# FY 2020 Published Research Findings

- In work suggesting new therapeutic targets to fight obesity, CPRIT Scholar Joshua Mendell, M.D., Ph.D., identified a novel mechanism that regulates the creation of fat in mammals. The research, reported in the September 5, 2019, edition of *Genes & Development,* found that loss of a family of microRNAs, miR-26, results in a dramatic increase in fat formation and that its overexpression protected against weight gain in mice. MicroRNAs are small molecules that function to regulate gene expression and are potential drug targets. The University of Texas Southwestern Medical Center recruited Dr. Mendell, professor of molecular biology and an investigator in the prestigious Howard Hughes Medical Institute, in 2011 from Johns Hopkins with support of a $4 million CPRIT Rising Star Award (R1008).

- Baowei Fei, Ph.D., professor of bioengineering at The University of Texas at Dallas shows that hyperspectral imaging predicted cancer cells with 80-90% accuracy. Dr. Fei's findings, published in the September 14, 2019, edition of the journal *Cancers*, used hyperspectral imaging - technology originally used in satellite imagery - to research how cells absorb ultraviolent and near-infrared lights. Its use during surgery may allow surgeons to see cancer cells that would be undetectable to the human eye. The speed and accuracy of hyperspectral imaging compared to the standard diagnostic method is significant. Currently, pathologists analyze a patient's tissue samples removed during surgery and may require many tissue resections and future surgeries if surgeons do not detect all cancerous cells during surgery. Dr. Fei received a CPRIT Early Translational Research Award (RP190588) in August 2019 to further his research in this area.

- An international team of researchers that includes CPRIT Scholar José Onuchic, Ph.D., described a potential new drug target against cancer in the September 18, 2019, edition of *Proceedings of the National Academy of Sciences*. The research identified how a cancer-linked version of the protein mitoNEET can close the primary gateways in the outer surface of mitochondria, the "power plants" that supply cells with chemical energy. These gateways normally open and close to allow the passage of metabolites and other small molecules between mitochondria and the rest of the cell and dysfunction of this channel is involved in cancer and fatty liver disease. This is important because it shows how a drug could disrupt the cancer-linked altered mitochondria gateway to restore its proper function. Rice recruited Dr. Onuchic from the University of California San Diego in 2011 with a $6 million Established Investigator recruitment award from CPRIT (R1110).

- Lydia Kavraki, Ph.D., the Noah Harding Professor of Computer Science, and director of the Ken Kennedy Institute for Information Technology led a team of computational scientists at Rice University testing the molecular interactions of the immune system with cancer cells. By using the Comet supercomputer at the San Diego Supercomputer Center to survey thousands of molecules on the surface of immune cells and their binding sites on cancers, Dr. Kavraki's team was able to predict connections between the immune system and cancer cells that other methods would miss. The findings, published in the September 2019 edition of *BMC Molecular and Cell Biology Journal,* are significant because the ability to identify the immune cells that bind to and attack cancers provides promising opportunities for the development of immune-based cancer therapies. Dr. Kavraki received a CPRIT Individual Investigator Research award as well as a CPRIT-supported training fellowship from the Gulf Coast Consortia through the CPRIT Computational Cancer Biology Training Program (RP170593) to support this research.

- A CPRIT-funded team led by The University of Texas at Austin's Livia Eberlin, Ph.D. reports a new test for thyroid cancer that is faster and more accurate than the diagnostic tests doctors use today. Although the new metabolic thyroid test, developed with CPRIT funding (RP170427) and published in the October 7, 2019, edition of *Proceedings of the National Academy of Sciences,* needs more validation before clinicians can use it, it shows promise for preventing thousands of unnecessary thyroid removals each year. Using a technology called mass spectrometry imaging, the new metabolic thyroid test identifies metabolites produced by cancerous cells that act as a diagnostic fingerprint. The researchers worked on identifying these diagnostic metabolic fingerprints for over two years using 178 patient tissues before starting a pilot clinical study. The clinical study tested 68 new patients, nearly one-third of whom had received inconclusive results after fine needle aspiration. The new metabolic thyroid test returned a false positive only about 1 time out of 10 and could have prevented 17 patients in the study from undergoing unnecessary surgeries.

