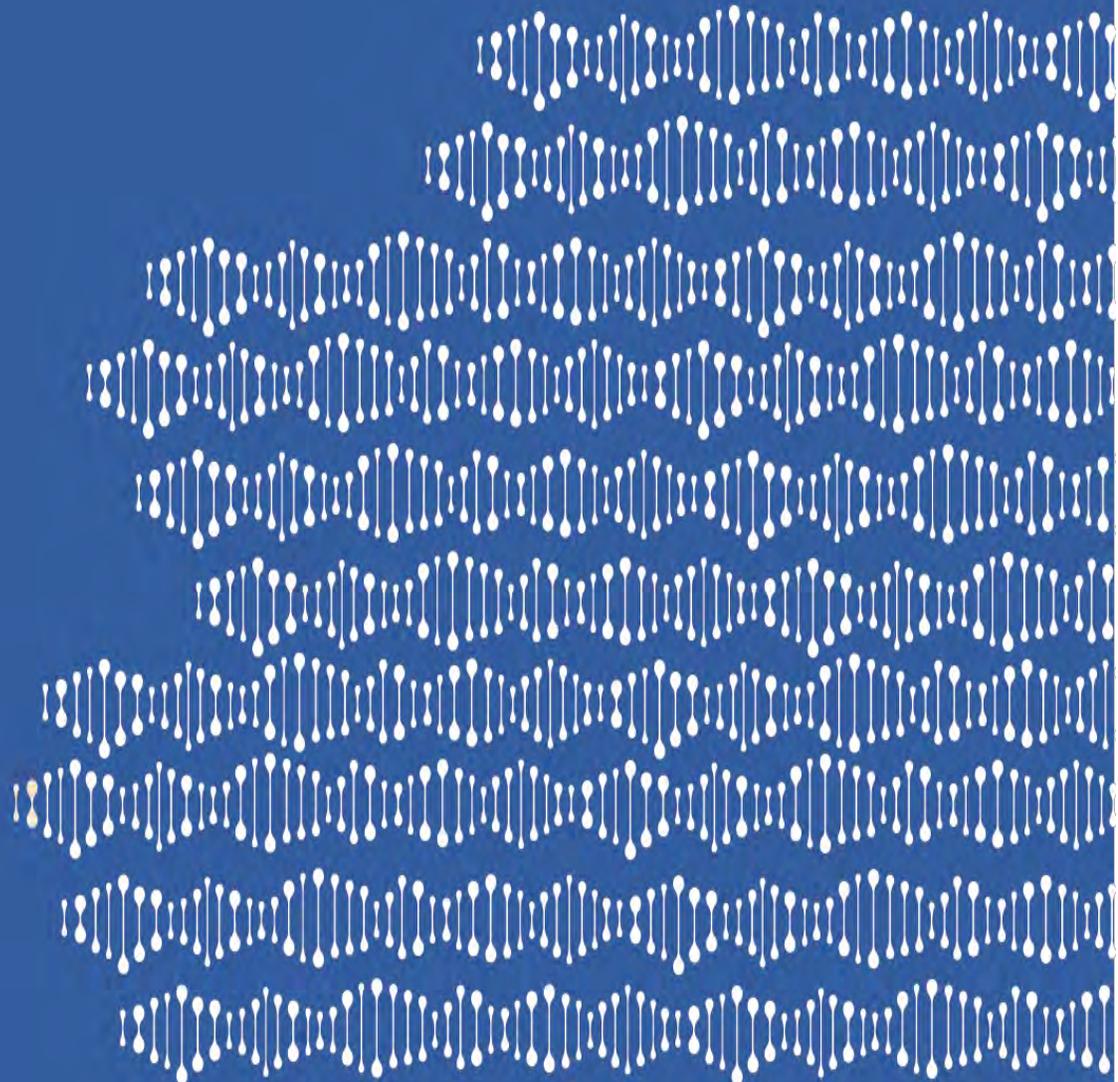




CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

# Oversight Committee Meeting

May 16, 2018







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## **Summary Overview of the May 16, 2018, Oversight Committee Meeting**

This summary provides an overview of major agenda items and background on key issues for Committee consideration at the May 16, 2018, Oversight Committee meeting.

### **CEO Report**

Wayne Roberts will present the CEO's report and address issues including personnel, available grant funds, and reports on the Texas Healthcare and Bioscience Institute annual conference and the Houston City Council's National Cancer Month Proclamation Event and other topics.

### **Grantee Presentation – James Brugarolas, M.D., Ph.D.**

Dr. James Brugarolas will report on building a kidney cancer program in Texas. Dr. Brugarolas is the primary investigator on five CPRIT grants totaling more than \$5.5 million.

### **Chief Compliance Officer Report**

Vince Burgess will report on the status of required grantee reports, financial status report reviews, desk reviews and site visits, annual compliance attestation, single audit tracking, and training.

### **Chief Scientific Officer Report and Grant Award Recommendations**

Dr. James Willson will provide an update on the Academic Research Program, including a proposed request for applications for FY 2019, and present the Program Integration Committee's (PIC) award recommendations for Academic Research grant awards. He will also present an issue related to CPRIT grant RP150058.

*CPRIT does not publicly disclose information related to the Academic Research grant applications recommended for funding until the Oversight Committee meeting. The information is available to board members through a secure electronic portal.*

### **Chief Prevention and Communications Officer Report and Grant Award Recommendations**

Dr. Becky Garcia will report to the Oversight Committee on the Prevention Program activities and present the PIC's award recommendations for Prevention grant awards. She will also present the agency's communications update.

*CPRIT does not publicly disclose information related to the Prevention grant applications recommended for funding until the Oversight Committee meeting. The information is available to board members through a secure electronic portal.*

### **Chief Product Development Officer Report**

An update on the Product Development Program, including an overview of FY 2019 Requests for Applications, will be provided to the Oversight Committee.

### **Appointments - Scientific Research and Prevention Programs Committee**

Mr. Roberts has provisionally appointed one new member to CPRIT's Scientific Research and Prevention Programs Committees. CPRIT's statute requires the Oversight Committee to approve the CEO's recommendation before the appointment is final. A biographical sketch for the appointee is included for the Oversight Committee's consideration.

### **Advisory Committee Reports**

The Advisory Committee on Childhood Cancer and the Product Development Advisory Committee will each present an annual report to the Oversight Committee. CPRIT's administrative rules and the committees' charter require advisory committees to provide updates to the Oversight Committee annually.

### **Advisory Committee on Clinical Trials**

A new advisory committee, charter, and appointments will be presented for Oversight Committee consideration.

### **Internal Auditor Report**

Weaver and Tidwell, CPRIT's internal auditor, will provide an internal audit update.

### **Oversight Committee Secretary Position**

With the resignation of Oversight Committee member Amy Mitchell, a vacancy exists in the board secretary position. The Presiding Officer will nominate an interim secretary for Oversight Committee approval.

### **Health & Safety Code § 102.1062 Waiver**

Mr. Roberts will present a conflict of interest waiver pursuant to Texas Health & Safety Code § 102.1062. The waiver is a blanket waiver CPRIT will invoke when a review council member must participate in a discussion of recommended applications that may include an application that the council member has reported a conflict.

### **Amendments to 25 TAC Chapters 701 and 703**

Cameron Eckel will present the final order approving amendments to Chapter 703 that the Oversight Committee provisionally approved at the February meeting. If approved, the amendments will become effective in June.

Ms. Eckel will also present proposed changes to the agency's administrative rules in Chapters 701 and 703. Texas Health and Safety Code § 102.108 authorizes the Oversight Committee to implement rules to administer CPRIT's statute. Legal staff will bring back these proposed rule changes to the Oversight Committee for final approval in August after the public has an opportunity to comment on the proposed rule changes.

**Chief Operating Officer Report, Contract Approvals, and Fiscal Year 2019 Bond Issuance Resolution**

Heidi McConnell will discuss the operating budget, performance measures, and debt issuance history for the second quarter of Fiscal Year 2018. Ms. McConnell will present the Fiscal Year 2019 Bond Issuance Resolution for approval by the Oversight Committee. She will also provide an update regarding preparations for CPRIT's State Agency Strategic Plan for 2019 – 2023 and CPRIT's Legislative Request for the 2020 – 2021 biennium. She will also present recommendations for contract approvals for the following services: due diligence, grant management support, and outside legal services.





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## Oversight Committee Meeting Agenda

Texas State Capitol Extension  
1100 Congress Avenue, Austin, Texas 78701  
Room E1.012

May 16, 2018  
10:00 a.m.

The Oversight Committee may discuss or act on any item on this agenda, and as authorized by the Texas Open Meetings Act, Texas Government Code Section 551.001 et seq., may meet in closed session concerning any purpose permitted by the Act. Anyone wishing to offer public comments must notify the Chief Executive Officer in writing prior to the start of the meeting. The Committee may limit the time a member of the public may speak.

1. Call to Order
2. Roll Call/Excused Absences
3. Adoption of Minutes from the February 21, 2018, meeting **TAB 1**
4. Public Comment
5. Honorary Resolution – Amy Mitchell **TAB 2**
6. Grantee Presentation **TAB 3**
7. Chief Executive Officer Report **TAB 4**
8. Chief Compliance Officer Report **TAB 5**
9. Chief Scientific Officer Report **TAB 6**
  - Grant Award Recommendations
  - Proposed Request for Applications FY 2019
  - RR150058
10. Chief Prevention and Communications Officer Report **TAB 7**
  - Grant Award Recommendations
11. Chief Product Development Officer Report **TAB 8**
12. Scientific Research and Prevention Program Committee Appointments **TAB 9**
13. Advisory Committee on Childhood Cancer **TAB 10**
  - Annual Report
14. Advisory Committee on Product Development **TAB 11**
  - Annual Report
  - Appointments
15. Advisory Committee on Clinical Trials **TAB 12**
  - Appointments
  - Charter
16. Internal Auditor Report **TAB 13**
17. Oversight Committee Secretary Position **TAB 14**
18. Health & Safety Code Section 102.1062 Waiver

19. Amendments to 25 T.A.C. Chapters 701 – 703 **TAB 15**
  - Final Order Approving Amendments to Chapter 703
  - Proposed Amendments to Chapters 701 and 703 and Authorization to Publish in *Texas Register*
20. Fiscal Year 2019 Bond Issuance Resolution **TAB 16**
21. Chief Operating Officer Report **TAB 17**
  - State Agency Strategic Plan 2019 – 2023
  - Legislative Appropriations Request for 2020-2021 Biennium
22. Contract Approvals **TAB 18**
  - Due Diligence Services
  - Grant Management Support Services
  - Outside Legal Services
23. Subcommittee Business
24. Compliance Investigation Pursuant to Health & Safety Code § 102.2631
25. Consultation with General Counsel
26. Future Meeting Dates and Agenda Items
27. Adjourn



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CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

**Oversight Committee Meeting  
February 21, 2018**

NOTE: Unless the information is confidential, the reports and presentations referenced in the minutes are available at [http://www.cprit.state.tx.us/cprit-media/oc\\_packet\\_02-21-2018.pdf](http://www.cprit.state.tx.us/cprit-media/oc_packet_02-21-2018.pdf). Information regarding the recommended awards is available at [http://www.cprit.state.tx.us/cprit-media/proposed\\_grant\\_awards\\_book\\_02212018.pdf](http://www.cprit.state.tx.us/cprit-media/proposed_grant_awards_book_02212018.pdf).

**Call to Order – Agenda Item 1**

A quorum being present, Presiding Officer Will Montgomery called the Oversight Committee to order at 10:02 a.m.

**Roll Call/Excused Absences – Agenda Item 2**

Committee Members Present

Amy Mitchell  
Angelos Angelou  
Bill Rice, M.D.  
Donald (Dee) Margo  
Will Montgomery

Mahendra Patel, M.D. was not present at roll call. Dr. Patel arrived at 10:09 a.m. as noted in the minutes.

Absent

Craig Rosenfeld, M.D.

**MOTION:**

On a motion by Mr. Margo and seconded by Mr. Angelou, the Oversight Committee unanimously voted to excuse the absence of Dr. Rosenfeld.

**Adoption of Minutes from the November 29, 2017 and January 17, 2018 Meeting – Agenda Item 3 – Tab 1**

**MOTION:**

On a motion by Dr. Rice and seconded by Mr. Angelou, the Oversight Committee unanimously voted to approve the minutes of the Oversight Committee meetings of November 29, 2017 and January 17, 2018, as presented.

## **Public Comment – Agenda Item 4**

Presiding Officer Montgomery noted that there were three requests for public comment.

Mr. Cam Scott, Senior Director of Texas Government Relations for the American Cancer Society Cancer Action Network, provided a handout (included in the Oversight Committee packet). He reported that the American Cancer Society (ACS) wants CPRIT to continue and requested that CPRIT submit a legislative appropriations request that includes an exceptional item for additional funding to keep grant funding at current levels in the FY 2020-2021 biennium. Mr. Scott spoke to CPRIT's important work and that ACS will continue to do what they can to see CPRIT continue.

Mr. Robert Sartin, an ACS volunteer, shared that doctors diagnosed his son, Spencer, with acute lymphocytic leukemia when Spencer was four years old. He is now 18. Mr. Sartin believes that his son would not be here if he had not been part of a research study in 1991, which helped refine the treatment protocol and reduce the length of chemotherapy. Mr. Sartin and Spencer were guests of their state representative and attended the State of the State Address when Governor Perry proposed CPRIT. He encouraged the Oversight Committee to act to continue funding for CPRIT without interruption.

Mr. Jason Chilton, a volunteer with Young Texans Against Cancer (YTAC) of Austin, said that one of the greatest functions of government is to protect the lives of its citizens. Cancer takes the lives of more citizens than the tragedies we see in the news every day. He supports the legislature providing continued funding to create a greater impact and to help Texans move closer to a cure.

There were no questions regarding the public comments. Presiding Officer Montgomery thanked Mr. Scott, Mr. Sartin, and Mr. Chilton for their comments.

*Presiding Officer Montgomery noted for the record that Dr. Patel arrived at 10:09 a.m.*

## **Grantee Presentation – Agenda Item 5 – Tab 2**

Michael Lang, Chief Product Development Officer, introduced Dr. Gary Latham, Sr. Vice President of Research and Development at Asuragen. Asuragen is a molecular diagnostic company located in Austin. Molecular diagnostics play a critical role in the assessment of cancer. Asuragen is one of CPRIT's early awardees, receiving a \$6.8 million grant in 2012.

Dr. Latham reported on the next-generation sequencing diagnostic tool that Asuragen developed with the support of a CPRIT grant award. Asuragen markets the tool currently. Dr. Latham noted that the CPRIT grant award resulted in many lasting and positive follow-on effects for the company. For example, he said that the cancer diagnostic tool developed with support from CPRIT resulted in a major industry partnership. The industry partnership led Asuragen to upgrade their laboratory facilities, which fueled the company's decision to remain in Texas for the long term. Dr. Latham also discussed a collaboration with MD Anderson, spurred by the CPRIT grant, which utilized Asuragen's tool to design targeted therapies for cancer patients in the BATTLE-2 Program.

Dr. Latham replied to an Oversight Committee member's question about how widely used the Asuragen tool was, explaining that the company distributes these products globally. He reports that Asuragen has a global footprint with a distribution network of more than 60 countries.

An Oversight Committee member inquired about Dr. Latham's views on the diagnostic potential of protein-expression and protein-protein interactions. Dr. Latham replied that he sees exciting potential in the use of proteins in addition to DNA and RNA.

Presiding Officer Montgomery thanked Dr. Latham and Asuragen's team for their work and presentation to the Oversight Committee.

### **Chief Executive Officer Report – Agenda Item 6 – Tab 3**

Presiding Officer Montgomery recognized Mr. Wayne Roberts to provide the CEO report.

Mr. Roberts noted that if the Oversight Committee approves all recommendations presented at the meeting, there will be \$199 million in available grant funds for the rest of the year.

Mr. Roberts presented his report on grant progress as required by Texas Health & Safety Code § 102.260(c). He explained that FY 2017 was another year of progress for CPRIT and its three programs. Key metrics indicate that CPRIT is affecting Texas' national standing in both cancer research and the biomedical industry. Mr. Roberts directed the Oversight Committee members to page 3-22 of their packet for the breakdown of each program.

There were no questions for Mr. Roberts.

### **Chief Compliance Officer Report – Agenda Item 7 – Tab 4**

Mr. Vince Burgess, Chief Compliance Officer, presented his certification report (in the meeting packet at 4-1) on the status of required grantee reports, financial status report reviews, desk reviews and site visits, annual compliance attestation, single audit tracking, and training.

Mr. Burgess noted that CPRIT has scheduled a grantee training webinar for March 7, 2018. The training will cover grant reporting requirements, administrative rule changes, grant closeout, and an overview of the compliance program. The Compliance Program plans two training webinars in June and October of 2018.

Mr. Burgess directed Oversight Committee members to page 4-3 in their agenda packet, reporting that the number of delinquent grantee reports has increased this month. He indicated that 11 grantees did not file 38 required reports by the due date. Mr. Burgess attributed the increase to a change in the sequencing of the Matching Compliance Certification form; of the 38 late reports, 32 reports are the Matching Compliance Certification forms. CPRIT now requires grantees to submit forms in a specific order and only after CPRIT approves the previous form may the grantee submit the next form. Of the 32 delinquent matching compliance forms, 90% were from two grantees. CPRIT has an on-going bi-weekly call with one of these grantees and has instituted a bi-weekly call with the other grantee to provide additional assistance.

An Oversight Committee member inquired about the balance between compliance and productivity. Mr. Burgess replied that the compliance program continues to work at striking an appropriate a balance.

## **Chief Scientific Officer Report, Grant Award Recommendations, and Request for Applications FY 2019 – Agenda Item 8 – Tab 5**

### Academic Research Award Recommendations

Presiding Officer Montgomery recognized Dr. Jim Willson, Chief Scientific Officer, to present the academic research award slates recommended by the CPRIT Scientific Review Council (SRC) and the Program Integration Committee (PIC). Dr. Willson indicated that the SRC and the PIC recommended 44 Individual Investigator and five Recruitment awards totaling \$60,195,197.

Dr. Willson provided a high-level overview of the recommended Individual Investigator Research Awards (IIRA) by the five IIRA mechanisms, noting an overall success rate of 8.6% (521 applications submitted/ 44 awards recommended).

In response to an Oversight Committee member's question regarding the computational biology slate success rate, Dr. Willson responded that CPRIT provides written feedback to the applicants regarding the strengths and weaknesses of their applications. This feedback can help the applicant if he or she decides to reapply.

Dr. Willson presented five recruitment grant awards recommended by the SRC and the PIC. He provided a brief introduction of the five candidates for Recruitment of Rising Stars and Recruitment of First-Time Tenure Track Faculty Member mechanisms, totaling \$14,000,000.

### Compliance Certification (Academic Research and Prevention Awards)

Mr. Burgess presented his certification of the review process for the proposed grant awards recommended to the Oversight Committee (included in the meeting packet). He reviewed the compliance pedigrees for the grant applications submitted to CPRIT for the seven academic research award mechanisms and four prevention award mechanisms.

### Conflict of Interest Notification

Presiding Officer Montgomery noted that Mr. Angelou reported a conflict of interest with three applications submitted by The University of Texas at Austin, grant applications RP18073, RP180381, and RP180590.

Presiding Officer Montgomery suggested that, unless a member objected, the Oversight Committee consider all the academic research award recommendations together in one vote except for the proposed awards to The University of Texas at Austin, which the committee would vote on separately. No member objected.

<b>ID</b>	<b>Award Mechanism</b>	<b>Score</b>	<b>Application Title</b>	<b>PI</b>	<b>PI Organization</b>	<b>Budget</b>
RP180313	IIRA	1.0	A somatic mutant p53 mouse model of metastatic triple negative breast cancer	Lozano, G.	The University of Texas M. D. Anderson Cancer Center	\$900,000
RP180505	IIRAP	1.4	Circulating Exosomes as Biomarkers for Lung Cancer Early Detection	Taguchi, A.	The University of Texas M. D. Anderson Cancer Center	\$799,085
RP180147	IIRA	1.6	Prevalence of Rare Passenger Mutations in Biopsy Tissue as Cancer Stratification Markers	Zhang, D.	Rice University	\$900,000
RP180047	IIRA	1.7	A Novel Dual Suppressor of Cancer Bone Metastasis	Wan, Y.	The University of Texas Southwestern Medical Center	\$898,672
RP180192	IIRA	1.8	Dissecting the interplay between BAP1 and PBRM1 in renal cancer	Brugarolas, J.	The University of Texas Southwestern Medical Center	\$897,633
RP180343	IIRA	1.8	Turn ON the Tumor Contrast in Lymph Node Metastases for Occult Disease Detection	Gao, J.	The University of Texas Southwestern Medical Center	\$885,684
RP180178	IIRA	1.8	Imaging glucose stimulated zinc secretion (GSZS) from the prostate by MRI: A potentially powerful method for early detection of prostate cancer	Sherry, D.	The University of Texas Southwestern Medical Center	\$900,000
RP180463	IIRACCA	1.9	Compound heterozygous mutations in pediatric cancer predisposition	Schlacher, K.	The University of Texas M. D. Anderson Cancer Center	\$556,763*
RP180248	IIRACB	1.9	Characterizing cancer genome instability and translational impact using new sequencing technologies	Chen, K.	The University of Texas M. D. Anderson Cancer Center	\$898,997
RP180191	IIRACCA	1.9	Understanding TFE3-mediated Tumorigenesis through Analysis of a Novel, Clinically-Relevant Mouse Model of Translocation Renal Cell Carcinoma	Brugarolas, J.	The University of Texas Southwestern Medical Center	\$1,155,128
RP180220	IIRA	1.9	Targeting the prion protein Doppel in brain tumor angiogenesis	McCarty, J.	The University of Texas M. D.	\$900,000

ID	Award Mechanism	Score	Application Title	PI	PI Organization	Budget
					Anderson Cancer Center	
RP180435	IIRA	2.0	Fasting-induced inhibition of leukemia development	Zhang, C.	The University of Texas Southwestern Medical Center	\$900,000
RP180275	IIRA	2.0	Targeting Stromal ERalpha for Cervical Cancer Therapy	Chung, S.	University of Houston	\$811,617
RP180381	IIRACT	2.0	Mass Spectrometry Imaging to Uncover Predictive Metabolic Markers of Ovarian Cancer Surgical Outcome and Treatment Response	Schiavinato Eberlin, L.	The University of Texas at Austin	\$1,092,048
RP180394	IIRACCA	2.0	Targeting the metastatic sarcoma niche using leukocyte biomimetic nanoparticles	Tasciotti, E.	The Methodist Hospital Research Institute	\$1,199,617
RP180131	IIRACCA	2.1	DNA methylation signatures of cell-free DNA in CSF as a new response biomarker for pediatric medulloblastoma	Sun, D.	Texas A&M University System Health Science Center	\$1,200,000
RP180196	IIRACCA	2.1	Microwafers as Novel Drug or Gene Delivery Vehicles for Noninvasive Treatment of Retinoblastoma	Hurwitz, R.	Baylor College of Medicine	\$1,195,721
RP180410	IIRA	2.2	Mechanisms of Nuclear Export in Cancer	Chook, Y.	The University of Texas Southwestern Medical Center	\$900,000
RP180181	IIRA	2.2	Targeting neutrophil elastase as a novel therapy for metastatic breast cancer	Watowich, S.	The University of Texas M. D. Anderson Cancer Center	\$900,000
RP180504	IIRA	2.2	Elucidating the Epigenetic and Metabolic Vulnerabilities of Myeloproliferative Neoplasms	Xu, J.	The University of Texas Southwestern Medical Center	\$900,000
RP180268	IIRA	2.2	Determining the role of polyploidization in liver cancer development	Zhu, H.	The University of Texas Southwestern Medical Center	\$900,000
RP180309	IIRA	2.2	Inhibiting Oxidative Phosphorylation: A Novel Strategy in Leukemia	Konopleva, M.	The University of Texas M. D. Anderson Cancer Center	\$900,000

ID	Award Mechanism	Score	Application Title	PI	PI Organization	Budget
RP180261	IIRA	2.2	Multi-Loading Strategy for Constructing Potent Antibody-Drug Conjugates	Tsuchikama, K.	The University of Texas Health Science Center at Houston	\$900,000
RP180473	IIRACT	2.2	Clinical trials of C188-9, an oral inhibitor of signal transducer and activator of transcription (STAT) 3, in patients with hepatocellular carcinoma (HCC)	Tweardy, D.	The University of Texas M. D. Anderson Cancer Center	\$2,399,905
RP180031	IIRA	2.2	Imaging of biochemical alterations in human breast malignancy using CEST-MRI	Vinogradov, E.	The University of Texas Southwestern Medical Center	\$900,000
RP180244	IIRA	2.3	Functional analyses of linkage-specific ubiquitination in the DNA damage response	Wang, B.	The University of Texas M. D. Anderson Cancer Center	\$900,000
RP180404	IIRACT	2.3	Noninvasive detection of anthracycline induced cardiotoxicity using hyperpolarized carbon 13 based magnetic resonance spectroscopic imaging	Zaha, V.	The University of Texas Southwestern Medical Center	\$2,397,204
RP180349	IIRA	2.4	Therapeutics Targeting Cancer-Associated HPV Replication	Chiang, C.	The University of Texas Southwestern Medical Center	\$900,000
RP180530	IIRA	2.4	Hippo signaling in non-alcoholic fatty liver disease (NAFLD) and it progression to hepatocellular carcinoma	Johnson, R.	The University of Texas M. D. Anderson Cancer Center	\$821,669
RP180607	IIRAP	2.4	Blood-based biomarkers for the early detection of pancreatic cancer	Killary, A.	The University of Texas M. D. Anderson Cancer Center	\$900,000
RP180590	IIRA	2.4	Development of an engineered & pharmacologically optimized human methionine-gamma-lyase drug candidate for the treatment of prostate cancer and glioblastoma	Stone, E.	The University of Texas at Austin	\$900,000
RP180553	IIRA	2.5	Structural and Functional Characterization of the DNA Double Strand Break Processing Complex of Mre11-Rad50	Latham, M.	Texas Tech University	\$850,876

ID	Award Mechanism	Score	Application Title	PI	PI Organization	Budget
RP180259	IIRA	2.5	PTEN Promotes Diabetic breast cancer metastasis	LIN, C.	The University of Texas M. D. Anderson Cancer Center	\$900,000
RP180588	IIRAP	2.5	Novel Computer Aided Diagnosis System For Early Detection Of Oral Cancer Based On Quantitative Autofluorescence Imaging	Jo, J.	Texas Engineering Experiment Station	\$897,394
RP180166	IIRACCA	2.6	Molecular mechanisms of anthracycline response in cardiomyocytes and link to genetic susceptibility to cardiotoxicity in long-term childhood cancer survivors	Hildebrandt, M.	The University of Texas M. D. Anderson Cancer Center	\$1,194,520
RP180466	IIRACT	2.6	Integrated single-cell biomarkers of T-cell efficacy	Varadarajan, N.	University of Houston	\$1,173,420
RP180055	IIRA	2.7	Mechanisms and Treatment of Hippocampal Cognitive Impairment Associated with Androgen Deprivation Therapy for Prostate Cancer	Morilak, D.	The University of Texas Health Science Center at San Antonio	\$899,547
RP180472	IIRA	2.8	Mucosal vaccine formulations for targeted therapy of HPV cancers	Sastry, J.	The University of Texas M. D. Anderson Cancer Center	\$883,146
RP180457	IIRA	2.8	Tumor Activated Enzyme Inhibitors for the Treatment of Cancer	Ready, J.	The University of Texas Southwestern Medical Center	\$898,776
RP180140	IIRACT	2.8	EXTernal beam radiation to Eliminate Nominal metastatic Disease (EXTEND): A randomized phase II basket trial to assess local control of oligometastatic disease	Tang, C.	The University of Texas M. D. Anderson Cancer Center	\$2,394,412
RP180634	IIRACCA	2.9	Understanding metabolic regulation of pediatric glioma through mouse modeling and patient tumor interrogation in vivo.	Bachoo, R.	The University of Texas Southwestern Medical Center	\$1,200,000
RP180073	IIRACCA	3.4	Myeloid support of refractory and aggressive T-ALL at distinct tumor sites	Ehrlich, L.	The University of Texas at Austin	\$1,200,000
RP180177	IIRA	3.5	Novel Small Molecule Probes Targeting Histone Acetyltransferase p300/CBP	Song, Y.	Baylor College of Medicine	\$900,000

ID	Award Mechanism	Score	Application Title	PI	PI Organization	Budget
RP180288	IIRA	3.5	Innate Immune Regulation of Cancer Cell Proliferation	Yan, N.	The University of Texas Southwestern Medical Center	\$900,000
RP180319	IIRACCA	3.5	Rhabdomyosarcoma vulnerabilities: Prioritizing and extending to the clinic	Skapek, S.	The University of Texas Southwestern Medical Center	\$1,193,363

\*RP180463 reflects budget as reduced by the SRC. SRC recommended to fund only Aim 1 and reduce the duration of the study from 4 years to 3.

Academic Research Recruitment Grant Awards					
App ID	Mechanism	Candidate	Organization	Budget	Overall Score
RR180011	RFTFM	Bose, Rohit	The University of Texas M.D. Anderson Cancer Center	\$2,000,000	1.0
RR180014	RFTFM	Zhong, Zhenyu	The University of Texas Southwestern Medical Center	\$2,000,000	1.0
RR180017	RFTFM	Jiang, Wen	The University of Texas Southwestern Medical Center	\$2,000,000	2.0
RR180016	RRS	Hoshida, Yujn	The University of Texas Southwestern Medical Center	\$4,000,000	2.0
RR180012	RRS	Jiang, Xiaoqian	The University of Texas Health Science Center at Houston	\$4,000,000	2.8

RRS: Recruitment of Rising Stars      RFTFM: Recruitment of First-Time Tenure Track Faculty Members

**MOTION:**

On a motion made by Mr. Margo and seconded by Dr. Rice, the Oversight Committee unanimously voted to approve the PIC’s recommendations for The University of Texas at Austin grant applications RP180073, RP180381, and RP180590.

Presiding Officer Montgomery noted for the record that Mr. Angelou did not vote on these recommendations.

**MOTION:**

On a motion made by Dr. Rice and seconded by Mr. Angelou, the Oversight Committee unanimously voted to approve the PIC’s recommendations for the remaining 46 academic research awards.

**MOTION:**

On a motion made by Mr. Margo and seconded by Dr. Rice, the Oversight Committee unanimously voted to approve the delegation of contract negotiation authority to the Chief Executive Officer and CPRIT staff and authorized the Chief Executive Officer to sign the contracts on behalf of CPRIT.

Academic Research Program Report

Dr. Willson presented his report (page 5-1 – 5-5 in the agenda packet).

In response to an Oversight Committee member’s question, Dr. Willson explained that the academic research program maintains a master list of CPRIT Scholars recruited to Texas, which includes the state and institution of Origin. Mr. Wayne Roberts also noted that the quarterly Achievement Report provides a high-level view of this information.

Proposed Plan for RFAs for FY 2019 Cycle 2

Dr. Willson presented the FY 2019 RFA release schedule (page 5-5) for consideration. The proposed RFAs in the schedule include: Recruitment of Established Investigator, Recruitment of Rising Stars, Recruitment of First-Time Tenure Track Faculty Members, Core Facilities Support Awards, High Impact/High Risk Research Awards, and Early Translation Research Awards.

**MOTION:**

On a motion made by Dr. Patel and seconded by Mr. Margo, the Oversight Committee unanimously voted to approve the Academic Research Program’s plan for proposed RFAs for the second cycle of FY 2019.

**Chief Prevention and Communications Officer Report, Grant Award Recommendations, and Request for Applications FY 2019 – Agenda Item 9 – Tab 6**

Prevention Award Recommendations

Presiding Officer Montgomery recognized Dr. Rebecca Garcia, Chief Prevention and Communications Officer, to present the Prevention Review Council (PRC) and PIC’s recommendations for prevention awards. She reported that the PRC and PIC recommended eight projects, representing four grant mechanisms totaling \$13,105,573. Dr. Garcia noted that the PIC agreed with the PRC’s recommendation to reduce the budgets of PP170078 and PP170121, deferred from Cycle 17.2, by ten percent. Dr. Garcia reported that all the recommended applications address one or more of the Prevention Program priorities.

App. ID	Mech	Application Title	PD	Organization	Score	Rank Order	Budget
PP170121 Deferred from 17.2	EBP	Evidence-Based Hepatocellular Cancer Prevention through Target Hepatitis C Screening and Navigation	Jain, Mamta	The University of Texas Southwestern Medical Center	1.3	1	\$1,300,994
PP180003	EBP	BEST 2: Breast Cancer Education Screening and Navigation (BEST) Program for El Paso and West Texas	Shokar, Navkiran K	Texas Tech University Health Science Center at El Paso	1.7	2	\$1,499,908

PP180031	EBP	Get FIT to Stay Fit. Stepping Up to Fight Colorectal Cancer in the Panhandle.	Obokhare, Izi D	Texas Tech University Health Science Center	1.8	3	\$1,498,476
PP180016	TCL	Equitable Access to Lung Cancer Screening and Smoking Cessation Treatment: A Comprehensive Primary Care and Community Health Approach	Zoorob, Roger	Baylor College of Medicine	2	4	\$1,472,918
PP170078 Deferred from 17.2	CRC	Alliance for Colorectal Cancer Testing 2.0 (ACT 2.0)	Foxhall, Lewis E	The University of Texas M. D. Anderson Cancer Center	3.1	5	\$4,034,507
PP180025	TCL	Lung Cancer Screening and Patient Navigation (LSPAN)	Argenbright, Keith E	The University of Texas Southwestern Medical Center	3.3	6	\$1,499,997
PP180037	EBP	Advancing an Established Colorectal Cancer Prevention Program for Rural and Underserved Texans through A&M's Family Medicine Residency	McClellan, David A	Texas A&M University System Health Science Center	3.3	7	\$1,499,202

Prevention Grant Award Recommendations – Dissemination Cycle 18.2

App. ID	Mech	Application Title	PD	Organization	Score	Rank Order	Budget
PP180065	DI	Disseminating Cancer Control Framework and Strategies, a UT System Partnership	Argenbright, Keith	The University of Texas Southwestern Medical Center	2.3	1	\$299,571

DI: Dissemination of CPRIT-Funded Cancer Control Interventions

Dr. Garcia responded to Oversight Committee members’ questions, explaining that the 42 counties in the Colorectal Cancer Testing 2.0 Coalition project are not contiguous but are spread throughout the state and that the statewide colorectal cancer coalition meets annually but there is subcommittee activity throughout the year.

Dr. Garcia directed the Oversight Committee members to the “Counties of Residence of Populations Served by CPRIT Prevention Projects” map on page 80a in their award packets. The map includes sixty-six active and proposed projects and noted that CPRIT grantees have provided more than 4.3 million prevention services across the state. An Oversight Committee member commended the prevention program and grantees for providing services to residents of all Texas counties.

### Compliance Certification

Presiding Officer Montgomery noted that Mr. Burgess previously certified compliance of the prevention awards process.

### Conflict of Interest Notification

Presiding Officer Montgomery noted that no Oversight Committee member reported a conflict of interest with the applications under consideration.

Presiding Officer Montgomery suggested that, unless a member objected, the Oversight Committee consider all the prevention recommendations in one vote. No member objected.

#### **MOTION:**

On a motion made by Mr. Angelou and seconded by Ms. Mitchell, the Oversight Committee unanimously voted to approve the PIC's recommendations for Tobacco Control and Lung Cancer Screening, Colorectal Cancer Prevention Coalition, Evidence-Based Cancer Prevention Services, and Dissemination of CPRIT-Funded Cancer Control Intervention awards.

#### **MOTION:**

On a motion made by Dr. Rice and seconded by Mr. Angelou, the Oversight Committee unanimously voted to approve the delegation of contract negotiation authority to the Chief Executive Officer and CPRIT staff and authorized the Chief Executive Officer to sign the contracts on behalf of CPRIT.

### Proposed Prevention RFAs FY 2019 Cycle 1

Dr. Garcia directed members to pages 6-1 – 6-3 in their meeting packets and discussed the proposed RFAs and timeline for the prevention awards in the first cycle of FY 2019 Cycle 1.

There were no questions for Dr. Garcia.

#### **MOTION:**

On a motion made by Mr. Margo and seconded by Dr. Rice, the Oversight Committee unanimously voted to approve the Prevention Program's plan for proposed RFAs for FY 2019 Cycle 1.

### Communications Program Report

Dr. Garcia provided a Communications Program update and reported on program activities (pages 6-5 – 6-42 in the agenda packet). Dr. Garcia gave an overview of the fifth *CPRIT Innovation in Cancer Prevention and Research Conference*, held in November 2017 in Austin. Presiding Officer Montgomery thanked all who were involved with the conference.

Dr. Garcia responded to an Oversight Committee member's question about the number of product development research conference attendees, explaining that the number of people attending

typically reflects the overall percentage of grantees in each CPRIT program. Although CPRIT does not limit the conference to CPRIT grantees; a minority of the attendees were not CPRIT grantees.

### **Chief Product Development Officer Report, and Request for Applications FY 2019 – Agenda Item 10 – Tab 7**

Presiding Officer Montgomery recognized Mr. Lang to present the product development research program report. Mr. Lang directed members to his report in the agenda packet. He noted that the FY 2018.1 Product Development award cycle is complete. The Product Development Review Council, after considering 18 applications, including two applications that completed due diligence, declined to recommend any product development research awards for the first cycle of FY 2018.

Mr. Lang provided an overview of planned future award cycles. He indicated that the product development research program plans to maintain its existing schedule of two award cycles per year through 2021. He expects to release the RFAs for FY 2019.1 in June 2018.

Mr. Lang delivered a power point presentation (in the agenda packet beginning at 7-3) about the Product Development Research Program's new Seed Award RFA, which CPRIT plans to release for the first award cycle in FY 2019.

Responding to an Oversight Committee member's question about how an applicant like Asuragen fits within the range of development stages funded by CPRIT, Mr. Lang explained that Asuragen was early in the development process at the time of the award of 2012.

An Oversight Committee member asked about CPRIT's due diligence process. Mr. Lang explained that CPRIT's peer reviewers have domain expertise and are rigorous in their application evaluations. Mr. Roberts noted that he is concerned with the recent number of projects that go through the due diligence process that are not recommended for an award by the Product Development Review Council. Mr. Roberts indicated that he has engaged the Product Development Review Council to seek ideas to improve the success rates of product development research applicants.

#### **MOTION:**

On a motion made by Mr. Margo and seconded by Mr. Angelou, the Oversight Committee unanimously voted to approve the Product Development Research Program's plan for the proposed RFAs for FY 2019.

#### ***Recess***

*Presiding Officer Montgomery recessed the Oversight Committee for ten minutes at 12:02 p.m.*

#### ***Reconvene***

*Presiding Officer Montgomery reconvened the Oversight Committee at 12:13 p.m.*

Presiding Officer Montgomery announced that the Oversight Committee would take up Agenda Items 12 and 13 out of agenda order.

## **University Advisory Committee Annual Report – Agenda Item 12 – Tab 9**

Dr. Willson introduced Dr. Michelle Barton, Chair of the University Advisory Committee (UAC). Dr. Barton is a professor at The University of Texas MD Anderson Cancer Center, Department of Epigenetics and Molecular Carcinogenesis, and is the Dean at the Graduate School of Biomedical Sciences partnered with MD Anderson and the UT Health Science Center in Houston. Dr. Willson noted that Dr. Barton has provided outstanding guidance and support to CPRIT through her membership and leadership of the UAC.

Dr. Barton presented the UAC's 2017 annual report and recommendations to the Oversight Committee (pages 9-1 – 9-24 in the agenda packet) and provided an overview of the UAC's mission.

In response to an Oversight Committee member's question about the number of National Cancer Institute (NCI) designated centers in other states, Dr. Barton referred the Oversight Committee to the NCI map for that information.

Dr. Barton noted that prior to CPRIT, The University of Texas MD Anderson Cancer Center was the only NCI-designated Comprehensive Cancer Center in Texas. She credited CPRIT with helping two additional centers, Baylor College of Medicine and The University Texas Southwestern Medical Center, receive Comprehensive Cancer Center status. An Oversight Committee member asked how CPRIT's support for these two new centers made them successful NCI designated centers candidates. Dr. Barton explained that CPRIT's grants have brought increased interest, attention, and other extramural funding to cancer research at these institutions and across the state. Dr. Barton added that CPRIT's recruitment awards, research training awards and core facility support awards are paving the way of the future for Texas.

An Oversight Committee member asked about the number of patients in clinical trials supported by CPRIT grants. Dr. Barton explained that it may be possible to get this information by researching the clinical trial registry. Mr. Roberts added that CPRIT does track the number of patients in clinical trials, explaining that it is a critical metric for CPRIT.

Dr. Barton stated the UAC is supportive of all the RFAs and Program Priorities for FY 2018-2019.

## **Internal Auditor Report – Agenda Item 13 – Tab 10**

Presiding Officer Montgomery recognized Ms. Alyssa Martin, CPRIT Internal Auditor from Weaver and Tidwell, LLP, to present a status update on the FY 2018 internal audit plan, the recent internal audit reports, and the reports on follow-up procedures. She directed members to the audit materials in the meeting packet at pages 10-1 – 10-42 and provided her report.

There were no questions for Ms. Martin.

### **MOTION:**

On a motion made by Dr. Patel and seconded by Mr. Margo, the Oversight Committee unanimously approves the revised FY 2018 audit plan and the internal audit reports and follow up procedures reports as presented by CPRIT's Internal Auditor.

## **Scientific Research and Prevention Program Committee Appointments – Agenda Item 11 – Tab 8**

Presiding Officer Montgomery recognized Mr. Roberts to present the seven appointees to CPRIT's Scientific Research and Prevention Program Committee. Mr. Roberts recommends the appointments to the peer review committees for Oversight Committee approval. He noted that CPRIT provided the biographical information for the seven appointees in the agenda packet (pages 8-5 - 8-64) and that the Nominations Subcommittee discussed the appointments at their February 16, 2018, subcommittee meeting and recommends approval.

There were no questions for Mr. Roberts.

### **MOTION:**

On a motion by Dr. Rice and seconded by Mr. Margo, the Oversight Committee unanimously voted to approve the seven Scientific Research and Prevention Program Committee appointments.

### ***Recess***

*Presiding Officer Montgomery recessed the Oversight Committee for a 30-minute recess at 12:44 p.m.*

### ***Reconvene***

*Presiding Officer Montgomery reconvened the Oversight Committee at 1:17 p.m.*

## **Fiscal Year 2020 -2023 Budget Scenarios – Agenda Item 14 – Tab 11**

Presiding Officer Montgomery recognized Mr. Roberts to present the FY 2020 – 2023 budget scenarios. Mr. Roberts reported that he discussed the funding scenario preferred by the Oversight Committee at its special meeting in January with an initial group of legislators familiar with CPRIT, as well as CPRIT grantees and cancer advocates. He indicated that he also raised the possibility of CPRIT requesting an estimated \$190 million exceptional item request for the 2020 – 2021 fiscal biennium to maintain current grant funding levels. Mr. Roberts recommends the Oversight Committee approve the preferred funding scenario and the exceptional item request.

There were no questions for Mr. Roberts.

### **MOTION:**

On a motion by Mr. Margo and seconded by Mr. Rice, the Oversight Committee unanimously voted to adopt Budget Scenario 4 for planning purposes, including drafting the agency's request for legislative appropriations for the fiscal biennium beginning September 1, 2019, and to instruct CPRIT staff to prepare an exceptional item request for general revenue funding in an amount to continue current grant levels in the FY 2020 – 2021 biennium, estimated to be \$190 million.

## **Amendments to 25 TAC Chapters 701 and 703 – Agenda Item 15 – Tab 12**

Presiding Officer Montgomery recognized Ms. Cameron Eckel, Staff Attorney, to present the rules changes for Oversight Committee action. Ms. Eckel referred members to the final rule changes and proposed amendments in the Oversight Committee packet at pages 12-1 – 12-17. She reported that the Board Governance subcommittee recommended final approval for amendments to Texas Administrative Code Chapters 701 and 703, originally considered by the Oversight Committee at the November 2017 meeting. In addition, Ms. Eckel reported that the Board Governance subcommittee recommended approval to publish two proposed rule changes to Texas Administrative Code Chapter 703 in the *Texas Register* for public comment.

There were no questions for Ms. Eckel.

### **MOTION:**

On a motion by Dr. Rice and seconded by Mr. Margo, the Oversight Committee unanimously voted to approve the final orders adopting rules changes to the Texas Administrative Code Chapters 701 and 703 and to approve the publication of the proposed changes to the Texas Administrative Code Chapter 703 in the *Texas Register*.

## **Chief Operating Officer Report – Agenda Item 16 – Tab 13**

Presiding Officer Montgomery called upon Ms. Heidi McConnell, Chief Operating Officer, to present the Chief Operating Officer's report. Ms. McConnell reported on the operating budget, performance measures, and debt issuance history, noting that the information is in the agenda packet at 13-1 – 13-20.

There were no questions for Ms. McConnell.

## **Subcommittee Business – Agenda Item 17 – Tab 14**

Presiding Officer Montgomery laid out agenda item 17, reminding members that at the January meeting the Oversight Committee discussed the need for a new Special Issues subcommittee to address issues, including legislative matters, as they arise. CPRIT staff drafted a Special Issues Subcommittee charter for members' consideration. Presiding Officer Montgomery noted that currently CPRIT's Board Governance Subcommittee is responsible for reviewing legislation affecting CPRIT. He explained that if the Oversight Committee approves the proposed Special Issues Subcommittee charter, the Oversight Committee should revise the Board Governance Subcommittee charter to avoid overlapping duties. He reported that the Board Governance Subcommittee recommended the Oversight Committee approve establishing the Special Issues Subcommittee and changes to the Board Governance Subcommittee duties.

There were no questions for Presiding Officer Montgomery.

### **MOTION:**

On a motion by Mr. Angelou and seconded by Mr. Margo, the Oversight Committee unanimously voted to approve the creation of the Special Issues Subcommittee of the Oversight Committee and to ratify its charter.







## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

The Oversight Committee of the Cancer Prevention and Research Institute of Texas, also known as CPRIT, by unanimous vote of its members, adopts the following resolution.

### RESOLUTION

WHEREAS, Amy Mitchell, has served as an Oversight Committee member of the Cancer Prevention and Research Institute of Texas since September 26, 2013; and

WHEREAS, Amy Mitchell assumed the role as Oversight Committee member during a critical period of regaining the confidence of the Texas Legislature and the citizens of Texas in order for CPRIT to resume its role in the fight against cancer; and

WHEREAS, Amy Mitchell was pivotal in restoring that confidence; and

WHEREAS, Amy Mitchell worked selflessly for and on behalf of CPRIT, giving her time, prestige, and energy without remuneration; and

WHEREAS, Amy Mitchell steadfastly performed the duties of her office with equanimity, determination, and poise; and

WHEREAS, Amy Mitchell earned the respect and admiration of CPRIT staff through her dedication in furthering the mission of CPRIT; and

WHEREAS, Amy Mitchell likewise earned the respect of her fellow Oversight Committee members through her wise counsel and able leadership of the Board Governance subcommittee and as Secretary of the Oversight Committee; and

WHEREAS, CPRIT's mission of promoting prevention, academic research, and product development research advanced under Amy Mitchell's guidance to the benefit of all Texans; now, therefore, be it

RESOLVED, That the Oversight Committee of the Cancer Prevention and Research Institute of Texas hereby recognizes Amy Mitchell for her distinguished service to the citizens of the State of Texas, and expresses its gratitude for her many and lasting contributions to the Cancer Prevention and Research Institute of Texas; and, be it further

RESOLVED, That an official copy of this resolution be prepared for Amy Mitchell as an expression of high regard by Oversight Committee members and CPRIT staff.

Signed this 16<sup>th</sup> day of May 2018

\_\_\_\_\_  
Mahendra Patel, M.D.

\_\_\_\_\_  
Angelos G. Angelou

\_\_\_\_\_  
Will Montgomery

\_\_\_\_\_  
Donald "Dee" Margo

\_\_\_\_\_  
Craig S. Rosenfeld, M.D.

\_\_\_\_\_  
William Rice, M.D.

\_\_\_\_\_  
Wayne R. Roberts  
Chief Executive Officer



## James Brugarolas, M.D., Ph.D.

Director of the Kidney Cancer Program



**James Brugarolas, M.D., Ph.D.**, is a Professor at UT Southwestern Medical Center with appointments in both the Department of Internal Medicine's [Division of Hematology/Oncology](#) and the Department of Developmental Biology. He is a Virginia Murchison Linthicum Endowed Scholar in Medical Research.

A physician-scientist specializing in renal oncology, Dr. Brugarolas leads the [Kidney Cancer Program](#) at the [Harold C. Simmons Comprehensive Cancer Center](#), where he also serves as Co-Leader of the Cancer Cell Networks Program and runs the Renal Cell Carcinoma Tumor Board.

