortality, improve health behaviors and cancer outcomes.

One way the CPPS Program is aiming to accomplish this mission by helping to lead the Texas Hepatocellular Carcinoma Consortium (THCCC).

Hepatocellular cancer (HCC) is the most common (greater than 95 percent) of primary liver cancers. HCC is also the fastest rising cause of cancer-related deaths in the United States, and Texas has the highest death rate from HCC in the nation. Texas residents, notably Hispanics and African Americans, are greatly affected with established HCC risk factors, including hepatitis C virus, hepatitis B virus and alcoholic liver disease. Furthermore, emerging HCC risk factors, specifically the metabolic syndrome and non-alcoholic fatty liver disease, are exceptionally common in Texas.

The THCCC was established to reduce the death and suffering related to liver cancer in Texas by conducting cutting-edge collaborative research. The THCCC includes researchers, clinicians and staff from the Dan L Duncan Comprehensive Cancer Center, the Michael E. DeBakey Veterans Affairs Medical Center, MD Anderson Cancer Center, University of Texas Southwestern Medical Center, Parkland Health Hospital System in Dallas and University of Texas San Antonio. The consortium has been funded by Cancer Prevention and Research Institute of Texas (CPRIT), and recently secured additional funding from NIH.

Dr. Hashem El-Serag, Margaret and Albert Alkek Distinguished Professor and chair of the Department of Medicine at Baylor and a past holder of a Duncan Professorship, is the overall THCCC leader and is leading one of the five projects in the Consortium. He is tasked with developing categories of risk algorithms based on demographic, clinical, molecular and epidemiological risk factors to identify cirrhosis patients who might benefit from prevention or intensive surveillance.

Utilizing several recruitment centers across the state, El-Serag and his team have recruited and followed 1,700 patients in the course of four years, studying relevant risk factors. Obesity, he says, is fueling this sharp increase in liver cancer morbidity in the state.

“For the first time, we are looking at obesity as not only a precursor for diabetes, heart attacks and strokes, but we’re seeing actual scientific evidence it raises your risk of certain types of cancer, mainly gastrointestinal cancers,” El-Serag said.

El-Serag’s team goal is to recruit 5,000 patients by 2020. With additional recruitment sites opening throughout Texas, they think that number is attainable.

With HCC growing in numbers everyday, El-Serag wants to tighten the belt of this burgeoning disease.

“We’re witnessing a true epidemic of a deadly cancer, which is being fueled by the epidemic of obesity in the state of Texas,” El-Serag said.

CANCER PREVENTION AND POPULATION SCIENCES

LEADER
Melissa Bondy, Ph.D.
McNair Scholar

CO-LEADER
Hoda Badr, Ph.D.

MEMBERSHIP
33 Research members
11 Clinical members
1 Adjunct members

AIMS
Cancer risk factors; Cancer outcomes; Integration of Quantitative Sciences

RESEARCH FUNDING
NCI: $7.2M
NIH: $6.3M
Peer-Reviewed: $9.4M
Non-Peer Reviewed: $2.8M
Total: $25.8M

PEDIATRIC CANCER PROGRAM

The definition of a rare tumor is that there are a few patients diagnosed with this tumor compared to other types of cancer, and there is often no known course of treatment. When physicians and researchers at Texas Children's Cancer and Hematology Centers, who comprise the Pediatric Cancer Program in the Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine, encounter a tumor they have rarely, or sometimes never, seen, the race is on to use research to identify the most effective course of action by studying the tumor's make up and identifying similarities with known tumors.

Eden Green first came to Texas Children's Cancer Center in June 2015, when she was just 10 years old, with pain in her shin. Dr. Jennifer Foster, assistant professor of pediatrics-oncology in the Pediatric Cancer Program, worked with her colleagues in pediatric surgery and pediatric pathology to biopsy and diagnose Eden's tumor. However, when the team looked at the tumor under the microscope, it did not clearly meet the criteria for common tumors in the area. The team also did sophisticated state-of-the-art genomic studies on her tumor, which did not provide any additional insights as to the tumor type.

Finding insight in research

"We knew the tumor in Eden's shin was cancerous and quickly spreading throughout her body, but it didn't have characteristics associated with any cancer that the team had seen or treated previously. It looked like a combination of sarcoma and neuroblastoma, so that's where we started," said Foster.

Eden's care team treated her tumor with a combination of chemotherapies known to be effective in fighting pediatric sarcoma and neuroblastoma, and her cancer responded well, disappearing from scans all together.

A few years later, in May 2018, Eden began having shoulder pain. Unfortunately, a scan revealed Eden's tumor had recurred, with cancer now invading her shoulder blade.

Eden Green with her Dr. Jennifer Foster

"We knew we had to take a different treatment approach because these cancer cells had escaped from or adapted to the first treatment approach," said Foster. "We wanted to add a promising new investigational agent to her chemotherapy, which required enrolling her in a clinical trial."

Piecing together the puzzle

A seed grant from Baylor College of Medicine helped fund Foster's research and supported the preclinical laboratory work necessary to develop the background for the clinical trial of this promising new agent. The project was further supported by Alex's Lemonade Stand Foundation, which provided the requisite funding that Foster and her colleagues needed to develop and initiate the clinical trial in which Eden was ultimately enrolled.

"Financial resources are crucial to developing clinical trials for promising new agents to treat children like Eden who have some of the most difficult to treat cancers. The other critical component of their treatment is an expert, dedicated multidisciplinary team. The Pediatric Cancer Program in the Dan L Duncan Comprehensive Cancer Center and Texas Children's Hospital has both of these. As a result, physicians and scientists across many specialties routinely come together to share clinical and research knowledge that enables them to develop the most comprehensive, cutting edge approach to each patient's case," said Dr. Susan Blaney, director of Texas Children's Cancer and Hematology Centers, professor of pediatrics at Baylor and leader of the Pediatric Cancer Program.

Eden was enrolled in the clinical trial in June 2018. Her treatment has consisted of a combination of chemotherapy and pevonedistat, an enzyme inhibitor that is designed to prevent tumor cells from replicating. She continues to benefit from the treatment she is receiving on this trial.

"When Eden's cancer came back, we knew we needed to do something to stop it in its tracks. The clinical trial has offered us that option," said Shannon Green, Eden's mother.

"Participating in this clinical trial has not only provided hope for our family, but we are part of a learning process that will impact the treatment of countless childhood cancer patients in the future. That's a really powerful thing," Shannon added.

PEDIATRIC CANCER PROGRAM

LEADER
Susan Blaney, M.D.

CO-LEADER
Sharon Plon, M.D., Ph.D.

MEMBERSHIP
28 Research members
18 Clinical members
0 Adjunct members

AIMS
Three disease-focused themes: biologic and therapeutic studies of solid tumors, neuro-oncology and leukemia and lymphoma; two discipline-based themes: cancer genetics and genomics and developmental therapeutics, and childhood cancer survivorship.

RESEARCH FUNDING
NCI: $3.5M
NIH: $1.4M
Peer-Reviewed: $3.2M
Non-Peer Reviewed: $5.9M
Total: $14.1M

TEXAS CHILDREN'S CANCER CENTER

Texas Children's Cancer Center (TCCC) is a joint program of Baylor and Texas Children's Hospital and is the Pediatric Cancer Program of the DLDCCC. As the largest pediatric cancer center in the country, it is consistently ranked as one of the best pediatric cancer programs in the U.S. by U.S. News and World Report. With world-renowned faculty who have pioneered many of the now standard protocols for treating pediatric cancer, TCCC performs advanced patient care, cutting edge clinical and laboratory research and has the largest training program in pediatric hematology-oncology in the country. Additionally, the TCCC has a long-standing commitment to improving global health and collaborates with nine African countries.