- Researchers at Baylor College of Medicine and the Texas Children's Cancer Center, including CPRIT grantee Dr. Karen Rabin, discovered that identifying certain biomarkers in the bone marrow of pediatric patients with acute lymphoblastic leukemia (ALL) may predict how well those patients respond to treatment. With samples from 155 ALL pediatric patients, research published in the October 17, 2019, edition of the journal *EBioMedicine* showed that drugs that interfered with central carbon metabolism reduced growth of cancer. CPRIT awarded Dr. Karen Rabin an Individual Investigator Research Award for Cancer in Children and Adolescents (RP170074) in 2016 for this research. Dr. Rabin noted that, "We've reached the limits

of intensive chemotherapy for improving survival in ALL - adding higher doses or additional drugs increases side effects and often doesn't improve response. This study is important in identifying a potential alternative approach to attacking leukemia cells in patients with high-risk disease."

- CPRIT Scholar Dr. Matthew Ellis, professor and director of the Lester and Sue Smith Breast Center, and associate director of precision medicine at the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine (RR140033), discovered that a subset of endocrine therapy-resistant breast cancers activates immune responses that scientists may manipulate with immunotherapy. Researchers previously did not consider immunotherapy for endocrine therapy-resistant breast cancers. Dr. Ellis studied 66 cases - half of which were resistant to endocrine therapy - finding that immune checkpoint genes are the most actively expressed genes in resistant tumors. Dr. Ellis' finding, published in the October 30, 2019, edition of the *Journal of the National Cancer Institute,* is important because it shows that a subset of patients whose tumors have active immune responses may be amenable to immunotherapy.

- Aravive, Inc. published data from a nonclinical study of AVB-500, the company's lead product candidate, in the October 2019 edition of *Cancer Research*. The data demonstrated reduction in tumor size and blood vessel density in animal models of clear cell renal cell carcinoma. The study suggests that an anti-GAS6 therapy may be a potentially effective approach to prevent and treat tyrosine kinase inhibitor-resistant disease, supporting the rationale for combining AVB-500 with antiangiogenic agents to treat advanced kidney cancer. Houston-based Aravive received a $20 million CPRIT Product Development award in 2015 to develop their AXL-pathway decoy receptor to treat acute myeloid leukemia and solid tumors.

- Researchers at The University of Texas Southwestern Medical Center have developed a software tool using artificial intelligence (AI) to recognize cancer cells from digital pathology images. This provides clinicians with a powerful tool for predicting patient outcomes. The spatial distribution of distinct types of cells observed in a tumor biopsy can reveal a cancer's growth pattern, its relationship with the surrounding microenvironment, and the body's immune response. But the process of manually identifying all the cells in a pathology slide is labor intensive and error prone. Therefore, a major technical challenge in systematically studying the tumor microenvironment is how to automatically classify the several types of cells and quantify their spatial distributions.

The AI algorithm that Dr. Guanghua Xiao, professor of bioinformatics at UT Southwestern, and his team developed, called ConvPath, overcomes these obstacles by using AI to classify cell types from lung cancer pathology images. The ConvPath algorithm can "look" at cells and identify their types based on their appearance in the pathology images using an AI algorithm that learns from human pathologists. This algorithm effectively converts a pathology image into a map that displays the spatial distributions and interactions of tumor cells, stromal cells (i.e., the connective tissue cells), and lymphocytes (i.e., the white blood cells) in tumor tissue. Whether tumor cells cluster well together or spread into stromal lymph nodes is a factor revealing the body's immune response. Knowing that information can help doctors customize treatment plans and pinpoint the right immunotherapy.

*EBioMedicine* published a description of the ConvPath algorithm in its November 22, 2019, edition and Dr. Xiao is developing it further in his project "Digital Pathology Analysis for Lung Cancer Patient Care" with a CPRIT Individual Investigator Research Awards for Computational Biology grant (RP190107).