Dr. Brugarolas earned his medical degree at Spain's Universidad de Navarra before earning a doctoral degree in biology at the Massachusetts Institute of Technology. He completed an internship and residency in internal medicine at Duke University Medical Center and a medical oncology fellowship at a combined program of Massachusetts General Hospital, Brigham and Women's Hospital, and the Dana-Farber Cancer Institute.

Dr. Brugarolas joined the UT Southwestern faculty in 2006 with the goal of creating a comprehensive, dedicated renal oncology program. Today's program, which comprises some 40 investigators, is closely integrated with the [Brugarolas Laboratory](#).

He also serves as an investigator on several [clinical trials](#).

An active national and international speaker, Dr. Brugarolas is a member of the American Society of Clinical Oncology, the American Association for Cancer Research, and the American Society for Clinical Investigation.

He has authored groundbreaking research and published in journals such as *The New England Journal of Medicine*, *Nature*, *Cancer Cell*, *Nature Genetics*, and *Proceedings of the National Academy of Sciences*.

Dr. Brugarolas is also active in a variety of grant-review and teaching activities, including serving as a reviewer for the National Institutes of Health's National Cancer Institute, the American Cancer Society, and the U.S. Army Medical Research Command.



# THE FIGHT





LARRY CARLSON  
DISCOVERED A RENEWED  
SENSE OF HOPE AT SIMMONS  
CANCER CENTER.

**One of the largest  
kidney cancer  
programs in the  
nation is changing  
lives — one  
patient at a time**

**WHEN 72-YEAR-OLD LARRY CARLSON** was diagnosed with stage 4 kidney cancer, he simply didn't believe the news. Initially, Mr. Carlson was in denial about his cancer, but once he accepted the diagnosis, he decided that giving up wasn't going to be a part of his plan. He was determined to fight cancer with everything he had, so he contacted a patient coordinator at Simmons Cancer Center. He was drawn to the program at UT Southwestern based on its survival rates, which are more than double the national benchmarks, along with its world-class team of clinicians and researchers. More than three years later, Mr. Carlson isn't just surviving — he's thriving.

"UT Southwestern is a teaching hospital, so everything is on the cutting edge. There's always a team of people there to cheer you on, to provide you with the latest and most experimental treatments," he says, praising his treatment team for his incredible results.

Mr. Carlson enrolled in a clinical trial designed for kidney cancer patients with clear cell renal cell carcinoma that metastasized to other sites, a disease stage that was once

# CONTINUES



**LARRY AND ANN CARLSON NOW CONSIDER THEMSELVES PART OF THE UT SOUTHWESTERN FAMILY AND PROVIDE GUIDANCE TO OTHERS WHO ARE JUST BEGINNING THEIR JOURNEY.**

**Survival rates for stage 4 kidney cancer patients at UT Southwestern are more than double the national benchmark.**

thought to be largely incurable. He underwent major surgery that involved resection of the kidney tumor along with part of the liver that was affected by the cancer. After conventional treatment, he enrolled in a clinical trial that is available only at UT Southwestern and Johns Hopkins University. "This was a good option for Larry," says James Brugarolas, M.D., Ph.D., Mr. Carlson's doctor and leader of the Kidney Cancer Program. The clinical trial, which is directed by Hans Hammers, M.D., Ph.D., co-leader of the Kidney Cancer Program, involves a combination of the most active immu-

notherapy for kidney cancer, along with radiation. The treatment led to a profound reduction in Mr. Carlson's tumor burden. As a trial participant, he receives follow-up from a multidisciplinary team of specialists he calls "a sensational team." He now considers himself part of the UT Southwestern family and provides guidance to others who are just beginning their journey.

### **Making Strides in the Fight Against Kidney Cancer**

Mr. Carlson isn't alone in his fight – kidney cancer is the sixth most common type of cancer in men and the 10th

most common in women. Unfortunately, the incidence of kidney cancer is reportedly increasing in both men and women and is particularly prevalent in Texas. Luckily for patients in the North Texas region, UT Southwestern offers one of the largest kidney cancer programs in the country, with over 20 internationally recognized physicians and 60 research labs working to improve outcomes for patients diagnosed with the disease. Research at the Kidney Cancer Program of UT Southwestern has led to discoveries that have shaped the medical community's understanding of how kidney cancer develops and how it can best be eradicated.

The Kidney Cancer Program was one of the first in the United States to offer a noninvasive surgical treatment of kidney tumors utilizing ablation and is considered one of the top 10 robotic kidney surgery programs in the nation. Advancing the treatment of kidney cancer, the program offers the most innovative and broadest radiation solutions in the country.

The program reports five-year overall survival rates of 25 percent for stage 4 kidney cancer patients, a rate that is more than double the national benchmark of 11 percent. UT Southwestern attracts some of the most complex and advanced cases of kidney cancer, making these results even more impressive.

### **Distinction as Part of the Cure**

Patients and professionals alike recognize the groundbreaking nature of the research happening at UT Southwestern. The Kidney Cancer Program is one of only two programs in the country to receive a Specialized Program of Research Excellence (SPORE) Award by the National Cancer Institute. This program is designed to support research that will deliver cutting-edge treatments for kidney cancer. The Kidney Cancer Program was selected because of its history of discovery and innovation, which is changing the way kidney cancer patients are treated.

"The SPORE program is tackling fundamental questions in kidney cancer," says Dr. Brugarolas, who is the principal investigator leading SPORE. For example, a multidisciplinary team involving urological surgeons, a medical oncologist, a radiologist, and a biologist are studying how small tumors consume nutrients to distinguish tumors that may enlarge and become life-threatening from those that are harmless. This project could mean personalized treatments for kidney cancer patients that lead to better outcomes and quality of life.

# CONQUERING CANCER, ONE CLINICAL TRIAL AT A TIME

**At any given time, there are several ground-breaking trials underway at the Simmons Cancer Center Kidney Cancer Program. Read on to learn about some of the exciting discoveries that are being made.**

Two researchers at UT Southwestern, Steven McKnight, Ph.D., and David Russell, Ph.D., discovered the HIF-2a protein, arguably the most important driver of kidney cancer. HIF-2a was then characterized at the atomic level by Richard Bruick, Ph.D., and Kevin Gardner, Ph.D., and a weakness in its structure was identified. Next, this weakness was exploited to find chemicals that would block its function. These chemicals were the foundation for a biotech company, Peloton Therapeutics, in the UT Southwestern BioCenter, which turned them into a HIF-2a blocking drug. The HIF-2a blocking drug was then tested by a team led by Payal Kapur, M.D., and



James Brugarolas, M.D., Ph.D. The drug was evaluated in mice that had been transplanted with kidney tumors from patients. The researchers found that the drug blocked tumor growth in 50 percent of the kidney cancers. The study, which was reported in *Nature* last year, also identified features of the tumors that are most likely to respond.

The HIF-2a blocking drug has also been evaluated in patients. The results of a phase one clinical trial were published by UT Southwestern investigator Kevin Courtney, M.D., Ph.D., in the *Journal of Clinical Oncology* in December 2017

and showcased some life-changing results. Among 51 patients with aggressive kidney cancer that had progressed, on average, through five previous treatments, 40 percent had tumor growth blocked for at least four months with the HIF-2a drug. Twenty-five percent of patients had no more cancer growth after a full

year. This journey, going from gene discovery to a patient treatment at a single institution, is part of what makes the Kidney Cancer Program so unique.

Other clinical trials in the Kidney Cancer Program are currently testing combination immunotherapy. The combination of two drugs, nivolumab and ipilimumab, is able to shrink kidney tumors in 1 out of 3 patients and in UT Southwestern's Kidney Cancer Program is being evaluated in combination with radiation. Radiation can facilitate recognition of the cancer by the immune system's defenses.



JAMES  
BRUGAROLAS, M.D.

THE RIGHT  
TREATMENT FOR  
THE RIGHT PATIENT

For some kidney cancer patients, clinical trials can provide hope in the face of a devastating illness. Clinical trials can offer kidney cancer patients treatment with the newest treatment strategies and medications, while delivering promise for the kidney cancer patients of the future who will benefit from the trials. To learn more about the program and clinical trials, visit [utsouthwestern.edu/kidneycancer](http://utsouthwestern.edu/kidneycancer) or call 214-645-8300.

## Whole Patient Care

Beyond clinical trials and experimental, cutting-edge treatments, patients receiving care in the Kidney Cancer Program have access to multidisciplinary expertise from urologists, medical oncologists, radiation oncologists, interventional radiologists, and neurosurgeons. The physician team works together to meet all the patient's needs with the most innovative, compassionate care. Broader support systems include specialists in cancer psychology, oncology nutrition, social work, transitional care coordination, spiritual support, and integrative therapy.

Patients are exceedingly satisfied with the Kidney Cancer Program, which they ranked at 4.9 out of 5

in a recent patient satisfaction survey involving 250 responses. In addition to the world-class physicians and innovative research, another key element of the Kidney Cancer Program's success is its committed patient advocates, who provide a first line of support for patients, walking them through this confusing time from their very first phone call to doctor's visits to treatment team meetings and more. The Kidney Cancer Program staff also works closely with the families of those in treatment and recently launched a private Facebook community where kidney cancer patients and their families can get information and support one another on their journeys.

# Partnering with CPRIT to Build a Program of Excellence in Kidney Cancer

**James Brugarolas, M.D., Ph.D.**

Director, Kidney Cancer Program  
Principal Investigator, Kidney Cancer SPORE  
Sherry Wigley Crow Endowed Chair in Cancer Research  
Professor of Internal Medicine / Hematology-Oncology  
Cancer Biology, Genetics, Development and Disease  
University of Texas Southwestern Medical Center

## SPORE Leaders



J. Brugarolas  
\$4.2 M



T. Carroll  
\$.9 M



R. DeBerardinis  
\$2.2 M



J. Mendell  
\$1.2 M



Y. Yu  
\$2 M



R. Lenkinski  
\$2 M



Y. Xie  
\$.7 M

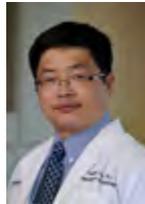
## Other SPORE PIs



C. Ahn  
\$.9 M



E. Maher  
\$1 M



X. Sun  
\$9.8 M



N. Williams  
\$1.3 M

## SPORE CEP/DRP Awardees



L. Banaszynski  
\$2 M



R. Mason  
\$2.2 M

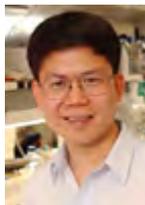


Y. Wan  
\$2 M

## KCP Members



J. Abrams  
\$.8 M



J. Chen  
\$.9 M



R. Hannan  
\$.1 M



J. Jewell  
\$2.2 M



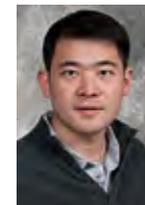
W. Luo  
\$2.2 M



S. Malladi  
\$2 M



B. Posner  
\$2.2 M



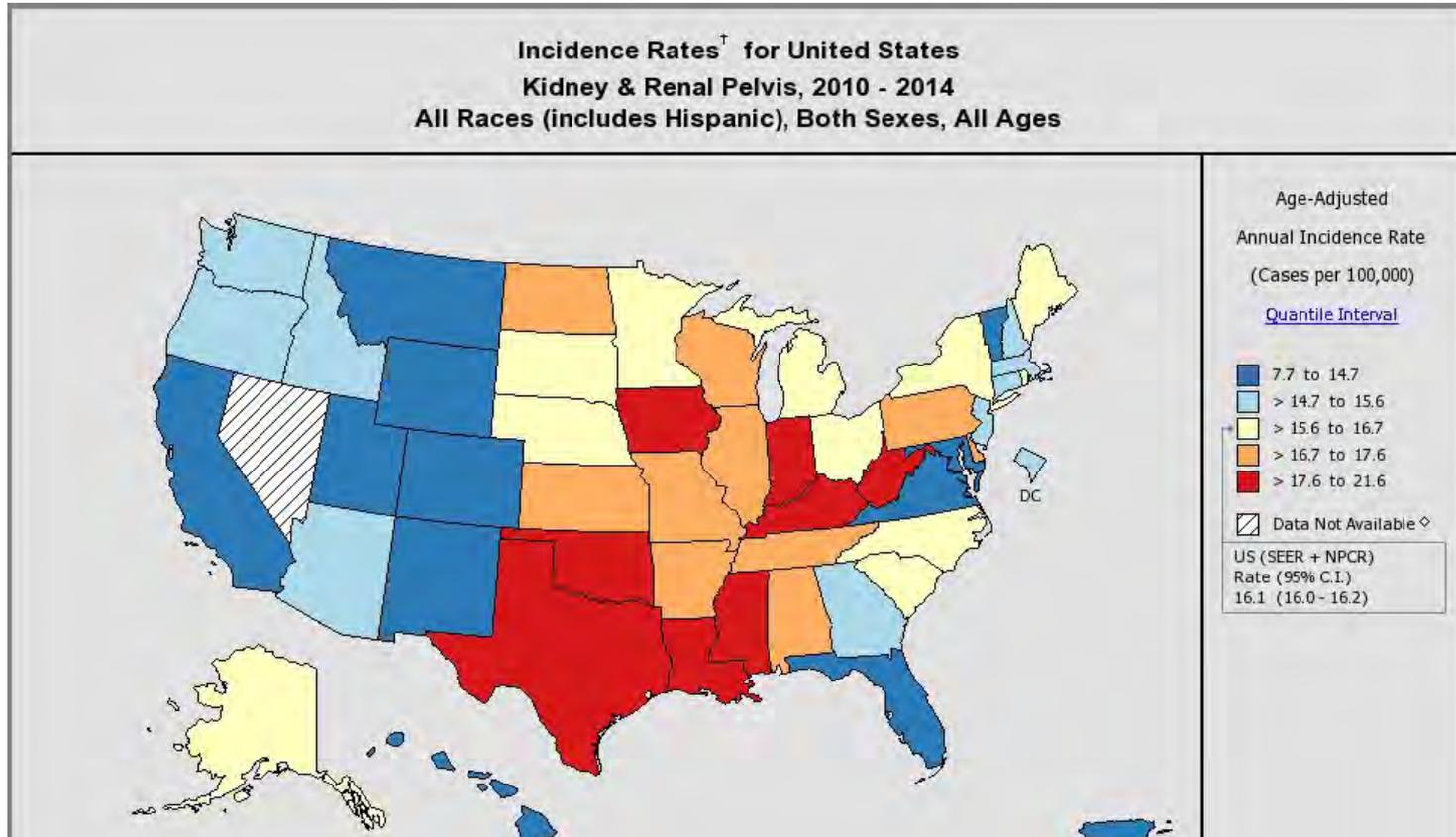
N. Yan  
\$.9 M



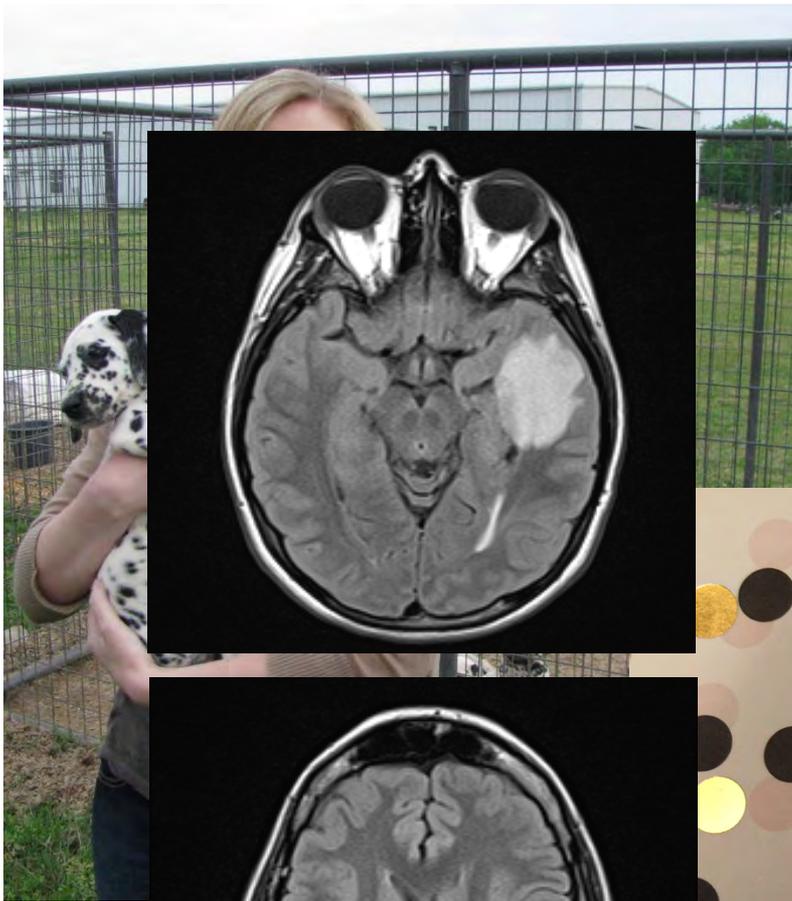
H. Zhu  
\$3.4 M

**TOTAL CPRIT SUPPORT:  
\$45.9 million**

# Texas has the **4<sup>th</sup> highest** rate of Kidney Cancer in the US (after Louisiana, Mississippi, & Kentucky)



**In Texas: 5<sup>th</sup> most common tumor in men and 7<sup>th</sup> in women.  
4<sup>th</sup> most common cancer type at UTSW.**



- She was 28 when she was diagnosed with metastatic kidney cancer.
- This was the second life/death struggle for Whitney - when she was 2, she was diagnosed with

7-11-2014

HAPPY NEW YEAR!

- Awards
- News
- Leadership
- Research
- Kidney Cancer Experts
- Collaborating Physicians
- For Patients
- Clinical Trials
- Patient Council
- Videos
- Support Us

# Kidney Cancer Program

Cutting-edge discoveries, transforming patient care

Why should you choose the UTSW Kidney Cancer Program?

- 1 Possibly the largest Kidney Cancer Program in the country. [\(1\)](#)
- 2 Survival rates double national benchmarks for stage IV kidney cancer patients, and improved across stages. [\(2\)](#)
- 3 Only program in the US developing immunotherapies with a Nobel Prize winner in Immunology. [\(3\)](#)
- 4 Only program to develop a new drug for kidney cancer going from gene discovery to clinical trials. [\(4\)](#)
- 5 One of two to receive an NCI Specialized Program of Research Excellence (SPORE) Award. [\(5\)](#)
- 6 Top 3 urology department in the US. [\(6\)](#)
- 7 Most innovative, broadest, and possibly largest radiation oncology program for kidney cancer. [\(7\)](#)



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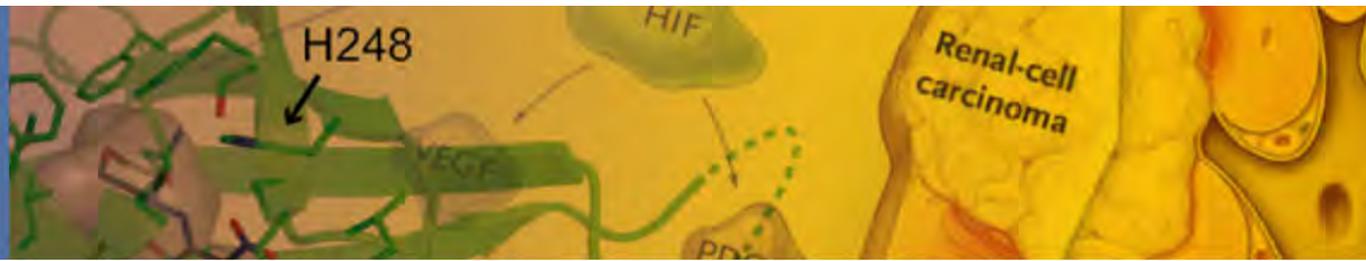
[Simmons Cancer Center – Patient Care](#)

[Simmons Cancer Center - Kidney Cancer](#)

[Simmons Cancer Center – Research and Education](#)

# National Leadership

- **Dr. Amatruda** - *Chair*, Germ Cell Tumor Biology and Rare Tumors Biology Committees in the *Children's Oncology Group*.
- **Dr. Brugarolas** - *Chair*, Programmatic Panel of the *Congressionally-directed Kidney Cancer Research Program*. Member, Renal Task Force of the *Scientific Steering Committee* for the *National Cancer Institute's Clinical Trials Enterprise*.
- **Dr. Cadeddu** - Member, *American Urological Association* Panel setting guidelines for the management of renal masses.
- **Dr. Courtney** - Member, Genitourinary Committee of the *ECOG-ACRIN cancer research group*.
- **Dr. Hammers** - Member, Renal Task Force of the *Scientific Steering Committee* for the *National Cancer Institute's Clinical Trials Enterprise*.
- **Dr. Hannan** - Member, Renal Task Force of the *Scientific Steering Committee* for the *National Cancer Institute's Clinical Trials Enterprise*.
- **Dr. Kapur** - Member, Renal Task Force of the *Scientific Steering Committee* for the *National Cancer Institute's Clinical Trials Enterprise*.
- **Dr. Pedrosa** - Member, Renal Task Force of the *Scientific Steering Committee* for the *National Cancer Institute's Clinical Trials Enterprise*, the Genitourinary Committee of the *ECOG-ACRIN cancer research group*, and the Renal Cell Carcinoma Disease-Focused Panel of the *Society of Abdominal Radiology*.
- **Dr. Zhou** - Member, *American Joint Committee on Cancer* (Kidney Cancer), the *College of American Pathologists* Cancer Committee, and primary author of genitourinary cancer protocols.



Awards

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Collaborating Physicians

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## Kidney Cancer Program

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- 6 Top 3 urology department in the US. [\(6\)](#)
- 7 Most innovative, broadest, and possibly largest radiation oncology program for kidney cancer. [\(7\)](#)



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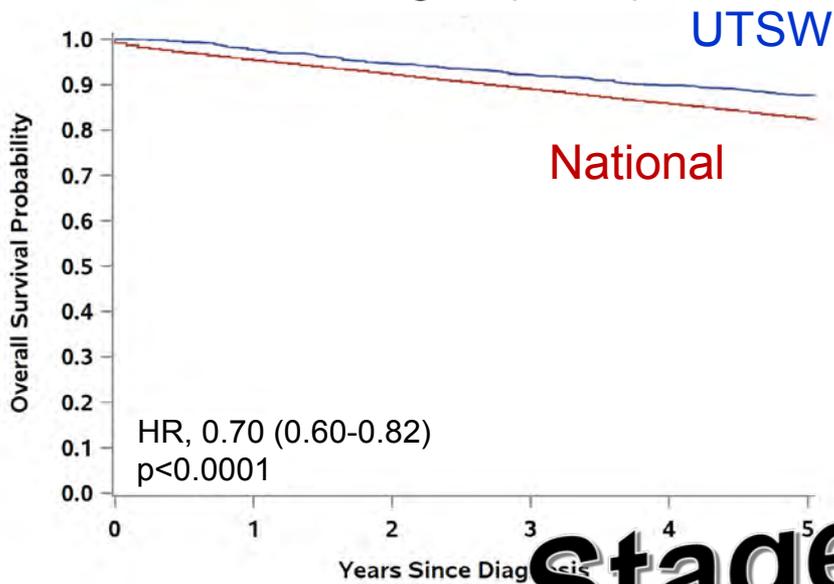
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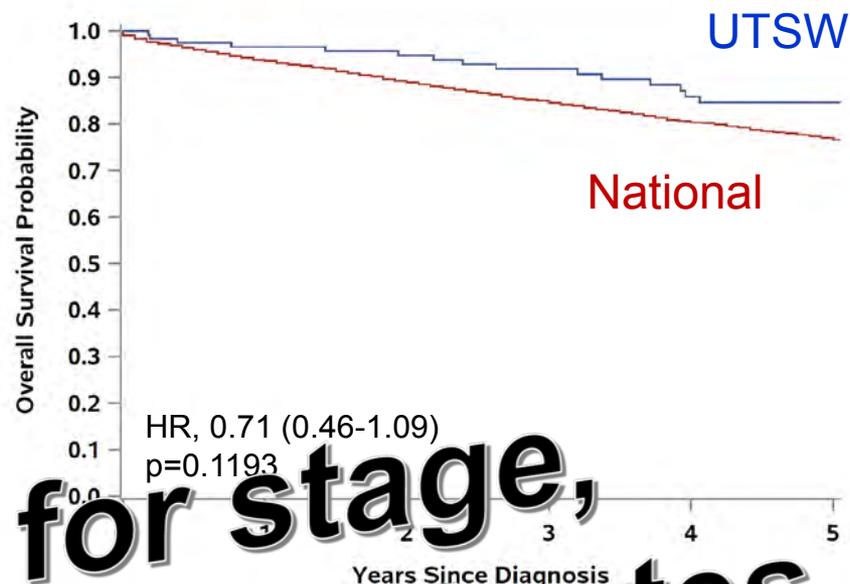
[Simmons Cancer Center – Research and Education](#)

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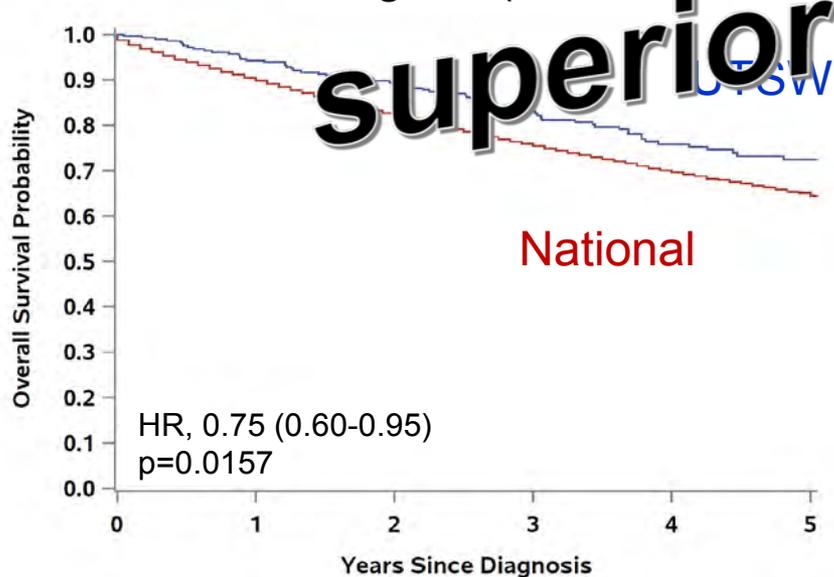
Stage I (small)



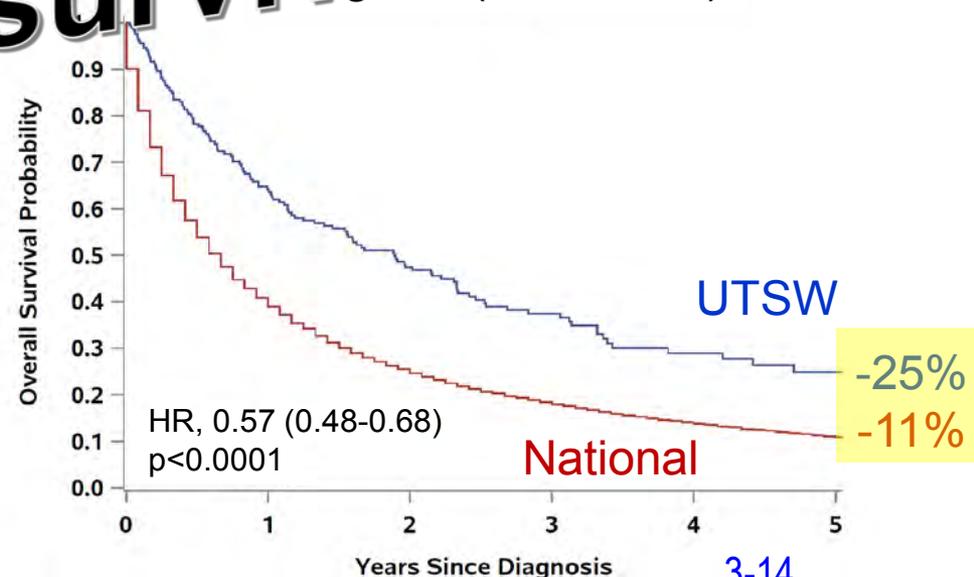
Stage II (large)



Stage III (invasive)



Stage IV (metastatic)



**Stage for stage,  
superior survival rates**



# Why are survival rates better?

- **Expertise.** Kidney cancer is not common. Many oncologists and urologists only see a handful of cases. KCP experts follow hundreds of patients.
- **Teamwork.** Urologists, oncologists, and radiation oncologists work together to deliver the best treatment approach tailored to each patient.
- **Collaboration.** An outstanding broader team: cardiothoracic and orthopedic surgeons, neurosurgeons, interventionalists, radiologists, and pathologists...
- **Access** to new drugs. Vetted clinical trials.
- **Patient-centeredness.**
- **Research.** Patients benefit from the latest discoveries at the KCP (more than 60 laboratories).

# A different type of r

Friendliness | ★★★★★ 4.9

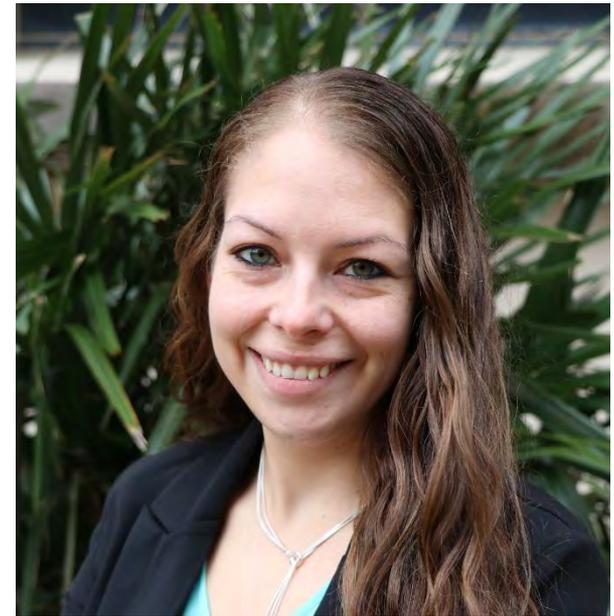
Explanation | ★★★★★ 4.8

Concern & understanding | ★★

Confidence in the doctor | ★★

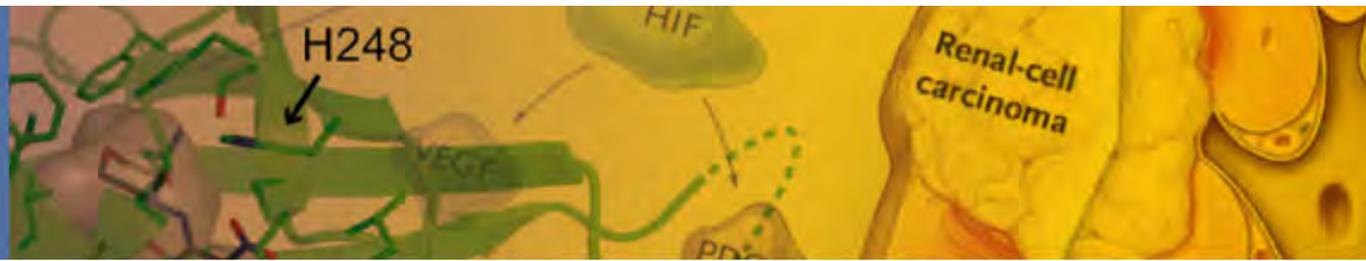
Likelihood of recommending | ★★★★★ 4.9

Overall satisfaction | ★★★★★ 4.9



Megan Dougherty, R.N.  
Director of Patient Experience

250 surveys, 2016



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# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

APRIL 5, 2018

VOL. 378 NO. 14

## Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma

R.J. Motzer, N.M. Tannir, D.F. McDermott, O. Arén Frontera, B. Melichar, T.K. Choueiri, E.R. Plimack, P. Barthélémy, C. Porta, S. George, T. Powles, F. Donskov, V. Neiman, C.K. Kollmannsberger, P. Salman, H. Gurnev, R. Hawkins, A. Ravaud, M.-O. Grimm, S. ... M. Wind-Rotolo, J. D...



U.S. Department of Health and Human Services

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**Approved Drugs**

Hematology/Oncology (Cancer) Approvals & Safety Notifications

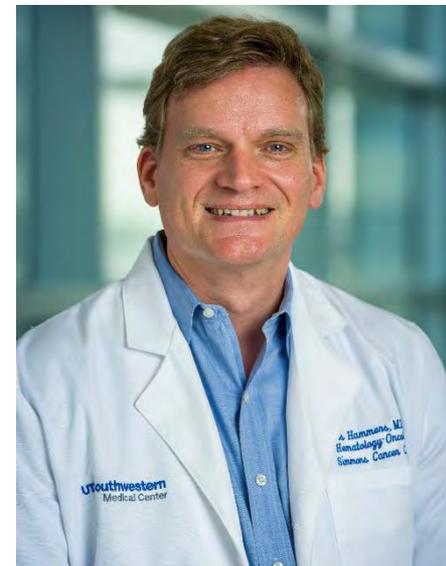
Drug Information Soundcast in Clinical Oncology (D.I.S.C.O.)

Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book)

**FDA approves nivolumab plus ipilimumab combination for intermediate or poor-risk advanced renal cell carcinoma**

SHARE | TWEET | LINKEDIN | PIN IT | EMAIL | PRINT

On April 16, 2018, the Food and Drug Administration granted approvals to nivolumab and ipilimumab (Opdivo and Yervoy, Bristol-Myers Squibb Co.) in combination for the treatment of intermediate or poor risk, previously untreated advanced renal cell carcinoma.



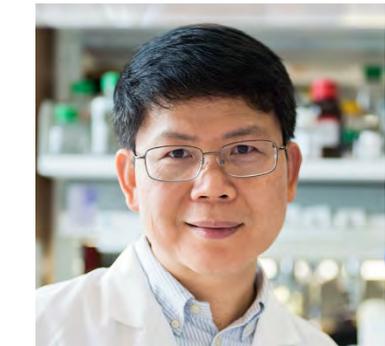
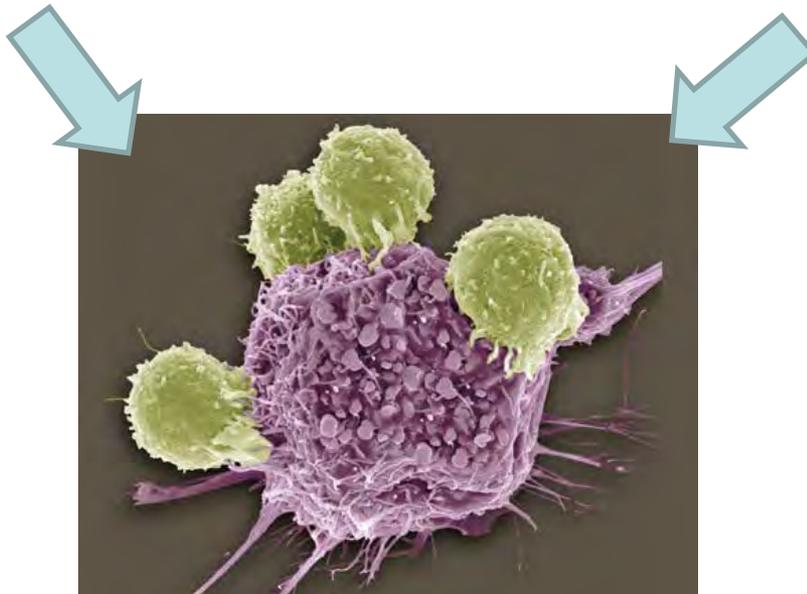
# Building on Nobel-caliber immunology research to develop the next wave of immunotherapies



Bruce Beutler, M.D.  
Nobel Prize, 2011

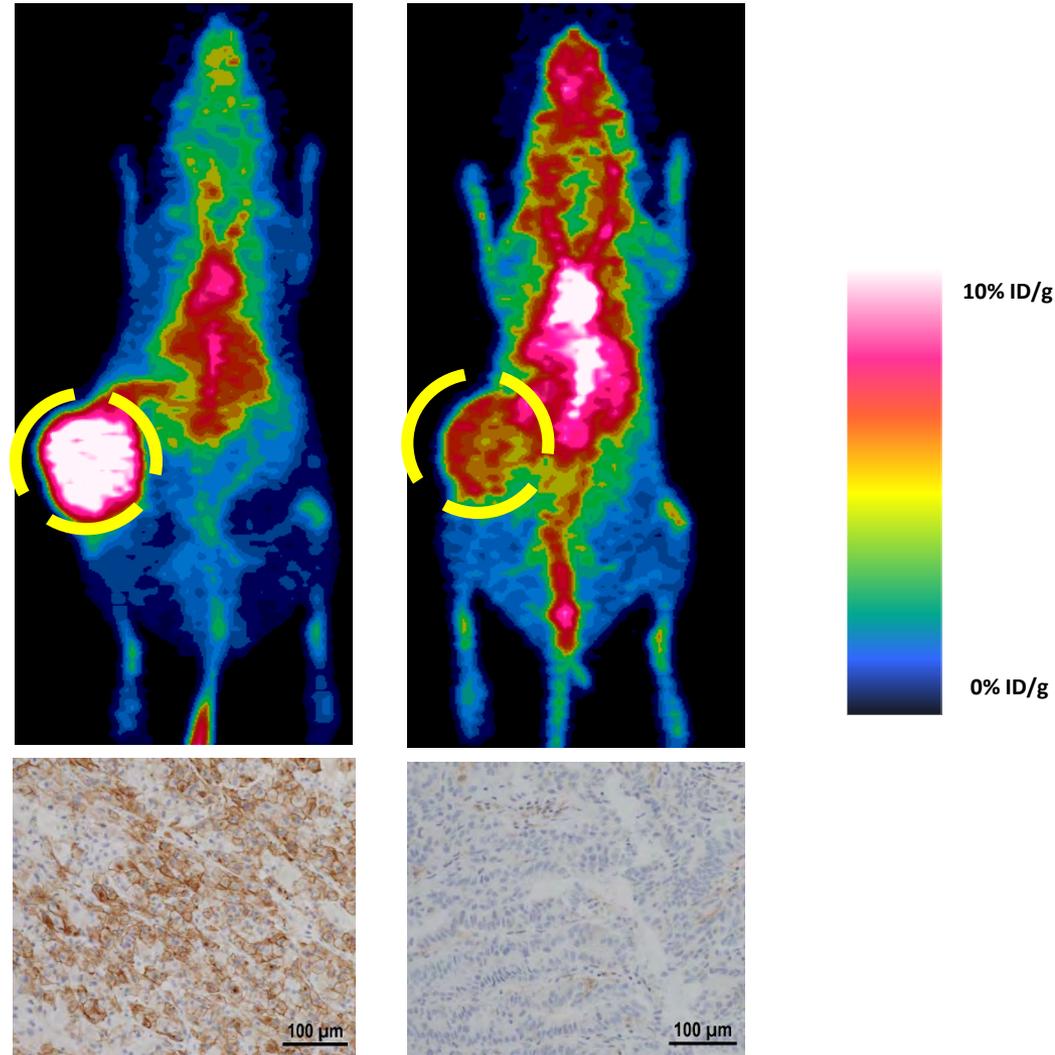
**Innate  
Immune  
System  
(TLR & STING)**

**Adaptive  
Immune  
System  
(Checkpoint  
Inhibitors)**



James Chen, Ph.D.  
HHMI, NAS

# Developing radiology tools to identify tumors that respond to immunotherapy





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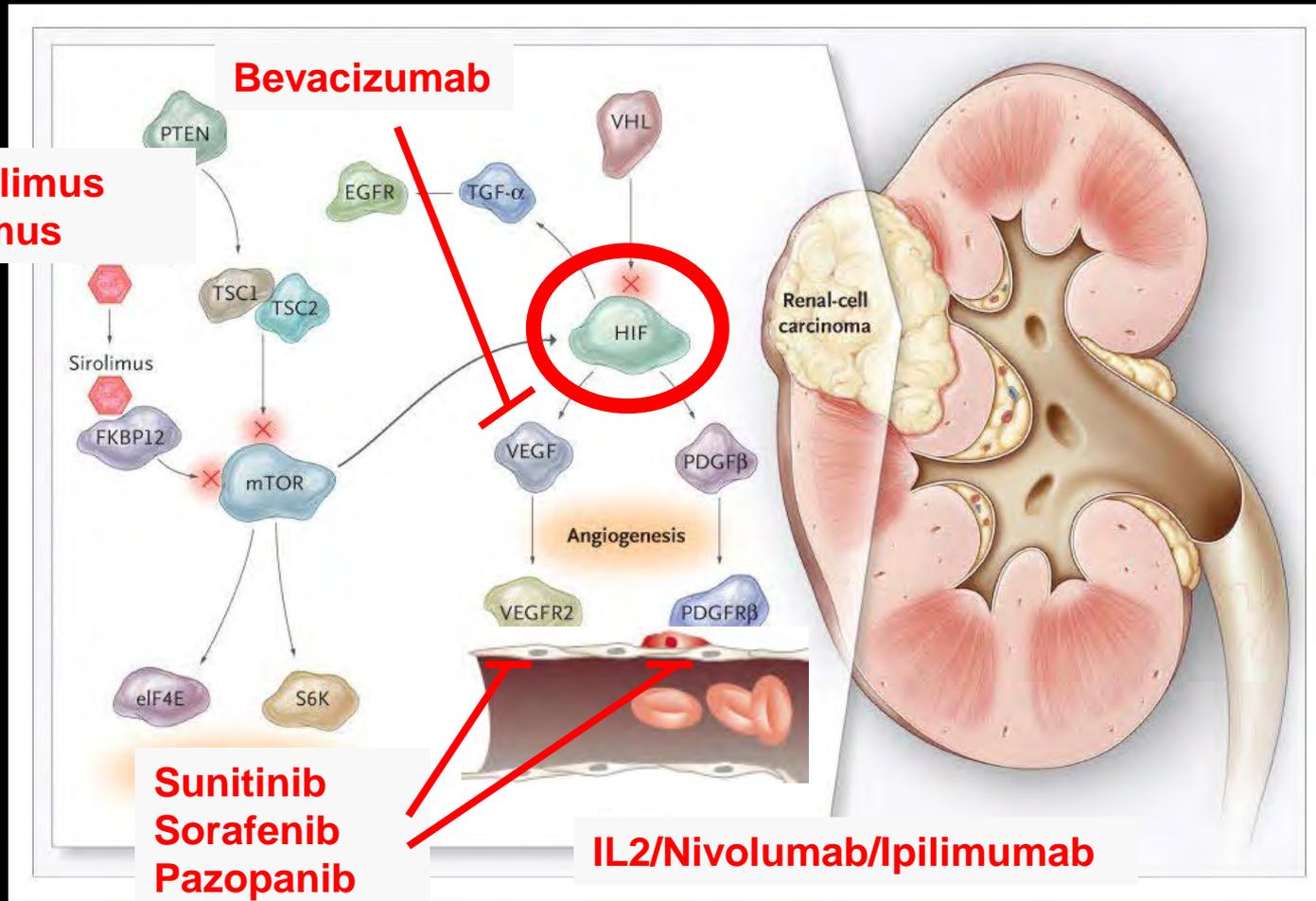
[Simmons Cancer Center - Kidney Cancer](#)

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3-21

# Developing a drug to block the most important driver of kidney cancer – HIF

**Temsirolimus  
Everolimus**



# From gene discovery to a first-in-class treatment for kidney cancer – a unique UTSW journey

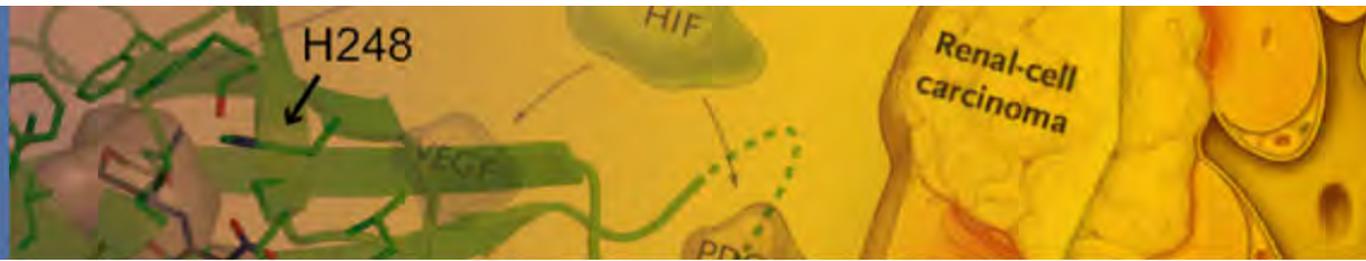
VOLUME 36 · NUMBER 9 · MARCH 20, 2018

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

## Phase I Dose-Escalation Trial of PT2385, a First-in-Class Hypoxia-Inducible Factor-2 $\alpha$ Antagonist in Patients With Previously Treated Advanced Clear Cell Renal Cell Carcinoma

*Kevin D. Courtney, Jeffrey R. Infante, Elaine T. Lam, Robert A. Figlin, Brian I. Rini, James Brugarolas, Naseem J. Zojwalla, Ann M. Lowe, Keshi Wang, Eli M. Wallace, John A. Josey, and Toni K. Choueiri*



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3-24

# Specialized Programs of Research Excellence (SPORE)

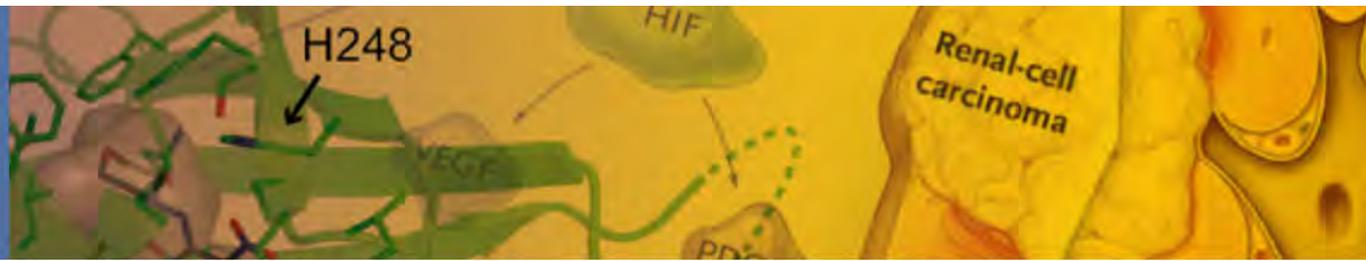
Strengths/Weaknesses	Impact	Descriptor	Score	<u>UTSW SPORE</u>
	High	Exceptional	1	<b>1.4</b>
		Outstanding	2	
		Excellent	3	
	Moderate	Very Good	4	
		Good	5	
		Satisfactory	6	
	Low	Fair	7	
		Marginal	8	
		Poor	9	

Not Recommended for Further Consideration=NRFC



*“I am celebrating as Mayor to receive a SPORE award. It puts us in a class by itself, and continues to show what we’re doing with science and patient care here in our city. As you look at building cities, the medical community is such an important part of it; we need to attract the greatest scientists, the greatest doctors, and the greatest healthcare workers to the place we call home. And we are doing that.”*

*Mayor Mike Rawlings, 2016*



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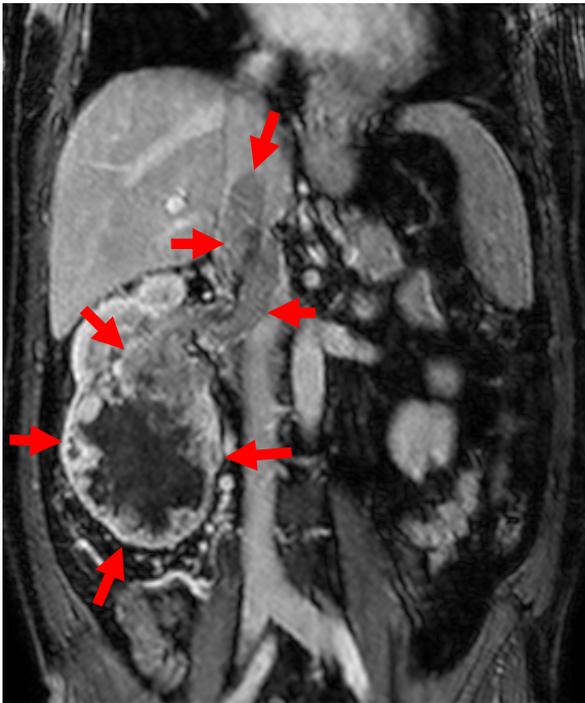
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3-27

# A Leader in Radiation Therapy



Physicians pioneer the use of stereotactic body radiation for deadly kidney cancer complication



Hannan, Timmerman

Most innovative and broadest radiation oncology program for kidney cancer.<sup>1</sup>

- **First program** to report the use of stereotactic radiation (SBRT) for tumor extensions into the vena cava (tumor thrombi) (Hannan, *Cancer Biol Ther* 2015).
- **Largest reported experience** of SBRT (Wang, *Int J Radiat Oncol Biol Phys* 2017) and one of the largest in combination with new immunotherapies (Mohamad, *Oncol Immunology* in press).
- **SBRT deployment for:** (i) small renal masses, (ii) tumor thrombi, (iii) oligometastasis, (iv) oligoprogression, and, (v) extensively, in combination with immunotherapy.