Texas Children's Hospital®

NUCLEAR RECEPTOR PROGRAM

The primary goals of the Nuclear Receptor Program are to promote rapid translation of basic discoveries on the role of nuclear receptors in cancer development, and to develop novel receptor-targeted therapies for cancer prevention and therapeutic intervention.

"In the 1920s, Otto Warburg and his colleagues discovered that cancer cells consume larger amounts of glucose than normal cells, and most cancer cells process it via fermentation," said Dr. Bert O'Malley, senior author of a paper on this subject in the journal *Nature*. O'Malley is chancellor at Baylor College of Medicine and professor of molecular and cellular biology, where he served as longtime department chair, and he is the Thomas C. Thompson Chair in Cellular Biology and associate director of basic research in the Dan L Duncan Comprehensive Cancer Center at Baylor.

To generate energy from glucose, cells can use one of two pathways. One of them takes place in the mitochondria, the energy-producing structures inside cells, and yields significantly more adenosine triphosphate, or ATP, an energy-carrying molecule found in all organisms, than the second pathway, called fermentation. Normal cells mostly use the path in the mitochondria, but about 80 percent of cancer cells seem to have revamped their metabolism to preferentially generate energy via fermentation. This phenomenon is known as the Warburg effect.

The Warburg effect has been a mystery for quite some time. Why would cancer cells, which need large amounts of energy to sustain their growth, prefer to use a pathway that produces less ATP than another available pathway? What would be the advantage for cancer cells to use the Warburg pathway? This study sheds new light on this mystery.

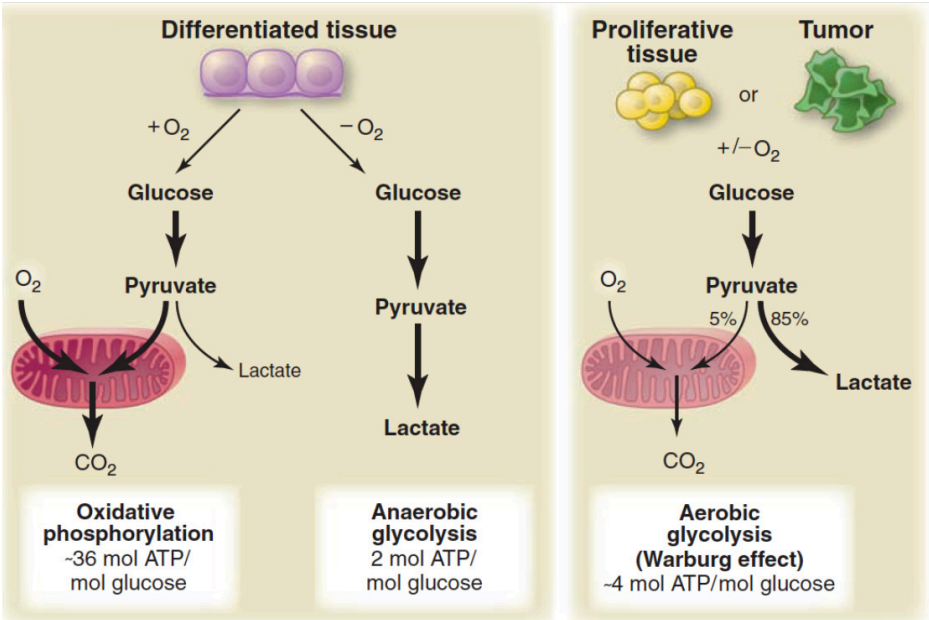
The Warburg pathway – cancer connection

Years ago, the O'Malley laboratory identified SRC-3, a protein that is an important regulator of gene expression. SRC-3 is overproduced in most cancer cells and this transforms it into an oncogene; it can turn on genes involved in abnormal growth, invasion, metastasis and resistance to anti-cancer drugs. If cancer cells modify SRC-3, for example by adding a phosphate chemical group to it, then SRC-3 becomes hyperactive, a hallmark of many tumors.

"We conducted an unbiased search to identify enzymes that add phosphate groups that are able to enhance the activity of SRC-3," said first author Dr. Subhamoy Dasgupta, who was a trainee and junior faculty while he was working on this project in the O'Malley lab and currently is an assistant professor of cell stress biology at Roswell Park Comprehensive Cancer Center.

"We were surprised to identify an enzyme named PFKFB4 as one of the most dominant regulators of SRC-3. This was unexpected because PFKFB4 was well known for its ability to only add phosphate groups to sugars in the Warburg pathway. Nobody had described before that this enzyme could also add phosphate groups to proteins," Dasgupta said.

Otto Warburg



Warburg Effect

"When PFKFB4 adds a phosphate group to SRC-3, it transforms it into a potent driver of breast cancer and other cancers as well," O'Malley said.

"I am most excited about our findings regarding breast tumor progression in mouse models," Dasgupta said. "Our data shows that by removing PFKFB4 or SRC-3 from the tumors, we are able to almost completely eliminate recurrence and metastasis of breast cancer. In addition, modification of SRC-3 so that it cannot receive a phosphate group, also results in control of the tumor."

These and other findings allowed the researchers to connect for the first time the Warburg pathway to cancer growth.

"One of the most interesting things to me is that we have solved some of this nearly 100-year-old mystery," O'Malley said. "Also, our findings give us more potential intervention points for future therapies. This is important because breast cancer recurrence and metastasis are clinically challenging problems.

"Previous studies by the O'Malley group have uncovered critical functions of the coregulator protein SRC-3 in promoting growth, invasion and metastasis of prostate, lung and breast cancers," said Dr. Orla Conneely, leader of the Nuclear Receptor Program. "These studies highlight SRC-3 as a potential target for cancer therapy. The current seminal study by this group now provides a novel mechanistic link between metabolic Warburg associated glycolytic pathway reprogramming in cancer cells and epigenetic activation of SRC-3 driven oncogenic transcriptional programs to drive cancer cell growth and metastasis. The studies reveal that metabolic intervention may provide a novel strategy to inhibit SRC-3 driven oncogene activity."

Bert O'Malley

NUCLEAR RECEPTOR PROGRAM

LEADER
Orla Conneely, Ph.D.

CO-LEADERS
Suzanne Fuqua, Ph.D.
Nicholas Mitsiades, M.D., Ph.D.

MEMBERSHIP
22 Research members
2 Clinical members
1 Adjunct members

AIMS
The identification of nuclear receptors that contribute to cancer pathogenesis and progression, disclosure of their molecular mechanism of action, and evaluation of their potential as novel targets for therapeutic intervention in cancer. The characterization of nuclear receptor coregulator-dependent epigenetic mechanisms of cancer development.

RESEARCH FUNDING
NCI: $6.4M
NIH: $2.2M
Peer-Reviewed: $4.5M
Non-Peer Reviewed: $6.4M
Total: $19.7M

OFFICE OF OUTREACH

AN INTEGRAL PART of the mission of both the Dan L Duncan Comprehensive Cancer Center and Baylor College of Medicine is to reach and prevent disease in Houston's underserved community. The DLDCCC's cancer prevention and outreach activities are led by the Office of Outreach and Health Disparities (OOHD). This team of eight implements innovative programs, such as a theater outreach program, culturally and linguistically-appropriate patient education materials and videos designed for use in the exam room, as well as patient navigation. These programs, particularly the theater outreach program, are implemented in the community and within clinical settings with partnering health systems and clinics. Harris Health System, our county's safety net health system, is the OOHD's primary clinical partner.

"We value the strong partnerships we've built over the years, bridging academic institutions with public and community-based institutions," said Dr. Maria Jibaja-Weiss, director of the Office of Outreach and Health Disparities.