- The University of Texas Health Science Center at San Antonio researchers supported in part by CPRIT (RP160716, RP170686 and RP180769), and working with collaborators at the University of Florida, have discovered a safe and potent next generation of drugs to fight multiple types of leukemia and lymphoma in adults and children. Their findings, published in the December 2, 2019, edition of *Journal of Biological Chemistry* and *Nature Medicine,* involve a new class of drugs called PROTACs that target an essential survival protein in cancer cells called BCL-XL. Previous drugs that have targeted BCL-XL cause a precipitous drop in platelets, with a significant risk of bleeding. The PROTAC drug markedly reduces that risk by inducing a selective degradation of the BCL-XL rather than blocking its enzymatic activity.

- Two CPRIT First Time Tenure Track Scholars at the Baylor College of Medicine - Dr. Koen Venken, assistant professor of biochemistry and molecular biology (R1313) and Dr. Damian Young, assistant professor, Department of Pharmacology and Chemical Biology (R1314) - collaborated to develop a novel technological approach that expands from two to six the number of molecular pathways that scientists can study simultaneously in a cell sample. This allows for the simultaneous readout of activity for five different cellular pathways, compared to just one pathway using a traditional approach, providing a much deeper understanding of pathways of interest in cancer. Published in the December 13, 2019, edition of *Nature Communications*, this innovative technology is important because cancer usually originates through

changes on many different genes and pathways, not just one, and currently most cell-based screening assays conduct single measurements.

- The University of Texas Southwestern Medical Center's CPRIT Scholar Dr. Sean Morrison and CPRIT grantee Dr. Ralph Deberardinis discover that melanoma cells are more likely to spread through the body if their surface bristles with a molecule called MCT. The CPRIT-supported researchers (R1109, RP100437, RP130272, RP140021, RP160089) studied the MCT molecule, which grabs lactate in the blood and ushers it into the cell where it increases the cell's chance of survival. When they dosed mice with melanoma with a drug that inhibits the action of MCT, the scientists observed that developing melanoma metastases stopped immediately. Melanomas in untreated mice spread to the mice's liver, kidneys, and pancreas. The drug had no effect on the growth of melanoma cells. This finding, published in the December 18, 2019, edition of *Nature,* has potential implications for how AstraZeneca should test a new MCT1 inhibitor under development. Rather than testing the MCTI1 inhibitor in melanoma that has already metastasized, these findings suggest that blocking MCT1 may be effective only at the stage when melanoma cells have reached the bloodstream and lymph nodes but not beyond.

- CPRIT Scholar Carlos L. Arteaga, M.D., Director of the Simmons Cancer Center at The University of Texas Southwestern Medical Center (RR170061), published findings in the January 23, 2020, edition of *Cancer Cell* that a two-drug combination halts the growth of cancer cells that carry HER2 mutations. HER2 mutations are key drivers in breast and other cancers. Scientists know that patients with cancers harboring HER2 mutations eventually develop resistance to neratinib, a promising new cancer drug currently in clinical trials. Dr. Arteaga discovered that everolimus, a drug already on the market, counters that resistance and blocks the cancer, thereby providing the basis for a novel drug combination against cancers with mutations in the HER2 gene. The combination of neratinib and everolimus worked in cell lines, organoids established from patient-derived tumors, and in mice harboring HER2 mutant tumors. The next step will be testing this two-drug combo in humans.

- CPRIT Scholar Chonghui Cheng, M.D., Ph.D., associate professor of molecular and human genetics at the Lester and Sue Smith Breast Center, Baylor College of Medicine (RR160009), found a protein naturally produced in the body that suppresses breast cancer metastasis in animal models of human tumors. She also discovered that elevated levels of this protein, AKAP8, predicts a better survival for breast cancer patients. These findings, reported in the January 24, 2020, edition of *Nature Communications*, show that AKAP8 impedes metastasis by interfering with

the production of proteins that stimulate metastatic behavior in cells and suggest strategies that can improve treatments for metastatic cancer.