<sup>1</sup>National clinical trials registry ([clinicaltrials.gov](https://clinicaltrials.gov)) search with the terms "Kidney Cancer" and "Stereotactic" fails to identify other programs with similar breadth of clinical trials.



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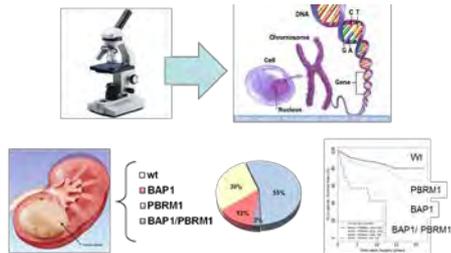
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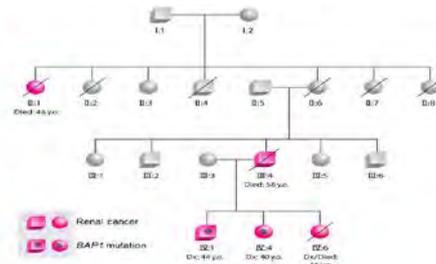
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3-29

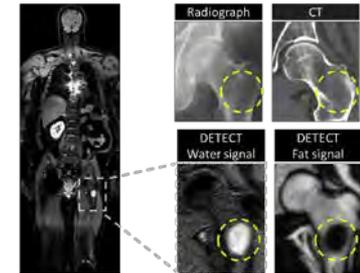
Developed a modern genomic-based classification of kidney cancer



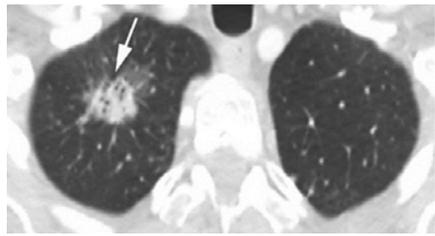
Identified a novel familial kidney cancer syndrome



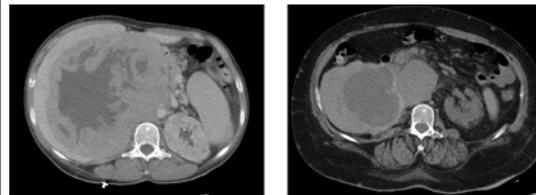
Developed a 7-minute whole body MRI for bone metastases



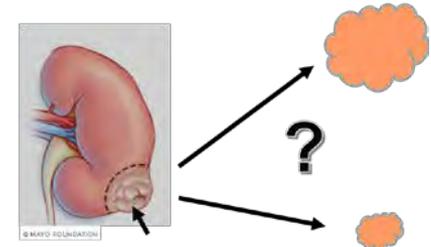
Discovered that up to 6% of patients with metastatic kidney cancer have lung cancer



Identified new treatment for an orphan disease (eAML)



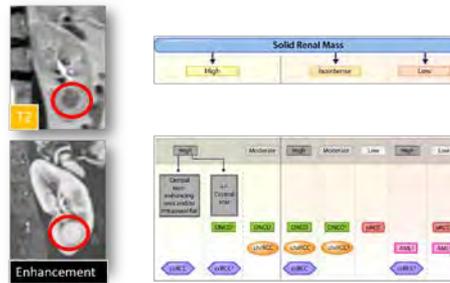
Conceived new approach to predict future behavior of small tumors



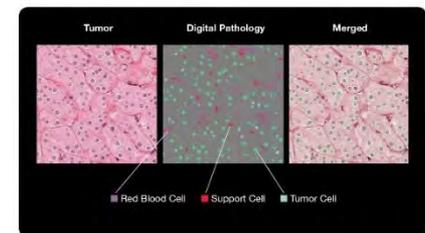
Pioneered new tools to integrate clinical and research data



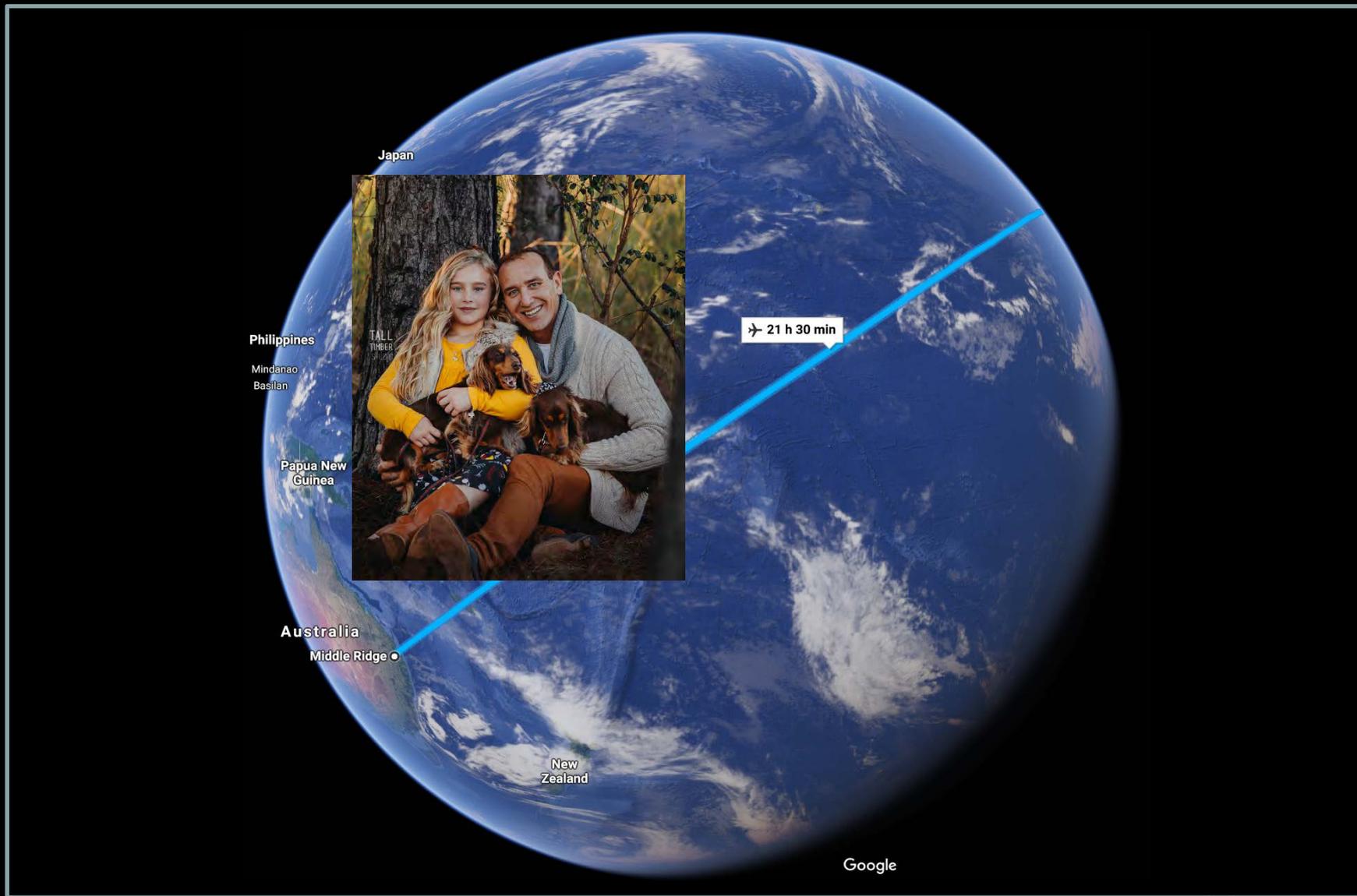
Developed MRI protocol that bypasses need for biopsies



Developing machine learning tools to revolutionize the practice of medicine



# Our Goal: To Eliminate Kidney Cancer



# KCP Clinical faculty and staff

## Adult Urology



**Aditya Bagrodia, M.D.**  
Assistant Professor, Urology



**Vitaly Margolis, M.D.**  
Associate Professor, Urology



**Jeffrey Cadeddu, M.D.**  
Professor, Urology and Radiology



**Ganesh Raj, M.D., Ph.D.**  
Professor, Urology



**Jeffrey Gahan, M.D.**  
Assistant Professor, Urology



**Arthur I. Sagalowsky, M.D.**  
Professor, Urology and Surgery



**Yair Lotan, M.D.**  
Professor, Urology

## Radiation Oncology



**Tu Dan, M.D.**  
Instructor, Radiation Oncology



**Aaron Laine, M.D., Ph.D.**  
Assistant Professor, Radiation Oncology



**Neil Desai, M.D.**  
Assistant Professor, Radiation Oncology



**Lucien Nedzi, M.D.**  
Associate Professor, Radiation Oncology



**Michael Folkert, M.D., Ph.D.**  
Assistant Professor, Radiation Oncology



**Robert Timmerman, M.D.**  
Professor, Urology and Surgery



**Raquibul Hannan, M.D., Ph.D.**  
Associate Professor, Radiation Oncology



**Zabihullah Wazdak, M.D.**  
Assistant Professor, Radiation Oncology

## Radiology



**Alberto Diaz de Leon, M.D.**  
Assistant Professor, Radiology



**Ivan Pedrosa, M.D., Ph.D.**  
Professor, Radiology



**John Leyendecker, M.D.**  
Professor, Radiology



**Lori Watumull, M.D.**  
Professor, Radiology

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## Pathology



**Payal Kapur, M.D.**  
Associate Professor, Pathology



**Ming Zhou, M.D., Ph.D.**  
Professor, Pathology

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## Clinical Genetics



**Brian Reys, M.S., CGC.**



**Amber Gemmill, M.S., CGC.**

## Medical Oncology



**Yuli Ariaga, M.D.**  
Associate Professor, Internal Medicine -  
Hematology/Oncology



**Eugene Frenkel, M.D.**  
Professor, Internal Medicine -  
Hematology/Oncology and Radiology



**Isaac Bowman, M.D.**  
Assistant Professor, Internal Medicine -  
Hematology/Oncology



**Hans Hammers, M.D., Ph.D.**  
Associate Professor, Internal Medicine -  
Hematology/Oncology



**James Brugarolas, M.D., Ph.D.**  
Professor, Internal Medicine -  
Hematology/Oncology



**Teresa Sanders, P.A.**  
Physician Assistant, Simmons  
Comprehensive Cancer Center



**Kevin Courtney, M.D., Ph.D.**  
Assistant Professor, Internal Medicine -  
Hematology/Oncology









CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** WAYNE ROBERTS, CHIEF EXECUTIVE OFFICER  
**SUBJECT:** CHIEF EXECUTIVE OFFICER REPORT, AGENDA ITEM 7  
**DATE:** MAY 9, 2018

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As of this writing the Chief Executive Officer's Report for the May 16, 2018, Oversight Committee meeting will consist of the following items:

- Personnel update
- FY 2018 Grant Award Funds Available (attached)
- Report on the May 1, 2018, Texas Healthcare & Bioscience Institute Annual Summit
- Report on the Houston City Council's National Cancer Research Month Proclamation Event on May 15, 2018

Other topics may be added as warranted.

In addition, for your reference copies of the March 28, 2018, and April 27, 2018, CPRIT Activities Updates previously provided to you are included at the end of this tab. These reports are done in months in which the Oversight Committee does not meet.

\*\*\*\*\*

CPRIT has awarded **1,247** grants totaling **\$1.954 billion**

- 198 prevention awards totaling \$208.5 million
- 1,049 academic research and product development research awards totaling \$1.746 billion

Of the \$1.746 billion in academic research and product development awards,

- 29.2% of the funding (\$510.0 million) supports clinical research projects
- 26.5% of the funding (\$461.7 million) supports translational research projects
- 25.9% of funding (\$452.1 million) supports recruitment awards
- 15.0% of the funding (\$262.2 million) supports discovery stage research projects
- 3.5% of funding (\$59.9 million) supports training programs.

CPRIT has 9 open Requests for Applications (RFAs)

- 3 Research Recruitment
- 5 Academic Research
- 1 Prevention Dissemination



**FY 2018 GRANT AWARD FUNDS AVAILABLE**

General Obligation Bond Proceeds

	Prevention	Academic / Product Development Research	1% Grant Funding Buffer	Operating Budget	Total Appropriations
Available Appropriated Funds	\$ 28,022,956	\$ 255,239,310		\$ 16,737,734	\$ 300,000,000
Appropriations Transfer to DSHS		\$ (2,969,554)		\$ 2,969,554	
Adjusted Appropriations	\$ 28,022,956	\$ 252,269,756		\$ 19,707,288	\$ 300,000,000
<b>Total Available for All Grants</b>			\$ 280,292,712		
<b>1% of Total Available Grant Funding</b>			\$ 2,802,927		
<b>Adjusted Grant Award Funding</b>	<b>28,022,956</b>	<b>\$ 249,466,829</b>			<b>\$ 277,489,785</b>

	Prevention Grants	Academic Research Grants	PD Research Grants	
<b>Total Available for Grant Awards (Total GO Bond Proceeds Less Operating Budget)</b>	\$ 28,022,956	\$ 189,202,317	\$ 63,067,439	\$ 280,292,712
<b>Total Available for Grant Awards Incorporating 1% Grant Funding Buffer</b>	\$ 28,022,956	\$ 187,100,122	\$ 62,366,707	\$ 277,489,785

**Announced Grant Awards**

11/29/17 Prevention Dissemination Award	\$ 294,804		\$ -
11/29/17 AR Recruitment Awards (3)		\$ 10,000,000	
11/29/17 AR Core Facility Supplement (RP170691)		\$ 943,570	\$ -
2/21/18 Prevention Dissemination Award	\$ 299,571		
2/21/18 Prevention Awards	\$ 12,806,002		
2/21/18 AR Recruitment Awards (5)		\$ 14,000,000	
2/21/18 Individual Investigator Research Awards		\$ 46,195,197	

<b>Announced Grant Award Subtotal</b>	\$ 13,400,377	\$ 71,138,767	\$ -	\$ -	\$ 84,539,144
---------------------------------------	---------------	---------------	------	------	---------------

**Grant Award Adjustments**

Declined Recruit Award (MDACC-Skok) 11/2017 Slate	\$ -	\$ (6,000,000)	\$ -		\$ (6,000,000)
Declined Recruit Award (MDACC-Bose) 2/2018 Slate		\$ (2,000,000)			\$ (2,000,000)

<b>Revised Grant Award Subtotal</b>	\$ 13,400,377	\$ 63,138,767	\$ -		\$ 76,539,144
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<b>Available Funds as of April 1, 2018</b>	\$ 14,622,579	\$ 123,961,355	\$ 62,366,707		\$ 200,950,641
--------------------------------------------	---------------	----------------	---------------	--	----------------

**Pending Grants-PIC Recommendations**

Prevention Dissemination Award	\$ 300,000	\$ -	
AR Recruitment Awards	\$ -	\$ 29,986,494	

<b>Pending Award Subtotal</b>	\$ 300,000	\$ 29,986,494	\$ -		\$ 30,286,494
-------------------------------	------------	---------------	------	--	---------------

<b>Total Grant Funding Committed</b>	\$ 13,700,377	\$ 93,125,261	\$ -		\$ 106,825,638
--------------------------------------	---------------	---------------	------	--	----------------

<b>1% Grant Funding Buffer</b>	\$ -	\$ 2,102,195	\$ 700,732		\$ 2,802,927
--------------------------------	------	--------------	------------	--	--------------

<b>Potential Available Funds as of May 16, 2018</b>	\$ 14,322,579	\$ 93,974,861	\$ 62,366,707		\$ 170,664,147
-----------------------------------------------------	---------------	---------------	---------------	--	----------------

**Operating Budget Detail**

Indirect Administration	\$ 3,030,652
Grant Review & Award Operations	\$ 13,707,082
Subtotal, CPRIT Operating Costs	\$ 16,737,734
Cancer Registry Operating Cost Transfer	\$ 2,969,554
Total, Operating Costs	19,707,288



**CPRIT MANAGEMENT DASHBOARD  
FISCAL YEAR 2018**

	SEPT	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	CUMULATIVE (ANNUAL)	CUMULATIVE (TO DATE)
<b>ACCOUNTABILITY</b>														
Announced Grant Awards	0		4			57							61	
New Grant Contracts Signed	9	19	7	11	6	44	2	35					133	
New Grant Contracts In Negotiation			12			24							36	
Grant Reimbursements Processed (#)	191	172	138	120	126	216	174	163					1,300	
Grant Reimbursements Processed (\$)	\$ 14,402,580	\$ 24,849,514	\$ 12,652,218	\$ 16,464,363	\$ 12,888,800	\$ 15,287,606	\$ 30,698,463	\$ 20,199,295					\$ 147,442,839	
Revenue Sharing Payments Received	\$ 1,500	\$ 35,140	\$ 7,557	\$ -	\$ 21,969	\$ -	\$ 6,298	\$ 18,165					\$ 90,628	\$ 3,324,844
Total Value of Grants Contracted (\$)	\$ 11,469,175	\$ 30,088,458	\$9,750,000	\$ 16,294,571	\$ 10,138,500	\$ 23,821,567	\$ 6,200,000	\$ 37,619,680					\$ 145,381,951	
Grants Awarded (#)/ Applications Rec'd (#)	13%	13%	13%	13%	12%	13%	13%	13%						
Debt Issued (\$)/Funding Awarded (\$)	73%	73%	72%	72%	72%	70%	75%	75%						
Grantee Compliance Trainings/Monitoring Visits	0	1	0	0	1	1	4	6					13	
Awards with Delinquent Reimbursement Submission (FSR)			1			1								
Awards with Delinquent Matching Funds Verification			8			19								
Awards with Delinquent Progress Report Submission			7			3								
IA Agency Operational Recommendations Implemented	0	0	0	0	0	9	0	0					9	
IA Agency Operational Recommendations In Progress	27	27	27	27	27	18	18	18						
Open RFAs	6	7	7	12	12	9	4	4						
Prevention Applications Received	38	4	0	1	0	31	1	0					75	791
Product Development Applications Received	0	0	0	0	0	20	0	0					20	422
Academic Research Applications Received	2	2	5	1	208	8	9	12					247	6,260
Help Desk Calls/Emails	161	192	121	132	285	243	189	125					1,448	
<b>MISSION</b>														
<b>ACADEMIC RESEARCH PROGRAM</b>														
Number of Research Grants Announced (Annual)	0		3			49							52	
Recruited Scientists Announced														207
Recruited Scientists Accepted														154
Recruited Scientists Contracted														148
Published Articles on CPRIT-Funded Projects (#)														
Jobs Created & Maintained (#)														
Trainees in CPRIT-Funded Training Programs (#)														
Clinical Trials (#)														71
Number of Patents Resulting from Research														

**CPRIT MANAGEMENT DASHBOARD  
FISCAL YEAR 2018**

	SEPT	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	CUMULATIVE (ANNUAL)	CUMULATIVE (TO DATE)
Number of Patent Applications														
Number of Investigational New Drugs														
<b>PRODUCT DEVELOPMENT RESEARCH PROGRAM</b>														
Number of Product Development Grant Announced (Annual)			0			0							0	
Life Science Companies Recruited (in TX)														9
Published Articles on CPRIT-Funded Projects														
Number of Jobs Created & Maintained														515
Clinical Trials (#)														15
Number of Patents Resulting from Research														
Number of Patent Applications														
Number of Investigational New Drugs														
<b>PREVENTION PROGRAM</b>														
Number of Prevention Grants Announced (Annual)			1			8							9	
People Served by CPRIT-Funded Prevention and Control Activities			483,648			218,357							702,005	
People Served through CPRIT-Funded Education and Training			201,481			111,558							313,039	
People Served through CPRIT-Funded Clinical Services			282,167			106,799							388,966	
<b>TRANSPARENCY</b>														
Total Website Hits (Sessions)	5,959	5,881	5,928	5,613	7,209	6,655	5,736	5,671					48,652	
Total Unique Visitors to Website (Users)	4,359	4,234	4,305	4,417	4,773	4,657	4,281	4,114					35,140	



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** WAYNE ROBERTS, CHIEF EXECUTIVE OFFICER  
**SUBJECT:** CHIEF EXECUTIVE OFFICER REPORT  
**DATE:** APRIL 27, 2018

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Topics in this memo include the resignation of Amy Mitchell from the Oversight Committee, preparation for the May 16, 2018, Oversight Committee meeting, recent milestones in our fight against cancer, a staffing summary, CPRIT outreach efforts, and updates from Compliance, Programs, and Operations.

**Amy Mitchell Resigns from the Oversight Committee**

Amy Mitchell informed Oversight Committee Chair Will Montgomery that she resigned her position as Oversight Committee member effective April 13, 2018. She notified Lt. Governor Dan Patrick in late March of her decision. Although Ms. Mitchell's term originally ended January 31, 2015, she graciously continued to serve as a holdover appointee for more than three years. There are now three vacant positions on the Oversight Committee. The Oversight Committee will take up a resolution honoring Ms. Mitchell for her service at the May 16 Oversight Committee meeting.

**Upcoming Oversight Committee Meeting**

The Oversight Committee will meet May 16, 2018, at 10:00 a.m. in Room E1.012 of the Texas Capitol Extension. CPRIT will post the final agenda for the Oversight Committee meeting by May 8; a tentative agenda is attached. We have six members of the Oversight Committee currently and do not expect new appointments before the May meeting. A quorum of five members is necessary to conduct official business. **Please notify me as soon as possible if you are unable to attend the May meeting or have travel arrangements that will cause you to arrive late or leave the meeting early.**

You will receive an email from CPRIT by May 3 with a link and password to access the Program Integration Committee's recommendations via the grant award portal. The portal has supporting documentation regarding each project proposed for an award, including the application, CEO affidavit, summary statement, and grant pedigree. A summary of the award slate will also be available through the portal. Please allow some time to complete the individual conflict of interest checks and review the supporting material.

Oversight Committee members will receive an electronic copy of the agenda packet by May 9. Hard copies of the agenda packet will be available at the meeting.

## Recent Milestones in the Fight Against Cancer

### CPRIT Grantees in the News

- Isaiah J. Fidler, DVM, Ph.D., professor, The University of Texas MD Anderson Cancer Center, (MD Anderson), received the Margaret Foti Award for Leadership and Extraordinary Achievements in Cancer Research on April 15 at the American Association Cancer Research (AACR) annual meeting. Dr. Fidler is married to Dr. Margaret Kripke, CPRIT's former Chief Scientific Officer. Dr. Fidler and Dr. Kripke are noted for their groundbreaking studies that demonstrated tumors are composed of different, unrelated cells.
- CPRIT grantee Zhijion "James" Chen, Ph.D., professor, UT Southwestern Medical Center is the recipient of the 2018 Lurie Prize in Biomedical Sciences, for his discovery of the enzyme, cyclic GMP-AMP synthase (cGAS), a sensor of innate immunity. cGAS patrols the cell's interior and sounds the alarm that triggers the immune system in response to invasion by foreign DNA. Dr. Chen's CPRIT-funded research investigates the role of the cGAS pathway in anti-tumor immunity. The prize includes a \$100,000 honorarium and will be presented by the Foundation for the National Institutes of Health on May 16 in Washington.
- CPRIT University Advisory Committee Co-Chair, Kent Osborne, M.D., Director, Dan L. Duncan Cancer Center at Baylor College of Medicine, was honored by the American Association of Cancer Research, for his contributions to breast cancer research and he presented the AACR Distinguished Lecture, "New Strategies for HER2 Targeted Therapy in Breast Cancer", at the association's annual meeting in Chicago in April.

### Notable CPRIT Supported Research and Prevention Accomplishments

- Houston-based Bellicum Pharmaceuticals announced on April 11 that the US Food and Drug Administration (FDA) lifted the clinical hold on U.S. studies of BPX-501, Bellicum's lead compound. BPX-501, is an adjunct T-cell therapy administered to cancer patients receiving stem cell therapy. This novel therapy comprising genetically modified donor T cells incorporates Bellicum's CaspaCIDE® safety switch. It provides a safety net to eliminate alloreactive BPX-501 T cells should uncontrollable Graft vs Host Disease (GvHD), or other T-cell mediated transplant complications, occur. This enables physicians to perform stem cell transplants more safely to speed immune reconstitution, provide control over viral infections, and enhance graft-versus-leukemic activity while minimizing GvHD side effects.

The FDA had initiated the clinical hold on January 30, 2018 after several patients experienced adverse neurological events. Bellicum modified their clinical protocols to monitor more closely and manage potential future adverse neurological events. Bellicum is the recipient of two CPRIT Product Development Research Awards; an award of \$5.7 million made in March 2011 and an award of \$16.9 million in November 2016.

- Pulmotect, a Houston-based clinical stage biotechnology firm developing novel anti-infective therapies for cancer patients, announced initial closing of a \$12 million Series B financing. Funding will support clinical development of the company's lead compound, PUL-042, an

inhaled drug designed to boost the immune response in the lungs, offering potential protection against a wide range of pathogens. Cancer therapies often weaken a patient's immune response putting these patients at higher risk for pneumonia and other airborne infections. PUL-042, was developed at The University of Texas MD Anderson Cancer Center and Texas A & M Health Science Center.

Fannin Partners, an affiliate of Fannin Innovation Studios, led the financing. Houston-based Fannin Innovation Studio is an early-stage biomedical development incubator commercializing medical technologies. Fannin partners with bioscience innovators to co-found startup companies and provides a pooled management team, funding, and administrative support. Fannin incubated Pulmotect and is their lead investor. Pulmotect has raised \$25 million to date including a \$7.1 million CPRIT Product Development Research Award received in March 2012.

- San Antonio-based Pelican Therapeutics presented at the AACR 2018 Annual Meeting held in Chicago April 14-18. The company reported the results of a mouse model study showing that addition of checkpoint inhibition and T cell co-stimulators into the company's novel vaccine platform elicits stronger antigen-specific CD8+ T cell activation and expansion, stimulates memory precursor cell activation, and enhances tumor rejection. Despite the dramatic successes of checkpoint inhibitors in limited populations of cancer patients, 60-90% of patients still fail to respond to these therapies. Pelican claims that their approach, which targets multiple facets of the immune system, will improve patient outcomes. Pelican received a \$15.2 million CPRIT Product Development Research Award in May 2016.
- DNATRIX, a Houston-based company specializing in oncolytic virus immunotherapies for cancer, presented positive study results at the AACR 2018 Annual Meeting. In mouse models of triple negative breast cancer, the OX40L-expressing oncolytic virus reversed the immunosuppressive tumor microenvironment, leading to increased survival and delayed tumor metastases.

The company reports that the results build on extensive research demonstrating that arming DNATRIX viruses with T-cell agonists trigger antitumor immune responses and immune memory in variety of cancers. Upcoming clinical studies with the OX40L-expressing virus, DNX-2440, will test the ability of this potent virus to elicit antitumor effects in patients. DNX-2401, the backbone for the OX40L-expressing virus, has been tested in over 150 patients and is currently in Phase 2 testing for recurrent glioblastoma with Merck's checkpoint inhibitor, pembrolizumab. DNATRIX received a \$10.8 million Product Development Research Award in February 2014.

- Synlogic, Inc. also reported positive preclinical immune-oncology data from two studies at the recent AACR meeting. The company is developing synthetic biology medicines. These leverage the tools and principles of synthetic biology to genetically engineer probiotic microbes to perform or deliver critical functions missing or damaged due to disease.

Synlogic described two new genetic circuits engineered into *E. coli* Nissle, an immune "initiator" STING activating circuit (SYN-STING) and an immune "sustainer" kynurenine

consuming circuit (SYN-Kyn). SYN-STING can be delivered directly into the tumor enabling its localized site of action. The approach of using intra-tumoral injection elicits innate responses in the tumor but not in the circulation, potentially decreasing the risk of adverse events that may arise from the production of systemic type I interferon.

The company announced that *in vitro* studies of SYN-Kyn and SYN-Ade show that the treatments deplete kynurenine and adenosine at clinically relevant concentrations. SYN-Kyn also demonstrated rapid and near-complete reductions in tumor kynurenine levels *in vivo*. A combination of either SYN-Kyn or SYN-Ade with checkpoint inhibition led to superior anti-tumor activity compared with checkpoint inhibitors alone. If confirmed in future clinical studies, these biological effects may improve outcomes across multiple cancer types.

Separately the company announced closing a \$30 million financing on April 6. The company plans to sell common stock shares to a large mutual fund company. Proceeds will be used to fund ongoing and planned clinical studies and preclinical research. Synlogic is the successor company to Mirna Therapeutics, which received CPRIT Product Development Research Awards in 2010 and 2014 of \$10.3 million and \$16.8 million, respectively.

- Colin Hill, Sr. Vice President of Commercial Operation for Asuragen, Inc., an Austin-based molecular diagnostics company, will chair a roundtable discussion during the 2018 World Clinical Biomarkers and Companion Diagnostic Europe Summit in May. Mr. Hill's session will focus on the imminent changes to the regulatory environment in Europe and the implications for pharmaceutical and diagnostic companies collaborating to advance precision medicine. The discussion will highlight several topical issues facing both the pharmaceutical and diagnostic industries, including addressing value share imbalances between industries, streamlining the collaboration process from concept to commercialization, and understanding the specific nuances of the European market to ensure mutual successes. Asuragen received a \$6.8 million CPRIT Product Development Research Award in February 2012.
- Cancer researchers at Baylor College of Medicine reported in *Nature Medicine* on a novel targeted treatment strategy for patients with triple negative breast cancer, a particularly aggressive form of breast cancer that lacks known targets for therapies, making it difficult to treat. This work was supported in part by a CPRIT Individual Investigator Research Award granted in 2012 to Dr. Thomas Westbrook.
- CPRIT grantees Jef De Brabander, Ph.D. and Jerry Shay, Ph.D. at UT Southwestern Medical Center have identified the mechanism of action for a new drug developed with CPRIT support, TASIN (Truncated APC Selective INhibitor). They found that TASIN selectively kills colorectal cancer cells without harming healthy cells. Houston-based Barricade Therapeutics, a privately held biotech company, is commercializing TASIN. The research was reported in the February 21 issue of the journal *Molecular Cancer Therapeutics*. Several CPRIT awards have supported this important discovery including a 2016 Individual Investigator Research Award to Dr. Shay.
- A team from Harvard and Baylor College of Medicine found that different tissues have variable sensitivities to genes that drive normal and malignant cell proliferation. The

research, reported in the March 22 issue of *Cell*, identified hundreds of cancer-driving genes and revealed that different tissue types have shockingly variable sensitivities to those genes. The findings help explain why individual cancer drivers appear in some tumors and not others and the importance of tissue-specific strategies for cancer treatment. The research was enabled by the CPRIT funded 2017 Proteomics and Metabolomics Core Facility at Baylor College of Medicine.

- Diversity in the genetic lesions that cause cancer is extreme. A pressing challenge is the development of drugs that target patient-specific disease mechanisms. To address this challenge, UT Southwestern Medical Center researchers set out to identify new therapeutic targets for non-small cell lung cancer as well as potential drugs for these targets. After testing more than 200,000 chemical compounds, they identified 170 chemicals that are candidates for development into drugs for lung cancer. The five-year project, initiated by a CPRIT Multi-Investigator Research Award granted in 2011, also identified a predictive biomarker for the majority of the drugs. This feature allows the development of “precision medicine,” or individualized treatment for each patient. The final step of the study was determining how the drugs act on the cancer. The results of this ambitious project were reported online this month in the journal *Cell*.
- Dr. Matt Anderson, in conjunction with multiple investigators at Baylor College of Medicine, is collaborating with the goal of using patient volume/care supported by his CPRIT cervical cancer screening project to apply for NIH Pre-Cancer Tumor Atlas that profiles cervical pre-cancers using a multi-omic approach.
- CPRIT funding allowed The Bridge Breast Network to expand early detection services into 30 North Texas counties rather than waiting for women to seek care for a breast problem. Many of the counties have no breast and cervical screening programs in their county. Increased access led to the decrease in late stage cancers from 70% to 30%. Two hundred twenty-one new cases of breast cancer were detected, with nearly 84% being Stages 0-II which generally respond well to treatment.
- The NCI invited Dr. Jane Bolin of Texas A&M University System Health Science Center and Dr. Simon Craddock Lee of The University of Texas Southwestern Medical Center, to speak at the NCI Division of Cancer Control and Population Sciences Accelerating Rural Cancer Control Research Meeting, May 30-31, 2018, in Bethesda, MD. These invitations came about as a direct result of their multiple CPRIT awards for breast, cervical and colorectal cancer screening.

## **Personnel**

CPRIT has 35 authorized full-time equivalent (FTE) positions, of which CPRIT has filled 33 positions as of April 30, 2018.

- Claudia Leal, Executive Assistant, resigned to take a position with the Texas Department of Motor Vehicles effective April 16, 2018.

- We are in the process of filling the vacant Executive Assistant and Grant Compliance Specialist positions.

### **CPRIT Outreach**

- On April 3 Chief Operating Officer Heidi McConnell and I briefed staff of the Legislative Budget Board on CPRIT operations and anticipated budget requests to the 86<sup>th</sup> Texas Legislature that convenes in January 2019.
- Product Development Program Manager Rosemary French attended The University of Texas at Austin Technology Incubator mentoring session in Austin on April 3.
- CPRIT staff and UT Rio Grande Valley School of Medicine leadership met at their Edinburg School of Medicine facility on April 9 to discuss CPRIT funding opportunities. A legislative luncheon at Doctor's Hospital at Renaissance followed, which Senator Juan Hinojosa and staff from Senator Eddie Lucio Jr., and Representatives Terry Canales and Bobby Guerra attended. CPRIT grantees and CPRIT staff also participated in an American Cancer Society public forum that featured CPRIT and hosted by Cam Scott. Drs. Willson and Garcia, Chris Cutrone, and I attended and participated in these events.
- At the request of Secretary of State Rolando Pablos, Deputy Executive Officer and General Counsel Kristen Doyle and I attended a briefing on outreach activities of the National Aeronautics and Space Administration (NASA) on April 10.
- Dr. Garcia, Dr. Willson and Chief Product Development Officer Michael Lang attended the American Association for Cancer Research 2018 Annual Meeting April 14-18 in Chicago.
- On April 17, Ms. Doyle, Ms. McConnell, and I briefed Governor Abbott's budget and policy staff on CPRIT operations and anticipated budget requests to the 86<sup>th</sup> Texas Legislature.
- Ms. French attended a Texas Medical Device Alliance networking event in Austin April 19.
- Texas Tech University Health Sciences Center El Paso held a press conference on April 19, 2018, to announce the CPRIT Scholar recruitment grant of Shrikanth Gadad, PhD. The announcement received extensive coverage in the El Paso media market in both English and Spanish. El Paso legislators Senator José Rodríguez, and Representatives César Blanco, and Lina Ortega attended the event. Dr. Jim Willson and El Paso Mayor Dee Margo spoke at the event on behalf of CPRIT along with Tech Texas University System Board of Regents Chairman Rick Francis. Prior to the press conference, TTUHSC El Paso President Richard Lange, Dee Margo, and I held a briefing on CPRIT for the El Paso legislators.
- Dr. Garcia participated in the Texas Health Improvement Network (THIN) quarterly meeting on April 20.
- Ms. Doyle and I briefed staff of Representative Sarah Davis on CPRIT operations and anticipated budget requests to the 86<sup>th</sup> Texas Legislature on April 23.

- On May 1 Presiding Officer Will Montgomery will give a keynote address to the Texas Healthcare and Bioscience Institute (THBI) concerning CPRIT's momentum and keeping the state's competitive edge in cancer research and prevention. THBI is the state's largest trade association for the life sciences industry and this is a major annual meeting of its general membership. Members of the Texas Legislature and their staff also attend and participate. Mr. Lang, Ms. Doyle, and I will attend the conference.

## **Compliance Program Update**

### Submission Status of Required Grant Recipient Reports

CPRIT's grant management system (CGMS) produces a summary of delinquent reports each week; this is the primary source used by CPRIT's compliance staff to follow up with grantees. CPRIT typically has 570+ grants that are either active or wrapping up grant activities and receives an average of 570 grantee reports each month.

As of April 23, 2018, four entities have not filed 10 required reports by the set due date; eight (80%) are Academic Research grants and two (20%) are Product Development Research grants. CPRIT's grant accountants and compliance specialists continue to review and process incoming reports and reach out to grantees to resolve filing issues. In most cases, CPRIT does not disburse grant funds until the grantee files the required reports. In some instances, grantee institutions may be ineligible to receive a future award if the grantee does not submit the required reports.

### FSR Reviews

CPRIT's Compliance Specialists performed 73 second-level reviews of grantee Financial Status Reports (FSRs) for the month of April. Staff has completed a total of 307 reviews for the current Quarter. Seven FSRs (9%) required resubmission due to insufficient or inaccurate documentation submitted by the grantee. CPRIT's grant accounting staff completes the initial review of the FSRs and supporting documentation before routing them to the compliance specialists for final review and disposition.

### Single Audit Tracking

As part of ongoing monitoring efforts, compliance specialists track the submission of grantees' independent audit reports and the resolution of issues identified in these reports. Grantees who expend \$750,000 or more in state awards in the grantee's fiscal year must submit a single independent audit, a program specific audit, or an agreed upon procedures engagement. The auditor must compile the findings in an independent audit report, which the grantee submits to CPRIT within 30 days of receipt, but no later than 270 days after the grantee's fiscal year.

Compliance Specialists are working with one grantee to remediate audit findings. CPRIT gives grantees 30 days from the receipt of the audit to submit supporting documentation to demonstrate remediation efforts. Currently, there are no grantees with a delinquent audit. Grantees are unable to receive reimbursements or advances if they are delinquent in filing the required audit and corrective action plan unless the grantee requested additional time by the due date of the required audit and CPRIT's CEO approved the request.

CPRIT recently revised the Annual Single Audit Determination (SAD) form process. Grantees will now complete one form for their institution on an annual basis and submit the completed

form to CPRIT via email. Prior to this change, the grantee completed a SAD form for each active grant held by the grantee and submitted the forms through CPRIT's grants management system. The revised due date for all future SAD forms will be 60 days after the organization's fiscal year end date. CPRIT provided the new SAD forms to grantees on April 20, 2018.

### Desk Reviews

Compliance Specialists performed 12 desk-based financial monitoring/reviews for the month of April, to verify that grantees expend funds in compliance with specific grant requirements and guidelines. Desk reviews may target an organization's internal controls, current and past fiscal audits, and timeliness of required grantee report submission. Compliance Specialists are working with five grantees to remediate desk review findings.

### On-Site Reviews

Compliance Specialists performed five on-site reviews during the month of April. On-site reviews typically include an examination of the grantee's financial and administrative operations, subcontract monitoring, procurement and contracting procedures, inventory procedures, personnel policies and procedures, payroll and timesheet policies, travel policies and records, and single audit compliance. Compliance Specialists are working with one grantee to remediate on-site review findings.

### Annual Compliance Attestation (Self-Certification)

CPRIT requires grantees to submit an annual self-certification by December 31<sup>st</sup>, demonstrating compliance with statutory and administrative grant requirements, CPRIT's policies and procedures, the grant contract, and Uniform Grant Management Standards (UGMS). This opportunity to self-report, in the form of a checklist, provides a baseline of grantee compliance and allows Compliance Specialists to proactively work with grantees towards full compliance prior to a desk review or on-site review. All grantees have submitted their 2018 Attestation form to CPRIT. Compliance staff are working with two grantees who require additional corrective action related to their attestation.

### Training and Support

CPRIT compliance, legal, and grant accounting staff conducted a grantee training webinar on March 7, 2018 with approximately 190 grantee staff in attendance. The training covered grant reporting requirements, administrative rule changes, grant closeout, and an overview of the compliance program including fraud, waste, and abuse reporting. This was the first training offered this year in support of the annual compliance training requirement which states that the Authorized Signing Official (ASO) and at least one other employee from each grantee organization must attend an annual compliance training by November 1 of each year. CPRIT has scheduled a second grantee training for the first week in June.

CPRIT conducted a new grantee training for ViraCyte, LLC, on March 29, 2018. This training included a hands-on navigation of CPRIT's grants management system as well as an overview of the compliance program, grantee reporting requirements and administrative rule changes. Pursuant to Texas Administrative Code §703.22, CPRIT requires new grantees to complete an initial compliance training program prior to receiving disbursement of Grant Award funds.

CPRIT conducted a new ASO training for Nexeon MedSystems, Inc. on April 17, 2018. This training covered grant reporting requirements, administrative rule changes, grant closeout, and an overview of the compliance program including fraud, waste, and abuse reporting. Pursuant to Texas Administrative Code §703.22, new ASOs are required to complete a compliance training within 60 days of the change.

### **Academic Research Program Update**

#### FY 2018 Cycle 2 (18.2) Request for Academic Research Applications

CPRIT received 203 applications through January 31, 2018, for Core Facility Support Awards, High-Impact/High Risk Awards, and Multi-Investigator Research Awards (see Table 1 below). Applications will be reviewed May 18 - 25 in Grapevine. The Scientific Review Council’s recommended awards will be presented to the Program Integration Committee and the Oversight Committee for approval in August 2018.

Table 1: FY 2018.2 Application Submissions by Mechanism

Mechanism	Number Received	Total Funds Requested
Core Facility Support Awards	27	\$134,701,329
High Impact/High Risk Awards	153	\$30,331,245
Multi-Investigator Research Awards	23	\$135,215,282
<b>TOTAL</b>	<b>203</b>	<b>\$300,247,856</b>

#### FY 2019 Cycle 1 Request for Academic Research Applications

CPRIT released five Requests for Applications (RFAs) on January 11, 2018. CPRIT will receive applications for the Individual Investigator, Individual Investigator-Childhood and Adolescent Cancers, Individual Investigator Computational Biology, Individual Investigator Prevention and Early Detection, and Individual Investigator Clinical Research Awards through June 6, 2018. Applications will be peer reviewed in October. The applications recommended by the SRC will be presented to the Program Integration Committee and the Oversight Committee for approval in February 2019.

#### Recruitment Summary Data

CPRIT received 22 recruitment applications for Recruitment Cycles: 18.6, 18.7, 18.8 and 18.9 (see Table 2 below). The Scientific Review Council reviewed the applications and their recommendations will be presented to the Program Integration Committee and the Oversight Committee for approval at the May 16, 2018, Oversight Committee meeting.

Table 2: Summary of Recruitment Application Submissions for Cycles 18.6, 18.7, 18.8 and 18.9.

Mechanism	Number Received
Recruitment Established Investigators	5
Recruitment Rising Stars	5
Recruitment of First-Time Tenure Track Faculty Members	12
<b>TOTAL</b>	<b>22</b>

The Collaborative Action Program (CAP) to Reduce Liver Mortality in Texas

Following the Oversight Committee’s direction at its January special meeting, Dr. Willson and Dr. Garcia have worked to develop a proposed request for applications for a new project addressing a specific, endemic problem or issue in cancer research, treatment, or prevention. Applicants will be expected to address the issue through an interinstitutional and interdisciplinary collaboration. Dr. Willson will host a meeting in Austin on May 1 to discuss the proposed project. CPRIT has invited representatives from the following institutions and organizations to attend:

- Baylor College of Medicine
- Texas A&M University
- Texas Tech University Health Sciences Center El Paso
- Texas Tech University Health Sciences Center
- The University of Texas at Austin
- The University of Texas at Galveston
- The University of Texas Southwestern Medical Center
- The University of Texas M.D. Anderson Cancer Center
- The University of Texas Rio Grande Valley
- The University of Texas Health Science Center at San Antonio
- Rice University
- University of Houston
- Texas Department of State Health Services/Cancer Registry

Dr. Willson will present the draft RFA at the May Oversight Committee meeting for approval.

**Product Development Research Program Update**

FY 2018 Cycle 2 (18.2) Product Development Research Applications

CPRIT received 20 applications for 18.2 Product Development Research awards by the February 7, 2018, deadline. CPRIT’s Product Development peer reviewers met March 26 and 27 and

selected 10 companies to present in person to the entire panel. The panels met April 23-26, 2018. Following the presentations, the peer review panels decided to move six applicants into due diligence. Applications recommended by the Product Development Review Council and the PIC will be presented to the Oversight Committee in August 2018 for approval.

FY 2019 Cycle 1 (19.1) Product Development Research Applications

The Oversight Committee approved three Product Development Award 19.1 RFAs at the February 21 meeting. Mr. Lang and Ms. French have finalized the review schedule and developed the RFAs consistent with the plan presented in February. CPRIT will release the Texas Company (TXCO) RFA, the Relocation Company (RELCO) RFA and the new Seed Award RFA in early June. Companies may submit applications June 28 through August 8, 2018. Selected applicants will be presented to the Oversight Committee in February 2019 for approval.

The new Seed Award program provides startup funding to early-stage projects. CPRIT is targeting company projects that may be too early for the TXCO and RELCO awards. We anticipate that many Seed Award applicants will be spinouts from Texas research institutions.

An outreach program is underway to build awareness of both programs with potential applicants. Mr. Lang and Ms. French are engaging with regional and statewide trade associations, public policy groups, biotech incubators, investment groups, and academic tech transfer offices to insure potential applicants are aware of these funding opportunities.

**Prevention Program Update**

FY 2018 Cycle 2 (18.2) Prevention Applications

CPRIT released three RFAs for the second cycle of FY 2018 on November 20, 2017. Peer review panels will meet May 22 - 25 to evaluate the 28 FY18.2 prevention applications requesting \$47,323,690 (see table below). The Prevention Review Council (PRC) will meet in July to make award recommendations. Dr. Garcia will present the recommendations to the Program Integration Committee and the Oversight Committee in November.

Mechanism	Number Received	Total \$ Requested
Evidence-based Cancer Prevention Services	12	\$16,037,453
Expansion of Cancer Prevention Services to Rural and Medically Underserved Populations	9	\$21,645,686
Tobacco Control and Lung Cancer Screening	7	\$ 9,640,551
<b>TOTAL</b>	<b>28</b>	<b>\$47,323,690</b>

CPRIT received one application this quarter for the Dissemination of CPRIT-Funded Cancer Control Interventions mechanism. The PRC reviewed the application on April 3, 2018. Dr. Garcia will present any recommendations to the Program Integration Committee and the Oversight Committee in May.

#### FY 2019 Cycle 1 (19.1) Prevention Applications

CPRIT will release three RFAs for the first cycle of FY 2019 on May 10. Applications are due September 5, 2018, with peer review panels meeting in December 2018. The Program Integration Committee and the Oversight Committee will consider the recommendations in February 2019. RFAs released in May include:

- **Evidence-Based Cancer Prevention Services**  
Seeks projects to deliver evidence-based cancer prevention and control clinical services. CPRIT gives priority to projects that address CPRIT areas of emphasis and serve areas of the state not well addressed by current CPRIT funded projects. Award: Maximum of \$1,500,000; Maximum duration of 36 months.
- **Tobacco Control and Lung Cancer Screening**  
Seeks programs on tobacco prevention and cessation, as well as screening for early detection of lung cancer. Through release of this RFA, CPRIT's goal is to stimulate more programs across the state, thereby providing greater access for underserved populations and reducing the incidence and mortality rates of tobacco-related cancers. Seeks to promote and deliver evidence-based programming designed to significantly increase tobacco cessation among adults and/or prevent tobacco use by youth. Award: Maximum of \$1,500,000; Maximum duration of 36 months.
- **Expansion of Cancer Prevention Services to Rural and Medically Underserved Populations**  
Seeks to support the coordination and expansion of evidence-based services to prevent cancer in underserved populations that do not have adequate access to cancer prevention interventions and health care thereby bringing together networks of public health and community partners to carry out programs tailored for their communities. Projects should identify cancers that cause the most burden in the community and use evidence-based models shown to work in similar communities to prevent and control these cancers. Currently funded CPRIT projects should propose to expand their programs to include additional types of prevention clinical services and/or an expansion of current clinical services into additional counties. Expansion must include delivery of services to nonmetropolitan and medically underserved counties in the state.  
Award: Maximum of \$3,000,000; Maximum duration of 36 months.
- **Dissemination of CPRIT-Funded Cancer Control Interventions**  
Seeks projects to facilitate the dissemination and implementation of successful CPRIT-funded, evidence-based cancer prevention and control interventions across Texas. Proposed projects should be able to develop one or more "products" based on the results of the CPRIT-

funded intervention and should also identify and assist others to prepare to implement the intervention and/or prepare for grant funding. This mechanism is continuously open; the PRC reviews applications quarterly. Award: Maximum of \$300,000; Maximum duration of 24 months.

### **Advisory Committees**

- The Product Development Advisory Committee (PDAC) met April 17. Andrew Strong will present the PDAC's annual report to the Oversight Committee on May 16.
- The University Advisory Committee met April 26.
- The Advisory Committee on Childhood Cancers (ACCC) will meet May 7. Dr. Susan Blaney will present the ACCC's annual report to the Oversight Committee on May 16.
- The inaugural meeting of the Clinical Trials Advisory Committee (CTAC) will convene May 7. The Oversight Committee will consider appointments to the CTAC on May 16.