The patient navigation program, which is implemented in the Harris Health System, is a tiered system that involves tracking patients, conducting reminders for upcoming appointments, calling patients who didn't attend their appointment, and assisting patients with barriers to care through patient navigation. The goal of this program is to get patients in the door for necessary screenings and diagnostic follow-up for colorectal, cervical, breast and liver cancers, as well as to ensure completion of the human papillomavirus (HPV) vaccine series.

"We're very fortunate in Harris County to have a state-of-the art safety net healthcare system, but it can be complicated to navigate, especially for those with language barriers," said Dr. Jane Montealegre, deputy director of the OOHD. "Before our program, it really was up to patients to figure out how

BodyGuards (an OOHD volunteer program for Baylor students) assisting attendees at Peck Elementary health fair with OOHD staff member Ivan Valverde.

AND HEALTH DISPARITIES

to navigate the system and follow up with their abnormal screening test. Now, there is a team that proactively tracks all of those patients and makes sure they are able to get the follow-up they need."

The patient navigators are instrumental in getting patients in to appointments, especially after a positive cervical, colorectal or Hepatitis B and C screening results. The navigators then go a step further by intervening at both the patient and provider levels; making future appointments and ensuring doctors have submitted the patient's next steps, whether for testing, treatment or referrals.

The patient navigation program works hand-in-hand with the patient education program, which strives to provide patient-centered, culturally appropriate education around cancer screening and prevention. Educational and screening materials reach a large number of underserved populations. In 2017, more than 75,000 Fecal Immunochemical Test (FIT) kits were distributed and completed by 42,000 patients.

"Sometimes I look at these numbers and I'm astounded. That seems incredible, but we are delighted to be making such a difference," Jibaja-Weiss said.

These combined strategies are paying off for the OOHD. For example, from 2010 to 2017, the Harris Health System achieved a more than two-and-a-half fold increase in proportion of age-eligible patients screened with pap tests. The work in the cervical program also achieved profound decreases in the proportion of screen-positive patients who were lost to follow-up care. Similar gains have been observed for colorectal cancer screening and the HPV vaccine, where more than 80 percent of age-eligible children receive the first dose of the vaccine.

The plan for the OOHD is to continue to expand these strategies and keep achieving measurable gains in cancer screening and prevention among the medically underserved. The work is rewarding and the team is happy that it is having such a large impact on the care provided by Harris Health and its other clinical partners.

Actor Ray Walker in between takes, while filming "The Bottom Line," a colorectal cancer awareness monologue that aims to provide information to the African-American population about screening for colorectal cancer.

PROTEOGENOMICS

PRECISION MEDICINE is a modern buzz word, but what does it really mean? In the Proteogenomics Center at Baylor College of Medicine, it is about the drive toward a more accurate diagnosis so the patient gets the correct treatment. In the setting of cancer care, increased precision is a critical focus, as so many more traditional treatments are not very precise. The standard approaches of surgery, radiation and chemotherapy, while somewhat effective, carry a burden of immediate side effects and often long-term debilitating problems that impair quality of life. Thus, an early example of a precision medicine tool developed in the last decade are prognostic "gene signatures," which are reliably deployed to dramatically reduce the use of chemotherapy in breast cancer patients assigned "low-risk."

Another inspirational focus point in cancer treatment has been the development of treatments that are precisely matched to the biology that caused the cancer initially. Dramatic changes in a cell's chromosomal structure are called disease drivers. Without them the cancer would not exist, and drugging them is dramatically effective. This understanding propelled the notion that ever deeper analysis of the cancer's DNA could deliver the answer for everyone, a goal which we are are still working tirelessly towards.

"The problem with current diagnostic approaches to cancer is that they do not measure enough cancer biology," says Dr. Matthew Ellis, McNair Scholar and director of the Lester and Sue Smith Breast Center at Baylor. "After all, DNA is not actually responsible for executing the cancer phenotypes but rather proteins do the job, interacting in complex ways in tiny natural nanoscale devices we call cancer cells."

Thus, the advancement of precision medicine is served by measuring more biology and using computer science to organize the data, creating a virtual therapeutic road map. The field of cancer proteogenomics therefore rests on key technical advances, including a huge improvement in mass spectrometry instrumentation that measures proteins through peptide sequencing and cloud-based computing. DNA, RNA and peptide data from an individual cancer is temporally uploaded to a massive commercial server farm to run algorithms that integrate the data and identify the deregulated pathways in hours rather than days.

"The increased peptide sequencing depth available from the latest instruments is driving a microscaled approach, such that from a core biopsy weighing less than 20 grams we can obtain data on over 10,000 proteins. Amazing, when you consider that today a breast cancer is subtyped based on only three to four proteins,"explained Ellis.

Research at Baylor is showing proteogenomics can unravel deeper levels of cancer biology in clinical specimens, identify new molecules involved in breast cancer and prompt new avenues for drug development. Baylor College of Medicine and the Dan L Duncan Comprehensive Cancer Center are world leaders in proteogenomic approaches to translational medicine, which is at the core of the precision medicine approach we are developing," said Ellis.

Proteogenomics is an ambitious initiative across the nation. The National Cancer Institute's (NCI) Clinical Proteomic Tumor Analysis Consortium (CPTAC), of which Baylor is a member, centers on using the analysis of genomic and proteomic data to eventually help solve clinically relevant cancer questions, such as drug response and drug sensitivity.

"The CPTAC program encourages and allows multiple institutions to come together to share and contribute varied types of data, which is then studied and analyzed in a cooperative, mutually beneficial way," said Dr. Bing Zhang, McNair Scholar and professor in the Lester and Sue Smith Breast Center and of molecular and human genetics at Baylor.

One of the key pillars of CPTAC is a group of institutions called the Proteogenomic Translational Research Centers (PTRCs), which furthers the convergence of proteomics with genomics to better understand the molecular basis of cancer and accelerate research in these areas by

spreading research resources within the scientific community. Among these PTRCs is the Lester and Sue Smith Breast Center, part of the Dan L Duncan Comprehensive Cancer Center at Baylor.

The PTRC at Baylor is jointly run by Ellis and Dr. Steve Carr at the Broad Institute and focuses on breast cancer specifically. The two institutions, alongside other PTRCs, work to generate, analyze and apply proteogenomics data to core biopsy specimens to further understand the behavior and functions of cancer cells in the advancement of precision oncology, through the analysis of NCI-sponsored clinical trial specimens.

“As a Proteogenomic Translational Research Center, we are transitioning the proteogenomics technology and bioinformatics from a research tool into clinical utility, giving us a dramatically deeper look at what the cancer cells are doing in patients,” said Ellis, “The ability to access clinical trial samples from the NCI will help us achieve big wins in cancer research by getting definitive answers on the clinical utility of proteogenomics in larger populations with well documented patient outcomes.”

Whereas the PTRCs integrate clinical trial data and clinical implications, the Proteogenomic Data Analysis Centers (PGDACs), another pillar of the CPTAC, focus on applying algorithms and computational tools to develop proteogenomic data to help the NCI expand its study of clinical trial and tumor samples beyond the existing colon, breast and ovarian cancer data sets CPTAC has already published.

In addition to the PTRC, Baylor also has a CPTAC-funded PGDAC led by Zhang, who is the primary investigator. The physical proximity of the facilities and research teams is beneficial to the project, encouraging integration among groups of scientists.

The CPTAC program is the largest effort in the nation to advance precision medicine through proteogenomics. Through the PTRC and PGDAC sites, Ellis and Zhang and their teams will develop novel bioinformatics infrastructure for the integrative analysis of cancer genomic and proteomic data to advance cancer research and clinical care.