- Baylor College of Medicine's CPRIT Scholar Matthew Ellis, MB, BChir, BSc., PhD, FRCP, develops a new method to analyze the tumor genetic material with protein characterization using a single-needle core biopsy from a patient's tumor. The CPRIT-supported study (RR140033) outlining this new micro-scale technology appears in the January 27, 2020, edition of *Nature Communications*. This type of proteogenomic analysis had only been possible before with much larger tissue samples taken at surgery. Developed with collaborators at the Broad Institute of MIT and Harvard, the new technique provides a more detailed and wider window into cancer biology, tumor type, and the mechanisms of response and resistance to therapy compared to conventional approaches.

- In January 2020, *Molecular Cancer Therapeutics*, a peer-reviewed American Association of Cancer Research journal, published preclinical data for Hummingbird Bioscience's lead candidate, HMBD-001, an anti-HER3 antibody. HER3 plays a role in a signaling pathway that promotes cancer cell division and growth. Preclinical models show that HMBD-001 is uniquely able to bind to a critical region on HER3, effectively inhibiting the activation of the signaling pathway – and consequently, tumor growth. Houston and Singapore-based Hummingbird received a $13.1 million CPRIT Product Development award in 2019 (DP190027) to develop a monoclonal antibody therapy designed to reverse one of the main causes of resistance to immunotherapy drugs.

- On February 4, 2020, Sunil Sharma, M.D., Salarius Pharmaceuticals, Inc. scientific founder and Deputy Director, professor and head of applied cancer research and drug discovery at the Translational Genomics Research Institute, published research from *in vitro* studies that demonstrate the potential for clinicians to use Salarius' lead clinical drug candidate SP-2577, also known as Seclidemstat, in combination with checkpoint inhibitors to treat cancers with identifiable mutations. The data are available in preprint at bioRxiv.com and published in the July 10, 2020, edition of PLOS ONE. Houston-based Salarius, a clinical-stage biotechnology company targeting cancers caused by mis-regulated gene expression, received an $18.7 million CPRIT Product Development Award in 2016 (DP160014) to develop and clinical study Seclidemstat for Ewing sarcoma.

- CPRIT Scholar Andy Futreal, Ph.D., chair of Genomic Medicine at The University of Texas M.D. Anderson Cancer Center (R1205), and collaborators at M.D. Anderson led a study that helps explain why osteosarcomas do not respond well to immunotherapy. By

analyzing comprehensive profiles of tumor samples taken from patients with osteosarcoma, Dr. Futreal's team found that poor infiltration of the tumor by immune cells and multiple immune-suppressing pathways all combine to dampen responses to immunotherapy. *Nature Communications* published the findings in its February 21, 2020, edition that also showed an increased expression of the gene *PARP2* in the tumors with the lowest levels of immune infiltration. This supports clinical trials exploring a combination of PARP inhibitors and immune checkpoint blockade. Osteosarcoma cancers occur primarily in adolescents. When diagnosed at initial stages, treatment with combination chemotherapy and surgery achieves survival rates of 70%, but metastatic osteosarcoma is associated with survival rates below 30%.

- Along with a team of researchers at The University of Texas Southwestern Medical Center, James Brugarolas, M.D., Ph.D., director of the Kidney Cancer Program, has discovered an "Achilles heel" of clear cell renal cell carcinoma. Clear cell renal carcinoma is a particularly difficult cancer to treat because it does not respond to chemotherapy or radiation treatment. UT Southwestern researchers focused on hyposia-inducible factor 2α (HIF-2α) that is a target of a tumor suppressor protein that scientists consider "undruggable". In a study published in the February 2020 issue of *Clinical Cancer Research,* the UT Southwestern team reported blood flow to tumors in patients receiving PT2385, a HIF-2 inhibitor drug, decreased by 29%. Biopsies of the tumors showed that PT2385 dissolved HIF-2α/HIF-1β and prevented the complex from activating cancer promoting genes. After a year, further tests showed that in at least two patients, a tumor developed resistance to the drug through a mutation within HIF-2 α. Dr. Brugarolas reports that the findings demonstrate how essential HIF-2α is to this type of cancer and how inhibitors like PT2385 are important to its treatment. CPRIT grantee Peloton Therapeutics developed PT2385. Dr. Brugarolas has received six CPRIT grants (RP101075, RP130603, RP130172, RP160440, RP180191, RP180192) totaling more than $5 million to support this work.