### **Communications Update**

#### Cancer Awareness Month Activities

- CPRIT released a video featuring Dr. Jinming Gao and Dr. Sumer Baran from UT Southwestern Medical Center about their nanotechnology research that has received funding from both Academic Research and Product Development over social media for National Oral, Head and Neck Cancer Awareness Week (April 8-15).
- Chris Cutrone is working with the City of Houston and CPRIT's institutional partners on a mayoral proclamation recognizing National Cancer Research Month on May 15, 2018. The institutions plan to send CPRIT grantees and representatives to attend the event, and we are working on media strategy with our partners. As part of this outreach, Chris is working with *TMC Pulse*, the Texas Medical Center's magazine, on a possible feature story on CPRIT-funded research collaborations for the May issue.

#### Social Media Metrics

##### **Facebook (last 28 days):**

- Reach: 883
- Engagement: 226
- Most popular post: ICYMI: More than a dozen UT Southwestern Medical Center researchers received CPRIT grants in the latest round of funding.

##### **Twitter (last 28 days):**

- 5,185 impressions

- Top tweet: ICYMI: Read about how more than a dozen @UTSWNews researchers received CPRIT grants in the latest round of funding: [cprit.us/2uGJVrJ](http://cprit.us/2uGJVrJ)

**Operations, Audit and Finance Update**

Staff continues working on the *Agency Strategic Plan for 2019-2023*, which CPRIT will submit to the Legislative Budget Board and Governor’s Office by June 8.

The Weaver audit team started field work on the Follow-up Procedures Over the Purchasing and P-Card Audit as well as on the Follow-Up Procedures Over the Pre-Award Grant Management Audit. They also completed field work on the Communications Audit. CPRIT and the Weaver team will hold exit meetings for all three audits on April 30.

**Upcoming Subcommittee Meetings**

CPRIT will hold the following regularly scheduled subcommittees in advance of the May 16, 2018, Oversight Committee meeting.

Board Governance	May 3 at 10:00 a.m.
Audit	May 7 at 10:00 a.m.
Prevention	May 8 at 10:00 a.m.
Academic Research	May 9 at 10:00 a.m.
Product Development Research	May 10 at 10:00 a.m.
Nominations	May 11 at 10:30 a.m.

CPRIT will send an agenda, call-in information, and supporting material to the subcommittees one week prior to the meeting date.

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CPRIT has awarded **1,247** grants totaling **\$1.954 billion**

- 198 prevention awards totaling \$208.5 million
- 1,049 academic research and product development research awards totaling \$1.746 billion

Of the \$1.746 billion in academic research and product development awards,

- 29.2% of the funding (\$510.0 million) supports clinical research projects
- 26.5% of the funding (\$461.7 million) supports translational research projects
- 25.9% of funding (\$452.1 million) supports recruitment awards
- 15.0% of the funding (\$262.2 million) supports discovery stage research projects
- 3.5% of funding (\$59.9 million) supports training programs.

CPRIT has 9 open Requests for Applications (RFAs)

- 3 Research Recruitment
- 5 Academic Research
- 1 Prevention Dissemination



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** WAYNE R. ROBERTS, CHIEF EXECUTIVE OFFICER  
**SUBJECT:** CHIEF EXECUTIVE OFFICER REPORT  
**DATE:** MARCH 28, 2018

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Topics in this memo cover the period January 2018 through the end of March and include recent milestones in our fight against cancer, a staffing summary, construction in the Capitol Complex, CPRIT outreach efforts, and updates from Compliance, Programs, and Operations.

**Recent Milestones in the Fight against Cancer**

CPRIT Grantees in the News

- Parkland Health & Hospital System and The University of Texas Southwestern Medical Center received the 2017 Bill Aston Award for Quality at the annual conference of the Texas Hospital Association on February 7 for a project that has significantly improved the rate of voluntary human papillomavirus (HPV) vaccine delivery in Dallas County. Through a CPRIT grant to Dr. Jasmin Tiro in 2011-2012, the project team evaluated the impact of educational pamphlets mailed to parents of young patients before clinic visits to increase voluntary initiation and telephone recalls to improve series completion. This project showcases how national, state, and non-profit funding agencies were leveraged to understand and intervene on this key cancer prevention area.
- Michael Pignone, M.D., M.P.H., chairman of the department of internal medicine at Dell Medical School has developed an app that can help explain to the public the benefits of each type of colon cancer screening and help schedule a screening. The number of patients in the study that went on to get testing was 30 percent with the app versus 15 percent with the traditional information. While the app study happened when Dr. Pignone was in North Carolina, he is continuing work on colon cancer now that he is in Austin. He received a grant in 2017 through CPRIT to work with CommUnityCare, a clinic system that serves the uninsured.
- CPRIT Scholar James Allison, Ph.D. of The University of Texas MD Anderson Cancer Center (MD Anderson) will receive the Jessie Stevenson Kovalenko Medal from the National Academy of Sciences in a ceremony April 29, during its 155th annual meeting. Dr. Allison's research has had a vast impact on cancer therapy and the evolution of the entire field of cancer immunology.

- CPRIT grantee Sattva Neelapu, M.D., professor at MD Anderson, reported in the *New England Journal of Medicine* on a remarkable improvement in outcomes for patients with aggressive large B-cell lymphoma treated with anti-CD19 CAR T-cells. Over 80 percent of patients had a response and 42 percent remain in remission at 15 months following treatment. Despite these impressive clinical results, half the patients did not have a durable response and Dr. Neelapu's CPRIT Individual Investigator Research Award, granted in 2015, RP150316, focuses on developing the next generation of CAR T-cell immune therapies for lymphoma patients.

#### Notable CPRIT Supported Research and Prevention Accomplishments

- Aravive Biologics announced initiation of a Phase I clinical trial of its lead drug candidate, AVB-S6-500. This 40-patient study will evaluate pharmacokinetics and pharmacodynamics to demonstrate proof of mechanism of AVB-S6-500. The company is developing AVB-S6-500 as a treatment for acute myeloid leukemia and certain advanced solid tumor indications, including ovarian and breast cancer. The drug candidate inhibits a key molecular pathway thought to promote tumor growth and metastasis, as well as tumor immune evasion and resistance to other anticancer agents. Aravive has also announced plans to expand their biologics manufacturing following the rapid success achieved in the process development of AVB-S6-500. Aravive received a CPRIT product development grant award in December 2015.
- DNATRIX, a Houston based company and CPRIT awardee, reported that the use of their drug candidate DNX-2401 in a Phase 1 clinical trial allowed 20 percent of patients with recurrent glioblastoma to live an additional three years. The drug was injected one time directly into the tumors of 25 patients whose glioblastoma had recurred after surgery and other treatments, a patient group that typically has a median survival of six months. DNATRIX developed the technology in collaboration with MD Anderson Cancer Center.
- The U.S. Food and Drug Administration (FDA) approved Salarius Pharmaceuticals' Investigational New Drug Application (IND) for the development of Seclimdestat, a drug aiming to treat Ewing's sarcoma, an orphan disease primarily affecting children. The "Safe to Proceed" ruling allows the company to initiate clinical trials, giving patients' access to this novel therapeutic drug. Salarius plans to initiate clinical trials with Ewing's Sarcoma patients in the next few months. Salarius received a CPRIT product development grant award in June 2016.
- Synlogic recently reported positive preclinical oncology data. Synlogic is developing synthetic biotic medicines. These leverage the tools and principles of synthetic biology to genetically engineer probiotic microbes to perform or deliver critical functions missing or damaged due to disease. Synlogic presented data showing that their STING (STimulator of INterferon Genes) probiotic bacteria successfully modulated the tumor microenvironment and demonstrated potent and effective antitumor immunity. Tumor cells can affect their local environment that make them harder to target. Modulating the tumor microenvironment can improve the usefulness of various therapies. Synlogic is the successor company to Mirna Therapeutics, which received CPRIT product development grant awards in 2010 and 2014.

- Bellicum Pharmaceutical is developing novel, controllable immunotherapies for cancers and orphan inherited blood disorders. The company’s lead therapy is BPX-501, an adjunct T cell therapy administered after an allogeneic (donor) stem cell transplant. Bellicum has treated more than 240 patients with BPX-501 cells on three allogeneic stem cell transplantation protocols. The FDA placed U.S. studies of BPX-501 on a clinical hold in late January following three cases of encephalopathy possibly related to BPX-501. Encephalopathy is a known risk factors in allogeneic stem cell transplants patients. These three cases are complex with multiple confounding factors. The company is in the process of implementing the criteria provided by the FDA for lifting the clinical hold.

On March 13, Bellicum announced interim results showing low rates of cancer recurrence in pediatric acute myelogenous leukemia patients receiving allogeneic stem cell transplants treated with BPX-501. The 38 pediatric patients in the study showed a 91.5% relapse free survival rate and an overall 97.3% survival rate one year after treatment. This compares to a reported 60% relapse free survival rate and an 80% overall survival rate one year after a stem cell transplant without BPX-501. Bellicum received two CPRIT product development grant awards in 2011 and 2016.

- In the cover article of the January 5, 2018, issue of *Science*, CPRIT grantee Jennifer Wargo, M.D., associate professor, MD Anderson, shows how the gut microbiome modulated the response of melanoma patients to anti-PD-1 immunotherapy. She studied melanoma patients receiving PD-1 blockade immunotherapy and found a greater abundance of “good” bacteria in the guts of responding patients. Non-responders had an imbalance of “good” bacteria in their gut, which correlated with a lack of response to anti-PD-1 immunotherapy. Fecal microbiota transplantations (feeding patients the content of stool from normal individuals) has proven effective in the treatment of antibiotic-associated diarrhea and Dr. Wargo is developing similar strategies to maintain a “good” bacteria balance to help patients combat cancer. This work was supported in part by a CPRIT Individual Investigator Research Award, *Exploring Molecular and Immune Mechanisms of Response and Resistance to Combined BRAF/MEK Inhibition in Patients with High-Risk Resectable Metastatic Melanoma*, granted to Dr. Wargo in 2015.
- CPRIT scholar Stephen Mack, Ph.D., recruited to Baylor College of Medicine and Texas Children’s Hospital from the Cleveland Clinic with a CPRIT First-Time, Tenure-Track Faculty Members recruitment award in 2017, reported in the journal *Nature* on a novel strategy for discovering targets in childhood ependymomas. This work is particularly important because ependymoma is a type of brain tumor that is highly resistant to chemotherapy and Dr. Mack’s research promises to reveal new therapy targets for this lethal childhood cancer.
- In the December 2017 issue of *Computer Methods in Applied Mechanics and Engineering*, CPRIT Scholar Thomas Yankeelov, Ph.D., recruited to UT-Austin with an Established Investigator Award in 2016, reported on a model that predicts how brain tumors will respond to radiation therapy with much greater accuracy than previous models. This project is an example of Dr. Yankeelov’s research to “mathematize cancer” to represent how cancer behaves and responds to treatment.

- CPRIT Scholar Kenneth Westover, M.D., Ph.D., recruited to The University of Texas Southwestern Medical Center in 2012 with a CPRIT award for Recruitment of First-Time, Tenure-Track Faculty Members, reported in the journal *Cell* a tactic for attacking *RAS*-driven cancers. This research, supported by a CPRIT Investigator Initiated Research Award CPRIT granted initially in 2014 and renewed in 2017, is heralded as a foundation for further studies to develop new cancer drugs that target *RAS*-driven cancers. This work is notable because mutated *RAS* genes are some of the most common genetic drivers of cancer, especially in aggressive cancers like pancreatic and lung cancer, but no medicines that target *RAS* are available despite decades of effort.
- CPRIT funded scientists at The University of Texas Southwestern Medical Center, Jinming Gao, Ph.D. and Baran Sumer., M.D., will begin clinical testing of a cancer specific dye that lights up cancer tissue to see whether it can be used to improve the accuracy of cancer surgeries and reduce cancer recurrence and surgical morbidity. A CPRIT Investigator Initiated Research Award granted in 2012 and renewed in 2014 supported the initial development of this diagnostic tool. The clinical evaluation is supported by a CPRIT New Company Product Development Award made in 2014.

The cancer specific dye is based on a nanosensor that works by reacting to the low pH of cancer cells and illuminating the cancer like a lightbulb. Because normal tissues do not react, the dye sharply distinguishes cancerous tissue from healthy tissue, making it easier for surgeons to remove cancer cells while leaving healthy, functional tissue intact. The first clinical application of the nanosensor will be evaluated in patients undergoing breast cancer surgery where up to one-third require additional surgery because residual cancer cells were not removed initially.

- CPRIT Scholar Hao Zhu, M.D., Ph.D., who received a First Time Tenure Track Recruitment Award to bring him to The University of Texas Southwestern Medical Center has discovered that cells in the liver with whole genome duplications, known as polyploid cells, can protect the liver against cancer. The study, published in *Developmental Cell*, addresses a long-standing mystery in liver biology and is expected to stimulate new ideas to prevent cancer in a variety of chronic liver diseases that frequently lead to liver cancer.
- Alexander Bishop, Ph.D., with the Greehey Children's Cancer Research Institute at UT Health San Antonio, has discovered a surprising connection between a breast cancer protein, BRCA1, and a pediatric cancer called Ewing sarcoma. His research, reported in *Nature*, is supported by a CPRIT Individual Investigator Research Awards for Cancer in Children and Adolescents awarded in 2015. Dr. Bishop found that a mutant protein produced in Ewing's causes normal cell functions to run unchecked and disable the repair function of BRCA1, which repairs damaged genetic material. Ewing sarcoma is a pediatric bone and soft tissue cancer. This work is part of Dr. Bishop's program to identify why Ewing sarcoma is usually sensitive to standard cancer drugs, with the hope of finding new targets for therapy and revealing new ways to treat the disease if it returns or does not respond to standard therapies.

- More than 7,000 mammograms, Pap tests, and diagnostic services were provided in the Texas Panhandle as a direct result of outreach efforts from 2010 to 2017 through Dr. Rakhshanda Layeequr Rahman’s Evidence-Based Prevention Services award. This project has been instrumental in closing gaps within the continuum of care that would not have been possible without CPRIT funding. The program’s successes have enabled Dr. Rahman to leverage several other grants to provide additional services. Federal DSRIP (Delivery Reform System Incentive Payment) funding is available to provide free clinic visits. A private grant covers required annual MRIs for high-risk patients. A pharmaceutical company is providing free genetic testing for uninsured patients. Fundraising efforts support a survivorship program, offered at no cost to participants.
- Dr. Lorraine Reitzel of the University of Houston presented the Taking Texas Tobacco Free project outcomes on clinician behavior changes at the Society for Research on Nicotine and Tobacco Annual Conference in Baltimore, MD and was invited to present at a meeting with US State Department Bureau of Educational and Cultural Affairs Russian Healthcare and Agricultural delegates.
- Dr. Amelie Ramirez of UT Health San Antonio gave written testimony at the San Antonio City Council to support the Tobacco 21 ordinance to increase the age for sale of tobacco products from 18 years to 21 years of age. The ordinance, the first of its kind in Texas, passed on January 11, 2018, and is a major step toward protecting the health of future generations and reducing the burden of tobacco in the state. Dr. Ramirez is also leading the UT Health San Antonio End Tobacco Use Committee formed as part of the UT System’s successful effort to become the first entirely tobacco-free university system in the state.

## **Personnel**

CPRIT has 35 authorized full-time equivalent (FTE) positions, 34 of which CPRIT has filled.

- Chris Bair, who has worked at CPRIT as a contract employee, accepted the permanent position of Programmer effective February 22.
- Ed Dorotik, who has worked at CPRIT as a contract employee, accepted the permanent position of Grant Accountant effective March 1.
- We are in the process of filling the vacant Grant Compliance Specialist position.

## **Construction at the Capitol Complex**

State officials have long held the goal of moving all state agencies out of rented office space and consolidating state employees in state-owned office buildings in Central Austin. To this end, the Texas Legislature gave final approval to the “Capitol Complex Master Plan” that includes the construction of three new office buildings, below ground parking, and a four-block walking promenade that will replace Congress Avenue from 15<sup>th</sup> Street to Martin Luther King Jr. Blvd. The rendering below depicts the new buildings in gold. The William B. Travis Building, where CPRIT is located, is the grey building on the left between two new buildings.



The first phase of the project begins this month. The Texas Facilities Commission (TFC) will break ground on the two new buildings on either side of Travis Building, eventually adding more than one million square feet of new space and five floors in each building of below ground parking (4,400 spaces) by 2022.

Building construction will be disruptive for everyone working for or doing business with agencies currently located in the Capitol Complex. Construction activities will require the elimination of all street level parking in the several blocks surrounding the Travis Building beginning this spring (400 employee spaces in addition to metered parking). This is another burden on the already crowded parking garages located around the Capitol Complex, including the Capitol Visitor's Public Parking garage where Oversight Committee members park when we meet at the Capitol.

The TFC also plans to permanently shut down Congress Avenue by June. Many of the side streets in the Capitol Complex will close on a rotating basis over the next four years to dig up and rebury underground power and communication lines. The road closures will create more traffic problems for the thousands of state employees that work in the Capitol Complex. In addition, excavation work to create the underground parking lots will take place during working hours on both sides of the Travis Building.

We are exploring options to minimize the disruption on CPRIT staff and will keep you updated on the construction progress.

## CPRIT Outreach

- During late January and early February Kristen Doyle, Heidi McConnell and I briefed legislators, legislative staff, advocates, and CPRIT grantees about the agency's funding scenarios for fiscal years 2020 through 2023 considered by the Oversight Committee at its January 17, 2018, special meeting. These discussions included a possible exceptional item to maintain current grant making levels in 2020-21 in CPRIT's biennial budget request. We expect to file the budget request in August 2018.
- On January 17 Oversight Committee member Dee Margo and I briefed Governor Abbott's executive staff on CPRIT activities and plans for the 86<sup>th</sup> Texas Legislature in 2019.
- On January 24 I briefed Tom Kowalski, President of the Texas Healthcare & Bioscience Institute, and Coach Ty Harrington of Texas State University, a cancer survivor, about CPRIT activities and future expectations.
- Chief Product Development Officer Michael Lang and Rosemary French, Product Development Program Manager, attended the Health Tech Austin networking event at the Medical Device Summit in Austin on February 1, 2018.
- Mr. Lang and Ms. French met with entrepreneurs at the Fannin Innovation Studio, a Houston-area accelerator, on February 7, 2018.
- On February 7 Mr. Lang presented an overview of CPRIT Product Development Program at the JLABs "Meet With..." series. Mr. Lang and Ms. French also held one-on-one meetings with prospective applicants.
- On February 8 I briefed Representative Todd Hunter on CPRIT activities.
- Chief Prevention Officer Becky Garcia presented an outline of the Texas Cancer Plan revision process and instructions for providing feedback to the Cancer Alliance of Texas Executive Committee and several workgroup members on February 8, 2018.
- Chief Scientific Officer Jim Willson, Dr. Garcia, Mr. Lang, Ms. Doyle, and I met on February 15 with a delegation from the United Kingdom, including Sir Mark Walport, Chief Executive Officer of UK Research and Innovation, a consortium of scientific and medical research councils, about shared interests and possibilities for future collaboration.
- Academic and Prevention program staff conducted a webinar on February 15 for 105 participants on a new area of emphasis to the Individual Investigator Research Awards for Prevention and Early Detection (IIRAP) RFA. The purpose of the webinar was to communicate interest in receiving applications on implementation research designed to accelerate the adoption and deployment of evidence-based cancer prevention and screening interventions.

- Ms. French attended the Texas Medical Device Alliance marketing networking event in Austin on February 15.
- Mr. Lang presented an overview of the CPRIT Product Development Program at the Health Wildcatters' Pulse Healthcare Innovation Breakfast Series in Dallas on February 22, 2018. Mr. Lang and Ms. French also met one-on-one with prospective applicants.
- On February 26 Ms. McConnell and I briefed the State Auditor staff member newly assigned to CPRIT on CPRIT activities including delegated financial and internal audit functions.
- Ms. French attended the Austin Community College Bioscience Incubator open house networking event on March 7.
- Dr. Garcia and Ramona Magid met with regional leadership of the American Cancer Society on March 8 to learn about their new structure and initiatives in the Southern Region.
- I met with the newly assigned Governor's Office policy analyst on March 12 to provide a brief on CPRIT's operations and history.
- Dr. Garcia and Ramona Magid attended a meeting of the Texas HPV Coalition on March 20. All CPRIT grantees with HPV projects are members of this coalition.
- Dr. Willson, Dr. Garcia, Mr. Lang, Ms. Doyle, Chris Cutrone, and I met with a health care reporter from Politico, Renuka Rayasam, on March 21 about CPRIT's purpose and operational status.
- Dr. Willson, Dr. Garcia, Chris Cutrone, and I will travel to the Rio Grande Valley for a series of meetings with UT Rio Grande Valley, Doctor's Hospital at Renaissance, and Rio Grande Valley legislators on April 9, 2018. The American Cancer Society has invited legislators, CPRIT grantees, and CPRIT staff to participate in a forum that will feature CPRIT.
- Mr. Cutrone is working with Texas Tech University Health Sciences Center at El Paso on a on an April 19, 2018, press conference announcing the CPRIT Scholar recruitment grant of Shrikanth Gadad, PhD. The El Paso legislative delegation along with CPRIT leadership and Tech Texas University System Board of Regents Chairman Rick Francis have been invited to participate.

## **Compliance Program Update**

### Submission Status of Required Grant Recipient Reports

CPRIT's grant management system (CGMS) produces a summary of delinquent reports each week; this is the primary source used by CPRIT's compliance staff to follow up with grantees. CPRIT typically has 570+ grants that are either active or wrapping up grant activities and receives an average of 570 grantee reports each month.

As of March 26, 2018, two entities have not filed three required reports by the set due date; all three delinquent reports are for Academic Research grants. CPRIT's grant accountants and grant compliance specialists continue to review and process incoming reports and reach out to grantees to resolve filing issues. In most cases, CPRIT does not disburse grant funds until the grantee files the required reports. In some instances, grantee institutions may be ineligible to receive a future award if the grantee does not submit the required reports.

### FSR Reviews

CPRIT's Grant Compliance Specialists performed 371 second-level reviews of grantee Financial Status Reports (FSRs) for the months of February and March. Forty-five FSRs (12%) required resubmission due to insufficient or inaccurate documentation submitted by the grantee. CPRIT's grant accounting staff completes the initial review of the FSRs and supporting documentation before routing them to the compliance specialists for final review and disposition.

### Single Audit Tracking

As part of ongoing monitoring efforts, grant compliance specialists track the submission of grantees' independent audit reports and the resolution of issues identified in these reports. Grantees who expend \$750,000 or more in state awards in the grantee's fiscal year must submit a single independent audit, a program specific audit, or an agreed upon procedures engagement. The grantee must submit the independent audit report and findings to CPRIT within 30 days of receipt, but no later than 270 days after the grantee's fiscal year.

Grant Compliance Specialists are working with one grantee to remediate audit findings. CPRIT gives grantees 30 days from the receipt of the audit to submit supporting documentation to demonstrate remediation efforts. Currently, there are no grantees with a delinquent audit. Grantees are unable to receive reimbursements or advances if they are delinquent in filing the required audit and corrective action plan unless the grantee requested additional time by the due date of the required audit and CPRIT's CEO approved the request.

### Desk Reviews

Grant Compliance Specialists performed 34 desk-based financial monitoring/reviews for the months of February and March, to verify that grantees expend funds in compliance with specific grant requirements and guidelines. Desk reviews may target an organization's internal controls, current and past fiscal audits, and timeliness of required grantee report submission. Grant Compliance Specialists are working with nine grantees to remediate desk review findings.

### On-Site Reviews

Grant Compliance Specialists performed three on-site reviews during the months of February and March. On-site reviews typically include an examination of the grantee's financial and administrative operations, subcontract monitoring, procurement and contracting procedures, inventory procedures, personnel policies and procedures, payroll and timesheet policies, travel policies and records, and single audit compliance.

## Annual Compliance Attestation (Self-Certification)

CPRIT requires grantees to submit an annual self-certification by December 31 of each year, demonstrating compliance with statutory and administrative grant requirements, CPRIT’s policies and procedures, the grant contract, and Uniform Grant Management Standards (UGMS). This opportunity to self-report, in the form of a checklist, provides a baseline of grantee compliance and allows Grant Compliance Specialists to proactively work with grantees towards full compliance prior to a desk review or on-site review. All grantees have submitted their 2018 Attestation form to CPRIT. Compliance staff is working with three grantees who require additional corrective action related to their attestation.

## Training and Support

CPRIT staff conducted a grantee training webinar on March 7, 2018. There were approximately 150 grantee staff in attendance. The training covered grant reporting requirements, administrative rule changes, grant closeout, and an overview of the compliance program including fraud, waste, and abuse reporting. This was the first training offered this year in support of the annual compliance training requirement which states that the Authorized Signing Official (ASO) and at least one other employee from each grantee organization must attend an annual compliance training by November 1 of each year. CPRIT has scheduled a second grantee training for the first week in June. Also, CPRIT Compliance Staff is coordinating efforts to conduct one new ASO training and one new grantee training by April 30.

## **Academic Research Program Update**

### FY 2018 Cycle 2 (18.2) RFAs Update

CPRIT received 203 academic research applications for FY 2018 Cycle 2 (18.2) (listed below on Table 1 by RFA mechanism). CPRIT will conduct peer review May 18 through 25 in Grapevine. Dr. Willson will present the Scientific Review Committee’s award recommendations to the Program Integration Committee and the Oversight Committee in August 2018.

**Table 1: FY 2018.2 Application Submissions by Mechanism**

Mechanism	Number Received	Total Funds Requested
Core Facility Support Awards	27	\$134,701,329
High Impact/High Risk Awards	153	\$30,331,245
Multi-Investigator Research Awards	23	\$135,215,282
<b>TOTAL</b>	<b>203</b>	<b>\$300,247,856</b>

## Recruitment Summary Data

Table 2 displays the number of recruitment applications submitted for FY Cycles 18.6, 18.7 and 18.8 and reviewed by the SRC on February 15 (18.6 and 18.7) and March 15, 2018 (18.8). SRC-recommended grant applications will be presented to the Program Integration Committee and the Oversight Committee for approval at the May 16, 2018, Oversight Committee meeting.

**Table 2: Summary of Recruitment Application Submissions Cycles 18.6, 18.7 & 18.8**

Mechanism	Number Received
Recruitment Established Investigators	3
Recruitment Rising Stars	5
Recruitment of First-Time Tenure Track Faculty Members	5
<b>TOTAL</b>	<b>13</b>

## FY 2019 Cycle 1 Request for Academic Research Applications

The Academic Research Program posted five RFAs on January 11, 2018. Dr. Willson initially presented these RFAs to the Oversight Committee for approval in August 2017. CPRIT will accept applications from March 7, 2018, through June 6, 2018. Peer reviewers will evaluate the applications in October 2018; the applications recommended by the Scientific Review Council will be presented to the Program Integration Committee and the Oversight Committee for approval in February 2019. The five RFAs are:

- **Individual Investigator Research Awards (IIRA) (RFA R-19.1 IIRA)**  
Supports applications for innovative research projects addressing critically important questions that will significantly advance knowledge of the causes, prevention, and/or treatment of cancer. Areas of interest include laboratory research, translational studies, and/or clinical investigations. Competitive renewal applications accepted.  
Award: Up to \$300,000 per year.  
Duration: Maximum 3 years.
- **IIRA Childhood and Adolescent Cancers (RFA R-19.1-IIRACCA)**  
Supports applications for innovative research projects addressing questions to advance knowledge of the causes, prevention, progression, detection, or treatment of cancer in children and adolescents. Laboratory, clinical, or population-based studies are all acceptable. CPRIT expects the outcome of the research to reduce the incidence, morbidity, or mortality from cancer in children and/or adolescents in the near or long term. Competitive renewal applications accepted.  
Award: Up to \$300,000 per year. Applicants that conducting a clinical trial as part of the project may request up to \$500,000 in total costs.  
Duration: Maximum 4 years.

- IIRA Computational Biology (RFA R-19.1-IIRACB)**  
 Supports applications for innovative mathematical or computational research projects addressing questions to advance knowledge in any aspect of cancer. Areas of interest include data analysis of cellular pathways, microarrays, cellular imaging, cancer imaging or genomic, proteomic, and metabolomics databases; descriptive mathematical models of cancer, as well as mechanistic models of cellular processes and interactions and use of artificial intelligence approaches to build new tools for mining cancer research and treatment databases.  
 Award: Up to \$300,000 per year.  
 Duration: Maximum 3 years.
- IIRA Prevention and Early Detection (RFA R-19.1-IIRAP)**  
 Supports applications for innovative research projects addressing questions to advance knowledge of the causes, prevention, early-stage progression, and/or early detection of cancer. Research may be laboratory, clinical, or population-based, and may include behavioral/intervention, dissemination, or health services/outcomes research to reduce cancer incidence or promote early detection. Competitive renewal applications accepted.  
 Award: Up to \$300,000 per year for laboratory and clinical research; Up to \$500,000 per year for population-based research.  
 Duration: Maximum 3 years.
- IIRA Clinical Translation (RFA R-19.1 – IIRACT)**  
 Supports applications for innovative clinical research to lead to a better understanding of the clinical efficacy of a cancer therapy or diagnostic device. Applications submitted under this mechanism should propose innovative clinical studies that are hypothesis-driven and involve patients enrolled prospectively on a clinical trial or involve analyses of biospecimens from patients enrolled on a completed trial for which the outcomes are known.  
 Award: Up to \$400,000 per year for a maximum of 3 years for laboratory and clinical research; Up to \$600,000 per year for up to 4 years if research includes the conduct of clinical trials.  
 Duration: Maximum 4 years.

## **Product Development Research Update**

### FY 2018 Cycle 2 Applications

Product Development Award FY 2018 Cycle 2 opened to receive applications from December 22, 2017, through February 7, 2018. Peer reviewers are evaluating the 20 applications submitted by the deadline. The peer reviewers met March 26 and 27 and selected 10 companies to present applications at the peer review panel meeting April 23-26, 2018. Mike Lang will present the Product Development Review Council’s recommendations to the Oversight Committee in August 2018 for approval.

### FY 2019 Cycle 1 RFAs

The Oversight Committee approved the timeline and proposed RFAs for Product Development Award FY 2019 Cycle 1 at the February 21, 2018, meeting. In addition to RFAs for Texas

Company Product Development Awards and Company Relocation Product Development Awards, the FY 2019 cycle includes a new Seed Award RFA. The Seed Award, together with the Early Translational Research Award (“ETRA,” offered through the Academic Research program) bridge between current academic and product development programs. CPRIT has modified the ETRA grant to enhance focus on clinical and commercial objectives and ensure support is available. In addition to the modified ETRA, the new Seed Award grants provide startup funding to new projects at emerging companies. We anticipate many of the Seed Award applicants will be spinouts from Texas research institutions.

CPRIT will begin accepting applications June 28 through August 8, 2018, for the first cycle of FY 2019. Any grant award recommendations will be presented to the Oversight Committee in February 2019 for approval.

An extensive outreach program is underway to build awareness with potential applicants. We are engaging with regional and statewide trade associations, public policy groups, biotech incubators, investment groups, and academic tech transfer offices. In addition, we are meeting with potential applicants and attending numerous networking events.

### Prevention Program Update

#### FY 2018 Cycle 2 (18.2) Prevention Applications

CPRIT released three RFAs in November 2017 for the second review cycle of FY 2018. Peer review panels will meet May 22 - 25 to evaluate the 28 FY18.2 prevention applications requesting \$47,323,690 (see table below). The Prevention Review Council (PRC) will meet in July to make award recommendations to the Program Integration Committee (PIC). Dr. Garcia will present the PIC recommendations to the Oversight Committee in November.

Mechanism	Number Received	Total \$ Requested
Evidence-based Cancer Prevention Services	12	\$16,037,453
Expansion of Cancer Prevention Services to Rural and Medically Underserved Populations	9	\$21,645,686
Tobacco Control and Lung Cancer Screening	7	\$ 9,640,551
<b>TOTAL</b>	<b>28</b>	<b>\$47,323,690</b>

CPRIT received one application this quarter for the Dissemination of CPRIT-Funded Cancer Control Interventions mechanism. The PRC will review it on April 3, 2018.

## FY 2019 Cycle 1 (19.1) Prevention RFAs

CPRIT will release three RFAs for the first cycle of FY 2019 on May 31. Applications are due September 5, 2018, with peer review panels meeting in December 2018. The Oversight Committee will consider the recommendations at the February 2019 meeting. RFAs released in May include:

- **Evidence-Based Cancer Prevention Services (EBP)**  
Seeks projects to deliver evidence-based cancer prevention and control clinical services. CPRIT gives priority to projects that address CPRIT areas of emphasis and serve areas of the state not well addressed by current CPRIT funded projects. Award: Maximum of \$1,500,000; Maximum duration of 36 months.
- **Tobacco Control and Lung Cancer Screening (TCL)**  
Seeks programs on tobacco prevention and cessation, as well as screening for early detection of lung cancer. Through release of this RFA, CPRIT's goal is to stimulate more programs across the state, thereby providing greater access for underserved populations and reducing the incidence and mortality rates of tobacco-related cancers. Seeks to promote and deliver evidence-based programming designed to significantly increase tobacco cessation among adults and/or prevent tobacco use by youth. Award: Maximum of \$1,500,000; Maximum duration of 36 months.
- **Expansion of Cancer Prevention Services to Rural and Medically Underserved Populations (EPS)**  
Seeks to support the coordination and expansion of evidence-based services to prevent cancer in underserved populations that do not have adequate access to cancer prevention interventions and health care thereby bringing together networks of public health and community partners to carry out programs tailored for their communities. Projects should identify cancers that cause the most burden in the community and use evidence-based models shown to work in similar communities to prevent and control these cancers. Currently funded CPRIT projects should propose to expand their programs to include additional types of prevention clinical services and/or an expansion of current clinical services into additional counties. Expansion must include delivery of services to nonmetropolitan and medically underserved counties in the state.  
Award: Maximum of \$3,000,000; Maximum duration of 36 months.
- **Dissemination of CPRIT-Funded Cancer Control Interventions (DI)**  
Seeks projects to facilitate the dissemination and implementation of successful CPRIT-funded, evidence-based cancer prevention and control interventions across Texas. Proposed projects should be able to develop one or more "products" based on the results of the CPRIT-funded intervention and should also identify and assist others to prepare to implement the intervention and/or prepare for grant funding. This mechanism is continuously open; the PRC reviews applications quarterly. Award: Maximum of \$300,000; Maximum duration of 24 months.

## Communications Update

### Cancer Awareness Month Activities

- CPRIT released a video featuring the Moncrief Cancer Institute at the end of February for National Cancer Prevention Month.
- CPRIT interviewed Dr. Jinming Gao and Dr. Sumer Baran at UT Southwestern Medical Center about their nanotechnology research that has received both CPRIT Academic Research and Product Development funding. The interview is part of a video CPRIT will release on social media for National Oral, Head and Neck Cancer Awareness Week in April.
- Chris Cutrone is working with the City of Houston and CPRIT's institutional partners on a mayoral proclamation recognizing National Cancer Research Month on May 15, 2018. The institutions plan to send CPRIT grantees and representatives to attend the event, and we are working on media strategy with our partners. As part of this outreach, Chris is working with *TMC Pulse*, the Texas Medical Center's magazine, on a possible feature story on CPRIT-funded research collaborations for the May issue.

### Social Media Metrics

- Facebook (last 28 days):
  - Reach: 4,645
  - Engagement: 768
  - Most popular post: Great look at CPRIT-funded Texas A&M University Health Science Center C-STEP program conducting colorectal, breast, and cervical cancer screenings in over 20 Texas counties. <https://cprit.us/2DFvbIM>
- Twitter (last 28 days):
  - 6,900 impressions
  - Top tweet: Interesting look at @UTHealthSA CPRIT grantees discovery of a surprising connection between breast cancer protein and pediatric cancer Ewing sarcoma: [cprit.us/2FpOPu0](https://cprit.us/2FpOPu0)

## Operations, Audit, and Finance Update

At the beginning of March, the Legislative Budget Board and Governor's Office Budget Division issued the instructions for preparing agency strategic plans for fiscal years 2019 through 2023. The preparation of strategic plans is the beginning of the state budget cycle, which will culminate during the 2019 legislative session with a state budget for the 2020-21 biennium. The only major change to the strategic plan requirements is the elimination of the assessment of advisory committee section. CPRIT will not be requesting any changes to performance measures, so we do not anticipate significant changes to the agency's strategic plan that we filed two years ago. The uniform submission date for all agency strategic plans is June 8.

On March 1, 2018, the Comptroller’s Financial Reporting section notified CPRIT by letter that CPRIT’s audited financial report for FY 2017 complied with the Financial Reporting section’s annual financial report requirements.

The Weaver audit team initiated their field work on the Communications audit on March 20 and will hold an exit meeting with CPRIT staff on April 6. CPRIT will report the audit results to the Oversight Committee in May.

### Upcoming Subcommittee Meetings

Listed below are the regularly scheduled subcommittees in advance of the May 16, 2018, Oversight Committee meeting.

Board Governance	May 3 at 10:00 a.m.
Audit	May 7 at 10:00 a.m.
Prevention	May 8 at 10:00 a.m.
Academic Research	May 9 at 10:00 a.m.
Product Development	May 10 at 10:00 a.m.
Nominations	May 11 at 10:30 a.m.

CPRIT will send an agenda, call-in information, and supporting material to the subcommittees one week prior to the meeting date.

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CPRIT has awarded **1,247** grants totaling **\$1.954 billion**

- 198 prevention awards totaling \$208.5 million
- 1,049 academic research and product development research awards totaling \$1.746 billion

Of the \$1.746 billion in academic research and product development awards,

- 29.2% of the funding (\$510.0 million) supports clinical research projects
- 26.5% of the funding (\$461.7 million) supports translational research projects
- 25.9% of funding (\$452.1 million) supports recruitment awards
- 15.0% of the funding (\$262.2 million) supports discovery stage research projects
- 3.5% of funding (\$59.9 million) supports training programs.

CPRIT has 9 open Requests for Applications (RFAs)

- 3 Research Recruitment
- 5 Academic Research
- 1 Prevention Dissemination





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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** VINCE BURGESS, CHIEF COMPLIANCE OFFICER  
**SUBJECT:** COMPLIANCE PROGRAM UPDATE  
**DATE:** MAY 7, 2018

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The Chief Compliance Officer is responsible for apprising the Oversight Committee and the Chief Executive Officer of institutional compliance functions and activities, and assuring the Oversight Committee that controls are in place to prevent, detect and mitigate compliance risk. The required reporting includes quarterly updates to the Oversight Committee on CPRIT's compliance with applicable laws, rules, and agency policies. In addition, the Compliance Officer monitors the timely submission status of required grant recipient reports and notifies the Oversight Committee and General Counsel of a grant recipient's failure to meaningfully comply with reporting deadlines.

Submission Status of Required Grant Recipient Reports

CPRIT's grant management system produces a summary of delinquent reports each week; this is the primary source used by CPRIT's compliance staff to follow up with grantees. CPRIT typically has 570+ grants that are either active or wrapping up grant activities and receives an average of 570 grantee reports each month.

As of April 30, 2018, 15 grantees had not filed 26 required reports by the due date; 20 (77%) are Academic Research grants, three (12%) are Product Development Research grants, and three (12%) are Prevention grants. CPRIT's grant accountants and compliance specialists continue to review and process incoming reports and reach out to grantees to resolve filing issues. In most cases, CPRIT does not disburse grant funds until the grantee files the required reports. In some instances, grantee institutions may be ineligible to receive a future award if the grantee does not submit the required reports.

FSR Reviews

CPRIT's Compliance Specialists performed 73 second-level reviews of grantee Financial Status Reports (FSRs) for the month of April. Staff has completed a total of 307 reviews for the current Quarter. Seven FSRs (9%) required resubmission due to insufficient or inaccurate documentation

submitted by the grantee. CPRIT's grant accounting staff completes the initial review of the FSRs and supporting documentation before routing them to the compliance specialists for final review and disposition.

### Single Audit Tracking

As part of ongoing monitoring efforts, compliance specialists track the submission of grantees' independent audit reports and the resolution of issues identified in these reports. Grantees who expend \$750,000 or more in state awards in the grantee's fiscal year must submit a single independent audit, a program specific audit, or an agreed upon procedures engagement. The auditor must compile the findings in an independent audit report, which the grantee submits to CPRIT within 30 days of receipt, but no later than 270 days after the grantee's fiscal year.

Compliance Specialists are working with one grantee to remediate audit findings. CPRIT gives grantees 30 days from the receipt of the audit to submit supporting documentation to demonstrate remediation efforts. Currently, there are no grantees with a delinquent audit. Grantees are unable to receive reimbursements or advances if they are delinquent in filing the required audit and corrective action plan unless the grantee requested additional time by the due date of the required audit and CPRIT's CEO approved the request.

CPRIT recently revised the annual Single Audit Determination (SAD) form process. Grantees will now complete one SAD form for their institution on an annual basis and submit the completed form to CPRIT via email. Prior to this change, the grantee completed a SAD form for each active grant held by the grantee and submitted the forms through CPRIT's grants management system. The revised due date for all future SAD forms will be 60 days after the organization's fiscal year end date. CPRIT provided the new SAD forms to grantees on April 20, 2018.

### Desk Reviews

Compliance Specialists performed 12 desk-based financial monitoring/reviews for the month of April, to verify that grantees expend funds in compliance with specific grant requirements and guidelines. Desk reviews may target an organization's internal controls, current and past fiscal audits, and timeliness of required grantee report submission. Compliance Specialists are working with five grantees to remediate desk review findings.

## On-Site Reviews

Compliance Specialists performed five on-site reviews during the month of April. On-site reviews typically include an examination of the grantee's financial and administrative operations, subcontract monitoring, procurement and contracting procedures, inventory procedures, personnel policies and procedures, payroll and timesheet policies, travel policies and records, and single audit compliance. Compliance Specialists are working with one grantee to remediate on-site review findings.

## Annual Compliance Attestation (Self-Certification)

CPRIT requires grantees to submit an annual self-certification by December 31st, demonstrating compliance with statutory and administrative grant requirements, CPRIT's policies and procedures, the grant contract, and Uniform Grant Management Standards. This opportunity to self-report, in the form of a checklist, provides a baseline of grantee compliance and allows Compliance Specialists to proactively work with grantees towards full compliance prior to a desk review or on-site review. All grantees have submitted their 2018 Attestation form to CPRIT. Compliance staff are working with two grantees who require additional corrective action related to their attestation.

## Training and Support

CPRIT compliance, legal, and grant accounting staff conducted a grantee training webinar on March 7, 2018 with approximately 190 grantee staff in attendance. The training covered grant reporting requirements, administrative rule changes, grant closeout, and an overview of the compliance program including fraud, waste, and abuse reporting. This was the first training offered this year in support of the annual compliance training requirement which states that the Authorized Signing Official (ASO) and at least one other employee from each grantee organization must attend an annual compliance training by November 1 of each year. CPRIT has scheduled a second grantee training for the first week in June.

CPRIT conducted a new grantee training for ViraCyte, LLC, on March 29, 2018. This training included a hands-on navigation of CPRIT's grants management system as well as an overview of the compliance program, grantee reporting requirements and administrative rule changes. Pursuant to Texas Administrative Code §703.22, CPRIT requires new grantees to complete an initial compliance training program prior to receiving disbursement of grant award funds.

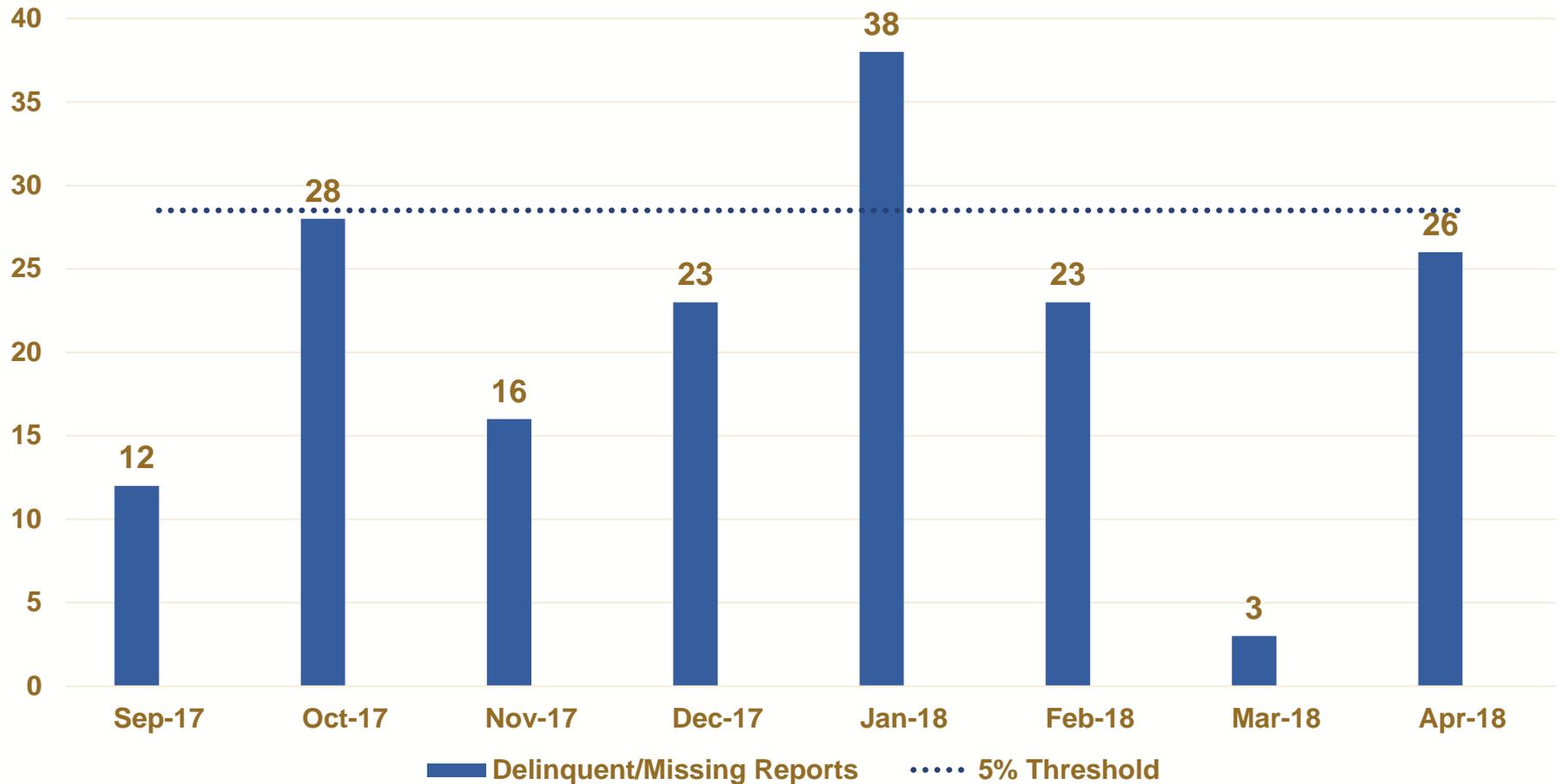
CPRIT conducted a new ASO training for Nexeon MedSystems, Inc. on April 17, 2018. This training covered grant reporting requirements, administrative rule changes, grant closeout, and an

overview of the compliance program including fraud, waste, and abuse reporting. Pursuant to Texas Administrative Code §703.22, new ASOs must complete a compliance training within 60 days of the change.

CPRIT staff will present at the National Council of University Research Administrators (NCURA) Region V meeting in San Marcos on May 8. The training will focus on required grantee reporting, specifically FSRs and Matching Compliance Certification forms and will include an interactive Q&A time with attendees.

# Grant Recipient Report Monitoring – 9-17 thru 4-18

## Delinquent/Missing Reports



Reports Submitted: Approximately 6,800/Annually, Average 570/Monthly







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**MEMORANDUM**

**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** JAMES WILLSON, MD., CHIEF SCIENTIFIC OFFICER  
**SUBJECT:** ACADEMIC RESEARCH PROGRAM UPDATE  
**DATE:** MAY 2, 2018

**FY 2018 Cycle 2 Academic Research Applications**

CPRIT released three RFAs for the second cycle of FY 2018 (18.2) in August 2017. As displayed in table 1, CPRIT received 203 applications by the deadline. Peer review panels will meet May 18-25 in Dallas/Fort Worth to conduct their review. The Oversight Committee will consider the PIC’s recommendation at the August 2018 meeting.

**Table 1: FY 2018.2 Application Submissions by Mechanism**

<b>Funding Mechanism</b>	<b>Number Applications Received</b>	<b>Total Funds Requested</b>
Core Facility Support Awards	27	\$134,701,329
High Impact/High Risk Awards	153	\$30,331,245
Multi-Investigator Research Awards	23	\$135,215,282
<b>Total</b>	<b>203</b>	<b>\$300,247,856</b>

**FY 2019 Cycle 2 Academic Research RFAs (Approved)**

The Oversight Committee approved the FY 2019 RFA release schedule on February 21, 2018 as follows:

- **Recruitment of Established Investigators (FY19)**  
Recruits outstanding senior research faculty with distinguished professional careers and established cancer research programs to academic institutions in Texas.  
Award: Up to \$6 million over a period of five years.
- **Recruitment of Rising Stars (FY19)**  
Recruits outstanding early-stage investigators to Texas, who have demonstrated the promise for continued and enhanced contributions to the field of cancer research.  
Award: Up to \$4 million over a period of five years.