Proteogenomic analyses, where Zhang’s group has done pioneering work, require momentous bioinformatics effort and innovation to help researchers sift through the wealth of ‘next-generation’ data and pinpoint only the most critical, causal and targetable molecular events.

“It’s an entirely new way of looking at clinical specimes to direct therapies,” said Ellis. “Not only are these centers executing very exciting work, but Baylor is the only site involved in this project in the south of the country, which speaks volumes to our strengths in both clinical science, translational medicine and computational biology.”

CENTER FOR PRECISION

THE CENTER for Precision Environmental Health focuses on the relationship among genes, environmental exposures that may lead to disease development and big data, with an overall objective to pair the right drug with the right patient to treat a particular disease. Through this work, it serves as an important partner to the Dan L Duncan Comprehensive Cancer Center.

Baylor College of Medicine scientist Dr. Dan Gorelick, assistant professor with the Center for Precision Environmental Health, studies the relationships among hundreds of thousands of environmental exposures and big data and their relationships to genes in humans. However, studying this information in humans or even other animal models isn't possible, so Gorelick instead relies on data he retrieves from zebrafish.

"You may be wondering exactly how a zebrafish's anatomy could possibly relate to a person," Gorelick said, "But actually, 70 percent of a zebrafish's genome is the same or extremely similar to that of humans. Typically, if you manipulate the gene in zebrafish, it has the same result in humans."

One of the advantages of using zebrafish as a model organism to study cancer and other diseases is their small size, high fertility and short time to maturity. In a few months, researchers can study thousands of fish, whereas it would take years to collect the same data from other animal models, such as rodents.

"The fact that you can accumulate thousands of zebrafish in a single study, and can study them over three to four generations in a year, makes it possible to do population-level research, informed by the response of the many rather than the few," said Dr. Cheryl Walker, director of the Center for Precision Environmental Health.

Fish are particularly useful for identifying cancer-causing agents in the environment and for testing whether drugs are effective in reducing tumor size and metastases. Fish also have been used to rapidly test whether a particular gene drives cancer. For example, scientists frequently observe correlations between genetic mutations and melanoma, a type of skin cancer, but determining whether a particular genetic mutation actually causes melanoma can be a challenging and slow process. Using zebrafish, it is possible to rapidly make mutations in hundreds of animals and test whether these mutations increase the frequency of melanomas, melanoma growth or metastasis.

ENVIRONMENTAL HEALTH

NEW CLINICAL HOME

ON JANUARY 22, 2019, a new era of integrated care for our patients at the NCI-designated Dan L Duncan Comprehensive Cancer Center commenced with the opening of the Center's new outpatient clinic facility on the 7th floor of the Baylor College of Medicine Medical Center, bringing our expert physicians together in one space. The Baylor College of Medicine Medical Center shares the McNair Campus with the Baylor St. Luke's Medical Center.

The floor and operational plan were designed to facilitate multidisciplinary clinics in order to treat most adult cancers. The Lester and Sue Smith Breast Center is an integral component of the outpatient clinic, and with the addition of gynecologic oncology, comprehensive women's cancer services are now part of the Duncan Cancer Center. Expanded clinics treating all gastrointestinal cancers including liver and pancreatic cancer, along with bone and soft tissue sarcomas, malignant and benign hematology and endocrine tumors also are offered at the facility. A greatly expanded cancer infusion suite with a state-of-the-art pharmacy to facilitate the latest clinical trials sits on the north end of the floor with sweeping views of downtown Houston and the Eastern horizon.

Importantly, the physicians, support staff and clinical trials team now have an academic home base in office space immediately adjacent the clinic. The new Duncan Cancer Center outpatient clinic brings the expertise of our core oncology teams closer to other cancer groups that already were housed on the McNair Campus treating genitourinary cancers, brain, pituitary and spinal cancers, as well as melanoma and other skin cancers at the Jamail Specialty Care Center. This proximity will enhance interactions and make care more convenient for all patients.

This move is the first step in a plan to create a completely comprehensive and seamless cancer facility, including an expanded outpatient capacity that will house all the multidisciplinary clinics of the Duncan Cancer Center, bring radiation oncology to the McNair Campus and open dedicated oncology inpatient units within close proximity to our outpatient hub. Baylor St. Luke's Medical Center – McNair Campus is scheduled for completion in 2022.

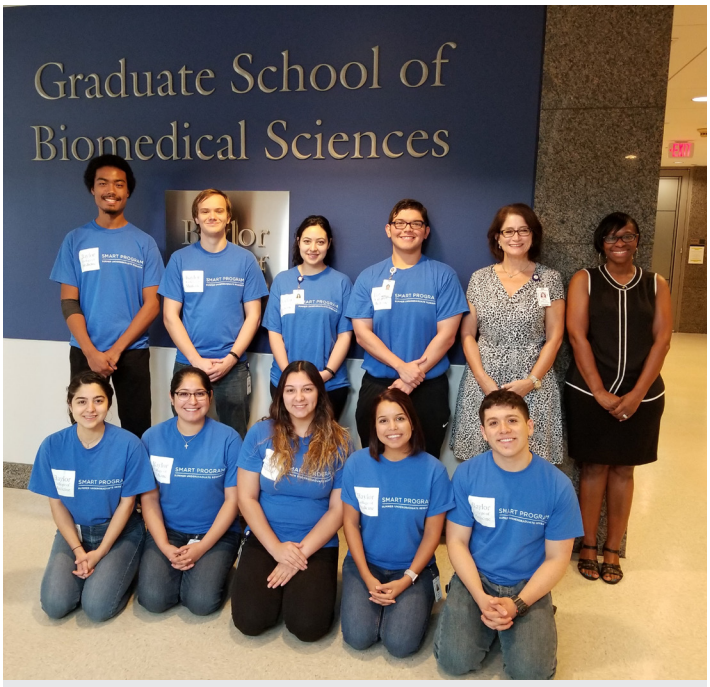
One of the great advantages of having a comprehensive cancer center integrated within a full spectrum academic hospital is our Duncan Cancer Center clinicians have access to the full array of Baylor's expert physicians in all specialties. By design we treat the whole patient - not just a patient's cancer.

FOR THE DAN L DUNCAN COMPREHENSIVE CANCER CENTER

EDUCATION & TRAINING

IN ORDER TO RECEIVE the National Cancer Institute's designation of Comprehensive Cancer Center, the Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine demonstrated ground-breaking research, impeccable patient care and education that inspires the next generation of doctors to find a cure for cancer.

Among the many educational achievements and initiatives of the Duncan Cancer Center is the National Institutes of Health P20 award with the University of Houston's College of Pharmacology, which focuses on cancer and pharmacology-related education and career enhancement programs with local middle and high schools to introduce a career in cancer medicine. In 2016, the Duncan Cancer Center collaborated with Baylor College of Medicine's summer undergraduate research program called Summer Medical and Research Training, or SMART, to develop the P30-CURE program funded through a National Cancer Institute grant. The summer program, which launched in 2017, lasts for two consecutive summers. The goal is to expose promising undergraduate students from underrepresented populations to state-of-the-art biomedical research, through working in labs and alongside scientists who mentor the students.



P30-Cure Program

Vidal Arroyo was one of the first students to complete the program.

"My parents didn't instill a drive for academics in me. I didn't have a reason to do well in school. They instilled a strong work ethic, but no one in my family had ever gone to college before," said Arroyo, Duncan Cancer Center P30 Cure grant recipient.

He only went to college, Arroyo said, because all of his friends were going. While at Chapman University, a small, private institution in Southern California, Arroyo decided for the first time he would begin applying himself academically. By Arroyo's sophomore year, he determined he wanted to become a physician after one of his favorite professors died in his 30s of colorectal cancer.