- An international collaboration led by CPRIT Scholar Matthew Ellis, MB., BChir., Ph.D., associate director of precision medicine in the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine (R140033), has new insights explaining the poor prognosis of a subset of ER+ breast cancer. They found that loss of a protein called neurofibromin led to endocrine treatment resistance and metastasis for ER+ breast cancer. These findings, published in the March 16, 2020, edition of *Cancer Cell*, also found a two-drug combination led to tumor regression in animal models with neurofibromin deficient ER+ breast cancers.

The team designed a clinical trial to determine the effectiveness of this therapeutic approach in patients with neurofibromin deficient ER+ breast cancers. Dr. Ellis at Baylor College of Medicine and Dr. Bora Lim at The University of Texas M.D. Anderson Cancer Center will lead the trial as part of the National Cancer Institute-MATCH program. The NIH program sponsors precision medicine cancer treatment clinical trials that select patients to receive treatment based on the genetic changes found in their tumors. In this trial, clinicians will treat ER+ breast cancer patients deficient in neurofibromin with the two-drug combo.

- A team of researchers at Rice University, including CPRIT Scholar Han Xiao, Ph.D., have discovered a way to create a photosensitizing molecule that kills cancer cells. Through their research on flurogenic dyes, the researchers discovered that replacing an oxygen atom with a sulfur atom in a flurophore results in a photosensitizing molecule that generates reactive oxygen species (ROS) when exposed to light. The ROS then destroys cancer cells. The method is significant because it does not require the use of heavy atoms usually needed in photodynamic therapy. With the findings published in the April 7, 2020, edition of the journal *Chemical Science,* Rice researchers are hopeful that this use of photosensitizers will have wide application on skin cancer. Rice recruited Dr. Xiao to Texas from Stanford with a First Time, Tenure Track recruitment grant (RR170014) in 2017.

- Researchers at Baylor College of Medicine, including William Decker, Ph.D., associate professor of pathology and immunology, discovered an additional class of proteins that plays a role in a cell-mediated immune response. Their research has shown that a class of proteins, Major Histocompatibility Complex (MHC), triggers a cell-mediated response. Research has shown that this type of immune response, rather than antibody-mediated response, results in immune response protection that lasts longer for the patient. By identifying that MHC plays a role in immune response, Baylor College of Medicine researchers believe that these findings, published in the April 16, 2020, issue of the journal *Federation of American Societies for Experimental Biology*, will help to design more effective vaccines for viral diseases and cancer. Dr. Decker received a CPRIT Individual Investigator grant RP110545 in 2011 that helped fund this research.

- Immunotherapy drugs that target a protein called “programmed death ligand 1” (PD-L1) on the surface of cancer cells have become the preferred method to treat many forms of cancer, often with dramatic results. But scientists do not fully understand how cancer cells turn on this protein. New research, led by CPRIT Scholar Kathryn O’Donnell, Ph.D., an associate professor of molecular biology at The University of Texas Southwestern Medical Center (R1101) and reported in the April 20, 2020,

edition of *Nature Cancer*, has identified genes that normally encourage PD-L1 production, or positive regulators, and those that stymie PD-L1 production, or negative regulators. Dr. O'Donnell's findings may offer new targets to improve how well current cancer immunotherapies work. Developing new drugs that specifically target proteins involved in making PD-L1 may improve the success of immunotherapy drugs.

- A team led by CPRIT Scholar Zhijie "Jason" Liu, Ph.D., assistant professor of molecular medicine in the Long School of Medicine at The University of Texas Health Science Center at San Antonio and the Mays Cancer Center (RR160017), published research in the May 18, 2020, edition of *Nature Cell Biology* identifying important drivers that enable tumors to change their behavior and resist anticancer therapies. By studying tumors in cell lines, mice, and human samples, the team documented genetic signals that promote the conversion of cancer cells from one stage to another. "Phenotypic plasticity" describes the cancer cell's ability to take different shapes, to grow faster or slower, and to vary in size. Cancers that acquire plasticity often are more dangerous, becoming metastatic and resistant to many targeted therapies. The team's next step is to screen new drugs, in the form of small molecules, that disrupt the genetic signals underlying tumor plasticity. Clinicians could administer such a drug along with current targeted therapies to eliminate resistance to those treatments.