- **Recruitment of First-Time Tenure Track Faculty Members (FY19)**  
Supports very promising emerging investigators, pursuing their first faculty appointment in Texas, who will make outstanding contributions to the field of cancer research.  
Award: Up to \$2 million over a period of five years.
- **Core Facilities Support Awards (CFSA) (RFA R-19.2 CFSA)**  
Solicits applications from institutions to establish or enhance core facilities (laboratory, clinical, population-based, or computer-based) that will directly support cancer research programs to advance knowledge of the causes, prevention, and/or treatment of cancer or improve quality of life for patients with and survivors of cancer.  
Award: Up to \$3M (total costs) for the first 2 years and up to \$1M (total costs) for each subsequent year; Maximum duration: 5 years.
- **High Impact/High Risk Research Awards (HIHR) (RFA R-19.2 HIHR)**  
Provides short-term funding to explore the feasibility of high-risk projects that, if successful, would contribute major new insights into the etiology, diagnosis, treatment, or prevention of cancers.  
Award: Up to \$200,000 (total costs); Maximum duration: 2 years.
- **Early Translational Research Awards (ETRA) (RFA-R-19.2 ETRA)**  
Supports projects that "bridge the gap" between promising new discoveries achieved in the research laboratory and commercial development for a therapeutic, device, or diagnostic assay through activities including preclinical proof-of-principle data that demonstrate applicability to the planned clinical scenario and preclinical toxicology and formulation to de-risk the development of lead compounds or devices. Any not-for-profit institution that conducts research is eligible to apply for funding under this award mechanism. CPRIT requires the applicant present a time line with stage gates for development. A public or private company is not eligible.  
Award: \$1 to 2 million in total costs over a period of 1-2 years.

### **FY 2019 Cycle 2 Academic Research RFA (Proposed)**

The Academic Research Program is proposing the following RFA for addition to the 19.2 review cycle (as discussed at the February 21, 2018, Oversight Committee Meeting):

#### **Collaborative Action Program to reduce liver cancer mortality in Texas**

##### **SUMMARY**

The overall goal of the Program is to position Texas as the national leader in reversing the trajectory of liver cancer incidence in the US.

Liver cancer, also known as hepatocellular cancer (HCC), is the fastest increasing lethal cancer in the US, with an annual incidence that has tripled during the past two decades. Texas is among

states with the highest incidence of liver cancer with an annual incidence that is nearly double the national average.

While the scientific community does not understand fully the reasons for the increase in HCC, the rise is particularly virulent among Texans of Mexican Hispanic ethnicity, who have a two-fold higher incidence of HCC compared to non-Hispanic Texans. Texans of Mexican Hispanic ethnicity are disproportionately affected by HCC risk factors including hepatitis C infection, non-alcoholic fatty liver disease, and exposure to aflatoxin.

The proposed “Collaborative Action Program to reduce liver cancer mortality in Texas” - “CAP liver cancer mortality” – will support investigator-initiated research projects (1) to explain the increased incidence of HCC in Texas, (2) to discover biomarkers of elevated risk for developing HCC, and (3) to identify best practices for implementation of prevention measures for HCC.

The CAP liver cancer mortality is comprised of two Research Funding Awards Announcements that will solicit applications for (1) Investigator initiated research awards and a Coordinating Center to facilitate coordination across the CAP Liver Cancer Mortality Research Projects. CPRIT will award the research projects as individual investigator research awards (IIRAs) to individual investigators. CPRIT will fund the coordinating center as a cooperative agreement with a Texas academic institution to allow CPRIT staff to advise and ensure coordination across the funded research projects, to foster interactions among the research participants, and to engage private and public entities across the state in developing a plan to implement the project findings.

## **BACKGROUND**

Even as overall cancer rates across the United States decline, liver cancer rates remain on the rise, especially among Texans of Mexican Hispanic heritage. Texas now has the highest incidence of liver cancer in the nation - estimated to be double the national average. In 2017, doctors will diagnose 4,020 Texans with HCC and 2,620 will die of liver cancer.

What is behind the increase in liver cancer in Texas? The medical community attributes liver cancer to a clustering of risk factors that cause liver fibrosis and cirrhosis which are the precursors of HCC. Hepatitis C infection is a major etiologic factor for cirrhosis and HCC in Texas. Individuals born between 1945 and 1965 have an extremely high risk for having chronic hepatitis C; this group is now aging to the point where many have developed cirrhosis and are at high risk for developing HCC. Studies estimate that 368,000 Texans are infected with hepatitis C in Texas and predict that 80% will go on to chronic infections and be at substantial risk for HCC.

Another risk factor for HCC on the rise in Texas is nonalcoholic fatty liver disease (NAFLD). NAFLD is related to obesity and type 2 diabetes and is estimated to affect 1 in 5 adults in Texas (1 in 3 Hispanic adults in Texas). While not all individuals with NAFLD develop liver-related complications, up to 30% will develop non-alcoholic steatohepatitis (NASH) and be at high risk for development of cirrhosis and HCC. Mexican Hispanics have a high frequency of a genetic polymorphism that increases the risk of obesity and alcohol-associated NASH and cirrhosis and the prevalence of this trait among Hispanics may partly explain the rise in HCC in Texas.

In addition to genetic predisposition, recent studies suggest the importance of environmental factors that may explain the incidence of HCC in Texas. Hispanics with liver cancer had much higher levels of aflatoxins than those without liver cancer. This finding suggests a link between aflatoxin, a human carcinogen found in corn, and liver cancer. Another possibility that the medical community has not evaluated fully is the impact of exposure to hazardous air pollutants as a contributing risk factor for liver cancer.

Because of the recent reports on the role of the microbiome in NAFLD and HCC, a comprehensive mechanistic study of the interaction between the microbiome and the liver and the identification of drivers of fatty liver disease progression is needed to identify new preventive strategies.

What can be done to lower the rise in liver cancer incidence and mortality? Screening and treating for hepatitis C and hepatitis B has the potential to have a dramatic impact on HCC incidence and mortality. Hepatitis C treatment results in cure in >90% of cases, and hepatitis B treatment results in adequate viral suppression in >95%. A vaccine for hepatitis B is also available for high risk individuals. Both outcomes have been associated with a considerable reduction in HCC risk.

Behavioral interventions that target obesity and alcohol and tobacco abuse represent obvious opportunities to decrease cirrhosis and HCC particularly in those populations at highest risk such as obese Hispanics carrying the genetic predisposition to developing a “fatty liver”.

Early detection strategies focused on high risk populations offer another promising strategy to change the current trajectory of liver cancer mortality in Texas. The 5-year survival rates for liver cancer is 18% but improves to 31% when diagnosed at an early stage. These data demonstrate both the limited impact of current therapies for late stage HCC and the potential impact of early detection on HCC mortality.

Texas is positioned well to lead a concerted effort to change the trajectory of liver cancer mortality. CPRIT sponsored research and prevention awards have catalyzed collaborative projects across the state that can be the basis of a state-wide investment in a multi-pronged approach to identify robust strategies for the prevention and early detection strategies that will change the current trajectory of HCC mortality in Texas.

A CPRIT Multi-investigator award established the Texas Hepatocellular Carcinoma Consortium (THCC) that includes national leaders in HCC research from Baylor College of Medicine, MD Anderson, UT Southwestern Medical Center, and UT San Antonio. The THCC has established cohort of individuals at high risk for HCC. This cohort as well as others could be expanded to accelerate the validation of biomarkers for early detection and prognosis in HCC.

CPRIT prevention awards currently support regional projects that are using novel strategies to promote HCC prevention through education, screening for hepatitis C, vaccination against hepatitis B and lifestyle modifications. These projects provide opportunities for implementation research to identify the best strategies to adopt and integrate evidence-based interventions into

clinical and community settings, scale up successful projects and sustain efforts, and to have a broad geographic impact.

**PROPOSED RFA: Collaborative Action Program to reduce liver cancer mortality in Texas**

The *CAP liver cancer mortality in Texas* project will promote research in hepatocellular cancer (HCC) prevention and early detection by supporting up to 6 individual investigator research awards designed to discover and validate clinically relevant strategies for preventing or the early detection of HCC in Texas. In addition, this program seeks research projects to identify genetic or environmental factors that explain the disproportionate ethnic and geographic risk for HCC in Texas.

Examples of projects responsive to this program include: implementation research designed to identify optimal outreach, screening and follow up practices for early detection in high-risk populations (including baby boomers); increase access to antiviral therapy for hepatitis C; identify innovative strategies to intervene in life style factors such as obesity and alcohol abuse in individuals at high risk for HCC; geospatial studies to identify environmental risks unique to Texas; and basic studies on the gene environment interactions to identify biomarkers for high risk populations.

In addition to the individual investigator research awards a single Coordinating Center based at a Texas academic institution will be supported to facilitate interactions across the research projects; provide administrative support to the program; assist with identification and collection of common data elements; to establish a collaboration with the state cancer registry to enhance real time assessment of HCC and HCC risk factors across Texas; provide a forum and develop a report for public policy considerations addressing issues critical to the implementation of research findings and reduction of HCC mortality in the state.

**RFA Concept Model Draft**

The Collaborative Action Program to reduce liver cancer mortality in Texas (CAP) RFA will support a Coordination Center and targeted Individual Investigator Research Award (IIRA) projects.

**Coordination Center**

The Coordination Center will facilitate coordination across the CAP targeted IIRA projects. In addition, the Coordination Center will provide (but not limited to) the following supports to the targeted IIRA projects:

- administrative and technical support
- facilitation and coordination of stakeholder partnerships
- guidance on study design and methods
- identify, develop, coordinate, and manage data sharing points
- provide bioinformatics resources
- provide geospatial (zip code level) resources
- provide epidemiology resources
- provide core facility tissue banking resources

- support the evaluation of IIRA innovative approaches to reduce liver cancer mortality in Texas
- provide a web based secure portal for data sharing, resources and code developed and utilized in the CAP IIRA projects.
- collect, synthesize, and disseminate main findings and lessons learned across the CAP IIRA projects.
- develop policy guidance and develop a report on policy recommendations and strategies to reduce the burden of liver cancer in Texas

### **Individual Investigator Research Award Projects**

The Individual Investigator Research Award projects will conduct targeted research in areas identified as a significant priority in reducing liver cancer mortality in Texas including:

Risk factors for HCC including:

- environmental risks;
- genetic markers.

Discovery of biomarkers of high risk for developing hepatocellular cancer.

Geospatial studies to identify environmental risks unique to Texas.

Implementation research including:

- Optimal outreach, early detection, screening, follow up interventions in high risk populations;
- Strategies for increasing access to antiviral therapy for Hep C;
- Effective interventions to reduce the impact of obesity and type 2 diabetes on nonalcoholic fatty liver disease.

### **BUDGET AND REVIEW CONSIDERATIONS**

#### Funding:

Individual Investigator Research Awards, up to 6 @ \$0.5M/year each over 5 years (\$15M)

Coordinating Center @ \$600,000/year over 5 years (\$3M)

Total cost - \$18 M

#### Review time line:

Oversight Committee Concept Approval: January 2018

Oversight Committee RFA Approval: May 2018

Announce RFA: August 2018

Application Receipt Dates: October 2018 - January 2019

Peer review: 19.2, Spring 2019

Award period: August 2019 - August 2023

# Academic Research Program RFA Release Schedule

Cycle and RFAs		Academic Research Program RFA release schedule																							
		FY 2018												FY 2019											
		Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug
<b>19.1</b>	RFA draft																								
Recruitment	RFA release																								
	Apps due																								
	SRC Review																								
	PIC meeting																								
	OC meeting																								
<b>19.1</b>	RFA draft																								
IIRA	RFA release																								
IIRACCA	Apps due																								
IIRACB	Peer Review																								
IIRAP	SRC Review																								
IIRACT	PIC meeting																								
	OC meeting																								
<b>19.2</b>	RFA draft																								
CFSA	RFA release																								
HIHR	Apps due																								
ETRA	Peer Review																								
CAP	SRC Review																								
	PIC meeting																								
	OC meeting																								
<b>Note:</b>																									
	<b>In Process</b>																								
	<b>Proposed</b>																								
		<p><b>IIRA-</b> Individual Investigator Research Awards, <b>IIRACCA-</b> IIRA Childhood and Adolescent Cancers  <b>IIRACB-</b> IIRA Computational Biology, <b>IIRAP-</b> IIRA Prevention and Early Detection, <b>IIRACT-</b> IIRA Clinical Translation  <b>CFSA-</b> Core Facilities Support Awards, <b>HIHR-</b> High Impact/High Risk Awards, <b>ETA-</b> Early Translation Awards  <b>*CAP -</b> Collaborative Action Program to reduce liver cancer mortality in Texas (Note: RFA in development will be considered in May 2018.)</p>																							





CANCER PREVENTION & RESEARCH  
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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** WAYNE R. ROBERTS, CHIEF EXECUTIVE OFFICER  
**SUBJECT:** DELEGATION OF CONTRACT AUTHORITY FOR RR150058  
**DATE:** MAY 9, 2018

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**Summary and Recommendation**

I recommend that the Oversight Committee vote to delegate to me the contract authority to designate an interim primary investigator and to disburse grant funds pursuant to an approved wind-down plan for CPRIT recruitment grant RR150058. These actions are necessary to facilitate the orderly closure of Dr. Andreas Doncic's recruitment award after his unexpected death.

**Discussion**

The Oversight Committee voted in May 2015 to approve a \$2 million recruitment award to The University of Texas Southwestern Medical Center (UTSW) for the recruitment of Andreas Doncic, M.D. from Stanford University. Dr. Doncic's research focus was understanding how cells make decisions, and he was a rising star in his field. He was particularly interested in applying this knowledge to understand how uncontrolled proliferation occurs in cancer.

Dr. Doncic died unexpectedly on April 21, 2018. Following his death, CPRIT staff have met with UTSW representatives to discuss Dr. Doncic's work and UTSW's plans to preserve its early findings. Dr. Doncic's grant was scheduled to end May 31, 2019. At the time of his death, he had expended \$1.2 million.

UTSW is in the process of developing a plan for winding down or transitioning his active projects. Based upon input from Dr. Willson and Ms. Doyle and the discussions with UTSW, it is appropriate for CPRIT to support wind down activities for Dr. Doncic's projects. Doing so helps to realize, as much as possible, the potential of his CPRIT-funded work.

Although UTSW is still devising the wind down plan, disbursing CPRIT grant funds to support approved wind down activities requires that the Oversight Committee approve some procedural steps and provide staff direction at this time. One component of the wind down plan is for UTSW to change the designated primary investigator from Dr. Doncic to an interim primary investigator. Occasionally an institution may request to replace a primary investigator on a CPRIT grant, usually because the original primary investigator has accepted a position out of state. CPRIT has a process in place to consider the request and amend the contract to reflect the

change in primary investigator. However, because a recruitment grant is linked specifically to an individual, replacing the primary investigator (the recruited investigator) is not an option. In this unusual situation, it is appropriate to designate someone to fill the primary investigator role temporarily until the grant ends. The interim primary investigator will serve as the scientific manager of the wind down activities, such as supervising the post-doctoral students and other personnel working in Dr. Doncic's lab as well as overseeing final reports to CPRIT and any external publications. Dr. Willson will work with UTSW representatives to finalize a wind down plan, including designation of an interim primary investigator, a revised scope of work, and a reduced budget.

Due to these unique circumstances, I request that the Oversight Committee delegate authority to me to negotiate contract changes that reflect and to execute these contract changes.



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** REBECCA GARCIA PHD, CHIEF PREVENTION AND COMMUNICATIONS OFFICER  
**SUBJECT:** PREVENTION PROGRAM UPDATE  
**DATE:** MAY 7, 2018

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FY 2018 Cycle 2 (18.2) Prevention Applications

CPRIT released three RFAs in November 2017 for the second review cycle of FY 2018. Peer review panels will meet May 22 - 25 to evaluate the 31 FY18.2 prevention applications requesting \$51,031,896 (see table below). The Prevention Review Council (PRC) will meet in July to make award recommendations to the Program Integration Committee (PIC). Dr. Garcia will present the PIC recommendations to the Oversight Committee in August.

Mechanism	Number Received	Total \$ Requested
Evidence-based Cancer Prevention Services	13	\$17,537,453
Expansion of Cancer Prevention Services to Rural and Medically Underserved Populations	9	\$21,645,686
Tobacco Control and Lung Cancer Screening	9	\$11,848,757
<b>TOTAL</b>	<b>31</b>	<b>\$51,031,896</b>

The PRC reviewed the one application CPRIT received this quarter for the Dissemination of CPRIT-Funded Cancer Control Interventions mechanism. Dr. Garcia will present the PIC recommendations to the Oversight Committee on May 16.

FY 2019 Cycle 1 Prevention RFAs

The FY 2019 Cycle 1 RFA release schedule was approved by the Oversight Committee at its February meeting. The RFAs have been drafted and are being edited. The release date is May 10, 2018.

## **PREVENTION RFA Descriptions**

### Evidence-Based Cancer Prevention Services

Evidence-Based Cancer Prevention Services - This award mechanism seeks to fund projects that will deliver evidence-based cancer prevention and control clinical services. Priority will be given to projects that propose to address CPRIT areas of emphasis and serve areas of the state not well addressed by current CPRIT funded projects.

Award: Maximum of \$1.5M; Maximum duration of 36 months.

### Tobacco Control and Lung Cancer Screening

This award mechanism seeks to fund programs on tobacco prevention and cessation, as well as screening for early detection of lung cancer. Through release of this RFA, CPRIT's goal is to stimulate more programs across the state, thereby providing greater access for underserved populations and reducing the incidence and mortality rates of tobacco-related cancers. This RFA seeks to promote and deliver evidence-based programming designed to significantly increase tobacco cessation among adults and/or prevent tobacco use by youth.

Award: Maximum of \$1.5M; Maximum duration of 36 months.

### Expansion of Cancer Prevention Services to Rural and Medically Underserved Populations

This award mechanism seeks to support the coordination and expansion of evidence-based services to prevent cancer in underserved populations who do not have adequate access to cancer prevention interventions and health care, bringing together networks of public health and community partners to carry out programs tailored for their communities. Projects should identify cancers that cause the most burden in the community and use evidence-based models shown to work in similar communities to prevent and control these cancers. Currently funded CPRIT projects should propose to expand their programs to include additional types of prevention clinical services and/or an expansion of current clinical services into additional counties. In either case, the expansion must include delivery of services to nonmetropolitan and medically underserved counties in the state.

Award: Maximum of \$3M; Maximum duration of 36 months.

### Dissemination of CPRIT-Funded Cancer Control Interventions

This award mechanism seeks to fund projects that will facilitate the dissemination and implementation of successful CPRIT-funded, evidence-based cancer prevention and control interventions across Texas. The proposed project should be in a position to develop one or more "products" based on the results of the CPRIT-funded intervention. The proposed project should also identify and assist others to prepare to implement the intervention and/or prepare for grant funding.

Award: Maximum of \$300,000; Maximum duration of 24 months.

### National Recognition

Dr. Jane Bolin of Texas A&M University System Health Science Center and Dr. Simon Craddock Lee of the University of Texas Southwestern Medical Center were invited to speak at the NCI Division of Cancer Control and Population Sciences Accelerating Rural Cancer Control Research Meeting, May 30-31, 2018, in Bethesda, Maryland. These invitations came about as a direct result of their multiple CPRIT awards for breast, cervical and colorectal cancer screening.

### Other activities

Prevention program staff continue to work with Dr. Jennifer Knight on drafting the 2018 Texas Cancer Plan. A workgroup from the Cancer Alliance of Texas recently provided feedback and the final draft is being prepared.

Dr. Garcia attended the American Association for Cancer Research 2018 Annual Meeting April 14-18 in Chicago. Dr. Garcia participated in the Texas Health Improvement Network (THIN) quarterly meeting on April 20.



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** REBECCA GARCIA PHD, CHIEF PREVENTION AND COMMUNICATIONS OFFICER  
**SUBJECT:** COMMUNICATIONS UPDATE  
**DATE:** MAY 7, 2018

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The following is an overview of the agency's communication activities through May 7, 2017.

**Earned Media**

**Grant Awards Announcement:** Following the Oversight Committee's approval of grant awards at its February 21, 2018 meeting, CPRIT distributed a press release to local, regional and national outlets announcing the grants.

**Coverage:** (February 12, 2018 - May 2, 2017)

- CPRIT earned 6 feature stories and 62 mentions across media.
- This totals 68 pieces of coverage for the quarter.

**Coverage Highlights:** (see clipped articles following report)

- Governor Greg Abbott sent out a tweet from his personal twitter account, sharing the Dallas Morning News article "Texas aims to lure cancer startups with \$3 million grants" by Sabriya Rice on April 30, 2018 (copy of tweet provided in the clips section): [https://twitter.com/GregAbbott\\_TX/status/991134280310050816](https://twitter.com/GregAbbott_TX/status/991134280310050816)
- February 14, 2018, *Houston Chronicle*, Q&A: German biotech company finds a good fit in Houston.
- February 21, 2018, *Dallas Morning News*, UT Southwestern withdrew \$2 million grant from a cancer researcher who allegedly falsified data
- February 27, 2018, *Denton Record-Chronicle*, Nelson receives award from American Cancer Society
- February 23, 2018, *San Antonio Business Journal*, Scott's Take: SA may have found a path to more research funding
- March 1, 2018, *Bisnow Houston*, Texas Med Center Playing Catch-Up On Commercialization
- March 2, 2018, *The Economic Times (India)*, Indian-American scientist awarded grant for cancer research

- March 4, 2018, *Del Rio News-Herald*, City proclaims ‘Colorectal Cancer Screening Month’
- March 30, 2018, *Dallas Innovates*, Discovery: Reducing Cancer Risk 1 Cup at a Time, Scientist Seeks Clearer Images of Deadly Tumors
- April 2, 2018, *Dallas Morning News*, UT Southwestern cancer research gets \$28 million booster shot
- April 23, 2018, *El Paso Inc.*, Texas Tech El Paso awarded \$2M for cancer research
- April 19, 2018, *El Paso Times*, \$2 million grant to help fund TTUHSC El Paso research on breast cancer
- April 30, 2018, *Dallas Morning News*, Texas aims to lure cancer startups with \$3 million grants

## **Cancer Awareness Months**

### **Cancer Prevention Awareness Month-February**

- A video featuring Dr. Jinming Gao and Dr. Sumer Baran from UT Southwestern Medical Center about their nanotechnology research that has received funding from both Academic Research and Product Development was released over social media for National Oral, Head and Neck Cancer Awareness Week (April 8-15).

### **National Cancer Research Month-May**

- Chris Cutrone is working with the City of Houston and CPRIT’s institutional partners on a mayoral proclamation recognizing National Cancer Research Month on May 15, 2018. The institutions plan to send CPRIT grantees and representatives to attend the event, and we are working on media strategy with our partners. As part of this outreach, Chris is working with TMC Pulse, the Texas Medical Center’s magazine, and our institutional partners to promote the event over social media.

## **Special Events**

- CPRIT staff and UT Rio Grande Valley School of Medicine leadership met at their Edinburg School of Medicine facility on April 9<sup>th</sup> to discuss CPRIT funding opportunities This was followed up by a legislative luncheon at Doctor’s Hospital at Renaissance which was attended by Senator Chuy Hinojosa and staff from Senator Eddie Lucio Jr., and Representatives Terry Canales and Bobby Guerra. CPRIT grantees and CPRIT also participated in an American Cancer Society public forum that featured CPRIT and hosted by Cam Scott. Wayne Roberts, James Willson, Becky Garcia and Chris Cutrone attended these events.
- A press conference was held on April 19, 2018 at Texas Tech University Health Sciences Center El Paso to announce the CPRIT Scholar recruitment grant of Shrikanth Gadad, PhD. The announcement received extensive coverage in the El Paso media market in both English and Spanish. The event was attended by El Paso legislators Senator Jose Rodriguez, and Representatives Cesar Blanco and Lina Ortega. Speaking at the event for CPRIT was Dr. Jim

Willson and El Paso Mayor Dee Margo along with Tech Texas University System Board of Regents Chairman Rick Francis. Prior to the press conference, TTUHSC El Paso President Richard Lange, Dee Margo and Wayne Roberts held a briefing on CPRIT for the El Paso legislators.

### **Social media metrics**

#### **Facebook (last 28 days):**

- Reach: 883
- Engagement: 226
- Most popular post: ICYMI: More than a dozen UT Southwestern Medical Center researchers received CPRIT grants in the latest round of funding.

#### **Twitter (last 28 days):**

- 5,185 impressions
- Top tweet: ICYMI: Read about how more than a dozen @UTSWNews researchers received CPRIT grants in the latest round of funding: [cprit.us/2uGJVrJ](https://cprit.us/2uGJVrJ)

# CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS



**CPRIT**

@CPRITTexas

CPRIT is a state agency designed to invest in the most promising cancer prevention, academic research and product development research opportunities in Texas.

- Austin, Texas
- cprit.texas.gov
- Joined January 2011
- 74 Photos and videos

**Greg Abbott** @GregAbbott\_TX

Following

Texas Aims To Lure Cancer Startups With Millions in Grant Funding. The Cancer Prevention & Research Institute of Texas announced a new Seed Award, which will target startups trying to introduce disruptive technologies in the cancer-care market. #txlege



**Texas aims to lure cancer startups with \$3 million grants**

A major funder of cancer research in Texas is offering up to \$3 million in seed funding to help lure startups to the Lone Star state--and keep them...

dallasnews.com

8:56 PM - 30 Apr 2018

91 Retweets 262 Likes

14 91 262

Tweet your reply

**TEXAS BACON** @bacon\_texas - May 2



1 2

**Joe orsak** @orsak\_a - Apr 30

Replying to @GregAbbott\_TX

I guess it makes sense, considering you allow all the chemical plants to poison us.

3

**Renaee Sparks** @TexasRenaeeUSA - May 1

Replying to @GregAbbott\_TX

Why don't we do something about the cancer causing toxins that are put in our foods and sprayed on our crops? Hmm? When will this sick scam ever end?

1

**Richard Jankovsky** @RichardJankovsk - Apr 30

Replying to @GregAbbott\_TX

@StBaldricks @SnowdropCC

**Don** @don\_peck - Apr 30

Replying to @GregAbbott\_TX

Excellent plan!

**dliuppold** @dliuppold - Apr 30

Replying to @GregAbbott\_TX

Accepting FREE federal Medicaid money that give millions of your constituents affordable healthcare also helps the cancer-care market

2 1

**Dawn** @dawnittedbear - Apr 30

Replying to @GregAbbott\_TX

Good Idea, but the Last person, a female doctor, that showed there was a cure, ended up DEAD. VERY soon after that revelation....

1

**lar306** @LarryJacobs1r - May 1

Replying to @GregAbbott\_TX

Trying to maintain a balance for all the polluting he allows corporations to do.



Edit profile

### Your Tweet activity

Your Tweets earned 3,052 impressions over the last 28 days

View your top Tweets

### Who to follow

- Peter WT Pisters, M.D.** @Peters - Follow
- OPUCTX** @OPUCTX - Follow

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# CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS

## Q&A: German biotech company finds a good fit in Houston

By Chris Tomlinson | February 14, 2018 | Updated: February 15, 2018 5:35am



Houston is a great place to start a biotech company, says Harpreet Singh, founder and managing director of Immaties, based in Tuebingen, Germany, and CEO of Immaties US, its Houston-based subsidiary.

He is an immunologist born in Frankfurt to Indian-immigrant parents and is developing immuno-therapies with MD Anderson Cancer Center.

**Q: *What is your vision for Immaties?***

**A:** Houston, with the Texas Medical Center, is one of the best places in the U.S. to build a biotech company. Our vision is to build one of the leading biotech companies in the U.S., even globally, in cancer immunotherapy.

We are not looking just for a short extension of life by a few weeks or a few months. We're looking for something that will last years. Or even, and I am reluctant to use the c-word, maybe a cure.

***Q: How did you get interested in immunology?***

**A:** I remember when I was 6 years old, I had a very high fever and was lying in bed with my mother next to me, and she told me about the policemen in the body that were taking care of the pathogen. And I was fascinated by the idea that there are these little policemen in my bloodstream that were going after the evil guys. That was a picture I never forgot.

I was incredibly fortunate that one of the leaders in immunology, Hans-Georg Rammensee, was from Tuebingen and came back to Tuebingen to open a large new institute for immunology. I applied and got a Ph.D. position with him.

***Q: How did Immatics come to be?***

**A:** Toni Weinschenk, who became a co-founder of Immatics, was looking very closely at tumors and how the immune system differentiates between normal tissue and tumors. I was working on proteins, and we came up with the idea of creating a company that focused on immunology. That was back in 2000.

The question was, what are the right targets for the immune system on a tumor that are different from normal tissue? We had access to those targets because they had been discovered in Tuebingen.

In 2004, if you asked pharmaceutical companies what they thought of t-cells, or the immune system, they thought it was like homeopathy, not real medicine.

***Q: What sets Immatics apart?***

**A:** Antibodies were the craze back then, but they only work on targets on the surface of the tumor cells. But only a fraction of all the targets that are really tumor-specific are on the surface.

The question was, how can we go after the targets that are inside the cell? What Rammensee discovered is that the immune system actually takes proteins from inside the cell, degrades them to shorter fragments called peptides, which are then shuttled back to the surface of the cell to special receptors. In this way, the inside of the cell is displayed on the outside, where the immune system can recognize these targets.

We're making use of that system to fight cancer. In 2004 we got our first funding, and since then we've raised approximately \$230 million.

***Q: What brought you to Houston?***

**A:** There was a scientific conference in Copenhagen. Also there was Patrick Hwu, who is now head of cancer medicine at MD Anderson. He is one of the rock stars. He's done both vaccine and cell therapy successfully.

He invited me to lunch and said they had all of these fantastic capabilities at MD Anderson to do clinical trials at a single institution. If you think about Immatics having the best nails, MD Anderson has the best hammer.

The vision that was presented to me by MD Anderson's leaders was to go beyond collaboration and have a joint venture ... but they said I had to commit to coming to this town. I said deal.

***Q: What's next?***

**A:** Right now, cell therapy companies are focused mostly on blood cancers, because those kinds of cancers have surface proteins that are easily differentiated from normal cells. But they have trouble going after the majority of other cancers, so-called solid cancers. Targets for solid cancers are often hidden inside the cell, and that's where we come in.

We've brought some of our best people from Germany, and here in Houston we've hired 50 people. Steffen Walter, our chief scientist in the U.S., was the first to move here with his family in 2015. I live here now with my family.

We have just opened two clinical trials at MD Anderson, and a third one is about to open. The fourth will likely open at the end of this year.



A researcher who was awarded a \$2 million dollar grant last year from the Cancer Prevention and Research Institute of Texas intentionally falsified data in previously published studies, according to the federal agency that oversees misconduct in research.

The Office of Research Integrity said in a [report this week](#) that Colleen Skau selectively omitted data, overstated numbers and falsified measurements that were included in studies published in the official journal of the National Academy of Sciences in [2015](#) and the peer-reviewed research journal *Cell* in [2016](#) . At the time, she was a postdoctoral researcher at the National Institutes of Health.

She is currently facing administrative action by U.S. Health and Human Services.

The Cancer Prevention and Research Institute of Texas has financially supported oncology research and prevention programs at institutions across the state for about a decade.

Last year, Skau was one of eight academics who were awarded a total of \$16 million in recruitment grants to become first-time, tenure track faculty members. Her research focused on trying to understand what causes melanoma cells to metastasize. She was slated to work at the University of Texas Southwestern Medical Center, according to a [press release issued in May](#).

After being notified of [the retraction](#) and subsequent review by the NIH, UT Southwestern said it withdrew the offer in July, prior to Skau being hired for the role, and it notified CPRIT.

Created in 2007, CPRIT has been the state's major funder of cancer research, but the agency was mired in scandal in the early 2010s after a series of questionable grants.

In 2013, the state Legislature put in place additional oversight and revamped the agency. Its \$3 billion budget allocation runs out in 2023.

***Correction: February 22, 3:57 p.m.: A previous version of this story said the budget allocation for CPRIT runs out in 2021. Last year, the Legislature voted to extend it to 2023.***

<https://www.dallasnews.com/business/health-care/2018/02/21/ut-southwestern-withdrew-2-million-grant-cancer-researcher-allegedly-falsified-data>



State Sen. Jane Nelson, R-Flower Mound, has received the Advocacy in Action Award from the American Cancer Society Cancer Action Network. The award was presented to Nelson in recognition of her work and support of the Cancer Prevention & Research Institute of Texas.

"I am proud of this organization and its important mission of supporting cancer victims and their families, and for their efforts to eradicate this terrible disease," said Nelson. "As a former volunteer for this organization, I am honored to receive this award and look forward to continuing our fight against cancer."

The American Cancer Society's Cancer Action Network focuses on cancer prevention, seeking new treatments and ensuring all Americans have access to quality medical care. It also works to improve the quality of life of those who have been affected by cancer, both during and after treatment.

Nelson, who is chairwoman of the Senate Finance Committee and the highest-ranking Republican in the Texas Senate, authored the legislation creating the Cancer Prevention & Research Institute of Texas. This is the fifth time she has received the Advocacy in Action Award from the American Cancer Society.

**FEATURED PHOTO:** State Sen. Jane Nelson, R-Flower Mound, speaks to the crowd at the Denton County Republican Party's Lincoln-Reagan Dinner on Feb. 10. DRC file photo

<http://www.dentonrc.com/news/news/2018/02/27/nelson-receives-award-american-cancer-society>

Feb 23, 2018,

## Scott's Take: SA may have found a path to more research funding



The old proverb is as applicable in today's scramble for cancer research funding as it's been in business and politics for centuries: If you can't beat them, join them.

That's essentially what UT Health San Antonio has done in striking a partnership with the MD Anderson Cancer Center. And the most recent allotment of funding from the Cancer Prevention and Research Institute of Texas suggests it was the right move.

CPRIT recently awarded 49 new academic research grants and eight prevention grants totaling more than \$73.5 million to several universities, health science centers and research institutions in the state.

MD Anderson Cancer Center received nearly a third of that funding – \$22.3 million.

Meanwhile, UT Health San Antonio was the only Alamo City recipient, with less than \$900,000.

The Baylor College of Medicine, Texas A&M University System Health Science Center, Houston's Methodist Hospital Research Institute, the University of Texas at Austin and the University of Texas Southwestern Medical Center were among the institutions that received more CPRIT funding than San Antonio in this latest round.

In fact, San Antonio has struggled since CPRIT's inception in 2007 to secure what one could argue is its fair share of cancer research funding. So, in late 2016, UT Health San Antonio President Dr. [William Henrich](#) made a calculated move, aligning his campus with one of the more renowned cancer research institutions in the world.



UT System Chancellor [Bill McRaven](#), who has pushed for such alliances across the state, told me after the deal between UT Health San Antonio and MD Anderson was reached, “This is the sort of collaborative approach that we have been trying to instill in all of our institutions. These institutions are on the forefront of that.”

Henrich is hopeful that pioneering effort will pay off.

“This affiliation puts two outstanding cancer centers together,” Henrich said. “The portfolio of what we can offer here in cancer care will expand. There will be more collaborative opportunities in research.”

The affiliation could provide UT Health San Antonio greater access to more resources. Time will tell if that includes more state cash to combat cancer, but the alliance was a factor in the Mays Family Foundation’s recent decision to contribute \$25 million in private money to the UT Health San Antonio Cancer Center.

“Our family has been touched by cancer,” said [Lowry Mays](#), chairman emeritus of Clear Channel Communications. “We’ve been very supportive of MD Anderson.”

Mays and his family saw the gift as an opportunity to help leverage UT Health San Antonio’s affiliation with the Houston institution and to bring a higher level of cancer care closer to patients in this region.

San Antonio health care and bioscience organizations have embraced local collaboration in a way that has set the city apart from other markets. But if the trend in CPRIT funding is an indication, the Alamo City may need to explore a wider geographic approach to cooperative pursuits and additional cash.



# Texas Med Center Playing Catch-Up On Commercialization

March 01, 2018 | Kyle Hagerty, Bisnow Houston

Despite being the largest medical complex in the world, Houston’s Texas Medical Center lags behind other healthcare strongholds in commercialization. In medical research hubs like Boston, every \$5 of research spending produces \$1 of commercialization, San Francisco is even better at a 3-to-1 ratio. At the TMC, it takes \$24 to produce \$1 of commercialization. To compete, the TMC will need to do better.



*Bisnow/Kyle Hagerty*

*Baylor College of Medicine Senior Vice President Kimberly Cotner David, Texas Medical Center Chief Operating Officer Shawn Cloonan, United Surgical Partners International Chief Strategic Officer Marian Lowe*

“If you look at the MITs and Stanfords of the world, the paradigm is no longer publish or perish, it’s now commercialize or perish,” Texas Medical Center Operating Officer and Executive Vice President Shawn Cloonan said at *Bisnow’s* National Healthcare South event Tuesday.

The Texas Medical Center handles more than 10 million patients and 750,000 emergency room visits every year. A surgery begins there every three minutes. Historically, the TMC has used its 50M SF of developed medical space to focus on treatment, not innovation. That is changing.

"Five years ago, and for the first time in our 70-year history, all TMC CEOs and executive leadership came together to form a strategic plan," Texas Medical Center President and CEO Bill McKeon said in a recent press release.



*Wikimedia Commons*  
*Texas Medical Center*

The Texas Medical Center's big push for commercialization centers around **TMC3**. Five academic institutions are planned to be involved with the project, which will feature a large central building surrounded by four other buildings offering research and lab space. The timeline and cost of the project have not been announced, but Texas A&M and Baylor already have permission to participate and the University of Texas is expected to sign on soon.

A recent study found that TMC3 could have a \$5.2B impact on the city of Houston.

“Very imminently we have a major announcement on that project, it’s too important to this city,” Cloonan said. “The bottom line is, we are building TMC3 to be a honeypot that attracts industry. We need something iconic.”



*Bisnow/Kyle Hagerty*

*Centura Health Senior Vice President James Corbett, Baylor College of Medicine Senior Vice President Kimberly Cotner David, Texas Medical Center Chief Operating Officer Shawn Cloonan*

“We’re in desperate need of research space,” Baylor College of Medicine Chief Business Officer Kimberly Cotner David said. “We’re landlocked in the Medical Center, that’ll be our next foray into a building.”

Research dollars are key to pursuing commercialization, and funding the right idea could lead to thousands of square feet of development as enterprises expand. Baylor is the top recipient of National Institutes of Health grants in the Texas Medical Center, accounting for roughly 25% of the area's \$2B in federal research grants. Statewide, Texas has committed \$3B in funding for cancer research and prevention as part of the Cancer Prevention and Research Institute of Texas. Houston institutions such as The University of Houston, UT MD Anderson Center, Baylor College of Medicine and Rice have received a large portion of the \$1.9B in grants to date.

“The economics of research funding isn’t well understood,” David said. “As hard as it is, it’s a very important part.”



*Courtesy of JLABS @ TMC*

*JLABS @ TMC*

Incubator space is also springing up in the TMC, helping bridge the gap from research to product. Last year Johnson & Johnson opened the **26K SF Center for Device Innovation**. In 2016, **JLABS @ TMC** opened as a **34K SF co-working/incubator space**. TMCx+, an accelerator, opened its 24K SF space in 2015, and TMCx opened in October 2014. The roughly 40K SF TMCxi, an area aimed at attracting tech leaders and venture capitalists, will open in June. All the spaces are in the larger **100K SF Innovation Institute at the TMC**.

TMC leadership is betting that the Texas Medical Center's \$3B in new projects and **100,000-plus healthcare professionals** will be enough to boost it up to the level of other prominent healthcare hubs like Boston and San Francisco.

“We're asking people to move across the country. **I'll take that bet. I'll bet on Texas,**” Cloonan said.

<https://www.bisnow.com/houston/news/healthcare/texas-med-center-playing-catch-up-on-commercialization-85650>

## Indian-American scientist awarded grant for cancer research

*An Indian-American scientist has been awarded a grant of over USD 1.1 million for his ground-breaking research on cancer.*



By Seema Hakhu Kachru

Houston, Mar 2 : An [Indian-American scientist](#) has been awarded a grant of over USD 1.1 million for his ground-breaking research on [cancer](#).

Navin Vardarajan, along with another University of Houston researcher Sanghyuk Chung, were awarded huge grants by Cancer Prevention & Research Institute of Texas (CPRIT), an organisation that funds pioneering cancer research and prevention programmes in the state.

Associate professor of chemical and biomolecular engineering, Navin was given USD 1,173,420 to improve effectiveness of [T-cell immunotherapy](#), while his fellow researcher Sanghyuk Chung, associate professor of biology and biochemistry, was awarded USD 811,617 to define molecular targets for the treatment of cervical cancer.

Varadarajan will use his grant to bring consistent results to cancer patients undergoing T-cell immunotherapy by manufacturing [programmed T cells](#) to meet, recognise and destroy tumours, a statement said.

"We have to understand every single T cell and what each one is capable of," said Varadarajan, who is looking for a perfect cell composition in order to manufacture only those that cure tumours.

"Once we know what is required to get a positive response, we can control the composition of the cells so that they all can work to fight cancer," he said.

Varadarajan said studying what makes better T cells will guide the development of the next generation of genetically modified cells, and all of immunotherapy in general.

"The big challenge with T cells is that there isn't one single thing that can be used to define what a T cell is supposed to do. Because it's a living cell, it's capable of so many different things but studying them at the single-cell level allows us to map all of these different things onto the same cell," he said.

Although cervical cancer is the fourth leading cause of cancer death in women worldwide, there has been little progress in the treatment of it over the past decade.

Chung will use his award to delve into the little-researched topic - the role of oestrogen in the development of cervical cancer.

"It is clearly demonstrated that human papillomavirus (HPV) is required for the development of cervical cancer, but evidence indicates that other co-factors are required for cervical cancer," Chung said. SHK MRJ MVV

<https://health.economictimes.indiatimes.com/news/industry/indian-american-scientist-awarded-grant-for-cancer-research/63139164>

## City proclaims 'Colorectal Cancer Screening Month'



Karen Gleason

### Colorectal Cancer Screening Month

City Manager Henry Arredondo, left, presents a proclamation to, from left, Maribel Garcia, data clerk; Anaid Olguin, outreach coordinator; Raquel Rodriguez, project manager for the FluFIT on the Frontera program, and Carlos Torres, VVRMC vice president of human resources. Not pictured is program director Ceci Lozano.

"Our main mission here is to prevent colorectal cancer, which is one of the most preventable, curable and treatable cancers and raising the awareness that the screenings are something that the Val Verde Regional Medical Center has to offer," said Raquel Rodriguez, project manager, at the start of Thursday's ceremony to accept the proclamation.

Rodriguez said, "Cancer hits home for a lot of us. I have had friends and family members who have passed away because of cancer. I think the reason I'm very passionate about this is that colorectal cancer is a type of cancer that is very curable, one of the only cancers that can be prevented, treated and cured successfully if caught in time," Rodriguez said.

"Our message is that screening saves lives. We definitely want people to get screened. It's all about prevention, and that's what we're all passionate about," she said.

Rodriguez said VVRMC is now offering free "InSure FIT" colorectal cancer screening tests for any patients who are eligible.

"Who is eligible? If you are over the age of 50, if you do not have a history of colorectal cancer in yourself or your immediate family, if you have not had a colonoscopy in the last 10 years, if you have not had a sigmoidoscopy in the last five years and if you have not had a fecal occult blood test screening in the last 12 months," Rodriguez said. She encouraged anyone interested in finding out more about the test to stop in at the Val Verde Regional Medical Center Walk-in Clinic, 1801 N. Bedell Ave., or at the VVRMC FluFIT on the Frontera Office, 801 N. Bedell Ave.

Del Rioans are being urged to take a simple step that could save their lives – schedule a colon cancer screening.

City Manager Henry Arredondo on Thursday presented the staff of Val Verde Regional Medical Center's FluFIT on the Frontera program, funded by Cancer Prevention & Research Institute of Texas (CPRIT), with a proclamation designating March 2018 as "Colorectal Cancer Awareness Month" in Del Rio.

Mayor Robert Garza, who was unable to attend due to a prior appointment, signed the proclamation.

Arredondo read the proclamation, which notes, "Colorectal cancer is the third most commonly diagnosed cancer and the second most common cause of cancer deaths for men and women combined in the United States."

The proclamation also reads that "colorectal cancer affects men and women equally, that someone dies from colorectal cancer every 10 minutes and that the vast majority of cancer deaths can be prevented through proper screening and early detection."

# Discovery: Reducing Cancer Risk 1 Cup at a Time, Scientist Seeks Clearer Images of Deadly Tumors

Let's take a closer look at some of the research taking place at laboratories and universities across North Texas. Here are some of the stories of how they better our world.

## RESEARCHERS SAY COFFEE MAY REDUCE CANCER RISKS



**I drink a lot of coffee, I admit it. I'm drinking some as I write. A new study from the Simmons Cancer Center at UT Southwestern Medical Center says that might be a good thing.**

Coffee consumption is steadily rising, UTSW said. When paired with prior studies showing that coffee consumption is associated with a lower risk of getting colon cancer, along with reduced risk of recurring tumors and death from colon cancer, one can take some solace in having that extra cup o' joe in the morning, or in the afternoon, or the evening (decaf of course).

And speaking of decaf, the research shows that both regular and decaf work.

**"We don't quite know how coffee exerts its health benefit because there are many different compounds in coffee."**

**Dr. Muhammad Beg**

research [here](#).

"We don't quite know how coffee exerts its health benefit because there are many different compounds in coffee," said Dr. Muhammad Beg, a GI cancer specialist at the Harold C. Simmons Comprehensive Cancer Center. "But researchers have shown that both caffeinated and decaf can be helpful."

So, why don't you grab a cup of your favorite coffee — arabica or robusta — and read more about the

## A \$1.9M CPRIT GRANT IS FUNDING SCIENTIST'S WORK

**Let's be clear about it — one of the most-challenging pieces in the fight against deadly tumors is to capture clear pictures of them in deep tissues.**

UT Arlington bioengineering professor Baohong Yuan has spent years **working on creating a better imaging system** to detect cancer that is tens of millimeters under the skin's surface, according to UTA's research website.

**“The problem with current imaging is that what you get is not clear, but more like an out-of-focus photo.”**

**Baohong Yuan**

Yuan's work is being funded with two grants from the Cancer Prevention and Research Institute of Texas worth a total of \$1.9 million.

“The problem with current imaging is that what you get is not clear, but more like an out-of-focus photo,” Yuan told *UTA Inquiry*, the university's research magazine.

“For imaging of deeper tissues, you have to sacrifice resolution. This means if you want to see deep tissue, you cannot see too small. There's a trade-off between the imaging depth and the resolution.”

Yuan is using ultrasound-mediated techniques that are combined with microparticles or nanoparticles that tumors attract to produce images of small, deep tumors.

His team has developed a non-invasive system that exposes the particles to ultrasound waves, making them temporarily fluorescent and, thus, detectable.

“We want to provide much clearer images of microvessels in deeply seated small tumors,” Yuan said. “With that information, physicians could better target the tumors for elimination.”

## UT DALLAS RESEARCHER GETS MS SOCIETY GRANT

**Bart Rypma of the Center for BrainHealth at the University of Texas at Dallas is one of 10 recipients who have been awarded funding from \$433,800 in grants from the National Multiple Sclerosis Society.**



Bart Rypma

Rypma's study uses neuroimaging methods to identify mechanisms involved in MS-related cognitive dysfunction, according to UTD. The society said the 10 high-risk pilot projects are part of the yearlong Pilot Research Grant program which supports early stage research projects to quickly evaluate their effectiveness.

In 2016, Rypma was awarded more than \$290,000 in grant funding from the society to investigate how changes in blood flow can affect cognition in people with MS.

## 3D PRINTING 'IN-SITU' RESEARCH GAINS MOMENTUM

In-situ 3D printing for bone regrowth is an emerging area of study by scientists looking at ways that 3D printers can aid in the healing process, according to a report in 3D Printing Industry.

**“Our goal is to heal the defect or fracture site rapidly, as if nothing ever happened.”**

**Venu Varanasi**

Dr. Venu Varanasi, assistant professor of biomedical sciences at Texas A&M University, recently presented at a session of the International & American Associations for Dental Research on bone regrowth utilizing in-situ 3D printing — meaning printing in its original place.

“Our goal is to heal the defect or fracture site rapidly, as if nothing ever happened,” Varanasi said in the article.

Varanasi's research will be undertaken in the Bone-Muscle Group of the University of Texas at Arlington in collaboration with Texas A&M, 3 Printing Industry said.

Find out more [here](#).