"I was shocked that someone so young could be taken by cancer. Up until that point, I thought cancer was completely preventable," Arroyo said.

Wanting a new adventure in Texas, Arroyo applied to the Duncan Cancer Center's P30-CURE program.

"Working with my mentors was very much like

a family environment. In fact, those close mentorship interactions allowed me to develop a love for research," Arroyo said.

Conducting research for two summers at the Duncan Cancer Center gave him the opportunity to explore his interests and his role in the field of oncology, Arroyo said. In that time, he gained the confidence and research experience needed to apply for the prestigious Rhodes Scholarship. In 2018, Arroyo was named one of only 32 United States Rhodes Scholars.

"For someone who didn't know what to do with his life, I would not have won this scholarship without Baylor," Arroyo said.

While at the University of Oxford, Arroyo plans to double master in statistics and theology. He then has plans to enter medical school under a dual M.D./Ph.D. program. Ultimately, he would like to make personalized medicine available for all patients, including those with cancer, in an ethical way.

"My mentors at Baylor were rooting for me long before even I knew my potential," Arroyo said.

DISEASE WORKING

GASTROINTESTINAL/PANCREAS: William Fisher, M.D.; Ben Musher, M.D.

The Gastrointestinal Cancer Multidisciplinary Team consists of experts in medical oncology, surgical oncology, radiation oncology, gastroenterology, nutrition and palliative care who evaluate and treat a wide range of gastrointestinal malignancies, including esophageal, gastric, pancreatic, hepatocellular (liver), bile duct, colorectal, neuroendocrine and anal carcinomas. Weekly tumor boards and shared clinic space ensure delivery of coordinated and comprehensive care while innovative clinical trials offer patients personalized, cutting-edge treatment.

LIVER: Karl-Dimiter Bissig, Ph.D.

The Dan L Duncan Comprehensive Cancer Center offers patients access to specialists in all areas of care for liver cancer through its Liver Cancer Working Group, including cancers that have spread to the liver from other organs. The group provides individualized care and consultation with an experienced liver surgeon, medical oncologist, radiation oncologist and diagnostic specialists, with hepatologists providing insight into hepatocellular cancer cases. Treatment, including surgical tumor removal or ablation, is customized for each patient, and patients receive state-of-the-art care and the opportunity to participate in clinical trials and other novel approaches.

HEMATOLOGICAL MALIGNANCY: George Carrum, M.D.; Daniel Lacorraza, Ph.D.

The goal of the Hematological Malignancies Working Group is to foster collaborations between clinical (pediatric and adult) and basic research groups and to translate cancer discoveries into clinical practice. The organizing committee composed by Drs. Michele Redell, Daniel Lacorazza, George Carrum, Joanna Yi and Gustavo Rivero, coordinates monthly meetings gathering oncologists, clinical fellows and basic research scientists with diverse expertise (e.g. pathology, human genetics, molecular and cell biology, cell and gene therapy) at Baylor to discuss advances in hematological malignancies research, identification of molecular targets for the development of therapies, and investigator initiated clinical trials.

HEAD AND NECK AND SALIVARY GLANDS: Andrew Sikora, M.D., Ph.D.

The Head and Neck Cancer Working Group is dedicated to the multidisciplinary treatment of patients with head and neck cancer and turning cutting-edge basic, translational and clinical research into cancer mechanisms and innovative therapeutic approaches. The Head and Neck Cancer Working Group encompasses a range of cancers, including squamous cell carcinoma of the head and neck, larynx, oral cavity, oropharynx, salivary gland, sinonasal, skull base and skin. Its membership is varied, with members from

GROUPS

pathology, obstetrics and gynecology, the Center for Cell and Gene Therapy, pediatrics, otolaryngology, medicine and hematology and oncology coming together to consider the latest research, treatments and patient care.

PROSTATE: Nicholas Mitsiades, M.D., Ph.D.; Michael Ittmann, M.D., Ph.D.

The Prostate Working Group facilitates the multidisciplinary treatment of patients with prostate cancer and the translation of bench discoveries into innovative clinical trials. The Prostate Working Group promotes scientific collaborations within the Group and with Programs, such as the Nuclear Receptor and the Cancer Biology Programs, that have led to several funded grants (e.g. Prostate Cancer Foundation Challenge Award, DoD, NCI U54 grant) and novel research directions (e.g. prostate PDX program, leading to a Minority PDX Development and Trial Center). The Prostate Working Group also reviews clinical trial protocols prior to IRB submission to ensure feasibility and proper scientific design.

BRAIN TUMOR: Melissa Bondy, Ph.D.

The Brain Tumor Working Group is dedicated to the multidisciplinary treatment of patients with a type of brain tumor called Glioma and turning cutting-edge basic, translational and clinical research into cancer mechanisms and innovative therapeutic approaches. The Its membership is varied, with members from pathology, the Center for Cell and Gene Therapy, pediatrics, medicine and hematology and oncology coming together to consider the latest research, treatments and patient care.

Lung and Mesothelioma: Bryan Burt, M.D., and R. Taylor Ripley, M.D.

Esophagus: Shawn Groth, M.D., and Mohamed Othman, M.D.

Gynecological Oncology: Jan Sunde, M.D.

Melanoma/Sarcoma: Eugene Choi, M.D., Daniel Wang, M.D., and Ida Orengo, M.D.

Genitourinary Oncology: Seth Lerner, M.D.

Survivorship and Integrative Medicine: Hoda Badr, Ph.D., Brian Bruel, M.D.

NEW FACES

CHRIS AMOS, Ph.D.

Associate Director of Quantitative Science, Dan L Duncan Comprehensive Cancer Center
Director for the Institute of Clinical and Translational Medicine

Dr. Amos is an internationally renowned expert in genetic epidemiology of lung cancer. He also has extensive expertise in genetic epidemiology and statistical genetics. His work strengthens bioinformatics and computational biology infrastructure to integrate genomics capabilities into applications for precision medicine. CPRIT Faculty Scholar

COURTNEY HODGES, Ph.D.

Assistant Professor, Department of Molecular and Cellular Biology
Center for Precision Environmental Health

Research in the Hodges lab focuses on altered epigenetic function in cancer and other diseases. They use interdisciplinary approaches, including epigenomics, live-cell super-resolution imaging, genome editing and structural biology, to understand epigenetic systems in disease settings. The research is especially focused on new technologies, for example, improving cell-culture tumor models, as well as single-cell and single-molecule methods. CPRIT Faculty Scholar

VALENTINA HOYOS VELEZ, M.D.

Assistant Professor, Center for Cell and Gene Therapy

Dr. Hoyos Velez's clinical interests lie in treating patients with breast cancer, and her current research goal is to develop effective CAR-T cell therapies against this disease by incorporating strategies to overcome the hostile breast tumor microenvironment. The long-term goal is to translate these therapies into the clinic to give breast cancer patients the opportunity to benefit from this immunotherapy. CPRIT Faculty Scholar

SHASHIKANT KULKARNI, M.S., Ph.D., FACMG

Professor and Vice Chair of Research, Molecular and Human Genetics
Chief Scientific Officer and Senior VP, Baylor Genetics

Dr. Kulkarni's research interest has been to utilize genomic, transcriptomic and epigenomic tools to study cancer biology and clonal evolution. Clinically, he is focused on providing clinical genomic analyses for both germline and acquired somatic disorders.

STEPHEN MACK, Ph.D.