- A new study, led by Venuprasad Poojary, Ph.D., associate professor of internal medicine and immunology at The University of Texas Southwestern Medical Center and published in the June 1, 2020, edition of *Nature Immunology*, offers clues to the mechanism behind Ulcerative Colitis (UC) and Crohn's disease. The research provides several new potential targets to treat these often-devastating inflammatory bowel conditions. The findings are part of a CPRIT-funded project (RP160577) investigating an enzyme that may block the severe intestinal inflammation that promotes colon cancer. Using a mouse model, the team discovered that the loss of a gene, Cyld, allowed the inflammation associated with Crohn's and UC to spiral out of control, leading to overproduction of a key inflammatory molecule called IL-18, and spurring inflammation in the intestines. Two-thirds of patients with UC and Crohn's disease showed an abnormally low amount of the Cyld protein, confirming the relevance of the mouse experiments and suggesting a potential target to reduce intestinal inflammation in these patients.

- C. Patrick Reynolds, M.D., Ph.D., Director, Cancer Center at Texas Tech University Health Sciences Center, has developed a new classification for neuroblastoma, a childhood cancer with heterogeneous clinical outcomes. Dr. Reynolds' CPRIT-

supported research (RP170510) reported in the June 15, 2020, edition of *Cancer Research*, used markers of telomere maintenance mechanisms to stratify high-risk neuroblastoma into three subgroups with different survivals. Building on the CPRIT grant findings, Dr. Reynolds secured a grant from the National Cancer Institute for a large confirmatory clinical study necessary to validate the new clinical risk stratification. If validated, the stratification may improve the analysis of future clinical trials in patients with high-risk neuroblastoma and reduce the intensity of therapy for the better risk patients.

- Researchers at The University of Texas Health Science Center at San Antonio, including CPRIT Scholar Patrick Sung, Ph.D., published their discovery in the June 18, 2020, edition of the journal *Nature Communications*, showing that DNA resection pathways are specific, and each resection enzyme addresses a particular type of complex break. This discovery helps scientists understand why many enzymes are involved and why several enzymes are necessary to repair the DNA break. Describing the discovery, Dr. Sung said, "It's like an engine mechanic who has a set of tools at his disposal. The tool he uses depends on the issue that needs to be repaired. In like fashion, each DNA repair tool in our cells is designed to repair a distinctive type of break in our DNA." UT Health San Antonio recruited Dr. Sung from Yale in 2019 with the support of a $6 million CPRIT Established Investigator Award (RR180029).

- OncoNano Medicine, Inc. published Phase 1 clinical trial data in the June 26, 2020 issue of *Nature Communications* featuring OncoNano's intraoperative tumor imaging product candidate, ONM-100. The study evaluated safety, pharmacokinetics and feasibility of ONM-100 in image-guided surgery, occult tumor detection and visualization of tumor margins in four different cancer types. Following tumor resection, ONM-100 detected residual tumor positive margins in 9 of 9 patients in whom histology confirmed tumor positive margins, as well as detecting occult lesions in an additional 5 patients whose tumors were undetected by standard of care. The Southlake-based OncoNano received a $6 million CPRIT Product Development award in 2014 and a $10 million award in 2020 to develop ONM-100 to detect breast, head and neck, and skin cancers. In addition, the company received a $15.4 million CPRIT Product Development award in 2019 to develop a novel T-cell activating cancer vaccine for solid tumors.

- To better understand and research viroplasms, researchers at Baylor College of Medicine created a rotavirus carrying an NSP2 protein with a mutation in amino acid 313, referred to as a phosphomimetic mutation. In findings published in the July 2020 edition of the *Journal of Virology,* Baylor College of Medicine researchers found that compared to the non-mutated rotavirus, the modified virus created viroplasms

at a slower rate and replicated more slowly. This allowed the researchers to better observe early viroplasm formation, which led to their discovery that lipid droplets are a critical aspect of viroplasms. The researchers will continue to use the mutated rotavirus to research viroplasm formation and how lipid droplets form. Support for this work included two CPRIT Core Facility grants (RP150578, RP170719) totaling more than $10 million awarded to the Texas A&M University System Health Science Center for use on behalf of Gulf Coast Consortium researchers, including these researchers from Baylor College of Medicine.