# UT Southwestern cancer research gets \$28 million booster shot



*Paul O'Donnell, Business Editor*

Texas' cancer-fighting agency is pumping \$27.8 million into research of breast, prostate, brain and other forms of cancers in North Texas, as well as creation of lung and liver cancer screening programs in underserved areas.

More than a dozen UT Southwestern researchers received grants in the latest round of funding from the Cancer Prevention and Research Institute of Texas. Voters approved a constitutional amendment in 2007 to create a \$3 billion cancer-fighting fund.

UTSW received the largest portion of the \$73.5 million doled out. M.D. Anderson Cancer Center in Houston, considered one of the nation's top treatment centers, pulled in more than \$22 million in grants.

"UT Southwestern cancer researchers are continually seeking better ways to diagnose and treat cancer, and these grants propel this important work forward," said Dr. Carlos L. Arteaga, director of UTSW's Harold C. Simmons Comprehensive Cancer Center, in a prepared statement.

UTSW will use \$8 million to recruit star researchers from out of state or create tenure-track faculty positions to keep them here. Simmons Cancer Center is one of the National Cancer Institute's 30 research centers designated to lead clinical trials. Researchers being recruited are:

- Dr. Yujin Hoshida from the Icahn School of Medicine at Mount Sinai in New York(\$4 million).
- Dr. Wen Jiang from M.D. Anderson Cancer Center (\$2 million).
- Zhenyu Zhong from the University of California, San Diego (\$2 million).

CPRIT grants also will fund a lung cancer screening and tobacco-cessation program at Moncrief Cancer Institute in Fort Worth, which serves Tarrant and 35 other counties, and a mobile screening initiative for liver cancer. Texas has one of the highest liver cancer rates in the nation.



HEALTH CARE

**\$22 million in grants brings new talent to a North Texas cancer center**

But most of the money will go toward academic research. Among the main areas being studied by UTSW researchers are:

### **Breast cancer: \$2.397 million**

Dr. Vlad Zaha, an assistant professor of internal medicine, will study methods for early detection of heart disease resulting from a chemotherapy drug commonly used to treat breast cancer.

### **Kidney cancer: \$2 million**

Two grants were awarded to Dr. James Brugarolas, director of UTSW's kidney cancer program and a professor of internal medicine, to focus on kidney cancers affecting adults and adolescents.

### **Brain cancer: \$1.2 million**

Dr. Robert Bachoo, an associate professor of neurology and neurotherapeutics, will study one of the most challenging tumors to treat: pediatric brain cancer.

### **Blood cancer: \$1.2 million**

Dr. Stephen Skapek, chief of pediatric hematology-oncology, will study the most common soft tissue cancer in children. Only about 1 in 5 children survive for three years, and this poor outlook has not improved despite many attempts to intensify chemotherapy and use new agents.

UTSW has received \$338 million from CPRIT. In all, the agency has awarded \$1.95 billion.

## Cancer research, prevention grants

The Cancer Prevention and Research Institute of Texas' most recent awards total more than \$73 million. Here are recipients of \$1 million or more.

<b>Institution</b>	<b>Amount</b>
UT Southwestern	\$27,827,022
MD Anderson Cancer Center	\$22,283,004
UT Health Science Center at Houston	\$4,000,000
Texas Tech University System	\$3,849,260
Texas A&M University	\$3,596,596
Baylor College of Medicine	\$3,568,639
UT Austin	\$3,192,048
University of Houston	\$1,985,037
Methodist Hospital Research Institute	\$1,199,617

SOURCE: CPRIT

<https://www.dallasnews.com/business/health-care/2018/04/02/ut-southwestern-cancer-research-early-detection-work-get-27-million-booster-shot>

# EL PASO INC.

Texas Tech El Paso awarded \$2M for cancer research



James K.V. Willson, chief scientific officer of the Cancer Prevention and Research Institute of Texas, or CPRIT, speaks Thursday at the announcement.



The Cancer Prevention and Research Institute of Texas has awarded Texas Tech University Health Sciences Center El Paso a \$2 million grant to open a new research lab.

The lab, which will focus on breast cancer research, will be headed by Shrikanth Gadad, a researcher recently recruited to the university, according to the announcement.

“The concept that Gadad is bringing in is really new, and it will help us understand the process of cancer growth and how it becomes aggressive,” said Rajkumar Lakshmanaswamy, dean of the Graduate School of Biomedical Sciences. “Using that, we can actually come up with some strategies to prevent the growth of these cancers.”

El Paso Mayor Dee Margo is the assistant presiding officer of the Cancer Prevention and Research Institute of Texas Oversight Committee.

“Having CPRIT Scholar Shrikanth Gadad recruited to TTUHSC El Paso demonstrates our city’s status as a serious player in life-sciences research,” Margo said in a statement. “Cancer disproportionately affects Texans on the border, and this requires us to build a stronger, cancer-fighting ecosystem right here to study how best to address these disparities.”

## \$2 million grant to help fund TTUHSC El Paso research on breast cancer



(Photo: Photo By: Tammie Morelos/Texas Tech HSC El Paso)



Texas Tech University Health Sciences Center El Paso on Thursday announced a \$2 million grant to fund a new lab to study breast cancer at the school's Center of Emphasis on Cancer.

The grant was instrumental in the recruitment of a [Cancer Prevention and Research Institute of Texas](#)

Scholar to run the lab, which is a first in West Texas, according to a news release from TTUHSC El Paso.

The lab will be headed by CPRIT Scholar Shrikanth Gadad, Ph.D.

Gadad said his long-term goal is to connect his research to the community, looking at how factors including stress and diet can affect the chances of contracting cancer.

His advanced, groundbreaking research on breast cancer could lead to new treatments.

**More:** [90 from Texas Tech El Paso's Paul L. Foster School of Medicine celebrate Match Day 2018](#)

The lab's research will complement current cancer research at the Center of Emphasis in Cancer, said Rajkumar Lakshmanaswamy, Ph.D., scientific director of the center and dean of the Graduate School of Biomedical Sciences.

Lakshmanaswamy's research at the Center of Emphasis in Cancer has focused on the types of genes that make proteins. Gadad's research will focus on long noncoding RNAs — genes that don't make proteins.



Officials announce on April 19 a \$2 million grant from the Cancer Prevention and Research Institute of Texas (CPRIT) will allow Texas Tech University Health Sciences Center El Paso (TTUHSC El Paso) to create a new lab focusing on breast cancer. (Photo: Photo By: Tommie Morelos/Texas Tech HSC El Paso)

"The concept that Gadad is bringing in is really new, and it will help us understand the process of cancer growth and how it becomes aggressive," Lakshmanaswamy said. "Using that, we can actually come up with some strategies to prevent the growth of these cancers."

**More:** [Texas Tech chancellor lauds fast-growing El Paso campus after tour; says popular with legislators](#)

El Paso Mayor Dee Margo, who is the CPRIT Oversight Committee's assistant presiding officer, said in a statement that Gadad's recruitment is important for the Borderland.

"Having CPRIT Scholar Shrikanth Gadad recruited to TTUHSC El Paso demonstrates our city's status as a serious player in life-sciences research," Margo said. "Cancer disproportionately affects Texans on the border, and this requires us to build a stronger, cancer-fighting ecosystem right here to study how best to address these disparities."

Students in the university's Graduate School of Biomedical Sciences will be involved with the new lab and Gadad's research.

In 2007, Texas voters approved a constitutional amendment establishing a cancer prevention institute. The state was authorized to issue \$3 billion in bonds to fund groundbreaking cancer research and prevention programs and services in the state.

**More:** [UMC Makes History as Borderland's First Comprehensive Stroke Center](#)

*Samuel Gaytan may be reached at 546-6175; [sgaytan@elpasotimes.com](mailto:sgaytan@elpasotimes.com); [@samuelgaytan](#) on Twitter.*

## **CPRIT facts**

- Since 2009, CPRIT has awarded more than \$14.5 million to TTUHSC El Paso, mostly through cancer prevention grants, and more than \$58 million to the Texas Tech University System.
- To date, CPRIT has awarded \$1.95 billion in grants to Texas researchers, institutions and organizations and provides funding through its academic research, prevention and product development research programs.
- Programs made possible with CPRIT funding have reached Texans from all 254 counties of the state, brought more than 150 distinguished researchers to Texas, advanced scientific and clinical knowledge and provide more than four million lifesaving education, training, prevention and early detection services to Texans.

*Source: Texas Tech University Health Sciences Center El Paso*

## Texas aims to lure cancer startups with \$3 million grants



*Sabriya Rice, Business of Health Care Reporter* [Twitter](#) [Email](#)

A major funder of cancer research in Texas is offering up to \$3 million in seed funding to help lure startups to the Lone Star State — and keep them here.

On Monday, the Cancer Prevention and Research Institute of Texas announced a new Seed Award, which will target startups trying to introduce disruptive technologies in the cancer-care market.

The institute has already doled out more than \$1.9 billion to cancer research and prevention programs statewide since 2007. But the new grant is unique in that it specifically targets companies that are just getting started, an area where venture capital funds are sparse.

The goal is to move them out of the seed stage “and into the stage where the products are going to be more attractive to external investors,” said Mike Lang, chief product development officer.

The award is designed for projects that are too early in their research to be competitive for the institute's two other product development award categories. The money could help new innovators in the cancer therapy and diagnostic tool space to become commercially viable businesses.

Eligible companies can qualify for a maximum of \$3 million per project, which will be distributed over a maximum of three years. Any startup around the world can apply.

But the goal is to bring business to Texas, Lang reiterated.

“This is state of Texas taxpayer money, and by statute it has to be kept here in the state,” he said. “So these companies either need to be here already, or willing to move here upon receipt of the award.”

Eleven larger, more established research firms have relocated to Texas since 2010, when the research institute began giving out its first product development grants.

For example, biotech startup Aravive, which investigates treatments for leukemia and cancers of the ovaries and pancreas, moved from San Francisco to Houston in 2015 on a \$20 million grant. Formation Biologics, which focuses on cancers of the breast, head and neck, lung and stomach, moved from Toronto to Austin in 2015 on a \$12.7 million grant.

The institute is still finalizing the application for the Seed Award, which should be available in mid-May. The deadline to apply will be in August, and the awards will be announced in February.



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** MICHAEL LANG, CHIEF PRODUCT DEVELOPMENT OFFICER  
**SUBJECT:** CPRIT PRODUCT DEVELOPMENT UPDATE – MAY 2018  
**DATE:** MAY 3, 2018

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**Product Development Research Award Update**

Product Development Research FY 2018 Cycle 2

Product Development Award FY 2018 Cycle 2 was open to receive applications from December 22, 2017 to February 7, 2018. Twenty applications were submitted and accepted for peer review. CPRIT's peer reviewers met March 26 and 27 and selected 10 companies to present at the Peer Review Panel meeting. CPRIT held the peer review panel meeting April 23-26, 2018. The panel selected six applicants to proceed to due diligence. Due diligence has commenced on these projects. I will present the applications approved by the Product Development Review Council (PDRC) to the Program Integration Committee and the Oversight Committee in August 2018 for approval.

Product Development Research Applications FY 2019 Cycle 1

The Oversight Committee approved the requests for applications and timeline for Product Development Award FY 2019 Cycle 1 at its February 21 meeting. The schedule has been finalized and RFAs have been developed. CPRIT will begin receiving applications June 28 through August 8, 2018. I will present applicants recommended by the PDRC to the Program Integration Committee and the Oversight Committee in February 2019 for approval. CPRIT will post three Product Development RFAs in late May:

- Texas company RFA
- Relocation company RFA
- New Seed Award RFA, see below for details.

## **Product Development Research Program Update**

### New and Modified Award Programs

CPRIT is implementing new grant programs approved by the Oversight Committee in February. The modified Early Translational Research Awards (ETRA) and new Seed Award programs bridge between current academic and product development programs.

CPRIT's academic research ETRA program provides translational research funding to promising technologies. The objective is to de-risk these projects and make them attractive spinout opportunities. This program has been modified to enhance focus on clinical and commercial objectives and insure commercial support is available to potential spinouts.

The new Product Development Research Seed Award program provides startup funding to early-stage projects. Seed awards target projects too early to effectively compete for the Relocation Company and Texas Company awards. We anticipate many Seed Award applicants will be spinouts from Texas research institutions.

### Outreach Activities

A CPRIT press release announcing the Seed Award program was distributed April 30. In addition, an extensive outreach program is underway to build awareness of both programs with potential applicants. We are engaging with regional and statewide trade associations, public policy groups, biotech incubators, investment groups, and academic tech transfer offices to build awareness such that potential applicants are aware of the new Seed Award program.



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** CAMERON ECKEL, STAFF ATTORNEY  
**SUBJECT:** APPOINTMENT TO THE SCIENTIFIC RESEARCH AND  
PREVENTION PROGRAMS COMMITTEE  
**DATE:** MAY 11, 2018

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**Summary and Recommendation**

The Chief Executive Officer has appointed one expert to the CPRIT's Scientific Research and Prevention Programs Committee. CPRIT's statute requires the appointment be approved by the Oversight Committee. The Nominations Subcommittee discussed the appointment at its meeting on May 11, 2018, and recommends that the Oversight Committee vote to approve the appointment.

**Discussion**

Scientific Research and Prevention Programs committee members (also referred to as "peer reviewers") are responsible for reviewing grant applications and recommending grant awards for meritorious projects addressing cancer prevention and research, including product development research. Peer reviewers perform an important role for the state; all CPRIT grant awards must first be recommended by a Scientific Research and Prevention Programs committee. Individuals appointed to serve as CPRIT's Scientific Research and Prevention Programs committee members must be exceptionally qualified, highly respected, well-established members of the cancer research, product development research, and prevention communities.

Texas Health and Safety Code Section 102.151(a) directs the Chief Executive Officer to appoint members to the Scientific Research and Prevention Programs committees. The CEO's appointments are final once approved by a simple majority of the Oversight Committee. The Nominations Subcommittee charter assigns the subcommittee with the responsibility "to circulate to Oversight Committee members in advance of a public meeting written notification of the committee's intent to make the nomination, along with such information about the nominee as may be relevant."

The Nominations Subcommittee considered the pending peer reviewer appointment and recommends Oversight Committee approval.





CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

**Recommendation for Academic Research Peer Review Panels**

- Daniel De Carvalho, Ph.D.



**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: De Carvalho, Daniel D

eRA COMMONS USER NAME: DDECARVALHO

POSITION TITLE: ASSOCIATE PROFESSOR/SENIOR SCIENTIST

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Brasilia, Brazil	BSc	12/2005	Veterinary Sciences
University of São Paulo, Brazil	PhD	12/2009	Immunology and Molecular Biology
University of Southern California	Post-doc	06/2012	Cancer Epigenetics and Bioinformatics

**A. Personal Statement**

I am Associate Professor in the Department of Medical Biophysics, University of Toronto, Senior Scientist at Princess Margaret Cancer Centre, University Health Network. Moreover, in recognition of my previous achievements, I hold the Helen M Cooke endowed professorship in Cancer Epigenetics and I am the Canada Research Chair in Cancer Epigenetics and Epigenetic therapy. My research program focuses on translational aspects of cancer epigenetics, with especial emphasis on DNA methylation. My group is motivated by large studies, such as The Cancer Genome Atlas, that showed the DNA methylation profile is largely changed between normal tissue and cancer tissue in virtually all cancer patients. My research program aim to understand whether cancer cells depended on this aberrant DNA methylation profile and whether it is amendable to therapeutic intervention. I am also interested in understand whether is possible to modulate an anti-tumor immune response using epigenetic therapy. Finally, I am trying to take advantage of this massive epigenetic reprogram in cancer cells to develop biomarkers for tumor sub-group classification and cancer early detection.

**Epigenetic Therapy.** In prior work, I discovery that cancer cells are addicted to the aberrant DNA methylation profile to survive and I was able to pinpoint some of the genes and pathways necessary to be hypermethylated in colorectal cancer cells. This work was published at *Cancer Cell* in 2012 (role: first author) and was highlighted by ASCO in its annual report as one of the most important biomedical discovery in oncology in that year. In a follow-up work, I showed that DNA demethylating drugs are not only able to reactivate tumor suppressor genes by promoter demethylation but also to decrease oncogenic pathways, such as MYC, by gene-body demethylation. This work was published at *Cancer Cell* in 2014 (role: co-first author). More recently, we found that the main anti-tumour mechanism of DNA demethylating agents is by reactivating endogenous retrovirus (HERVs), producing dsRNA (double-stranded RNA) and activating anti-virus pathways, a process we named 'viral mimicry'. One very important implication of our finding is that by activating these highly immunogenic anti-viral pathways, DNA demethylating agents can increase anti-tumour immune response and, therefore, can sensitize to immunotherapy. This work was published at *Cell*, 2015 (role: corresponding author) and was highlighted in a preview at *Cell* and by two reviews at F1000. Moreover, *Nature Medicine* (December/2015) highlighted this work among its top 10 notable advances of 2015 and Canadian Cancer Society highlighted it among the top 10 research impact stories of 2015. Furthermore, *Nature Medicine* (January/2016) wrote an extensive editorial about the potential of combining epigenetic therapy with immunotherapy, listing my group among the world leaders in the field. Several clinical trials around the world are testing the combination of DNA demethylating drugs and immunotherapy, highlighting the translational aspect of my research program. More recently, we showed that DNA demethylating drugs can converts cold tumors into hot tumors, increasing infiltration of CD8 T cells and increasing activation and cytolytic activity of human CD8 T cells. This work is currently under-review at *Cell* (role: corresponding author)

**Sub-group Classification and Early detection.** My group uses genome-wide DNA methylation profiling for subgroup classification. Recently, we showed that the change in DNA methylation and histone methylation of IDH mutant tumors is associated with impaired DNA repair and increased sensitivity to DNA damage. This work was published at *Cancer Cell* in 2016 (role: co-author). We also showed that genome-wide DNA methylation profile could be used to robustly classify atypical teratoid rhabdoid tumors (ATRTs) into three epigenetic subgroups with distinct genomic profiles that correlated

with differential cellular responses to a panel of signaling and epigenetic inhibitors. This work was published at *Cancer Cell* in 2016 (role: corresponding author). More recently, we developed a new method, cfMeDIP-seq, to profile the DNA methylome in circulating cell-free DNA. We showed this method is robust at very low DNA input, is very sensitive for detection of circulating tumor DNA and allows multi-cancer classification as well as sub-group classification. This work is currently under-review (second round) at *Nature* (role: corresponding author). Moreover, we have applied for two provisional patents on the method and its application for tumor detection and classification in order to translate this invention to the clinical setting.

I am also a dedicated mentor and two former postdocs have already started independent faculty positions in France and Brazil and a third one is currently interviewing for faculty positions.

## B. Positions and Honors

### Positions

12/09-06/12	Postdoctoral Fellow, Norris Comprehensive Cancer Center, University of Southern California (USC),
07/2012- 2017	Scientist, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada
05/2017-	Senior Scientist, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada
12/2012- 2017	Assistant Professor, Department of Medical Biophysics, University of Toronto, Toronto, Canada
07/2017	Associate Professor, Department of Medical Biophysics, University of Toronto, Toronto, Canada
04/2015-	Helen M. Cooke Endowed Professorship, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada

### Other Experience and Professional Memberships

2014 -	Editorial Board member of Epigenomes Journal
2013-	Member, Canadian Cancer Society, Novel Therapeutics Panel (4x)
2014-2014	Co-organizer, Epigenetic Mechanisms in Cancer conference, Toronto
2013-	Ad-hoc peer-reviewer for CIHR, Canada; National science Foundation (NSF), USA; Medical Research Council (MRC), UK; Cariplo Foundation, Italy; INSERM, France; and FAPESP, Brazil
2013-2015	Member, UofT Student ranking Committee, Department of Medical Biophysics
2013-2015	Member of the Cancer Genomics Program (CGP) Immunotherapy and PDX Subcommittee at Princess Margaret Hospital
2013-2014	Member of PMGC (Princess Margaret Genomics Centre) Advisory Board

### Honors/Awards

#### **Honors**

2016	Top 10 Research Impact Stories of 2015 by Canadian Cancer Society
2016	Top 10 Notable advances for 2015 by Nature Medicine
2012	Work featured on ASCO's "Clinical Cancer Advances 2012: ASCO's Annual Report on Progress Against Cancer" as a major advance in Tumor Biology and Developmental Therapeutics

#### **Awards**

2017	<b>Bernard and Francine Dorval Prize.</b> Canadian Cancer Society Research Institute Total amount: \$10,000
2017	<b>Early Career Award in Cancer.</b> CIHR Institute of Cancer Research (ICR) Total amount: \$25,000
2017	<b>Canada Research Chair in Cancer Epigenetics and Epigenetic Therapy.</b> CIHR Total amount: \$500,000
2016	CIHR New Investigator Salary Award. Total amount: \$300,000
2016	<b>Helen M Cook Professorship.</b> Princess Margaret Foundation

Total amount: \$1,000,000  
2015 **Till and McCulloch Paper of the Year Award.** Princess Margaret Cancer Centre  
Total amount: \$1,000

### C. Contribution to Science

**Statistics:** 32 peer-reviewed original research publications. h-index 15 (15 since 2013); i10-index 16 (16 since 2013); 1879 citations (1588 since 2013).

#### Published work:

<https://scholar.google.ca/citations?user=XImzWX0AAAAJ&hl=en>

#### Epigenetic modifications as therapeutic targets

One of my main areas of research is to understand the role of epigenetic modifications in cancer biology and how to therapeutically target these modifications. My previous work have shown that colorectal cancer cells are addicted to the DNA methylation reprogram and these are important therapeutic targets (*Cancer Cell*, 2012). WE also identified that DNA demethylating drugs can directly decrease expression of oncogenic pathways by gene body DNA demethylation (*Cancer Cell*, 2014). My most important discovery on this area was that DNA demethylating drugs could reactivate endogenous retrovirus and induces a viral mimicry in cancer cells (*Cell*, 2015). This viral mimicry leads to decrease in tumor growth and increase in antitumor immune response. Because of this work, several clinical trials are trying to combine DNA demethylating drugs with immunotherapy, including one trial at Princess Margaret where I am the scientific PI (METADUR trial: An open-label, phase II basket study of a hypoMETHylating Agent azacitidine and DURvalumab (anti-PDL1) in advanced solid tumours). This quick translation from publication to clinical trial (less than a year) highlights the strong translational aspect of my research program.

- a. Loo Yau H\*, Chakravarthy A\*, Almeida FC, Allard D, Singhanian R, Ettayebi I, Shen SY, Medina T, Mehdipour P, Morancho B, Pommey S, Klein C, Amarante-Mendes G, Roulois D, Butler M, Arribas J, Stagg J, **De Carvalho DD**. Transcriptional Programs Linking IRF7 Signaling to Enhanced Anti-Tumor Immune Response are Modulated by DNA-Demethylating Agents in Effector CD8+ T Lymphocytes. *Submitted* (current status: Under Review – Nature Medicine).
- b. Roulois D, Yau HL, **De Carvalho DD**. Pharmacological DNA demethylation: Implications for cancer immunotherapy. **Oncoimmunology** 2015 (PMID: 27141349)
- c. Roulois D, Loo Yau H, Singhanian R, Wang Y, Danesh A, Shen SY, Han H, Liang G, Jones PA, Pugh TJ, O'Brien C, **De Carvalho DD**. DNA-Demethylating Agents Target Colorectal Cancer Cells by Inducing Viral Mimicry by Endogenous Transcripts. **Cell** 2015 (PMID: 26317465).
- d. Yang X, Han H, **De Carvalho DD**, Lay FD, Jones PA, Liang G. Gene body methylation can alter gene expression and is a therapeutic target in cancer. **Cancer Cell** 2014 (PMID: 25263941).
- e. Fukumasu H, Rochetti AL, Pires PR, Silva ER, Mesquita LG, Strefezzi RF, **De Carvalho DD**, Dagli ML. Constitutive androstane receptor ligands modulate the anti-tumor efficacy of paclitaxel in non-small cell lung cancer cells. **PLoS One** 2014 (PMID: 24959746).
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#### Epigenomics-based Biomarkers for Cancer early detection, sub-classification and prognostic

Another major area of my research is devoted to use genome-wide epigenomics profiling to identify biomarkers for subgroup classification and cancer early detection. Recently, we showed that the change in DNA methylation and histone

methylation of IDH mutant tumors is associated with impaired DNA repair and increased sensitivity to DNA damage. This work was published at *Cancer Cell* in 2016 (role: co-author). We also showed that genome-wide DNA methylation profile could be used to robustly classify atypical teratoid rhabdoid tumors (ATRTs) into three epigenetic subgroups with distinct genomic profiles that correlated with differential cellular responses to a panel of signaling and epigenetic inhibitors. This work was published at *Cancer Cell* in 2016 (role: corresponding author). More recently, we developed a new method, cfMeDIP-seq, to profile the DNA methylome in circulating cell-free DNA. We showed this method is robust at very low DNA input, is very sensitive for detection of circulating tumor DNA and allows multi-cancer classification as well as sub-group classification. This work is currently under-review (second round) at *Nature* (role: corresponding author). Moreover, we have applied for two provisional patents on the method and its application for tumor detection and classification in order to translate this invention to the clinical setting.

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- c. Inoue S . . . **De Carvalho DD** . . ., Mak TW. ( 37 authors total). Mutant IDH1 Downregulates ATM and Alters DNA Repair and Sensitivity to DNA Damage Independent of TET2. **Cancer Cell** 2016 (PMID: 27424808).
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- e. Strong E, Butcher DT, Singhania R, Mervis CB, Morris CA, **De Carvalho D**, Weksberg R, Osborne LR. Symmetrical Dose-Dependent DNA-Methylation Profiles in Children with Deletion or Duplication of 7q11.23. **Am J Hum Genet** 2015 (PMID: 26166478)

#### **Epigenetics of the immune response**

My research program also focus on understand the interplay between epigenetic modifications and the regulation of immune response against cancer and microorganisms. Besides our work on modulating the anti-tumor immune response using epigenetic therapy (cited above at the 'Epigenetic modifications as therapeutic targets' section), we are also investigating the T cell epigenetics in Cancer and inflammatory Bowel Disease (IBD).

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- b. Buzzo CL, Medina T, Branco LM, Lage SL, Ferreira LC, Amarante-Mendes GP, Hottiger MO, **De Carvalho DD**, Bortoluci KR. Epigenetic regulation of nitric oxide synthase 2, inducible (Nos2) by NLRC4 inflammasomes involves PARP1 cleavage. **Sci Rep**. 2017
- c. Scheer S, Medina TS, Murison A, Taves MD, Antignano F, Chenery A, Soma KK, Perona-Wright G, Lupien M, Arrowsmith CH, **De Carvalho DD**, Zaph C. Early-life antibiotic treatment enhances the pathogenicity of CD4+ T cells during intestinal inflammation. **J Leukoc Biol**. 2017
- d. Benevides L, da Fonseca DM, Donate PB, Tiezzi DG, **De Carvalho DD**, de Andrade JM, Martins GA, Silva JS. IL17 Promotes Mammary Tumor Progression by Changing the Behavior of Tumor Cells and Eliciting Tumorigenic Neutrophils Recruitment. **Cancer Res**. 2015
- e. De Souza AP, Planello AC, Marques MR, **De Carvalho DD**, Line SR. High-throughput DNA analysis shows the importance of methylation in the control of immune inflammatory gene transcription in chronic periodontitis. **Clin Epigenetics**. 2014

#### **D. Research Support**

##### **Ongoing Research Support**

Ontario Institute for Cancer Research (OICR)

DeCarvalho (Co-PI)

April 2017-March 2021

OICR TRI-Ovarian Cancer Translational Research Initiative

Main Objective: We aim to develop predictive and pharmacodynamic biomarkers to impact therapeutic strategies to improve precision and outcome.

Ontario Institute for Cancer Research (OICR) DeCarvalho (Co-PI) April 2017-March 2021  
 Acute Leukemia Translational Research Initiative  
 Main Objective: The long-term goal is to isolate and characterize, from within the diagnostic sample, the subset of cells that are destined to survive initial therapy and contribute to generating the eventual AML relapse.

Canadian Institutes for Health Research DeCarvalho (PI) July 2016-June 2021  
 Epigenetic approaches to Enhance cancer immunotherapy and to target cancer initiating cells  
 Main Objective: Dissect the molecular mechanisms of how DNA demethylating agents increase anti-tumour immune responses and decrease tumour cell intrinsic self-renewal  
 Outline of Methodology: This project will use cell lines, PDX, organoids and syngeneic mice models for colorectal cancer and human derived T cells.

Canadian Institutes for Health Research DeCarvalho (PI) July 2016-June 2017  
 Project Title: Toward the use of epigenetic therapy as a primer for cancer immunotherapy  
 Main Objective: The main goal is to test the hypothesis that FDA approved DNA demethylating drugs can sensitize CRC patients to anti-PD1 therapy

American Association for Cancer Research (Philadelphia, PA) SU2C Canada Cancer Stem Cell Dream Team  
 DeCarvalho (Co-Investigator) Oct. 2016-Sept. 2019  
 Targeting Brain Tumour Stem Cell Epigenetic And Molecular Networks  
 Main Objective: To focus our attention on the worst prognosis brain tumours, glioblastoma (GBM) of adults and children, and posterior fossa subtype A (PFA) ependymomas of infants, with a goal of finding new treatments.  
 Outline of Methodology: Patient derived samples and cell lines will be profiled using genome-wide DNA methylation mapping

MedImmune Inc, Princess Margaret Foundation DeCarvalho (CoInvestigator) Apr. 2017-Mar 2018  
 METADUR: an open-label, phase II basket study of a hypomethylating agent azacitidine and durvalumab (anti-PDL1) in advanced solid tumors  
 Main Objective: The goal of this trial is to investigate the potential of DNA hypomethylating agents to improve response to immuncheckpoint inhibitors

NSERC – Discovery Grant DeCarvalho (PI) Apr. 2015-Mar. 2020  
 Understanding the molecular mechanisms of polycomb recruitment in ES cells and during cellular differentiation  
 Main Objective: The goal of this project is to generate maps of chromatin modifications during ES cell differentiation to understand the basic mechanisms recruiting chromatin modifiers to specific genomic coordinates.

Canadian Cancer Society Research Institute DeCarvalho (PI) Aug. 2015-July 2018  
 Project Title: BAZ2 Bromodomain as a novel target for colorectal cancer treatment  
 Main Objective: The goal of this project is to investigated the possibility of targeting BAZ2A/B bromodomains to decrease colorectal cancer cell proliferation while increase T cell activation

Canadian Institutes for Health Research (CIHR) DeCarvalho (Co-PI) Apr. 2013-Mar 2018  
 Project Title: Influence of the microbiome on epigenetic mechanisms in inflammatory bowel disease (IBD)  
 Main Objective: The goal of this project it to perform epigenomic mapping (ATAC-seq, ChIP-seq and DNA methylation) and trancriptomic profiling (RNA-seq) of T cells infiltrating the inflamed gut in IBD patients to identify new therapeutic targets



**2017 Annual Report**  
**CPRIT Advisory Committee on Childhood Cancer (ACCC)**  
*Submitted to the CPRIT Oversight Committee*  
*May 2018*

**I. Introduction**

The CPRIT Advisory Committee on Childhood Cancer (ACCC) convened via teleconference twice and face-to-face on one occasion during the past year to review progress as well as to formulate recommendations to the CPRIT Oversight Committee on priority areas for funding of research, prevention/survivorship, and product development in childhood cancer.

The ACCC as well as the pediatric cancer research and advocacy committees remain grateful to CPRIT for its ongoing focus on research excellence as guided by the peer-review process. We appreciate the ongoing opportunities that have been provided for childhood and adolescent cancer research funding by CPRIT, particularly the RFAs specifically requesting grant applications focused on these cancers as well as the RFAs to support shared resources to enhance and streamline efforts in our goal to cure and improve the outcome for children and adolescents with cancer. The peer-reviewed funding provided for high-impact research pediatric and adolescent cancer research, including the funded initiatives in prevention and product development, has enabled timely advances that are positively impacting as well as improving the lives and outcome for children and adolescents with cancer. The magnitude of these efforts will continue to amplify and will not only benefit children with cancer from Texas – but will benefit children and their families across the world.

**II. Progress to date**

Under the leadership of Dr. Willson as Chief Scientific Officer the success of CPRIT research applications focused on childhood cancer has continued to increase. This success is in large part due to focused RFA mechanisms that have resulted in the funding of more than 44 childhood and adolescent cancer research projects to date. Specifically, an increase has been realized in the number of grants devoted to childhood and adolescent cancers (from 4 percent in 2014 to 24% in 2017). This success reflects the quality of the applications that are being submitted to CPRIT for pediatric cancer research. The impact of the awards funded by CPRIT is tremendous since the life-years for survivors of childhood cancer greatly exceeds that of their adult counterparts.

Further evidence of the success in childhood and adolescent cancer research funding by CPRIT is measured by publications and new grant dollars. Although the impact of this outcome measures will continue to grow over the ensuing five years, at this early juncture there have been more than 170 peer review publications, with numerous others in progress, that have emanated from these CPRIT-funded pediatric-focused research projects. These

include publications in high impact journals such as *Journal of Clinical Oncology*, *Blood*, *Nature Reviews*, and *Nature Communications*. Additionally, these CPRIT-funded investigators have already been able to garner at least an additional \$21 million dollars in peer review funding, including NIH funding, to support the pursuit of their important research initiatives that are focused on pediatric cancer research.

The CPRIT-funded research initiatives focused on pediatric cancer are quite diverse and range from prevention strategies; to development of targeted therapies including small molecules and cellular therapies; through survivorship. The majority of funded awards have been Individual Investigator Research Awards (IIRA); however, there have also been three funded Multi-Investigator Research Awards (MIRAs) that have been particularly impactful including one focused on osteosarcoma, one on liver tumors, and another on soft tissue sarcomas, including Ewing sarcoma. Potential new therapeutic targets that are undergoing further study have been identified by many investigators. Prevention and education, targeted at potentially high-risk populations, particularly for human papilloma virus (HPV) have also been extremely successful.

During the past year, there were also recruitment awards of three outstanding investigators whose research focuses on pediatric oncology. The short and long-term impact of these investigators to the field of pediatric oncology will be substantial. These recruits include:

- Benjamin Fregly, PhD; Rice University
- Stephen Mack, PhD; Baylor College of Medicine
- Rosa Uribe, PhD; Rice University

A project by project summary of the impact of the funded projects on the field of pediatric oncology and the resultant publications and clinical trials is shown in Appendix A. It should be noted that these findings will continue to increase in magnitude since many of the awards are in the early stages of execution.

### **III. The ACCC recommends that current strengths in the CPRIT Research Portfolio remain a high priority:**

#### **1) Investigator-Initiated Research**

Support for clinical and translational research carried out by individual investigators as well as by collaborative teams of investigators should remain a high-priority.

#### *ACCC Recommendations*

- a. The CPRIT RFA for individual investigator grants specific to childhood and adolescent cancer, similar to RFA R-17-IIRACCA-1, should be issued on a continuous basis.

- b. Release of an RFA for multi-investigator research awards (MIRAs) focused on childhood and adolescent cancer (with an emphasis on inter-institutional collaboration) is recommended. These awards have been very successful in leading to new discoveries and translation of these results into meaningful clinical trials for children with high risk cancers.
- c. Partnering with foundations such as the Carson Leslie Foundation to release an RFA, similar to RFA R-13.1-IIRA, focused on pediatric central nervous system tumors. Tumors of the central nervous system are the leading cause of death from childhood solid tumors.

## **2) Recruitment Awards**

The recruitment award program has been successful in bringing high quality investigators to Texas. However, relatively few investigators trained in childhood cancer basic, translational or clinical have been brought to Texas by the recruitment grants. The ACCC recommends that consideration be given to setting aside at least one recruitment grant for pediatric oncology for each recruitment RFA (First Time, Tenure Track Faculty Members; Rising Stars, and Established Investigators).

## **3) Core Facility Grants**

*The ACCC recommends that CPRIT continue to prioritize initiatives for core facilities to support childhood cancer.* Continuation of the opportunity for institutions to submit an application for a shared resource to support research directed toward childhood and adolescent cancer in addition to an additional application to support another area of research (e.g., RFA R-17-CFSA-2)

# **IV. Prevention Portfolio**

## **Prevention initiatives in childhood and adolescent cancers**

With the increased survival rates of childhood cancer, issues related to survivorship including long-term side effects of treatment, quality of life, fertility, employment and a host of other concerns have become increasingly prominent. The number of years of life saved by successfully treating a child with cancer is substantially greater than that of an adult, which magnifies the importance of survivorship issues. We suggest that CPRIT continue to support prevention initiatives relating to childhood cancer survivorship. In addition, it has recently become evident that a significant number of childhood cancers are related to cancer pre-disposition syndromes. We encourage CPRIT to support research and prevention services targeting patients at high risk of initial and secondary cancers.

## **V. Product Development Portfolio**

### **Commercial Development of Diagnostics and Therapeutics for Childhood Cancer**

We appreciate CPRIT's recognition of and commitment to product development efforts that will support advances in childhood, as well as adult, cancers (DP160014, 160057). Nevertheless, a paucity of pediatric cancer drug development programs exist in the pharmaceutical industry. Additionally, none of the commercial entities currently funded by CPRIT have active clinical trials of diagnostics or therapeutics in childhood cancer.

The ACCC recommends ongoing exploration and discussion of innovative ways to facilitate and encourage commercial development of drugs and diagnostics for childhood cancer.

## **VI. Summary**

The ACCC is grateful to CPRIT for its commitment to prioritizing and funding groundbreaking cancer research and prevention programs that are focused on childhood cancer. CPRIT funding mechanisms have further catalyzed collaboration between clinical and laboratory investigators across the state of Texas, which benefits children with cancer as well as their families. The unprecedented commitment by CPRIT to pediatric cancer research has accelerated research discovery and translation. The resultant positive impact for the field of pediatric oncology is profound and has been recognized not only at the local level but also nationally and internationally.

# APPENDIX A

## IMPACT OF AWARDS TO DATE

**RP100329** (PI, Huff, Vicki; Next generation genomic sequence identification of the 19q familial Wilms tumor predisposition gene) –status closed

**RP110324** (PI, Huff, Vicki; Impact of differentiation status on tumorigenesis)

While patients diagnosed with Wilms tumor (WT) have an overall good prognosis, this is achieved at the expense of substantial late effects of treatment that may occur for decades after treatment. The investigators performed studies to further our understanding of the biology and genetic etiology of WT so that treatment modalities with fewer and lesser long-term effects can be developed. They identified germline mutations in three different genes that can predispose to WT and determined progenitor cell populations in the developing kidney that are susceptible to tumorigenesis. Additionally, because WT has proven to be a very productive model for understanding the genetic etiology and biology of cancer, the results from these studies on WT may elucidate common mechanisms by which genetic mutations of stem-like cells in an organ can become malignant.

**RP100429** (PI, Dent, Sharon; Regulation of Ash2L and MLL oncoproteins by PRMT-mediated methylation in normal cells and acute leukemias)

These investigators identified new post-translational cross-talk in histones that impact gene expression patterns in acute leukemia, the most common malignancy of childhood. This information may yield insights into optimizing therapy for high risk leukemias.

**RP100484** (PI, Bollard, Catherine; Human T lymphocytes with anti-viral and anti-leukemic specificity as protection against infection and relapse after stem cell and cord blood transplantation)

This award supported the first CD19-CAR T cell trials allowing the enrollment of pediatric patients with ALL after allogeneic SCT, driving the field of CAR T cell therapy forward beyond the adult setting.

**RP100762** (PI, Reynolds, C. Patrick, Enhancing the anti-neuroblastoma activity of fenretinide by identifying and targeting sphingolipid pathways that confer resistance)

Through this award the investigators generated both clinical and non-clinical data that have moved a novel investigational drug forward toward potential FDA registration, enabled the activation of five clinical trials pediatric as well as adult cancer patients, and supported formation of a Texas-based company. The ability to carry out clinical trials with a novel investigational agent in West Texas has provided access to early-phase clinical trials to a large region with virtually no

access to such innovative clinical studies. In addition, this work has resulted more than 13 manuscripts.

**RP100865** (PI, Fernandez, Maria; Cancer communication interventions to increase HPV vaccination among Hispanic adolescents)

**RP130459** (PI, Fernandez, Maria; Cancer communication interventions to increase HPV vaccination among Hispanic adolescents)

The investigators developed and evaluated a program *Por Nuestras Hijas* to educate and motivate Hispanic parents to vaccinate their daughters. Their findings showed that the program was effective at increasing HPV vaccination rates, both for initiation and completion of the vaccine series.

With CPRIT funding, the investigators expanded the reach of their prior successfully funded CPRIT intervention to increase HPV vaccination among Hispanic adolescents and to reduce HPV-related cancers. Because Hispanic populations experience higher HPV-related cancer morbidity and mortality than their white counterparts, this program is critical to reducing HPV-related cancer disparities.

**RP101017** (PI, Lee, Brendan; Genetics of Osteosarcoma)

The investigators identified new physiological roles of Notch in skeletal stem cells and the bone marrow niche. These functions when perturbed can drive and facilitate both primary cancers of the bone such as in osteogenic sarcoma as well as in metastasis of other primary tumors to bone. They also establish new genetic models that are improved for the development of therapies targeted at these cancers.

**RP101042** (PI, Kang, Min H; Validation of a MCL1 Promoter Deletion as a Molecular Marker for Sensitivity to Bcl-2 Inhibitors in Pediatric Acute Lymphoblastic Leukemia)

The investigators identified S159 and T163 phosphorylation sites of MCL-1 are important in determining *in vitro* sensitivity to ABT-737 in acute lymphoblastic leukemia. Their data suggest that serine-threonine kinases play an important role in determining the stability of Mcl-1 and thus warrant further investigation.

**RP101089** (PI, Plon, Sharon; Whole Genome Approaches to Define the Inherited Basis of Childhood Cancer)

This CPRIT investigator grant was one of the first projects to use whole exome sequencing to identify childhood cancer susceptibility genes with identification of leukemia susceptibility genes. The large number of rare sequence variants identified resulted in the development of new

statistical methods for analysis of missense variants. NIH-supported funding of a clinical trial of whole exome sequencing of childhood cancer patients is a direct result of this work.

**RP101195** (PIs, Tomlinson, Gail; Parsons, Donald; Lopez-Terrada, Dolores; Comerford, Sarah; Finegold, Milton; Rakheja; Dinesh; Chen, Yidong; Genetics and Biology of Liver Tumorigenesis in Children)

**RP120715** (PIs, Tomlinson, Gail; Parsons, Donald; Finegold, Milton; Rakheja; Dinesh; Chen, Yidon; Genetics and Biology of Liver Tumorigenesis in Children)

This MIRA was the largest-scale effort to genomically characterize hepatoblastoma (HB), including mRNA and miRNA profiling. A year MIRA extension further extend the analyses to also include hepatocellular carcinoma (HCC), the second most common malignant tumor of childhood. Major findings of this MIRA and the extension include:

- Identification of NFE2L2 as an activating mutation present in aggressive hepatoblastoma tumors, implicating oxidative stress, a previously unrecognized pathway, in hepatic tumor development as well as demonstrating a link between aggressive HB and HCC.
- Confirmation that a very low-number of somatic mutations is characteristic of hepatoblastoma.
- Completion of sequence analysis of pediatric HCC, distinguishing fibrolamellar from non-fibrolamellar subtypes and identifying a novel translocation.
- The integrated results of the genomic characterization of pre-treatment specimens were used to develop a classification plan for hepatoblastoma (Hepatology, Sumazin, *et al* 2017) with an upcoming validation through an international clinical trial, Children's Oncology Group (COG) AHEP1531 study, "Pediatric Hepatic Malignancy International Therapeutic Trial (PHITT)", that it being performed in collaboration with the European and Japanese oncology groups.
- In addition, the group has recently submitted a new MIRA grant ("Predictive biomarkers and novel therapies for high-risk pediatric liver cancers") that proposes to further study the prognostic and therapeutic biomarkers for these tumors, including work to enable development of molecularly-targeted therapies and immunotherapies.
- Development of a transgenic mouse model of hepatoblastoma (J Clin Invest Insights, Comerford et al 2016).
- Identification of recurrent DNAJB1/PRKACA gene fusions as well as novel fusions involving TERT and APC in childhood HCC.

In summary, projects RP101195-P2 and RP120715-P2 have provided a novel view of the genetic alterations underlying the most common liver tumors of childhood, facilitating further biologic and pre-clinical studies of the identified targets and development of a comprehensive risk-stratification system for childhood liver tumors. Findings from this MIRA are being incorporated into international clinical trials that are actively being developed for children with liver tumors.

**RP101335** (PIs, Poplack, David; Donehower, Larry; Lau, Ching; Gottschalk, Stephen; Yustein, Jason, Rao, Pulvarthi; Hicks, John; Targeted therapies for metastatic osteosarcoma)

Metastatic osteosarcoma is one of the most difficult to treat pediatric cancers because of its resistance to most chemotherapy agents as well as radiation therapy. No progress has been made in the past 30 years to treat this disease. A list of discoveries and other highlights of this award are summarized below.

- Identified aberrant expression of Wnt regulators and their functional significance, i.e., enhanced Wnt signaling activity within metastatic tumors through the downregulation of negative regulators NKD2 and APCDD1, in metastatic osteosarcoma (Zhao et al, Oncogene 2015)
- Performed comprehensive cytogenetic characterization of mouse osteosarcomas revealing amplification of Myc-Pvt1 in a subset of tumors (Rao et al, Genes Chromosomes and Cancer 2015)
- Identified a circulating microRNA signature to detect osteosarcoma and potentially monitor therapeutic responsiveness (Allen-Rhoades et al, Cancer Med 2015)
- Identified and validated prognostic signatures that can predict outcome of osteosarcoma based on gene expression and DNA methylation
- Identified a potentially novel therapeutic approach for osteosarcoma by using demethylation strategies to increase expression of FAS and decrease metastatic potential
- Demonstrated a higher level of the p27 autoantibody which correlates with poor outcome in osteosarcoma (Li et al, Cancer Res 2016)
- Developed a novel prognostic model based on CXCL10, FLT3LG and metastasis in osteosarcoma (Flores et al, Cancer 2016)
- Completed a Phase I/II clinical trial to evaluate safety and efficacy of HER2-CAR T cells in patients with HER2+ sarcomas (Ahmed et al, JCO 2015)
- Developed and published a strategy to generate genetically modified canine T cells for preclinical study in large animal model (Mata et al, JIT 2014)
- Developed a new strategy to enhance the expansion and antitumor activity of HER2-CAR T cells *in vivo*

**RP110050** (PI, Song, Yoncheng; Novel Epigenetic Modulators Targeting Leukemia Initiating Cells)

**RP150129** (PI, Song, Yoncheng; Drug Discovery and Mechanistic Studies of Protein Methylation Targeting Leukemia)

Acute leukemia is the most common cancer in children and adolescents. Current chemotherapies, which kill all rapidly proliferating cells including normal stem cells in bone marrow and other organs, cause severe toxicities and side effects, as well as secondary cancers due to mutagenesis. The ultimate goal of the investigators is find non-toxic drugs targeting oncoproteins (such as rearranged MLL and RUNX1-ETO) that drive the malignancy in order to develop the first-in-class therapeutics for these subtypes of leukemia.

**RP110187** (PI, Nuchtern, Jed G; Neuroblastoma-Derived Secretory Protein Receptor, a New

The investigators successfully completed their primary goal which was to identify the putative receptor for neuroblastoma derived secretory protein, (NDSP), which they had previously published identified as an autocrine growth factor for neuroblastoma.

**RP110390** (PI, Klisch, Tiemo; A functional genetic approach to identify new potential therapeutic targets for medulloblastoma)

A new oncogenic signal resulting from the faulty phosphorylation of Atoh1 by a prominent kinase that is NOT seen in normal development was discovered. The research can be directly applicable in assessing the effects of inhibitors that target the kinase, which are already in clinical trials and/or in use for other cancers.

**RP110394** (PI, Amatruda, James; Identification of novel targets for therapy of pediatric germ cell tumors)

Work supported by this CPRIT award has led to new insights into the signaling network that drives germ cell tumor (GCT) growth and a rationale for therapeutic targeting of GCTs with agents that antagonize the EGFR and mTORC1 pathways. In addition, this project resulted in the largest study to date of the molecular landscape of pediatric germ cell tumors (manuscript in preparation), which has revealed novel drivers of this disease that could lead to new and more effective therapies.

**RP110395** (PI, Amatruda, James; A genetic approach to target EWS-FLI1 oncoprotein in Ewing sarcoma)

The investigators used a transgenic zebrafish Ewing sarcoma model to screen a library of 1100 different drugs for activity against EWS-FLI1. Through this approach they identified a family of compounds with activity against human Ewing sarcoma tumor cells. They also investigated the role of novel fusion proteins including CIC-DUX4 fusion gene. This work has resulted in the first animal model of CIC-DUX4 sarcomas and has identified key target genes conserved from zebrafish to human.