Assistant Professor, Pediatrics-Oncology

Dr. Mack's research goals and interests lie at the intersection between the study of childhood brain tumors, cancer epigenetics, neuro-development and translational oncology. Distinct molecular variants that comprise the tumor entity, ependymoma, create a diverse disease system to study several aspects of cancer biology, including tumor cellular origins, epigenetic programs and transcriptional regulation. His lab's overall goal is to use the ependymoma tumor type as a model to develop therapeutic platforms in other pediatric brain tumors. CPRIT Faculty Scholar

AT THE DAN L DUNCAN COMPREHENSIVE CANCER CENTER

ROBERT TAYLOR RIPLEY, M.D.

Associate Professor of Surgery, Division of General Thoracic Surgery
Director, Mesothelioma Treatment Center, Baylor St. Luke's Medical Center

Dr. R. Taylor Ripley is a nationally recognized, board-certified thoracic surgeon and expert in thoracic surgical oncology specializing in treatment of mesothelioma. In addition to mesothelioma, he practices all facets of general thoracic surgery including infectious lung disease and benign esophageal and endobronchial diseases, as well as multidisciplinary management of patients with lung, esophageal, thymic, and other thoracic malignancies and endoscopic interventions.

ALASTAIR THOMPSON, BSc, MBChB, M.D.

Section Chief, Breast Surgery, Division of Surgical Oncology
Co-Director, Lester and Sue Smith Breast Center, Dan L Duncan Comprehensive Cancer Center

Dr. Alastair Thompson is an internationally recognized breast surgeon-scientist. He leads a forward-thinking clinical practice treating breast cancer patients, including an emphasis on skin and nipple sparing mastectomy, autologous reconstruction and innovative localization techniques for breast conservation and axillary node surgery. Amongst his innumerable research leadership roles, Thompson has served as principal investigator on landmark breast cancer clinical trials, including SOLE, MA 32, MINDACT and KRISTINE trials.

DANIEL WANG, M.D.

Assistant Professor, Medicine - Hematology/Oncology

Dr. Wang is a medical oncologist who specializes in the care of patients with sarcoma, melanoma, and other skin cancers. He is focused on providing excellent multidisciplinary care and clinical trials to these uncommon cancers. In addition, he has published research on immunotherapy related toxicities and interested in developing a team approach on management of these toxicities.

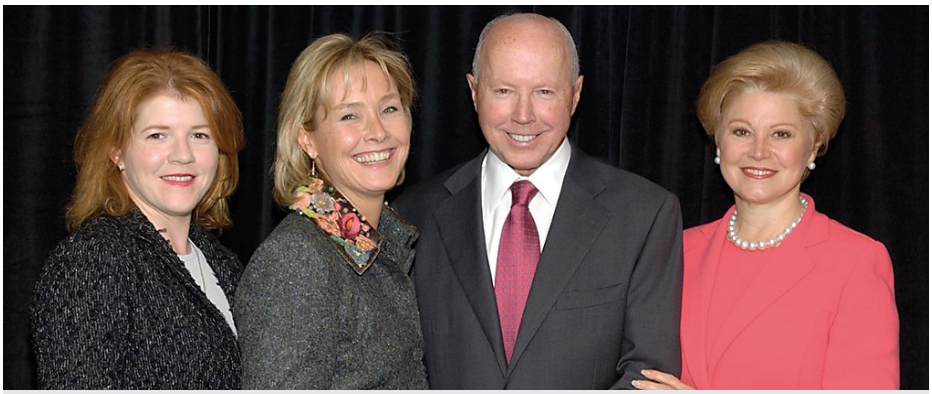
JIHYE YUN, Ph.D.

Assistant Professor, Molecular and Human Genetics

Colorectal cancer is the second leading cause of cancer-related deaths in developed countries. Epidemiological studies strongly suggest that diet is the most important environmental factor in colorectal cancer development. Indeed, diet is known to affect many important aspects of cancer development by influencing epigenetics, metabolism, immune systems, gut microbiota and others. As such, if we can identify and understand the mechanisms by which dietary factors can prevent or facilitate cancer development, we will be able to control cancer initiation, progression and metastasis more effectively. CPRIT Faculty Scholar

PHILANTHROPY

TRIBUTE TO DAN L DUNCAN AND THE DUNCAN FAMILY



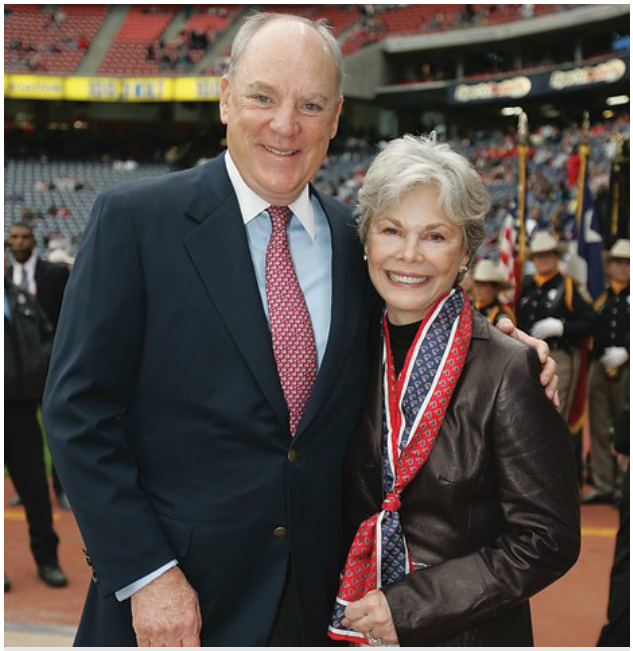
The late Dan L Duncan with daughters Milane Duncan-Frantz, Randa Williams and wife Jan Duncan.

No one could fully predict the impact of the historic $100 million pledge made in 2006 by late oil man Dan L Duncan, his wife, Jan, and their family to Baylor College of Medicine's fledgling Cancer Center. This financial commitment occurred just two years after Dr. C. Kent Osborne took the reins of the newly formed cancer program and initiated a strategy to attain National Cancer Institute (NCI) "cancer center" designation. The renamed Dan L Duncan Cancer Center achieved this remarkable goal just one year later, making it the nation's 58th cancer center to receive the lofty NCI designation. This milestone would not have been possible without the extraordinary community support demonstrated by the Duncan gift, a linchpin for the Center's NCI application, the footing for its stability and growth, and the basis for the Center's 2015 NCI "comprehensive" designation.

Over the ensuing years, the Duncans' extraordinary philanthropy significantly boosted faculty recruitment and retention by creating prestigious endowed positions, including two Dan L Duncan Chairs and six Dan L Duncan Professorships. The foremost experts holding these positions oversee the Center's seven research Programs in breast cancer, pediatric cancer, cancer cell and gene therapy, nuclear receptors, cancer prevention and population science, cancer biology and cancer evolvability. Part of the Center's growth attributed to the Duncan gift also includes the creation of 15 cancer-specific working groups to explore and consider cancer from multiple perspectives and encourage collaboration across clinical and research disciplines. More than 40 new cancer-focused scientists and physicians were recruited to the groups, including internationally known experts in lung, liver and esophageal cancers.

The Duncan family's sincere concern for the wellbeing of present and future generations who may be touched by cancer was fundamental to the evolution of what today is an incredible resource for Houston as well as the global community. The momentous donation of $100 million paired with Dr. Osborne's clear vision and leadership gave rise to a unique cancer center where ingenuity, discovery, talent and healing can thrive. We are indebted to the Duncan family for their support and friendship as we continue our quest to bring new treatments and new hope to patients and families.

TRIBUTE TO MR. AND MRS. ROBERT C. MCNAIR



The late Robert C. McNair and his wife, Janice.