- Robert Waterland, Ph.D., professor of pediatrics-nutrition at Baylor College of Medicine, is part of a team using computational tools to identify cell-type specific methylation patters (referred to as "molecular barcodes") in cell mixtures. DNA methylation is an epigenetic mechanism in which cells switch genes on or off. This whole genome bisulfite sequencing (WGBS) is the primary way to study DNA methylation. The Baylor College of Medicine researchers developed software to identify cell type specific methylation patterns within WGBS. Before this study, published in the July 1, 2020, issue of the journal *Genome Biology*, scientists could not distinguish methylation signals between different cell types. Dr. Waterland explained the study's significance, "It's a bit like wearing noise cancelling headphones to the symphony…Now, for the first time, researchers can 'tune in' to the full richness and complexity of WGBS data." Dr. Waterland received a $1 million CPRIT Individual Investigator Award for Prevention and Early Detection (RP170295) to support this work.

- Scientists already know that the immune protein STING helps protect against viruses and tumors by signaling the immune molecule interferon. In a study published in the July 7, 2020, edition of *Immunity*, Nan Yan, Ph.D., The University of Texas Southwestern Medical Center associate professor of immunology and microbiology, found that STING also activates a separate pathway that directly kills tumor-fighting immune cells without interferon. This is important because it may lead to development of longer-lasting immunotherapies to fight cancer. A CPRIT Investigator-Initiated Research Award (RP180288) supports Dr. Yan's research.

- Researchers at Baylor College of Medicine, Texas Children's Hospital, and Houston Methodist Hospital report that a child with rhabdomyosarcoma showed no detectable cancer following treatment on a clinical trial. The trial evaluates the effectiveness of chimeric antigen receptor (CAR) T cells engineered to target the HER2 protein on the surface of the cancer cells. Because 75 percent of tumor cells in the child's muscle cancer displayed the HER2 protein, the scientists reprogrammed the child's T cells to target the HER2 protein. Although cancer returned six months

after first stopping the T cell infusions, the child achieved a second remission after re-treatment with HER2-CAR T cells. At the time of the report in the July 15, 2020, edition of *Nature Communications*, the child last received T cell treatment 19 months ago and remains healthy and cancer free. A CPRIT Multi Investigator Research Award (RP101335) and a CPRIT Core Facility Support Award supported the clinical trial and CART T cell treatment preparation.

- In a recent study at Baylor College of Medicine on the relationship between cancer and children with birth defects, Sharon Plon, M.D., Ph.D., professor of pediatrics-oncology, and Philip Lupo, Ph.D., associate professor of pediatrics, studied data from population-based registries in four states. Their research, detailed in the August 1, 2020, edition of the journal *Cancer*, found that acute lymphoblastic leukemia (ALL) accounted for a smaller portion of diagnoses (12.4%) of children with birth defects compared to 24.5% of the general population of children with cancer. They also found that children with birth defects had a larger proportion of tumors that were of embryonic origin (including neuroblastoma and hepatoblastoma). Results from this study, supported by three CPRIT awards (RP140258, RP170071, RP160097), will help further understanding of the link between cancer and children with birth defects.

- In a report in the September 3, 2020, edition of *Nature*, a team led by CPRIT Scholar Sean Morrison, professor of pediatrics at The University of Texas Southwestern Medical Center (R1109), found melanoma cells passing through lymph nodes pick up a protective coating of oleic acid. This allows the cells to survive elevated levels of oxidative stress in the blood. Scientists know that many kinds of cancer cells often spread first to lymph nodes before other organs. The protective coating of oleic acid may assist the cancer cells' transit through the bloodstream to other parts of the body where they form metastatic tumors. These findings raise the possibility of treating patients with drugs that target protective mechanisms in the lymph to inhibit the initial stages of metastasis. CPRIT Individual Investigator Research Award (RP170114) and a Multi Investigator Research Award (RP180778) awarded to Dr. Morrison supported this research.