**RP120685** (PIs, Skapek, Stephen; Parsons, Donald; Amatruda, James; Cehn, Ydindog; Molecularly targeted therapy for soft tissue sarcoma in Texas)

This MIRA is the only program project scale multi-institutional research effort focused on soft tissue and Ewing sarcoma in the United States. One of the primary goals of this project is to characterize the genetic landscape of childhood sarcomas, with a particular focus on high-risk sarcomas with unknown biology and limited treatment options. These ongoing efforts have

already identified important and previously unknown genetic mutations underlying specific sarcoma subtypes, most recently the discovery of internal tandem duplications of the BCOR gene in >85% of cases of clear cell sarcoma of the kidney (published in Nature Communications). The results from this MIRA are already being translated into improved diagnostic tests for childhood sarcoma patients and have opened new avenues of research into sarcoma biology and treatment. Several manuscripts describing the results have already been published in high impact journals and additional manuscripts describing the development and application of a transcriptome (RNA)-sequencing pipeline for analysis of formalin-fixed paraffin-embedded (FFPE) sarcoma specimens are currently in preparation. Other notable highlights from this grant include the following:

- The investigators uncovered a novel, complex rearrangement of PDGFRB in infantile myofibromatosis case and are studying its tumorigenic properties in mouse models.
- The investigators have carried out next generation sequencing of undifferentiated sarcoma specimens from the Children's Oncology Group, and found among other things that NGS approaches unveil abnormalities that alter the diagnosis or represent targetable lesions in the majority.
- The investigators have developed a novel integrative computational analysis pipeline and applied this to rhabdomyosarcoma specimens. This new pipeline identifies 29 drivers genes for this disease, and the majority were validated to be important in CRISPR/Cas9-based functional screens.

**RP130266** (PI, Srivenugopal, Kalkunte; Rational redox-driven non-toxic therapeutic strategies for pediatric brain cancers (Carson Leslie Award)

The anti-mutagenic DNA repair protein MGMT is highly expressed in pediatric brain cancers. It is a major target to improve the efficacy of anti-glioma alkylating agents. O6-benzylguanine, an MGMT inhibitor is currently in clinical trials; however, the results have been disappointing due to extended bone marrow suppression. The investigators demonstrated that compounds like disulfiram and nitroaspirin potently inhibit MGMT and improve the alkylator efficacy in cell culture and xenograft models.

**RP130368** (PI, Ris, M Douglas; Proton Beam Radiation Therapy vs. Conventional Beam Radiation Therapy: Toxicities During & After Craniospinal Radiation Therapy in Children)

Toxicities resulting from the treatment of pediatric brain tumors have significant quality of life implications for survivors. This project is assessing the comparative, short-term toxicities of two types of radiotherapy - conventional X-ray therapy and proton beam radiotherapy. More information about the toxicities associated with radiotherapy will allow serve as the basis for the development of strategies to minimize the short and long term effects of radiotherapy as part of our goal to promote better overall outcomes in survivors. The investigators are in the process of data analyses.

**RP130629** (PI, Maher, Elizabeth A; Genotype and Metabolic Phenotype in Pediatric Brain Cancer (Carson Leslie Award))

Sample preparation for high resolution metabolomics analysis in process.

**RP140258** (PI, Lupo, Phillip; The Intersection between Childhood Cancer and Congenital Anomalies: Identifying Novel Cancer Predisposition Syndromes)

Congenital anomalies are one of the strongest risk factors for developing cancer during childhood. In fact, as many as 15% of all cancer cases during childhood may be attributable to both major and minor anomalies. This CPRIT award will leverage the Texas Birth Defects Registry and Texas Cancer Registry to build a population-based cohort of children with birth defects and cancer to: 1) identify novel birth defect-childhood cancer patterns, and 2) characterize the genetic alterations underlying these co-occurring conditions. Ultimately, this will inform cancer surveillance efforts in high-risk populations for childhood cancer.

**RP140430** (PI, Grosshans, David; Synaptic Mechanisms of Cognitive Decline after Cranial Radiation)

This project addresses alterations in nitric oxide and glutamate signaling negatively influence synaptic plasticity and promote long-term modifications in the structure and functions of neurons through epigenetic mechanisms.

**RP150006** (PI, Konopleva, Marina Y; Defining and Treating Targetable Lesions in AYA Acute Lymphoblastic Leukemia)

This is the first trial combining tyrosine kinase inhibitors dasatinib or ruxolitinib with chemotherapy in a rare subgroup of patients with ALL. This so-called “Ph-like” ALL subset has a very poor outcome with chemotherapy alone. Extensive biomarker studies, including gene expression and proteomics, that may identify novel therapeutic targets in this difficult to treat disease will be performed as a part of this trial.

As a result of the award, the investigators have initiated a clinical trial a MDACC “A Phase 2 Study of the Combination of Ruxolitinib and Dasatinib with Chemotherapy in Patients with Philadelphia Chromosome (Ph)-Like Acute Lymphoblastic Leukemia (ALL) 2014-0521.” To date they have treated 10 patients (9 ruxolitinib arm, 1 dasatinib arm with a median number of 3 prior therapies (range, 2-10). The preliminary findings of this trial were presented at the 2017 American Society of Hematology Annual Meeting. They have also reported on the outcomes of Ph-like ALL patients as well as the co-occurrence of CRLF2-rearrangement with Ph+ ALL.

**RP150081** (PI, Heaney, Jason; Genetic susceptibility to testicular germ cell tumors)

The investigators are performing studies to characterize the genes and developmental defects that contribute to testicular germ cell tumors (TGCT) susceptibility. TGCTs, the most frequent solid tumor diagnosed in boys and young men, can metastasize if not detected early. Furthermore, current treatment regimens can cause long-term side effects including hearing loss, cardiovascular disease, cognitive impairment, and infertility. This ongoing research project provide insight into the developmental origins and genetic risk factors of TGCTs in humans; it may also provide new targets for the early diagnosis and individualized treatment of TGCTs.

**RP150164** (PI, Leavey, Patrick; Using imaging and computational tools to improve risk stratification in children with bone cancer)

The investigators are developing a computer tool to interpret features of osteosarcoma that will potentially predict response or more accurately and in shorter time assess tumor response to treatment. They have almost completed the first step of this study to interpret histological features of osteosarcoma. Their work will be a critical advance in the care of patients with osteosarcoma both to improve treatment currently available and provide novel and predictive ways to evaluate the effect of new therapies.

**RP150301** (PI, Gopalakrishnan, Vidya; Epigenetics in Medulloblastoma Development and Therapeutics)

The CPRIT funded grant was focused on (1) identifying how elevation of the transcription factor REST contributes to medulloblastoma development, and (2) to target REST activity pharmacologically. The investigators discovered that REST drives leptomeningeal dissemination and medulloblastoma metastasis. Because REST expression in the normal brain is restricted mostly to neural stem cells and possibly a few neurons, it may be considered a tumor associated protein and therefore an attractive therapeutic target. REST is associated with a number of druggable chromatin remodelers, and drugs targeting these molecules are FDA approved and can be repurposed in novel combinations. The proposed screen was also designed to identify novel cooperating epigenes, and at least a few of the ones identified thus far can be targeted by existing FDA-approved drugs, possibly in novel combinations.

**RP150334** (PI, Deneen, Benjamin; Personalized Functionalization of Pediatric High Grade Glioma)

Cutting-edge technologies have ushered in an era of personalized medicine, where genomic data from individual tumors influences diagnostic and therapeutic decisions in a patient-specific manner. Our studies on pediatric glioma are a crucial component of this effort, as we will integrate a multi-disciplinary, discovery platform that combines our novel mouse models of pediatric glioma with cutting-edge gene editing approaches and established WGS technologies to determine how

specific mutations and patient-specific mutation cohorts drive tumorigenesis. Establishing this functional genomics pipeline will be a powerful tool for decoding driver and passenger mutations from individual patients with pediatric glioma that will be directly harnessed towards actionable diagnostic and therapeutic endpoints.

**RP150343** (PI, Willson, Richard; An ultra-sensitive nanomagnetic sensor for the early detection of anaplastic large cell lymphoma)

The goal of this project is to identify, less-invasive diagnosis of anaplastic large cell lymphomas (ALCL). ALCL is the most common childhood T-cell lymphoma and the second most common T-cell lymphoma in adults. ALCL usually is characterized by a very distinctive fusion protein, NPM-ALK, which is exceptionally stable and accumulates in lymphoma cells. Ultrasensitive detection could allow earlier diagnosis, diagnosis from blood samples instead of painful, invasive biopsies, better treatment monitoring, and earlier detection of recurrent disease.

The investigators have an issued US Patent on nanoscale GMR sensors derived from an application that predates the CPRIT funding. They also have two see CPRIT- project - derived patent applications now pending. One describes a high-density array of nanoscale GMR sensors based on a novel addressing scheme that radically increases the detection - active fraction of the sensor area, improving analytical performance. The other describes a novel approach to AC susceptometry, which improves the analytical sensitivity for magnetic nanoparticles of these relatively simple devices by orders of magnitude.

**RP150416** (PI, Maurer, Barry; Translational investigations on fenretinide and safingol for pediatric cancer use)

This award fund a pediatric phase 1 trial of the novel fenretinide and safingol in children following completion of the recently activated adult phase 1 trial of this combination in adults with refractory cancer (SPCO-2010-002, ClinicalTrials.gov identifier: NCT01553071). Accrual to the adult trial has been slower than anticipated. Once completed, the investigators plan to proceed with drug formulation so that they can initiate the planned pediatric trial.

**RP150445** (TimbiSha, Alexander; Ewing sarcoma, a homologous recombination defective disease)

This project focuses on developing an understand of why Ewing sarcoma, a relatively rare disease (2% of pediatric cancers, ~200 patients/year in the USA), is almost always initially sensitive to a wide variety of chemotherapies but then develops resistance. It is hoped that this understanding will lead to the replacement of “general therapies” with more targeted less toxic treatments. The investigators have also discovered that Ewing sarcoma traps BRCA1 in a transcription complex, impairing homologous recombination via a novel mechanism. Not only does this finding provide novel insight into the biology of Ewing sarcoma but it also reveals a new mechanism producing a

homologous recombination defect that may be important in adult cancers and cancer predisposition syndromes. The initial discoveries emanating from this project were recently published in *Nature*, a high impact journal.

**RP160022** (PI, Pati, Debananda; Role of cohesin in hematopoiesis and myeloid leukemia in children with Down syndrome)

This project is addressing several key gaps in current scientific knowledge of the driver mutations and genetic alterations that contribute to leukemogenesis in children with Down syndrome and may lead to genomic-proteomic biomarkers predictive of subsequent leukemia in infants with transient myeloproliferative disorder (TMD). The investigators have shown that *Rad21* loss leads to the impaired hematopoietic differentiation of HSCs and they are deciphering the mechanisms that underly these effects. They are also examining the role of a cohesion-resolving protease, separase, in hematopoiesis.

**RP160237** (PI, Shi, Xiaobing; A novel epigenetic reader as therapeutic target in MLL-translocated pediatric leukemias)

**RP160739** (PI, Shi, Xiaobing; Targeting Histone Acetylation Readers in MLL-translocated Leukemias)

Leukemias are the most common childhood cancers that account for ~30% of all cancers in children. This research proposal aims to understand the molecular mechanisms of MLL rearranged leukemias that account for up to 80% of infant ALL and 35-50% of infant AML and will likely provide potential therapeutic targets for disease intervention. The investigators have published multiple publications in high impact journals (e.g., *Nature*, *Nat Commun*, and others) describing the results of their work.

**RP160249** (PI, Mendell, Joshua; DIS3L2 in childhood Wilms tumor: mechanism to medicines)

The investigators are studying the gene DIS3L2 through which loss of function contributes to Wilms and are trying to uncover molecular pathways that are controlled by this gene using new murine models generated in their laboratory. The ultimate goal is to attempt to identify new targets and effective agents for the treatment of Wilms tumor and other childhood cancers utilizing their model systems.

**RP160487** (PI, Cytokine signaling in Ewing sarcoma)

This goal of this investigation is to dissect the role of cytokine signaling in Ewing sarcoma and evaluate the feasibility of its therapeutic targeting. In addition, the proposed research will provide a model to dissect and target cytokine signaling in children's cancers, an important yet

underexplored area of cancer research.

**RP160771** (PI, Scheurer, Michael; The Adolescent and Childhood Cancer Epidemiology and Susceptibility Service (ACCESS) for Texas)

ACCESS will provide childhood cancer researchers a much needed resource for the conduct of epidemiological and outcomes research in Texas. Risk factor and clinical data along with relevant biological specimens are being collected from children with a variety of childhood cancers across the state. The resource is available to researchers after review and approval by the ACCESS scientific committee.

**RP160841** (PI, Shiio, Yuzuru; Targeting EWS-FLI-1 for degradation)

The goals of this award are to investigate the molecular mechanism of lysosomal degradation of EWS-FLI-1 in Ewing sarcoma and to screen compounds that can be used clinically to target EWS-FLI-1 for degradation. These compounds can be developed as a new type of drug to treat Ewing sarcoma in the future.

**RP160190** (PI, Jiang, Steve; Pediatric Radiation Oncology With Movie Induced Sedation Effect (PROMISE))

**Technology Development:** In the past year, an initial PROMISE (Simulated Radiotherapy Treatment Assisted with Pediatric Radiation Oncology with Movie Induced Sedation Effect) prototype system was developed. The prototype is comprised of three major components: 1) a radiation transparent video system that can play movies during radiation beam delivery (home developed); 2) a motion monitoring system that can real-time capture patient surface and broadcast wireless motion signals (a commercial product); and 3) a PROMISE software platform that controls movie viewing using the received motion signal (home developed). The prototype system has been integrated and passed the initial functional test. A next step is to conduct a thorough specification test on a motion phantom, including signal latency and motion accuracy.

**Clinical Trial:** With the initial prototype system developed, an IRB (institutional review board) protocol for a clinical trial was developed. The endpoint of this clinical trial is to determine the feasibility of using the PROMISE system. In the trial, we will simulate PROMISE radiation treatment procedures, including patient positioned in radiation treatment couch and movie playing without radiation beam delivery. Also, we will evaluate treatment delivery accurate and overall treatment time.

**RP170071** (PI, Lupo, Phillip; Genetic epidemiology and molecular basis of cancer predisposition in pediatric rhabdomyosarcoma)

One of the strongest risk factors for rhabdomyosarcoma (RMS), a malignant tumor of muscle, is having a genetic cancer predisposition syndrome. While it is believed that about 7% of RMS patients have changes (or mutations) in the genes responsible for these syndromes, there have been: 1) no population-based assessments to support this estimate, and 2) no family-based studies to determine how many patients develop RMS due to new mutations (*de novo* mutations) in cancer predisposition genes. In this award the investigators will combine population-based research strategies with innovative molecular biological approaches to gain a better understanding of the causes of pediatric RMS that may aid in the development of future therapies.

**RP170074** (PI, Rabin, Karen; Molecular epidemiology and somatic alterations driving acute lymphoblastic leukemia in Down syndrome)

This study will address the fundamental question of why acute lymphoblastic leukemia (ALL) occurs more often in children with Down syndrome, a genetic disorder that is among the most common, and increasing in prevalence. The project employs complementary approaches that are likely to identify novel genes that drive the development of ALL in Down syndrome. These discoveries may serve as therapeutic targets to improve outcomes both in this vulnerable and high-risk population, as well as in other malignancies.

**RP170510** (PI, Reynolds, Charles; Telomere maintenance mechanisms in neuroblastoma)

The investigators have made outstanding progress which was ONLY possible through CPRIT funding. In collaboration with the Children's Oncology group (COG) and the NCI TARGET program they have translated their *in vitro* and *in vivo* findings from preclinical cell line and patient-derived xenograft model (MDX) systems in back into the clinic. They have identified 3 groups of high-risk neuroblastoma with distinct clinical outcomes by measuring telomerase mRNA (TERT) and through use of novel assay for the alternate lengthening of telomere (ALT) mechanism called c-circles. These groups include: (1) tumors with high TERT, (2) tumors with low TERT and c-circle positive, and (3) low-risk tumors with low-TERT and no c-circles. Importantly the low-TERT/c-circle negative tumors comprise a new group that has not previously identified. Additionally, the investigators have identified ATM kinase as a novel target in the c-circle positive (ALT) group, which has very poor overall survival rates and comprises ~24% of children with high-risk neuroblastoma. Importantly, they have been successful in reversing drug resistance with a clinical-stage ATM kinase inhibitor in PDX models of neuroblastoma.

In summary, the data from resulting from this CPRIT grant have a high-likelihood of altering the current molecular markers used for clinical risk-stratification of high-risk neuroblastoma and have resulted in the identification of a novel molecular target for high-risk neuroblastoma.

This work, which was presented in April to the COG. was very well received. COG is actively working with the CPRIT-funded investigators to validate their **findings**. In addition, this work was selected for a plenary session talk at the international Advances in Neuroblastoma Research Meeting ([www.ANRmeeting.org](http://www.ANRmeeting.org)) held May 2018 in San Francisco. A paper for a high-impact journal is currently in preparation.

**PP100047** (PI, Tiro, Jasmin; An intervention promoting HPV vaccination in safety-net clinics)

This 9 year partnership, leveraged grant funding from national (NCI), state (CPRIT), and non-profit (ACS) agencies to understand and intervene on HPV-related cancer prevention effort in the Dallas area. As a result of analysis of and modifications to patient-, provider-, and system-level interventions Parkland's HPV vaccine initiation vastly improved from 45.7% to 72.4% and HPV up-to-date similarly improved from 23.9% to 61.4%.

**PP120150** (PI, Berenson, Abbey; Prenatal education and postpartum administration of HPV vaccine: Strategies to increase initiation and series completion among low income women

**PP160058** (PI, Berenson, Abbey; Postpartum administration of HPV vaccine: Strategies to increase initiation and series completion among low income women across Southeast Texas

The initial grant resulted in a continuation/expansion award to extend HPV vaccination opportunity to all women who deliver an infant at John Sealy Hospital in Galveston. Patients reside in 32 counties. The follow-up grant focuses on Postpartum administration of HPV vaccine: Strategies to increase initiation and series completion among low income women across Southeast Texas

**PP140049** (PI, Morales-Campos, Daisy; Educating Hispanic adolescents and their families on cervical cancer prevention and HPV vaccination in community and clinic settings)

**PP160080** Promoting HPV vaccination among Hispanic adolescents and young adults using Health Care System-Based Interventions and Community Outreach

Our program uses a multi-level approach to address barriers to HPV vaccine initiation and completion in a safety net healthcare system (Harris Health). Through provider training, patient recall/reminder and navigation, and culturally- and linguistically-targeted patient (parent) education, our program will dramatically improve HPV vaccination rates among pediatric patients at Harris Health. Ultimately, our comprehensive HPV vaccine program will prevent the pediatric patient population from developing HPV-related cancers as adults.

In the follow-up program, findings from the multiple health care system-based interventions, including health care professional education and training to disperse accurate HPV and HPV vaccine information, and public, county-wide, education and outreach will assist in identifying factors that inhibit and/or enhance adolescent and young adult HPV vaccination rates.

**PP160079** (PI, Jibaja-Weiss, Maria L; Leveraging a Community Network for Cancer Prevention to Increase HPV Vaccine Uptake and Completion among Pediatric Patients in a Safety Net Healthcare Setting)

The investigators use a multi-tier approach to address barriers to HPV vaccine initiation and completion in a safety net healthcare system (Harris Health). Through provider training, patient recall/reminder and navigation, and culturally- and linguistically-targeted patient (parent) education, it is believed that this program will dramatically improve HPV vaccination rates among pediatric patients at Harris Health and ultimately prevent the pediatric patient population from developing HPV-related cancers as adults.

**RP11076** (PI, Reynolds, Patrick; Texas Cancer Cell Repository)

CPRIT funding was critical to the investigators ability to expand the Children's Oncology Group Cell Line and Xenograft Repository ([www.COGcell.org](http://www.COGcell.org)). This repository establishes and banks cell lines and patient-derived xenografts (PDXs) from pediatric cancers, largely from samples provided by Children's Oncology Group (COG) protocols. The repository has provided pediatric cancer laboratory models to > 350 investigators in 20 countries and has enabled multiple biological and preclinical therapeutic studies and numerous publications. Several clinical trials have been developed by investigators using models from our repository. In Texas there are 57 investigators in 10 Texas institutions using our cell lines and PDXs; 17 of these investigators have active CPRIT grants.

## TRAINING GRANTS

**RP170345** (PI, Oyajobi, Babatunde; UTHSCSA Cancer Research Training Program)

A pediatric oncology fellow was awarded a training slot on the UTHSCA training grant.

Fellow: Kristi George, MD

Mentor: Gail E. Tomlinson, MD, PhD (Greehey Distinguished Chair in Genetics and Cancer, Interim Chair of Pediatrics and Division Chief, Pediatric Hematology/Oncology)

Project: Screening for novel therapeutic agents for the treatment of aggressive childhood hepatoblastoma.

## TOO EARLY FOR RESULTS

**RP150032** (PI, Li, Xiao-Nan; Developing New Combinatory Therapies for Pediatric High Grade Glioma)

**RP160487** (PI, Shiio, Yuzuru; Cytokine signaling in Ewing sarcoma)

**RP160716** (PI, Houghton, Peter; Texas pediatric patient derived xenograft facility)

**RP160739** (PI, Shi, Xiaobing; Targeting histone acetylation readers in MLL-translocated leukemias)

**RP160844** (PI, McHardy, Stanton; Center for Innovative Drug Discovery Enhancement of a Shared Cancer Resource for South Texas)

**RP170152** (PI, Amatruda, James; Targeting the HNF4A and WNT/Beta-catenin pathways in childhood malignant yolk sac tumors)

**RP170169** (PI, Li, Xiao-Nan; High throughput combinatory drug screening for pediatric medulloblastoma with a dysregulated EZH2 pathway)

**RP1701691** (PI, Lewis, Michael; Patient-Derived Xenograft and Advanced in Vivo models (PDX-AIM) Core Facility)

**RP170180** (PI, Huang, Suyun;).

This award will study the pathogenesis and mechanisms of glioblastoma, a malignant brain tumor that occurs in children and adults. This understanding may impact future treatments that will improve the outcome of this deadly malignancy.

**RP170231** (PI, Lozano, Guillermina; Identifying vulnerabilities in mutant p53 driven tumorigenesis)

The proposal is focused on a new p53 mutant somatic model of bone cancer that metastasizes in mouse models. The data generated from these studies may impact future treatment strategies for children with malignant bone cancers.

**RP170470** (PI, Lee, Brendan; Mechanisms of Notch dysregulation in pediatric osteosarcoma)

**RP170488** (PI, Li, Xiao-Nan; High throughput combinatory drug screening for pediatric medulloblastoma with a dysregulated EZH2 pathway)

**RP170493** (PI, Fernandez, Maria; For Our Children: A tailored multi-level intervention for parents and healthcare providers to increase HPV vaccination rates)

**DP170043** (PI, Leen, Ann; Improving the Outcome of Stem Cell Transplants for Cancer Treatment Using Multi-Virus Specific T-cells)

The intent of this grant is to support a randomized Phase 3 study to treat BK virus-associated hemorrhagic cystitis (BK-HC) in pediatric and adult recipients of allogeneic hematopoietic stem cell transplants using adoptively transferred virus-specific T cells. BK-HC occurs in approx. 25% of all transplant patients, is associated with significant morbidity and prolonged hospitalization, and is a disease without available therapies and hence represents a significant unmet medical need for the pediatric transplant population.

## RECRUITMENT AWARDS

### 2016

**RR1109** – Dr. Dean Morrison, University of Texas Southwestern Medical Center

Too early for update.

**RR160019** - Dr. Dung-fang Lee, UT Health Science Center at Houston

The investigators have a Li-Fraumeni syndrome pluripotent stem cell model that they anticipate will serve as “disease in a dish” platform to elucidate p53 mutation-mediated cancer pathogenesis and reveal the potential therapeutic targets to prevent and treat childhood cancers (e.g., osteosarcoma and brain tumor) with p53 mutation. They hope that this model system will help to elucidate the pathogenesis of childhood cancers that has in limited by a number of factors including access to patient samples, tumor heterogeneity, and the lack of reliable model organisms.

**RR160047** - Dr. Omid Veiseh, Rice University

Too early for update.

**RR160062** – Dr. Myron Ignatius, UT Health Science Center at San Antonio

Embryonal rhabdomyosarcoma (ERMS), a pediatric muscle tumor, is a RAS driven cancer. The investigators will assess whether Notch signaling, which is critical for normal stem cell function and expressed in ERMS tumors, has a role in the self-renewal of tumor propagating cells/cancer stem cells.

### 2017

**RR170023** - Dr. Stephen Mack, Baylor College of Medicine

Dr. Mack will focus on providing an integrated genomics and epigenomics platform to pinpoint and functionally evaluate novel targets for CNS tumors.

**RR170026** - Dr. Benjamin Fregly, Rice University

Osteosarcoma, a malignant bone tumor of children and adults, may especially impair one’s ability to walk, run, or engage in physical activities when it occurs in the pelvic region. The current project is seeking to improve this situation by providing orthopedic oncologists with objective, personalized predictions of each child’s post-surgery function for different surgical decisions under consideration. By using child-specific computational models to generate these

predictions, the investigators hope to maximize each patients's ability to return to desired pre-surgery activities.

**RR170062** - Dr. Rosa Uribe, Rice University

Dr. Uribe's research focuses on looking at neural crest cells during peripheral nervous system development using zebrafish models. Her goal is to find treatments for neural crest-derived conditions and cancers.

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## CLINICAL TRIALS EMANATING FROM CPRIT AWARDS

NCT00902044: Administration of HER2 chimeric antigen receptor expressing T cells for subjects with advanced Sarcoma (HEROS)

NCT01187810: A phase I study of intravenous emulsion fenretinide (4-HPR, NSC 374551) in children with recurrent or resistant acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), and non-Hodgkin's lymphoma (NHL) IND #70,058

NCT01553071: Phase I Trial of Intravenous Fenretinide (4-HPR) plus Intravenous Safingol for Patients with Relapsed Malignancies

Phase I/II trial of fenretinide/LXS oral powder (NSC 374551) plus ketoconazole in recurrent ovarian cancer and primary peritoneal carcinoma

NCT01729429: An Intervention Promoting HPV Vaccination in Safety-net Clinics

NCT01962896: A Phase II Study of Sirolimus and Erlotinib in Recurrent/Refractory Germ Cell Tumors

NCT02075177: Phase I study of fenretinide (4-HPR, NSC 374551) Lym-X-Sorb™ oral powder plus ketoconazole plus vincristine in patients with recurrent or resistant neuroblastoma (IND # 68,254)

NCT02075177: Expanded access study of fenretinide (4-HPR, NSC 374551) Lym-X-Sorb™ oral powder plus ketoconazole in patients with recurrent or resistant neuroblastoma (IND # 68,254).

NCT02108522: Phase I/II Study of the Administration of Multi-Virus-Specific Cytotoxic T Lymphocytes (CTLs) Expressing CD19 Chimeric Receptors for Prophylaxis of Therapy of Relapse of CD 19 Positive Malignancies Post Hematopoietic Stem Cell Transplantation (Multi-PRAT)

NCT02420717: A Phase II Study of the Combination of Ruxolitinib or Dasatinib with Chemotherapy in Patients with Philadelphia Chromosome (Ph)-Like Acute Lymphoblastic Leukemia (ALL) 2014-0521

NCT0249515: Phase II study of intravenous fenretinide in peripheral T cell lymphoma (PTCL).

NCT02535845: Developing a self-persuasion intervention promoting adolescent HPV vaccination

NCT02537756: Developing a self-persuasion intervention promoting adolescent HPV vaccination

Incorporation of Genomic Sequencing into Pediatric Cancer Care

## Use of Disulfiram in Glioblastoma

Prospective evaluation of the use of imaging and computational tools to improve risk stratification in children with bone cancer

Using Imaging and Computational Tools to Improve Risk Stratification in Children with Bone Cancer. STU 042015-026

A Phase I/II Study of BMN673, an Oral Poly(ADP-Ribose) Polymerase Inhibitor, Plus Temozolomide in Children with Refractory or Recurrent Malignancies

Evaluation of the clinic-level effect of the program on HPV vaccine initiation and completion rates at Harris Health pediatric clinics

Evaluation of a patient education video to promote HPV vaccination among pediatric patients in a Safety Net healthcare setting

Rapid virus specific T cell methodology and an optimized CD19 CAR

Soft tissue sarcoma biospecimens collection and banking – multi-site trial

Prospective evaluation of the use of imaging and computational tools to improve risk stratification in children with bone cancer.

Using Imaging and Computational Tools to Improve Risk Stratification in Children with Bone Cancer

Pediatric Hepatic Malignancy International Therapeutic Trial (PHITT)

# Advisory Committee on Childhood Cancer

COMMITTEE REPORT MAY 2018

SUSAN BLANEY, M.D.  
CHAIR, ACCC

# ACCC Update

- Introduction of ACCC sites and members
- Background childhood cancer
- Challenges
- Highlights and progress
- ACCC recommendations
- Summary



# **Review of ACCC Members and Sites**

# Committee Membership

MEMBER	INSTITUTION	MEMBER	INSTITUTION
Susan Blaney, MD	TCCC/BCM	Greg Aune, MD, PhD, FAAP	UT San Antonio
Stephen Skaeck, MD, PhD	UT Southwestern	Juan Carlos Bernini, MD	Vannie Cook Clinic
Karen Albritton, MD	Cook Children's	Stan Goldman, MD	Medical City Dallas
Tim Culliver*	Adam's Angels Ministry	Virginia Harod, MD	Dell Children's Hospital
Eugenie Kleinerman, MD	MD Anderson Cancer Center	Lisa Hartman, MD	El Paso Children's Hospital
Annette Leslie*	Carson Leslie Foundation	Barkat Hooda, MD	UTMB Galveston
David Poplack, MD	TCCC/BCM	Julie Luke, CPNP	Methodist Children's Hospital
Pat Reynolds, MD, PhD	Texas Tech HSC	Meaghan Granger, MD	Cook Children's Hospital
Mohamad Al-Rahawan, MD, MPH	Texas Tech HSC Covenant Hospital	Sheila Thampi, MD	CHofSA
James Amatruda, MD, PhD	UT Southwestern		

# ACCC Representation Across Texas



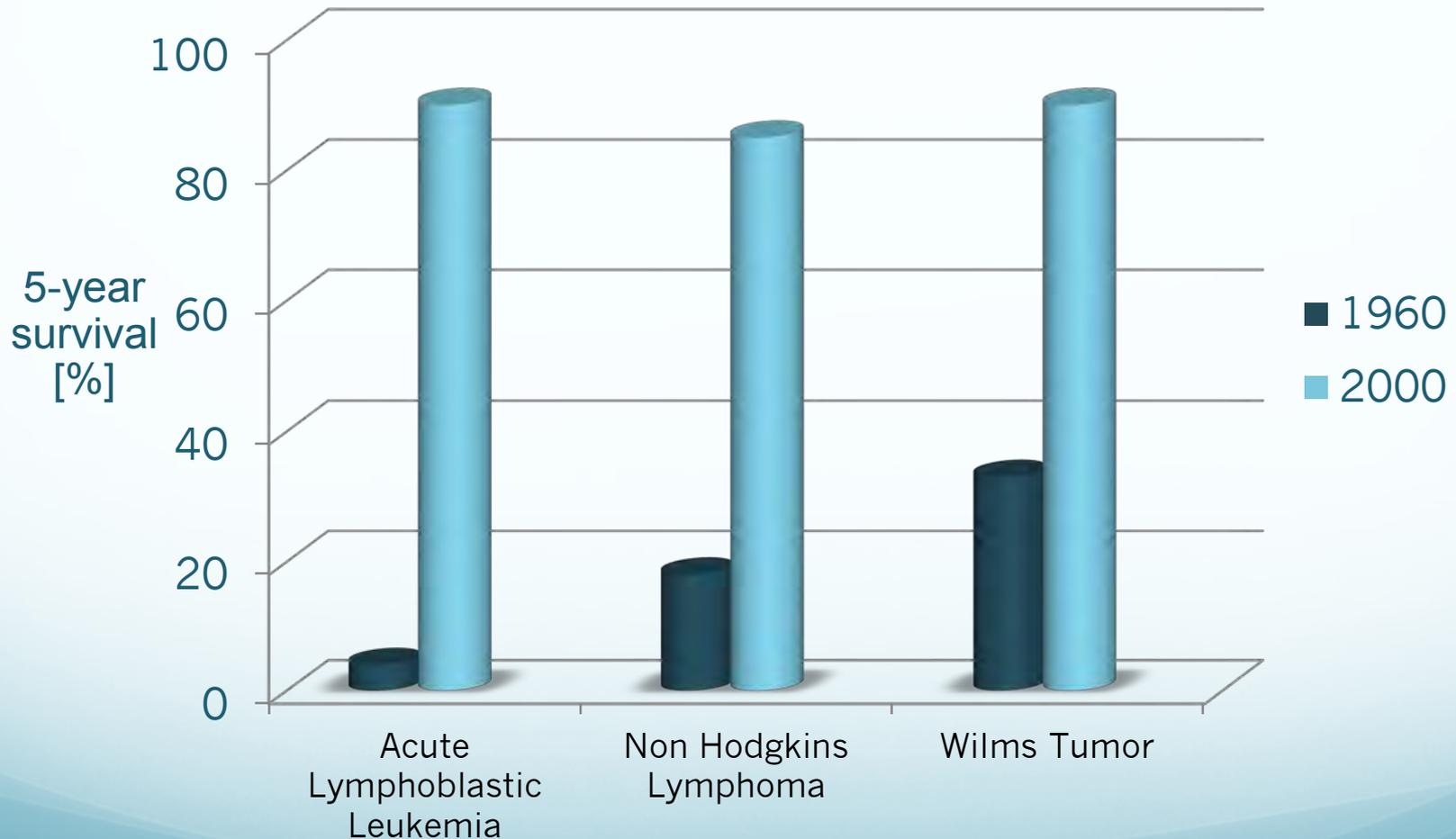


# Pediatric Cancer in the U.S.

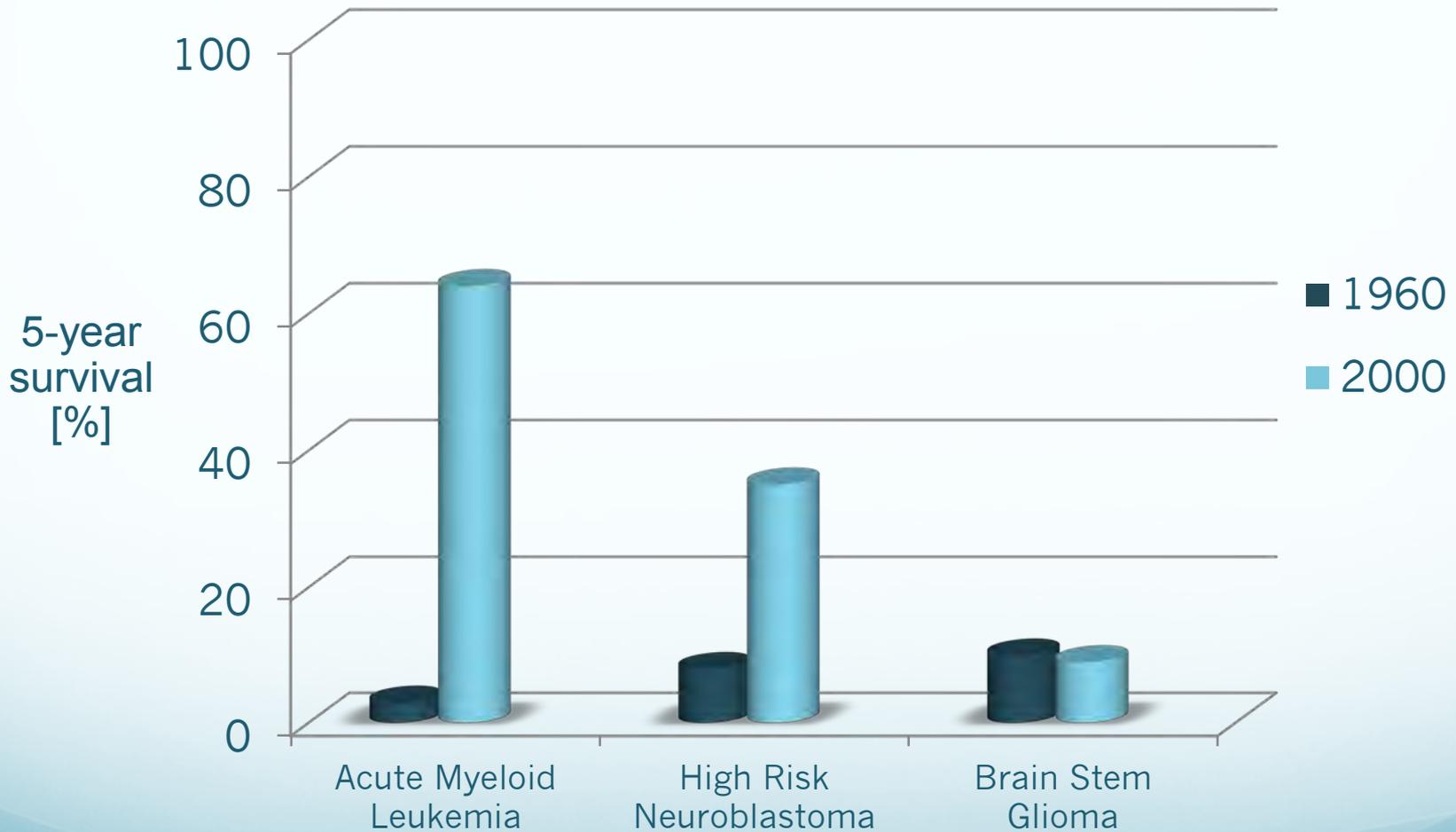
- The leading cause of death from disease in children\*
- 1 in every 330 Americans develops cancer before age 20
- 1 in 750 20-year-olds alive in the US today is a survivor of childhood cancer

\* 0 – 19 years of age

# Curing Cancer - Progress

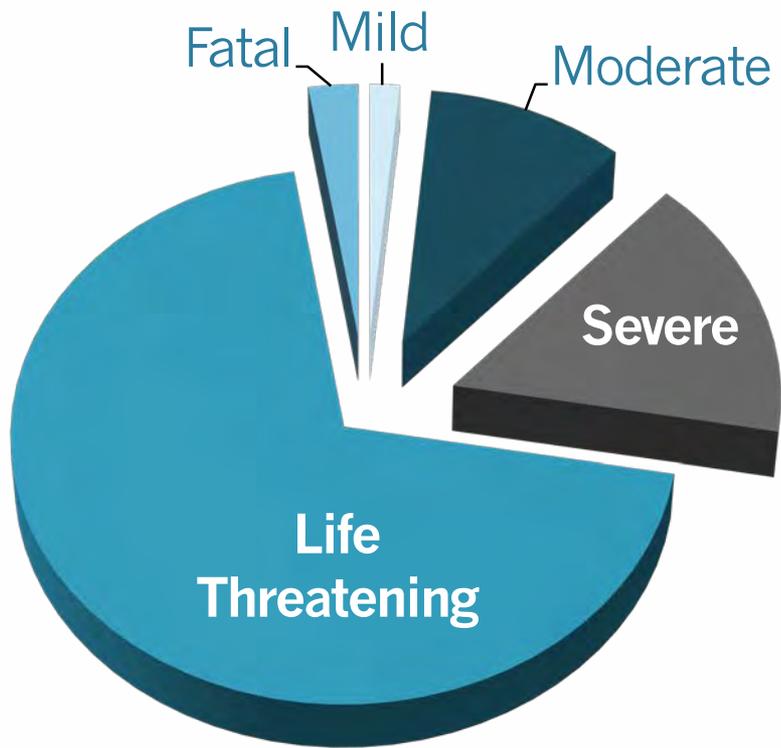


# Curing Cancer - Opportunities



# Curing Childhood Cancer

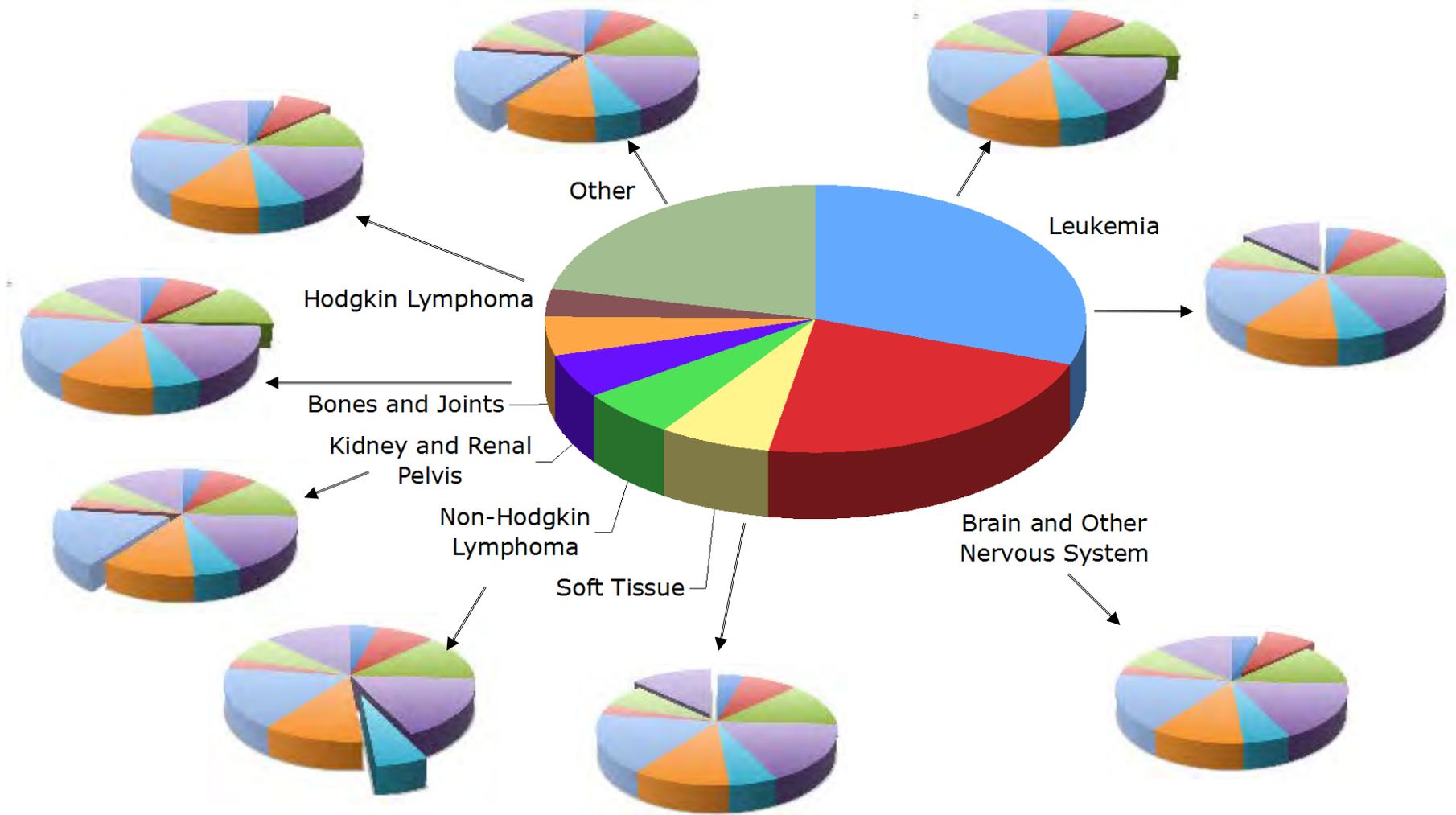
## Side Effects



## Late Effects



# Molecular Evolution of Childhood Cancer



# Scientific and Practical Challenges

- Improve cure rates
- Diminish acute toxicity
- Minimize risk for late effects
- Integrate targeted therapies
- Drug access for pediatric population
- Drug shortages

# Several Highlights of CPRIT Project Progress



# Highlights

- Increased number and % of grants funded
  - > 44 projects funded
  - Increase from 4% to 24% success rate over 4 yrs
- Peer reviewed publications
  - > 173 publications
  - High impact journals, e.g. - *JCI, JCO, Blood, Nature Reviews, Nature Communications*
- Other peer-reviewed funding
  - > \$21 million to date

# Highlights

- Gene and Target Discovery
- Development of Pediatric Preclinical Models
- Biorepository Development
- Biomarker Discovery
- Drug Discovery / Optimization
- Development of New Strategies for Immunotherapy
- Development and Implementation of Clinical Trials
- Prevention Strategies and Implementation for HPV

# Highlights

- **Training Grants**
  - Pediatric oncology fellow, Dr. Kristi George, 2<sup>nd</sup> year training slot on the UTHSCA training grant.
  - Mentor - Gail Tomlinson, MD, PhD
- **Recruitment Grants – Established Investigator**
  - Benjamin Fregly, PhD - Rice University
    - Use of personalized computer models to predict outcome for bone cancer patients

# Highlights

## Recruitment Grants – First Time, Tenure Track Recruits

Stephen Mack, PhD - Texas Children's Cancer Center / BCM

Will focus on providing an integrated genomics and epigenomics platform to pinpoint and functionally evaluate novel targets for pediatric CNS tumors.

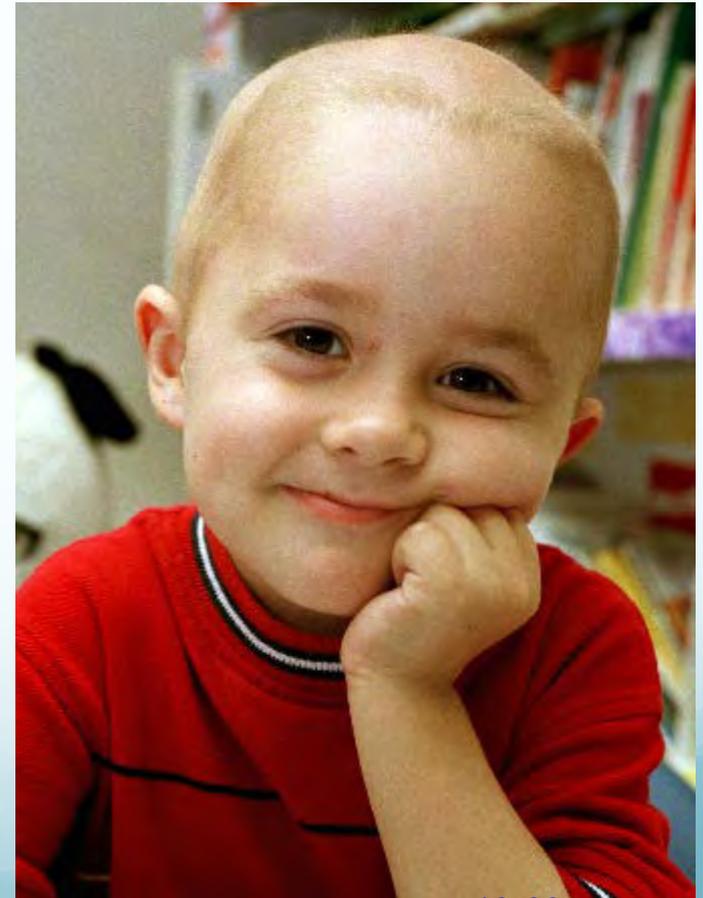
Siyuan Zheng, PhD – UT Health San Antonio

Will use genomic and proteomic data to understand the mechanisms behind the initiation, progression, treatment responses of pediatric and adult cancers.

Dr. Rosa Uribe, PhD – Rice University

Basic work looking at neural crest cells during peripheral nervous system development using a zebrafish model. Goal to find treatments for neural crest-derived conditions and cancers.

# ACCC Recommendations



# ACCC Recommendations

- Investigator-Initiated Research
  - Continue RFAs specific to childhood cancer research
  - Release a MIRA focused on childhood cancer research
  - Consider partnering with Carson Leslie Foundation for another CNS specific award
  - Immuno/cellular therapy a high priority
- Core Facility Grants
  - Continue the opportunity for institutions to submit a pediatric specific shared resource
- Recruitment Awards
  - Consider dedicating awards specific to a pediatric oncology laboratory or clinical/translational researcher

# ACCC Recommendations

- Prevention Portfolio
  - Continue ongoing prevention support opportunities
  - Target research support for highest risk patients and families (e.g., cancer pre-disposition syndromes)
- Product Development Portfolio
  - Explore innovative ways to facilitate and encourage development of therapeutics and diagnostics for childhood cancer
- Other
  - Increase the number of pediatric oncologists and laboratory scientists on CPRIT peer-review grant panels

# Summary

CPRIT's commitment to funding groundbreaking childhood cancer research and prevention programs is having - and will continue to have - a profound positive impact for children with cancer - as well as for their families - for generations to come....

# Thank you to CPRIT!

on behalf of the ACCC,  
our colleagues,  
and most importantly  
our patients and their families...