Two of Baylor College of Medicine's most generous and visionary donors, Robert and Janice McNair, are renowned for their many contributions to the City of Houston and are among the community's most respected philanthropists. At Baylor, the McNairs' legacy began with the election of Mr. McNair to the Board of Trustees in 1994. Following his appointment was the launch of several landmark programs underwritten by the couple and The Robert and Janice McNair Foundation that forever link this compassionate and civic-minded family to the College.

A particular area of focus for the McNairs has been cancer research, a cause that reflects the experiences of family and friends. Their emphasis on cancer was initiated through the McNair M.D./Ph.D. Scholars program created in 1998 to support students pursuing dual degrees in medicine and biomedical research. The study of cancer is one of three research foci for the McNair M.D./Ph.D. Scholars who today number 25 alumni.

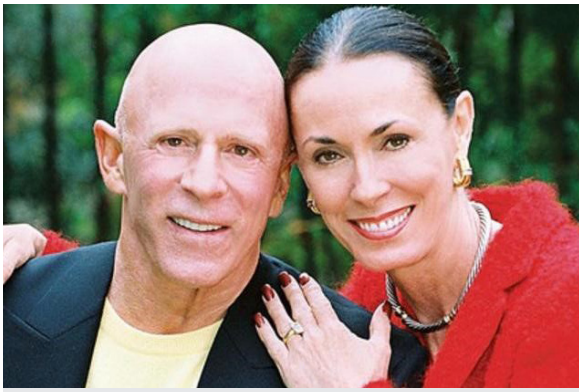
Turning next to medical research as a philanthropic priority, the McNairs established the McNair Medical Institute at Baylor in 2007 and founded the prestigious McNair Scholars Program with a transformational $100 million gift. The program recruits highly talented scientists and physician-scientists from around the world to the Texas Medical Center to pursue cross-institutional collaborative and transformational research in three areas, one of which is cancer. The exciting discoveries and medical advances accelerated by the McNair Scholars Program are showcased at the annual McNair Symposium.

In January 2019, Baylor's Dan L Duncan Comprehensive Cancer Center will relocate to the Baylor St. Luke's Medical Center on the McNair Campus where patients will receive the highest quality, personalized care in new outpatient clinics. With the Duncan Cancer Center's move to the McNair Campus, a key Baylor site named in honor of Robert and Janice McNair, the couple's passion for solving the cancer puzzle will come full circle. We are grateful for our continued relationship with Mrs. McNair as she carriers on the work begun by her and her late husband.

PHILANTHROPY

TRIBUTE TO LESTER AND SUE SMITH

"Forces of nature with hearts as big as Texas" aptly describes this compassionate and fun-loving couple who live and give by the motto, "to whom much is given, much is expected." Houston philanthropists Lester and Sue Smith have built a lasting legacy at Baylor, guided by their desire to help others avoid the suffering caused by devastating illnesses far too familiar to them. Top among these is cancer.



The late Lester Smith and his wife, Sue.

Their multi-million-dollar transformational gifts date back to 2002, when the Smiths raised substantial funding for prostate cancer research and endowed three chairs in the Scott Department of Urology. The Lester and Sue Smith Urology Clinic bearing their name recognizes this generosity.

Five years later, an ambitious gift to Baylor's Breast Center funded crucial research and treatment advances to bring healing and hope to patients. Today, the Lester and Sue Smith Breast Center is a major component of the Dan L Duncan Comprehensive Cancer Center and one of its most recognized service lines.

The Partnership's 2017 Café Society Soirée raised more than $420,000 to support an adult Phase 1 clinical trial unit at the Duncan Cancer Center, an essential element for moving new therapies from the lab to the bedside. Pictured left to right are Partnership President Peggy Carrington, Jan Duncan, Dr. C. Kent Osborne, Soirée Chairs Cora Sue and Harry Mach and Dr. Paul Klotman.

With their unique style and boundless energy, the Smiths also have chaired a number of fundraising events to support cancer research and care delivery at Baylor. The Partnership for Baylor College of Medicine, the institution's largest volunteer and advocacy group, twice was chosen by the Smiths as a benefactor of their magnanimous fundraising skills.

Lester and Sue Smith encouraged others to give by modeling philanthropy that comes from the heart, whether in funding cancer research, volunteering time to counsel patients, or in sharing a note or a spoken word of encouragement. We are grateful to these friends whose passionate dedication has contributed to the Duncan Cancer Center's evolution and success. Lester's infectious love for life, his deeply caring nature and his unique spirit that shined so brightly on the world will be missed. We are pleased to continue working with Sue, who remains engaged in the initiatives she and her husband brought to life through their generosity.

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SHARED RESOURCES BAYLOR COLLEGE OF MEDICINE

The shared resources of the Dan L Duncan Comprehensive Cancer Center provide extensive services essential to cancer research. As an NCI-designated center, our Cancer Center Support Grant allows us to fund advanced technologies, equipment, data analysis, and biostatistics and informatics services that would be difficult and expensive for individual investigators or programs to develop and maintain on their own.

Antibody-Based Proteomics

Director: Dean P. Edwards, Ph.D.
Co-Director: Shixia Huang, Ph.D.

The Antibody-Based Proteomics Core provides highly customized services for targeted proteomics platforms that are valuable as tools for both validation and protein biomarker discovery, particularly for low abundance regulatory proteins and activation states of proteins with phosphorylated antibodies. Services provided include reverse phase protein arrays (RPPA) with over 210 antibodies for total and phosphoproteins of major cell signaling pathways, Luminex bead technology for multiplex quantitative analyses of intracellular and extracellular signaling proteins, and antibody arrays.

Cell-Based Assay Screening Services (C-BASS)

Director: Trey Westbrook, Ph.D.
Co-Director: Dan Liu, Ph.D.

The Cell-Based Assay Screening Services (C-BASS) core is built upon the interconnected and complementary technology platforms of RNAi-based functional genomics and CRISPR/Cas9-mediated genome editing. The core houses whole-genome RNAi libraries that enable expedient investigation of gene function either individually or in large scale. For genome editing, we have available a collection of CRISPR sgRNA and Cas9 vectors for distribution and cloning services, and assist investigators in deciding on the choice of cell line(s), optimal vectors, and types of Cas9. C-BASS is able to customize CRIPSR/Cas9-mediated gene knockout and knock-in services, from target site design to generating KO/KI cell lines, based on the specific needs of individual investigators.

Cytometry and Cell Sorting

Director: Christine Beeton, Ph.D.
Co-Director: Joel M. Sederstrom, M.B.S.

This is a state-of-the-art facility offering assisted and unassisted flow cytometric services. Instrumentation includes FACSAria cell sorters with up to 13 colors plus forward and side scatter, LSRII Analyzers with high through-put 96 well sample loading plates, VI-Cell counter, AutoMACS magnetic bead cell sorter and workstations with data analysis software. The Core provides training on all instruments, assists with data analysis and design of experiments, and is available 24 hours-a-day, 7 days-a week for all trained users.

Genetically Engineered Mouse (GEM)

Director: Jianming Xu, Ph.D.
Co-Director: Jason D. Heaney, Ph.D.

The GEM Core provides investigators with advice and services requiring the manipulation of mouse gametes to facilitate research involving genetically engineered mice. Services include DNA microinjection (traditional transgene DNA constructs, lentivirus constructs or BAC DNA into the one cell mouse embryo), ES cell microinjection into blastocysts, strain rederivation into a pathogen free stratus, colony expansion, in vitro fertilization, embryo cryopreservation and sperm cryopreservation for safe preservation of valuable mouse strains. The Core also provides consultation on approaches and can work with the investigator to facilitate their research needs.

Genomic and RNA Profiling (GARP)

Director: Lisa White, Ph.D.
Co-Director: Daniel Kraushaar, Ph.D.

The Genomic and RNA Profiling Core provides cancer research investigators with access to state-of-the art next generation DNA and RNA sequencing technologies and instrumentation (NextSeq500 and NovaSeq6000) for whole genome and whole exome sequencing, whole genome bisulfte DNA sequencing, whole transcriptome, polyA selected and small RNA sequencing, ChIP sequencing for chromatin interactions and protein-DNA interactions (e.g., transcription factors), targeted genomic DNA and RNA sequencing, and amplicon sequencing. Additionally the NanoString nCounter platform, a direct digital detection system, is available for targeted multiplex analysis of from 20-800 genes or gene loci. GARP also assists with best practice experimental design and provides help with data management and analysis.

Human Tissue Acquisition and Pathology (HTAP)

Director: Michael Ittmann, M.D., Ph.D.
Co-Director: Patricia Castro, Ph.D.

The Human Tissue Acquisition and Pathology (HTAP) Core provides tissue and serum related services to researchers that includes histology and immunohistochemistry (IHC) and organization of the different tissue banks at BCM. Histology and IHC of human and experimental animal tissues are available on a fee-for-service basis. Services include tissue processing, embedding, sectioning and staining for routine histology (H&E, PAS, ORO, Trichrome, VVG, Giemsa), IHC and TUNEL assay for apoptosis. Also available are laser capture microdissection, archival tissue microarrays (TMA), image analysis by Inform and Vectra and consultation with pathologists.

Integrated Microscopy

Director: Michael Mancini, Ph.D.
Co-Director: Fabio Stossi, Ph.D.

The Integrated Microscopy Core provides state-of-the-art light and transmission electron microscopy imaging support. This fully digital-imaging-based resource provides routine microscopy (Nikon CiL, Biotek Citation 5), fixed and live cell-capable Nikon A1rs multispectral laser scanning confocal with full live cell enclosure (photobleaching and timelapse), Applied Precision deconvolution microscopy, Vala Sciences IC-200 high throughput microscopy, and GE Healthcare OMX BLAZE(SIM) super-resolution microscope. Digital transmission electron microscope (Hitachi) includes specimen processing services.

Mass Spectrometry Proteomics

Director: Anna Malovannaya, Ph.D.
Co-Directors: Sung Yun Jung, Ph.D.

The Mass Spectrometry Proteomics Core features state-of-the-art Thermo Scientific Orbitrap and AB Sciex 5600 instrumentation and offers comprehensive service packages for proteome-wide label free quantitative proteomic profiling of cells and tissues, isolation and identification of protein complexes via immunoprecipitation followed by mass spectrometry, post-translational modification analysis, and routine protein identification from purified samples. The services are provided with the full support that includes project evaluation and design, biochemical purifications, mass spectrometry sequencing, and data analysis performed within the core by experienced core personnel.

Metabolomics

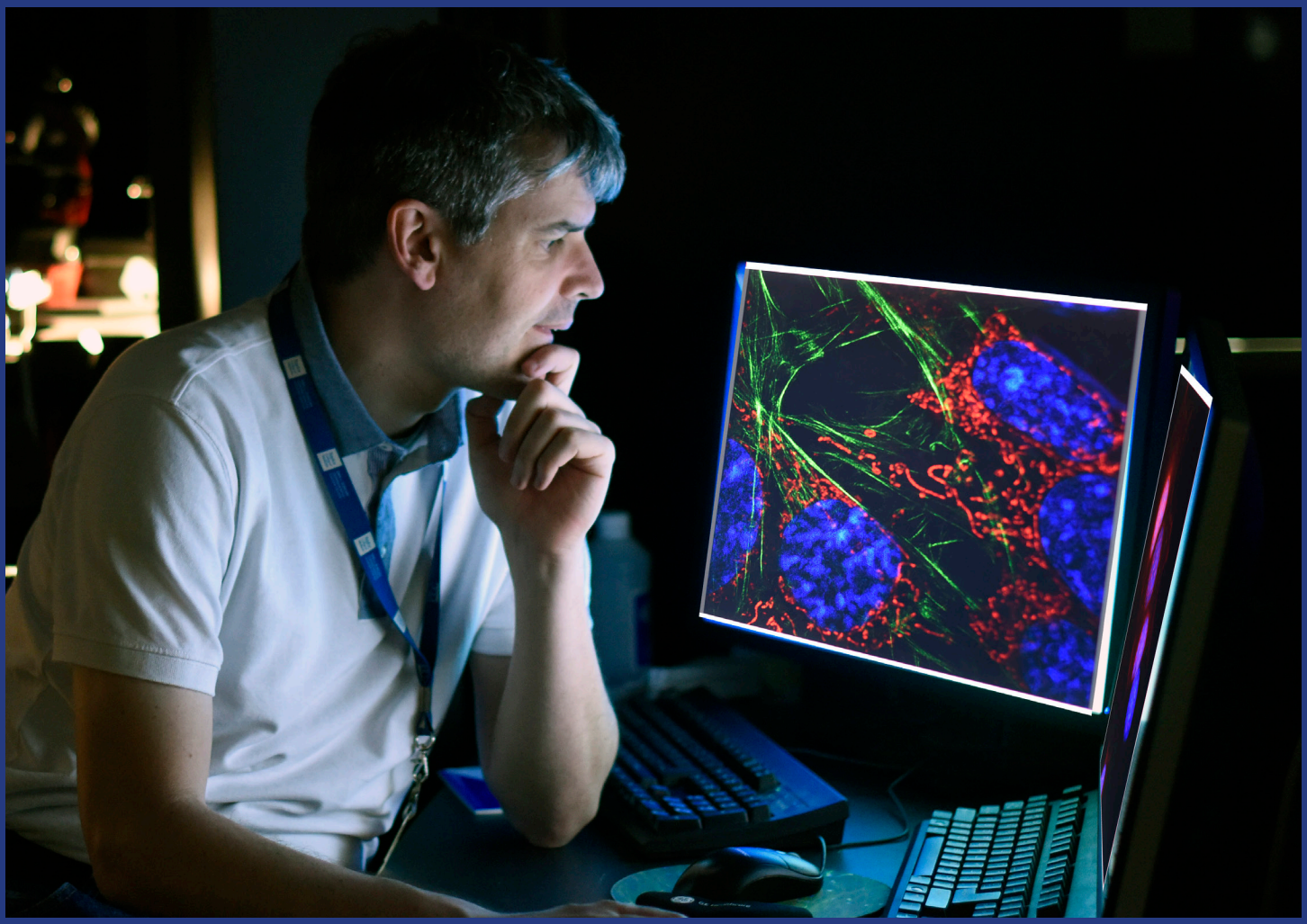
Director: Arun Sreekumar, Ph.D
Co-Director: Nagireddy Putluri, Ph.D

This Core provides metabolomics technologies for discovery and validation of biomarkers of various diseases with state-of-the-art high mass spectrometry as the main platform. Core services include quantitative targeted assays (up to 500 metabolites) for many analyte classes, metabolic flux analysis, lipidomics, and drug metabolism and pharmacokinetics.

Population Sciences Biorepository (PSB)

Director: Michael Scheurer, Ph.D.
Co-Director: Marlisa Hardy, Dr.PH., M.P.H.

The PSB Core provides risk factor and clinical data collection and a centralized facility for biospecimen processing and storage from epidemiological and clinical studies. Services are available for individual investigators as well as for clinical centers that require prospective banking of patient specimens. Clinical coordinators can assist with consenting, phlebotomy, and data collection. The PSB also provides laboratory services including: full fractionation and aliquoting for blood samples; DNA extraction from whole blood, buffy coat, or saliva; and RNA extraction from whole blood.



Baylor College of Medicine

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