**Product Development Research Advisory Committee  
Annual Report**

**Submitted to CPRIT Oversight Committee May 16, 2018**

The members of the Product Development Advisory Committee (PDAC) appreciate the opportunity to provide the PDAC’s annual report and recommendations to the Oversight Committee regarding CPRIT’s Product Development Research Program. We welcome a continuing dialogue with the Oversight Committee and CPRIT staff to enhance and improve Texas’ position as a leader in cancer prevention, cancer research, and cancer product development.

Texas is recognized around the country for its commitment to prevent and cure cancer. Along with its world-renowned academic medical centers such as M.D. Anderson Cancer Center, Baylor College of Medicine, and UT Southwestern Medical Center, the formation and funding of CPRIT established Texas as a top destination for the advance of innovative, cutting-edge research and the development of products targeting cancer.

CPRIT’s Product Development Research Program has the potential to be at the forefront of new, game changing cancer drugs, diagnostics, and tools. The Product Development Research Program is attracting some of the best cancer-focused technologies to Texas for company formation and relocation. Companies funded by CPRIT have the potential for a lasting economic and medical benefit through the resulting healthcare innovation and biotechnology ecosystem that otherwise would not exist.

CPRIT has awarded 32 grants totaling \$330 million to 29 companies since 2010. These companies have raised \$1.7 billion in follow-on funding after receiving CPRIT awards.

**Product Development Advisory Committee Membership**

The PDAC is an *ad hoc* advisory committee that offers guidance to the Oversight Committee on issues related to CPRIT’s Product Development Research Program. CPRIT’s Product Development Research Program reduces the burden of cancer by bringing improved products to market and growing the Texas life sciences ecosystem.

Members of the Oversight Committee and representatives from the life science industry trade association, CPRIT staff, and Texas venture capital companies nominated members of the PDAC. Listed below are the current PDAC members (asterisks identify CPRIT current and former grantees):

Jonathan MacQuitty, Ph.D., <b>Chair</b> <i>Venture Partner, Lightspeed Venture Partners</i>	David Lowe, Ph.D.,* <b>Vice Chair</b> <i>Co-Founder, Aeglea Biotherapeutics</i>
------------------------------------------------------------------------------------------------	------------------------------------------------------------------------------------

David Arthur* <i>CEO and Director, Salarius Pharmaceuticals</i>	Bruce Butler, Ph.D. <i>Vice President, Research and Technology, Director, Office of Technology Management UT Health Sciences Center at Houston</i>
Paul Lammers, M.D.* <i>CEO and President, Triumvira Immunologics, Founder Mirna Therapeutics</i>	Gary Latham, Ph.D.* <i>Sr. V.P., Research and Development, Asuragen</i>
Kevin LaLande <i>Managing Director, Santé Ventures</i>	Andrew Strong, JD* <i>Partner, Pillsbury Winthrop Shaw Pittman, LLP Founding CEO &amp; President, Kalon Biotherapeutics</i>
Brenton Scott, Ph.D.* <i>President and COO, Pulmotect</i>	Greg Stein, M.D.* <i>CEO, Curtana Pharmaceuticals</i>
Ilia Tikhomirov* <i>President and CEO, Formation Biologics</i>	James Topper, M.D., Ph.D. <i>Managing General Partner, Frazier Healthcare Partners</i>
Matt Winkler, Ph.D.* <i>Founder, Asuragen and Mirna Therapeutics</i>	

\* Past or current CPRIT grantees

### **Product Development Research Program Priorities**

The Oversight Committee's 2018 program priorities for the Product Development Research Program are:

- Funding novel projects that offer therapeutic or diagnostic benefits not currently available; i.e., disruptive technologies;
- Funding projects addressing large or challenging unmet medical needs;
- Investing in early stage projects when private capital is least available;
- Stimulating commercialization of technologies developed at Texas institutions;
- Supporting new company formation in Texas or attracting promising companies to Texas that will recruit staff with life science expertise, especially experienced C-level staff to lead to seed clusters of life science expertise at various Texas locations; and
- Providing appropriate return on Texas taxpayer investment.

## **Previous PDAC Recommendations – Status Update**

The Oversight Committee reactivated the current PDAC in 2014. The PDAC's first project was to provide advice regarding adoption of uniform revenue sharing terms for the Product Development Research Program. The Oversight Committee recognized the PDAC's contribution to the discussion as largely responsible for reaching a consensus policy for CPRIT's current standard revenue sharing terms.

The PDAC offered five recommendations for CPRIT's Product Development Program in its 2017 annual report to the Oversight Committee. We are gratified that the Oversight Committee implemented four of the PDAC's five recommendations. We believe that policy actions taken by the Oversight Committee support the momentum CPRIT is building to grow the life sciences infrastructure in Texas and accelerate the potential for breakthroughs in cancer prevention and cancer cures.

Due to circumstances described below, the Oversight Committee was unable to act on the PDAC's fifth recommendation, to increase investment in Product Development Research.

## **PDAC Discussion**

The PDAC met on April 17, 2018, to discuss issues related to the Product Development Research Program. A primary topic of discussion was the number of product development research awards approved in 2017. The Oversight Committee approved only one product development research grant in 2017, to ViraCyte, in August. Prior to the ViraCyte award, Bellicum Pharmaceuticals and Molecular Templates received the most recent product development research awards in November 2016. Over the past eighteen months (November 2016 to May 2018), CPRIT has awarded three product development research awards totaling \$41.1 million, including one application cycle when no award recommendations were put forward by the Product Development Review Council (PDRC). During the same eighteen-month period, the Academic Research Program approved 167 grants totaling \$270 million and the Prevention Program approved 26 grants totaling \$39.4 million.

The PDAC recognizes that the Oversight Committee may act only on grant recommendations made by the Program Integration Committee and the Product Development Review Council. The Oversight Committee has approved every product development research award recommendation presented by the Program Integration Committee, which itself has endorsed every grant proposal put forward by the Product Development Review Council. We believe that the issue underlying the declining number of product development research awards arises after the applicants are advanced into due diligence and before the Oversight Committee considers the award recommendations. Since the November 2016 award cycle, 14 companies were advanced into due diligence and only 3 were recommended for funding by the Product Development Review Council (a success rate of 21%). Prior to this period, the likelihood of being recommended for funding if a company was advanced into diligence was roughly 3 out of 4 applications (a success rate of 75%).

While we do not have enough information to understand if this is a continuing trend or an unusual event, the drop in the number of product development awards is significant and troubling. Even if one excludes the most recent 18 months, the success rate for a product development research award applicant averages about ten percent. A substantial amount of work is necessary to complete a product development award application. These applications generally run 60 pages and the process from release of an RFA to the recommendation for funding by the Product Development Review Council takes roughly 6 to 7 months. A prolonged decline in the number of product development awards discourages potential applicants from submitting a proposal because they perceive the amount of effort necessary to complete the review process is unlikely to lead to an award. Moreover, this negatively impacts our academic institutions like MD Anderson, UT Southwestern and Baylor College of Medicine's efforts to recruit the very best companies and their technologies to the Texas. Ultimately this subverts CPRIT's mission to enhance the potential for medical breakthrough and to attract companies that will create a substantial increase in cancer research and high quality new jobs in the state.

Dr. Jack Geltosky, Chair of the Product Development Review Council, joined our meeting and provided helpful insight. Both Dr. Geltosky and Chief Product Development Office Mike Lang report that the recent drop in the number of award recommendations is not indicative of a decline in the quality of the applications. With this information, the PDAC focused our discussion on increasing the number of quality applicants, improving the applicants' prospects during the review process, and identifying ways to improve the review of applications.

### **2018 PDAC Policy Recommendations**

To fulfill its statutory mandate and to achieve the Oversight Committee's Program Priorities, the PDAC offers three recommendations. In addition, we reiterate our recommendation from 2017 that the Oversight Committee increase the investment in Product Development Research.

Recommendation 1: CPRIT should conduct more outreach to increase the number of high quality applicants.

The number of applications submitted for the past several product development review cycles has remained relatively steady at 20 applications per cycle. Several PDAC members felt that CPRIT is missing opportunities to increase the pipeline of promising company applications, which in turn will boost the number of company awards. CPRIT should raise its profile among the national network of life science venture capitalists and oncology companies. Not only will this help to highlight CPRIT's unique product development research program and the work done by its funded companies in Texas, but it also provides CPRIT the opportunity to promote its grant program, particularly to companies and investors outside of Texas. In addition to the outreach efforts that CPRIT staff are doing throughout the state, the PDAC believes that it is important for CPRIT staff to attend high profile oncology, life

science, and venture capital conferences outside of the state to network with early stage companies and their investors.

Recommendation 2: CPRIT should provide more guidance to potential applicants prior to submitting applications to increase the number of high quality applications.

Unlike a typical angel or venture funding decision process, CPRIT's product development review allows limited interaction between the company and investment decision makers. As a result, missing information or an ambiguity in an application that would be relatively simple to address may cause reviewers to reject the application from consideration. Although CPRIT allows applicants to resubmit their applications in future application cycles, the additional time before the applicant can provide the missing information sought by the reviewers can be substantially disadvantageous to an early stage company. The PDAC recommends that CPRIT enhance support to applicants as they prepare their applications to help ensure high quality submissions. These resources can be webinars with reviewers and CPRIT Product Development Research Program staff that provide insight into the review process and what items constitute an excellent application. CPRIT may also consider working with local business incubators that can provide technical assistance to product development applicants.

Recommendation 3: CPRIT should consider changes to the product development review process to increase the likelihood of success for high quality companies.

All PDAC members are external to the CPRIT product development review process. For those PDAC members who are familiar with recent applications submitted for review, it appears that the Product Development Review Council is becoming less tolerant regarding the degree of risk it will accept in the companies recommended for CPRIT awards. If this is accurate, we believe this is the wrong path for CPRIT to take. Innovations rarely arise from taking the safe course, especially in the initial stages of development. Investing in early stage oncology companies is inherently risky. This was true when CPRIT was created with its mission to expedite innovative treatments for cancer patients and it remains true today.

CPRIT plays a special role by investing in early stage companies before many venture capitalists or other large investors are willing to do so. CPRIT's investments support the preclinical and early clinical trial work that is crucial for attracting additional funding to continue the project. If CPRIT is becoming less tolerant of risk, then a crucial source of investment dries up at a critical stage in company development.

We do not recommend CPRIT lower its standards for the company awards. CPRIT is known in the community as a discerning investor. The significant amount of additional funding raised by companies after receiving their CPRIT awards is testament to CPRIT's rigorous review process. Rather, we recommend that the Oversight Committee endorse its willingness to accept a high degree of risk in the

outcome of high-quality projects that are innovative and, if successful, will expedite cancer cures and treatments. CPRIT's willingness to tolerate risk for projects where the impact on cancer treatment is likely to be truly profound should be communicated to potential applicants and, more importantly, to the Product Development Review Council for their consideration during the review process.

In addition to affirming CPRIT's willingness to accept uncertain outcomes, the PDAC also recommends changes to the current review process to increase the number of successful companies. As noted in our second recommendation, there are few opportunities for company applicants to interact with decision makers. As a result, some Product Development Review Council members make their recommendations for grant awards based upon a *de novo* review of the application (6 to 7 months after the application was originally submitted) without having spoken to the company under consideration or having watched their presentation. The PDAC understands that, to some extent, the lack of interaction is due to time constraints and CPRIT's need to maintain a consistent review process for all applicants. At a minimum, the PDAC strongly recommends that a company that has progressed to due diligence has an opportunity to address the full Product Development Review Council and to answer questions and address concerns that arise during the due diligence process. Adding this opportunity during the final phase of the product development review process when only the most likely candidates for awards are still under consideration should not increase significantly the time required for the review. Ensuring that all Product Development Review Council members hear from the company applicant to have their questions addressed may increase the number of companies recommended for awards. Further to this process, the PDAC recommends that applicants be afforded the opportunity to address in their applications the concerns expressed by the Product Development Review Council prior to the Council's final recommendation on the grant award.

Recommendation 4: CPRIT should increase its investment in product development research.

The PDAC discussed how to best utilize remaining CPRIT product development research grant funding, which CPRIT estimates to be approximately \$210 million if the current 75/25 split between academic research and product development awards remains in place. The committee unanimously recommended increasing CPRIT's investment in product development, specifically by focusing on providing grant money to support clinical studies and trials.

PDAC members noted that the California Institute of Regenerative Medicine (CIRM), an agency similar to CPRIT in many respects, has received criticism for not emphasizing clinical trials and product development over constructing research buildings and funding basic research. Cures, or at least documented progress towards advancing cures to approval, have been limited in the California experience.

Unlike CIRM, CPRIT has not used its funds to construct buildings. CPRIT has funded more product development than CIRM, as well as a sustained commitment to clinical trial support. However,

CPRIT's historical funding weight of 81% towards academic research and recruitment versus 19% for Product Development Research may subject CPRIT to criticism similar to that of CIRM. This will become increasingly important as CPRIT approaches the end of its funding authorization. CPRIT should place significantly greater emphasis on clinical studies and Phase I and II clinical trials when investing CPRIT's remaining grant funds. Clinical trials are the best evidence that the cures many Texans expected when creating CPRIT are under development. Supporting early stage clinical trials is inherently risky and some promising treatments will fail. But not funding clinical trials poses greater risks to the pipeline of potential cancer treatments and cures. CPRIT's investment in a well-designed clinical trial for an innovative treatment that ultimately fails is forgivable; failing to support clinical trials is not.

The PDAC recommends CPRIT emphasize funding clinical projects that will demonstrate human proof of principle in an appropriate period, preferably before the agency's closure, currently set at August 31, 2023. Doing so prioritizes direct patient needs. Currently CPRIT allocates approximately \$60 - \$70 million per year for product development. This means that CPRIT can award three to four major Product Development grants annually, typically in the \$12 - \$20 million range. The PDAC recommends increasing the total amount CPRIT allocates for Product Development by 50% annually (\$90 - \$100 million). This will increase the number of major awards to five or six grants per year. Doing so increases the probability that the grantees will develop useful cancer products in the period remaining for CPRIT. Continuing at the current level increases the risks that useful cancer products will not be generated before CPRIT ends.





CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

**Product Development Advisory Committee**  
Member Nomination

**Andrew Strong**

Partner

Pillsbury Winthrop Shaw Pittman LLP





**Andrew L. Strong | Partner**  
Corporate  
+1.713.276.7677  
[andrew.strong@pillsburylaw.com](mailto:andrew.strong@pillsburylaw.com)

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Andrew Strong, a Pillsbury partner in the firm's Houston and Austin offices, has extensive experience representing many of the firm's life sciences clients and routinely advises on corporate and securities, mergers & acquisitions, private and public financing, university licensing, executive compensation and regulatory matters.

Andrew's clients include public- and private-sector entities in the emerging technology and life sciences industries and public and private academic institutions. Andrew previously served as the General Counsel and Compliance Officer for the Texas A&M University System where he was responsible for, among other things, business transactions, technology commercialization, research compliance, real estate and litigation for the System's 11 public universities, 7 state agencies and health science center.

Andrew was the Founding President and CEO of a start-up biotech company (Kalon Biotherapeutics) which was formed by the Texas A&M System in 2011 and was integral to the multi-billion dollar award from the Biomedical Advanced Research & Development Authority (BARDA) in 2012. Over the course of three years, Andrew successfully grew Kalon to over 100 employees and secured significant partnerships with MD Anderson Cancer Center and the pharmaceutical company GlaxoSmithKline. He then successfully ran a process to secure a strategic exit for Kalon that resulted in the sale of the company to Fujifilm and Mitsubishi in December 2014.

Following his return to Pillsbury in 2015, Andrew set his focus on helping grow the Texas biotechnology industry and now represents over 20 Texas private and public biotech companies, a number of which are CPRIT-funded companies.



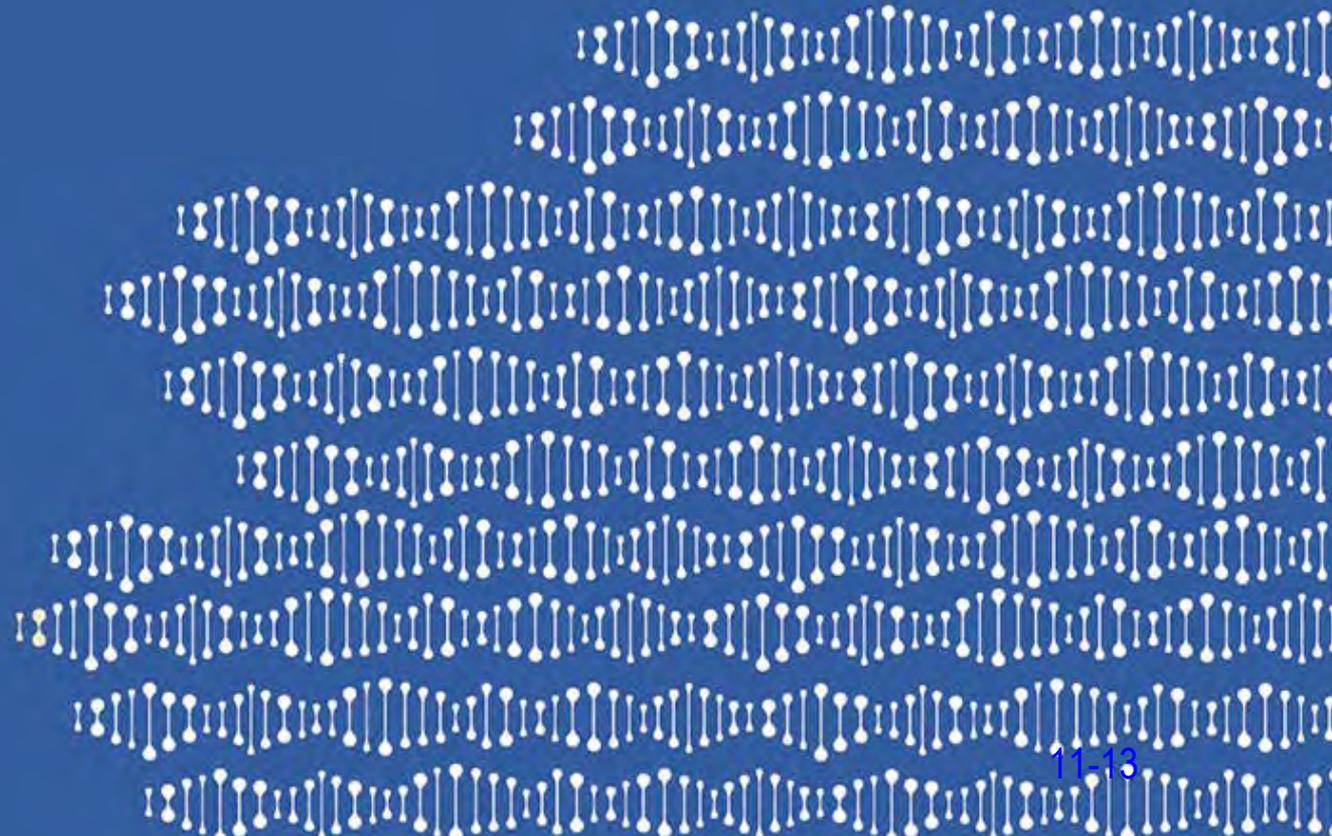


CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

# Product Development Advisory Committee – Annual Report

May 16, 2018

Presented By:  
Andrew Strong, JD



# PDAC – *ad hoc* Advisory Committee

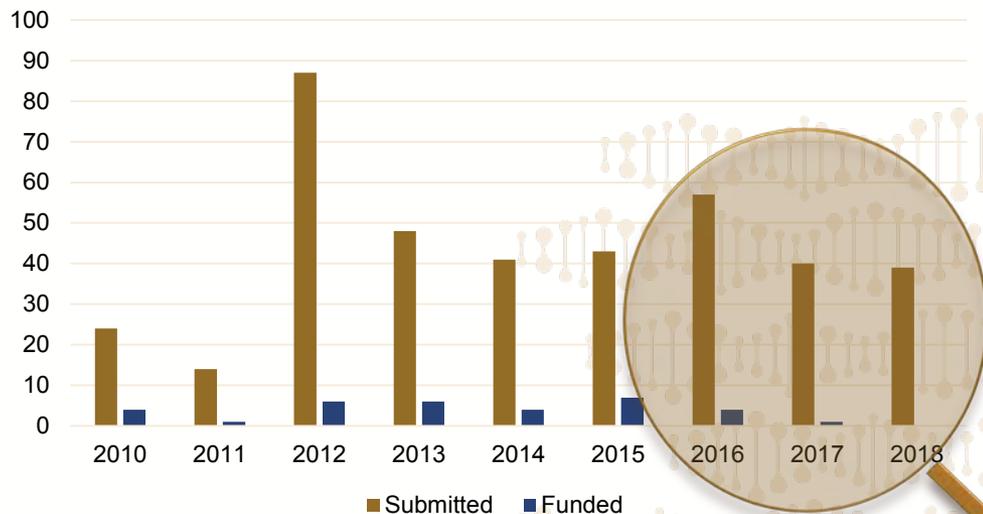
<b>Jonathan MacQuitty, Ph.D., Chair</b> Venture Partner, Lightspeed Venture Partners	<b>David Lowe, Ph.D.,* Vice Chair</b> Co-Founder, Aeglea Biotherapeutics
<b>David Arthur*</b> CEO and Director, Saliarius Pharmaceuticals	<b>Bruce Butler, Ph.D.</b> Vice President, Research and Technology, Director, Office of Tech Management UT Health Sciences Center at Houston
<b>Paul Lammers, M.D.*</b> CEO and President, Triumvira Immunologics, Founder Mirna Therapeutics	<b>Gary Latham, Ph.D.*</b> Sr. V.P., Research and Development, Asuragen
<b>Kevin LaLande</b> Managing Director, Santé Ventures	<b>Andrew Strong JD</b> Partner, Pillsbury Winthrop Shaw Pittman, Founding CEO & President, Kalon Biotherapeutics
<b>Brenton Scott, Ph.D.*</b> President and COO, Pulmotect	<b>Greg Stein, M.D.*</b> CEO, Curtana Pharmaceuticals
<b>Iliia Tikhomirov*</b> President and CEO, Formation Biologics	<b>James Topper, M.D., Ph.D.</b> Managing General Partner, Frazier Healthcare Partners
<b>Matt Winkler, Ph.D.*</b> Founder, Asuragen and Mirna Therapeutics	

\* *Current or former grantee*



# Product Development Application History

PD Applications Over Time



FY	Submitted	Funded	Success Rate
2010	24	4	17%
2011	14	1	7%
2012	87	6	7%
2013	48	6	13%
2014	41	4	10%
2015	43	7	16%
2016	57	4	7%
2017	40	1	3%
2018	39	?	?
<b>Total</b>	<b>393</b>	<b>33</b>	
<b>Total 2010-2017</b>	<b>354</b>	<b>33</b>	<b>9.3%</b>

Overall Success Rate: 9%  
(354 apps, 33 approved awards)

Since 11/2016 award cycle, 14 applications were advanced into DD and the PDRC recommended only 3 (a success rate of 21%). Prior to this period, roughly 3 out of 4 applications advanced to DD were recommended for funding (a success rate of 75%)



# 2018 PDAC Policy Recommendations

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## *Increase Awareness and Receipt of High Quality Product Development Applications*

- 1. CPRIT should conduct more outreach to increase the number of high quality applicants.**
- 2. CPRIT should provide more guidance to potential applicants prior to submitting applications to increase the number of high quality applications.**

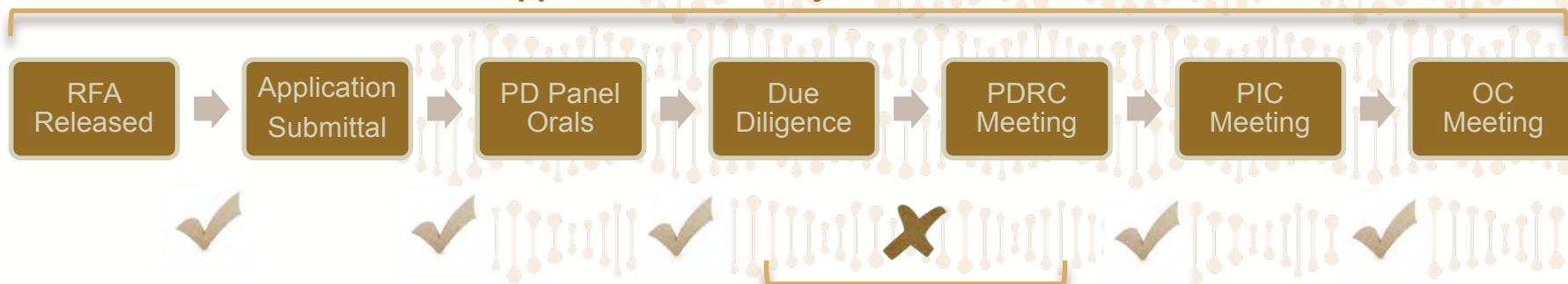


# 2018 PDAC Policy Recommendations

## *Enhance PDRC Review Process to Increase Likelihood of Awards*

- 3. CPRIT should consider changes to the product development review process to increase the likelihood of success for high quality companies.**

*PD application review cycle – 6 to 7 months*



# 2018 PDAC Policy Recommendations

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## *CPRIT's PD Awards are Materially Contributing to the Growth of the Texas Biotech Industry*

### **4. CPRIT should increase its investment in product development research.**

- Currently PD allocation is \$60 - \$70M/yr (3 to 4 awards/yr)
- PDAC strongly urges the Oversight Committee to increase the total amount CPRIT allocates for PD by **50% annually** (\$90 - \$100 million) (equates to 6 to 7 major awards/yr)

*Building off of our world renown centers such as MD Anderson, UT Southwestern and Baylor College of Medicine, CPRIT has begun to dramatically reshape the Texas biotech industry landscape. The recruitment of drug development experts is critical to this growth*



# 2018 PDAC Policy Recommendations

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***Thank you!***







CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

**Clinical Trials Advisory Committee  
Members**

**C. Kent Osborne, M.D., CHAIR**

Tina and Dudley Sharp Chair in Oncology  
Director, Dan L Duncan Comprehensive Cancer Center  
Professor of Medicine and Molecular and Cellular Biology  
Baylor College of Medicine

**Carlos L. Arteaga, M.D.**

Director of the Harold C. Simmons Comprehensive Cancer Center  
Associate Dean of Oncology Programs  
The University of Texas Southwestern Medical Center

**S. Gail Eckhardt, M.D., FASCO**

Chair, Department of Oncology  
Professor and Associate Dean of Cancer Programs  
Director, LIVESTRONG Cancer Institutes  
Dell Medical School | The University of Texas at Austin  
The University of Texas at Austin

**David S. Hong M.D.**

Deputy Chair of the Department of Investigational Cancer Therapeutics  
Clinical Medical Director of the Clinical Center for Targeted Therapy (CCTT)  
Associate Vice President of Clinical Research  
University of Texas M.D. Anderson Cancer Center

**Ruben A. Mesa, M.D., FACP**

Director  
Mays Cancer Center (An Affiliation UT Health San Antonio/ MD Anderson Cancer Center)  
Mays Family Foundation Distinguished University Presidential Chair  
Professor of Medicine  
The University of Texas Health Science Center San Antonio

**C Patrick Reynolds, M.D., Ph.D.**

Director, Cancer Center  
Professor of Pediatrics, Internal Medicine, and  
Cell Biology & Biochemistry  
School of Medicine  
Texas Tech University Health Sciences Center



## Biosketch for Dr. C. Ken Osborne

5/4/2018

Dr. Osborne has been a clinician scientist focusing on breast cancer for more than 40 years. He is also active clinically seeing patients and carrying out translational and clinical research. After completing medical school at the University of Missouri, residency at Johns Hopkins, and an oncology fellowship at the National Cancer Institute, he accepted his first faculty position at the University of Texas Health Science Center at San Antonio in 1977. Initially, his laboratory focused on the effects of insulin and other polypeptide growth factors on breast cancer development and progression, and he was the first to show that insulin and epidermal growth factor were regulators of breast cancer growth in preclinical models via their membrane receptors. He went on to demonstrate that the insulin like growth factors (somatomedins) were also important contributors to breast cancer growth, and he was the first to show in an in vivo model that inhibition of the IGF1 receptor could inhibit breast cancer growth, demonstrating that targeting growth factor pathways may be effective in some cancers, just like targeting the estrogen receptor is effective in another subset of breast cancer.

He then turned his studies to endocrine therapy of breast cancer and different strategies to inhibit ER signaling. He showed that tamoxifen was an effective inhibitor of the growth of estrogen receptor (ER) positive breast cancers both in vitro and in vivo and that its activity was mostly cytostatic rather than cytotoxic. This suggested that combinations of tamoxifen with chemotherapy may be detrimental if tamoxifen had an effect on reducing the number of cycling cells. He then showed that indeed tamoxifen did antagonize certain chemotherapy drugs although not through its inhibition of cell proliferation. This led to a large intergroup clinical trial that confirmed the observation that simultaneous treatment of tamoxifen with CAF chemotherapy resulted in antagonism of chemotherapy compared to the sequence of chemotherapy followed by tamoxifen. This sequence became the standard of care and remains so today.

His group was also interested in studying a new anti-estrogen that had no estrogen agonist activity like tamoxifen and other SERMS. This new agent was called fulvestrant. In a series of In vitro and in vivo studies and then in clinical trials, his group demonstrated that fulvestrant was more effective than other forms of endocrine therapy and was able to inhibit growth of tamoxifen resistant tumors. These studies, in part led to the further clinical development of fulvestrant and the preclinical data were confirmed in a series of international and national clinical studies, two of which were led by Dr. Osborne. Fulvestrant is now one of the most potent endocrine therapies available to clinicians.

Dr. Osborne's group then began a series of studies that demonstrated the importance of crosstalk between growth factor receptor and estrogen receptor pathways. Growth factor pathways through their phosphorylation of ER and its coregulators increased the agonist activity of selective estrogen receptor modulators like tamoxifen causing drug resistance. These data also suggested that blocking growth factor receptor signaling would restore tamoxifen antagonist effect. Similarly, growth factors receptor signaling activates the estrogen receptor in a ligand independent manner, causing resistance to estrogen deprivation therapies. The subsequent clinical demonstration that inhibitors of the growth factor pathway significantly improved the progression free survival of patients treated with endocrine therapy validated this preclinical data in patients.

Continuing the cross talk theme, the group showed that ER signaling reduces expression of the HER family of receptors and that blocking ER signaling upregulates growth factor receptor signaling to cause endocrine resistance. Furthermore, growth factor receptor signaling downregulates ER and blocking growth factor signaling upregulates ER to cause resistance to HER targeted therapies. These discoveries strongly suggest that both ER and growth factor receptor pathways should be blocked simultaneously to prevent escape and resistance to treatment, another laboratory observation that is now being confirmed in the clinic.

Another area of interest in Dr. Osborne's group is resistance to HER2 targeted therapies. They showed that multiple inhibitors of the HER receptor family are superior to the single agent trastuzumab and this has now been translated into clinical trials of dual targeted therapies that are more effective than trastuzumab by itself. He also showed that some patients with HER2 positive breast cancer may not need chemotherapy at all, but can be treated with dual targeted therapy alone. This de-escalation strategy is now being tested in a prospective clinical trials. Thus Dr. Osborne's group has made several important observations and contributions to both resistance to endocrine therapy and resistance to HER2 targeted therapy that have had important implications and impact in the clinic.

Dr. Osborne has also been a leader in national clinical trials. For more than a decade, he was Chairman of the Breast Cancer Committee of the Southwest Oncology Group, where he directed numerous nationwide clinical trials and was a founding member of the Breast Intergroup. He is currently the Principal Investigator of the Baylor Breast Cancer Specialized Program of Research Excellence grant which he has led for 22 years and focuses on translational research. Finally, he has chaired several national and international clinical trials. Dr. Osborne has received many awards for his accomplishments. Among his awards are the Komen Foundation Award, the Brinker International Award for Breast Cancer Research, the European Institute of Oncology Annual Breast Cancer Award, the ASCO Bonadonna Award for Breast Cancer Research, The William L. McGuire Memorial Lectureship from the SABCS Symposium and most recently, The 2018 AACR Distinguished Investigator Award for Extraordinary Scientific Achievement and Leadership in Breast Cancer Research. At Baylor College of Medicine, he is currently the Director of the Dan L Duncan Comprehensive Cancer Center and Professor of Medicine and Molecular and Cellular Biology and holds the Tina and Dudley Sharp Chair in Oncology at Baylor College of Medicine.

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Carlos L. Arteaga

eRA COMMONS USER NAME (credential, e.g., agency login): ARTEAGCL

POSITION TITLE: Associate Dean, Director, Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Guayaquil, Ecuador	M.D.	1980	Medicine
Emory University Affiliated Hospitals, Atlanta, GA		1984	Internal Medicine
University of Texas Health Sciences Center, San Antonio, TX		1987	Medical Oncology/Hematology

**A. Personal Statement**

I serve as Director of the NCI-designated Simmons Comprehensive Cancer Center (SCCC) and Associate Dean of Oncology Programs at UT Southwestern Medical Center (UTSW). My laboratory and translational program are funded by NCI and other agencies to study the pathogenesis of breast cancer, mechanism of action of and resistance to targeted therapies and their treatment implications, as well as investigator-initiated clinical trials. I am the PI of the UTSW Cancer Center Support Grant (P30 CA142543) and Leader of Project 1 of the Vanderbilt Breast SPORE (P50 CA98131). I have extensive experience in translational research, trans-institutional collaborations, and mentoring and training of junior faculty, many of whom hold independent academic faculty positions as well as leadership roles in industry.

**B. Positions and Honors****Positions and Employment**

1988-1994 Assistant Professor of Medicine, Department of Medicine, Division of Hematology/Oncology, Vanderbilt University Medical Center, Nashville, TN

1991-1994 Research Associate, VA Medical Center, Nashville, TN

1994-1998 Associate Professor of Medicine and Cell Biology, Department of Medicine, Division of Hematology/Oncology, Vanderbilt University Medical Center, Nashville, TN

1995-2000 Clinical Investigator, VA Medical Center, Nashville, TN

1998-2017 Professor of Medicine and Cancer Biology, Department of Medicine, Division of Hematology/Oncology, Vanderbilt University Medical Center, Nashville, TN

1996-2017 Director, Breast Cancer Program, Vanderbilt-Ingram Cancer Center, Nashville, TN

1999-2004 Ingram Professor of Cancer Research, Vanderbilt-Ingram Cancer Center, Nashville, TN

2005-10 Vice Chancellor's Chair in Breast Cancer Research

2009-2017 Donna S. Hall Chair in Breast Cancer Research

2010-11 Interim Director, Division of Hematology/Oncology, Vanderbilt University Medical Center

2011-2017 Associate Director for Translational/Clinical Research, Vanderbilt-Ingram Cancer Center

2013-2017 Director, VICC Center for Cancer Targeted Therapies, Nashville, TN

2017- Director & Professor, Harold Simmons Comprehensive Cancer Center and Associate Dean for Oncology Programs, UT Southwestern Medical Center

**Other Experience and Professional Memberships**

1998-2003 Member, Experimental Therapeutics-2 NIH Study Section

1999-2004 Member, Board of Scientific Counselors, NCI, NIH

2004-08 Member, NCI Parent Sub-Committee A (Review of Cancer Centers)

2004-07	AACR Board of Directors
2005-	Associate Editor or Editorial Board: <i>Cancer Cell</i> , <i>Cancer Discovery</i> , <i>Journal of Mammary Gland Biology &amp; Neoplasia</i> , <i>Breast Cancer Research</i> , <i>Cancer Biology &amp; Therapy</i>
2005-13	Deputy Editor, <i>Clinical Cancer Research</i>
2012-	Member, Scientific Advisory Board, Susan G. Komen for the Cure Foundation

### Honors

2003	AACR Richard & Hinda Rosenthal Foundation Award
1998	American Society of Clinical Investigation (ASCI)
2005	Association of American Physicians (AAP)
2007-17	American Cancer Society Clinical Research Professor
2009	American Society of Clinical Oncology Gianni Bonnadona Award
2011	Brinker Award for Scientific Distinction, Susan G. Komen for the Cure Foundation
2014-15	President American Association for Cancer Research
2015	Fellow of the AACR Academy
2015	Prize for Scientific Excellence in Medicine, American-Italian Cancer Foundation

### **C. Contributions to Science**

1. Early in my career, my laboratory was the first to report the role of IGF-I receptors and transforming growth factor (TGF)  $\beta$  on the progression of human breast cancer. These papers supported the development of therapies targeted to these signaling pathways in breast cancer.

- **Arteaga CL**, Kitten L, Coronado E, Jacobs S, Kull F, Alred C, Osborne CK: Blockade of the type I somatomedin receptor inhibits growth of human breast cancer cells in athymic mice. *J Clin Invest* 84:1418-1423, 1989
- **Arteaga CL**, Hurd SD, Winnier AR, Johnson MD, Fendly BM, Forbes JT. Anti-transforming growth factor (TGF)- $\beta$  antibodies inhibit breast cancer cell tumorigenicity and increase mouse spleen natural killer cell activity: Implications for a possible role of tumor cell/host TGF $\beta$  interactions in human breast cancer progression. *J Clin Invest* 92:2569-2576, 1993

2. A series of subsequent papers expanded on the mechanisms by which TGF $\beta$  signaling contributes to cancer progression and provided additional basis for the development of anti-TGF $\beta$  therapeutic strategies. The recent paper in *JCI* (Bhola *et al.* 2013) is probably the first demonstration of an association between a gene expression signature of TGF $\beta$  activation and resistance to anti-cancer chemotherapy.

- Muraoka RS, Dumont N, Ritter CA, Dugger TC, Brantley DM, Chen J, Easterly E, Roebuck LR, Ryan S, Gotwals PJ, Kotliansky V, **Arteaga CL**. Blockade of transforming growth factor  $\beta$  inhibits mammary tumor cell viability, migration, and metastases. *J Clin Invest* 109:1551-1559, 2002
- Biswas S, Guix M, Rinehart C, Dugger TC, Chytil A, Moses HL, Freeman M, **Arteaga CL**. Inhibition of TGF $\beta$  with neutralizing antibodies prevents radiation-induced acceleration of metastatic cancer progression. *J Clin Invest* 117:1305-1313, 2007
- Bhola N, Balko JM, Dugger TC, Kuba MG, Stanford J, Cook RS, **Arteaga CL**. TGF $\beta$  inhibition enhances chemotherapy action against triple-negative breast cancer. *J Clin Invest* 123:1348-58, 2013. PMC3582135

3. Our laboratory was one of the first to report hyperactivation of phosphoinositide 3-kinase (PI3K)/AKT as a mechanism of escape from hormone dependence in ER+ human breast cancer and, in turn, resistance to antiestrogen therapy. We were the first to show synergistic activity of antiestrogens and PI3K/AKT inhibitors against ER+/PIK3CA mutant tumors, supporting use of these combinations in currently ongoing clinical trials. Gene expression profiling revealed an estrogen-independent, ER/E2F-directed transcriptional program in breast cancer cells that adapt to estrogen deprivation. Kinome siRNA screening showed that CDK4, an activator of E2Fs, is required for estrogen-independent growth, supporting the use of recently approved CDK4/6 inhibitors for the treatment of ER+ breast cancer. Finally, we reported the first phase Ib trial of a PI3K inhibitor (buparlisib, BKM120) in combination with endocrine therapy (letrozole) in patients with metastatic ER+/HER2- breast cancer. The third paper is the basis for a global, Vanderbilt-led, phase II randomized, double-blind, placebo-controlled neoadjuvant trial of letrozole  $\pm$  the p110 $\alpha$  inhibitor BYL719 (alpelisib) for post-menopausal women with ER+/HER2- breast cancer (NCT01923168).

- Miller TW, Hennessy BT, González-Angulo AM, Fox EM, Mills GB, Ghazoui Z, Dunbier A, Anderson H, Dowsett M, Chen H, Higham C, García-Echeverría C, Shyr Y, **Arteaga CL**. Hyperactivation of

phosphoinositide 3-kinase promotes escape from hormone-dependence in estrogen-receptor positive breast cancer. *J Clin Invest* 2010; 120(7):2406-13. PMC2898598

- Miller TW, Fox EM, Balko JM, Ghazoui A, Dunbier A, Anderson H, Dowsett M, Jiang A, Smith RA, Sánchez V, Maira S-M, Manning HC, González-Angulo AM, Mills GB, Higham C, Ye F, Miller WR, Shyr Y, **Arteaga CL**. ER $\alpha$ -dependent E2F transcription can mediate resistance to estrogen deprivation in human breast cancer. *Cancer Discov.* 2011; 1(4):338-351. PMC3204388
- Mayer IA, Abramson VG, Isakoff SJ, Forero-Torres A, Balko JM, Kuba MG, Sanders ME, Yap J, Van den Abbeele AD, Li Y, Cantley LC, Winer E, **Arteaga CL**. Stand Up to Cancer phase Ib study of pan-phosphoinositide 3-kinase inhibitor buparlisib with letrozole in ER+/HER2-negative metastatic breast cancer. *J Clin Oncol* 2014; 32(12):1202-9. PMC3986383
- Schwarz LJ, Fox EM, Balko JM, Garrett JT, Kuba MG, Estrada MV, González-Angulo AM, Mills GB, Red-Brewer M, Mayer IA, Abramson V, Rizzo M, Kelley MC, Meszoely IM, **Arteaga CL**. LYN-activating mutations mediate antiestrogen resistance in estrogen receptor-positive breast cancer. *J. Clin. Invest.* 124:5490-502, 2014 PMC4348968 PMID 25401474

4. Using genetically engineered mice and pharmacological inhibitors of ERBB3, we showed for the first time that ERBB3 is required for PI3K-mediated mammary epithelial cell survival during puberty and in the mature mammary gland and for the pre-neoplastic events that precede the formation of mammary tumors driven by Neu/ERBB2. We were also one of the first to report on FoxO-mediated reactivation of ERBB3 and other receptor tyrosine kinases upon inhibition of the PI3K/AKT pathway. These data support a role for ERBB3 in adaptive resistance to PI3K inhibitors and anti-estrogens. They also suggest that the antitumor effect of PI3K inhibitors as single agents might be limited, thus supporting early use of combinations with this class of drugs. This knowledge has been followed in clinical trials led by members of our group.

- Cook RS, Garrett JT, Sánchez V, Stanford JC, Young C, Chakrabarty A, Rinehart C, Zhang Y, Wu Y, Greenberger LM, Horak ID, **Arteaga CL**. ErbB3 ablation impairs phosphoinositide 3-kinase (PI3K)/AKT-dependent mammary tumorigenesis. *Cancer Res.* 2011; 71(11):3941-51. PMC3204389
- Garrett JT, Olivares MG, Rinehart C, Granja-Ingram NM, Sánchez V, Chakrabarty A, Davé B, Cook RS, Pao W, McKienly ET, Manning HC, Chang JC, **Arteaga CL**. Transcriptional and post-translational upregulation of HER3 (ErbB3) compensates for inhibition of the HER2 tyrosine kinase. *Proc Natl Acad Sci USA.* 2011; 108(12):5021-6. PMC3064360
- Chakrabarty A, Sánchez V, Kuba MG, Rinehart C, **Arteaga CL**. Feedback upregulation of HER3 (ErbB3) expression and activity attenuates antitumor action of phosphoinositide 3-kinase pathway inhibitors. *Proc Natl Acad Sci USA.* 2012; 109(8):2718-23. PMC3286932
- Abramson VG, Ballinger T, Supko JG, Shapiro GI, **Arteaga CL**. Phase Ib study of safety and pharmacokinetics of the PI3K inhibitor SAR245408 in combination with the HER3 neutralizing antibody SAR256212 in patients with solid tumors. *Clin. Cancer Res.* 2016 Dec 28. pii: clincanres.1764.2016. doi: 10.1158/1078-0432.CCR-16-1764. [Epub ahead of print]

5. We were one of the first to propose that residual cancer in the breast after neoadjuvant chemotherapy (NAC) is a surrogate for actionable alterations in drug-resistant micro-metastases that ultimately progress to clinically overt metastatic breast cancer. Using digital transcript Nanostring counting on RNA from post-chemotherapy breast cancers, we identified dual specificity phosphatase 4 (DUSP4) associated with high Ki67, basal-like gene expression and, causally, with drug resistance. A second original study performed next-generation sequencing (NGS) and digital RNA expression analysis in a cohort of pre-treatment and residual triple negative breast cancer (TNBC) after NAC. Ninety percent of the tumors contained a somatic alteration potentially treatable with a molecularly targeted therapy, suggesting that genomic data in these chemotherapy-resistant tumors can inform adjuvant studies in patients with TNBC. Of note, 11% of residual TNBC exhibited *JAK2* amplification, a gene that has been associated with a stem-like phenotype and drug resistance. This second paper is the basis for EA1131, a national ECOG-ACRIN randomized phase III post-operative trial of platinum-based therapy vs. observation in patients with residual triple-negative, basal-like breast cancer after NAC. This national trial is supported by NCI and the Biomarker, Imaging and Quality of Life Studies Funding Program (BIQSFP); it evaluates the efficacy of cisplatin or carboplatin vs. observation in patients with TNBC whose residual cancer in the breast after NAC exhibits basal-like gene expression by PAM50 analysis.

- Balko JM, Cook RS, Vaught DB, Kuba MG, Miller TW, Bhola NE, Sanders ME, Granja-Ingram NM, Smith JJ, Meszoely IM, Salter J, Dowsett M, Stemke-Hale K, González-Angulo AM, Mills GB, Pinto JA, Gómez HL, **Arteaga CL**. Profiling of residual breast cancers after neoadjuvant chemotherapy identifies DUSP4 deficiency as a mechanism of drug resistance. *Nature Med.* 2012; 18(7):1052-9. PMC3693569

- Balko JM, Giltane JM, Schwarz LJ, Young CD, Cook RS, Owens P, Sanders ME, Kuba MG, Sánchez V, Pinto JA, Doimi F, Gómez H, Goga A, Lehmann B, Bauer J, Pietenpol JA, Stephens PA, Cronin M, Miller VA, Yelensky R, Wang K, Palmer G, **Arteaga CL**. Molecular profiling of drug-resistant tumor cells remaining in the breast after neoadjuvant chemotherapy of triple-negative breast cancers identifies actionable therapeutic targets. *Cancer Discov.* 2014; 4(2):232-45. PMC3946308
- Balko JM, Schwarz LJ, Cook RS, Estrada MV, Giltane JM, Sanders ME, Sánchez V, Wang K, Combs S, Hicks D, Pinto JA, Landis MD, Chang JC, Doimi FD, Gómez H, Rimm DL, Yelensky R, Miller VA, Stephens PJ, **Arteaga CL**. Triple negative breast cancers with amplifications of JAK2 at the 9p24 loci exhibit JAK2-specific dependence. *Sci. Transl. Med.* 2016 Apr 13;8(334):334ra53 doi: 10.1126/scitranslmed.aad3001

**Complete List of Published Work in MyBibliography:**

[https://www.ncbi.nlm.nih.gov/sites/myncbi/1ZC1o\\_pibk9Qo/bibliography/52810824/public/?sort=date&direction=ascending](https://www.ncbi.nlm.nih.gov/sites/myncbi/1ZC1o_pibk9Qo/bibliography/52810824/public/?sort=date&direction=ascending)

**D. Research Support**

**Ongoing Research Support**

**P50 CA098131 (Arteaga)**

**09/11/2008 – 08/31/2018**

NIH/NCI

SPORE in breast cancer

To determine if therapeutic blockade of PI3K adds to neoadjuvant therapy with the aromatase inhibitor letrozole in ER+/HER2–PIK3CA<sup>mut</sup> breast cancers. To discover biomarkers in tumor DNA, RNA, and proteins that are associated with response or resistance to estrogen deprivation in patients with operable ER+/HER2– breast cancer treated with letrozole.

**BCRF Grant (Arteaga)**

**10/01/2004 – 09/30/2018**

Breast Cancer Research Foundation

Oncogene signaling and resistance to antiestrogens in breast cancer

To determine mechanisms by which oncogene signaling induces resistance to antiestrogens in hormone receptor-positive human breast cancer cells and primary tumors

**P30 CA142543 (Arteaga)**

**9/01/2017 – 07/31/2020**

NIH/NCI

Cancer Center Support Grant

This CCSG provides support for senior leadership, five scientific research programs, six shared resources, protocol specific research, protocol review and monitoring, planning and evaluation activities, developmental funds, and administration to promote innovations in cancer diagnosis, treatment and control and builds on the outstanding science and the tradition of excellence in clinical training at UTSW.

**SAB (Arteaga)**

**12/01/2014 – 1/31/2018**

Susan G. Komen for the Cure Foundation

Discovery of Mechanisms of Resistance of Antiestrogen Therapy in ER+ Breast Cancer

**N/A (Arteaga)**

**02/24/2016-02/23/2018**

Puma Biotechnology

Mechanisms of acquired resistance to neratinib

To discover the mechanisms of acquired resistance to neratinib and to develop a structural/computational/cell biology pipeline to triage or to graduate HER2 (ERBB2) variants of unknown significance (VUS).

**3P50CA098131-S1 (Arteaga)**

**09/01/2016-08/31/2018**

NCI

Discovery of Targetable Mechanisms of Endocrine Resistance in ER + Breast Cancer

**Aim 1:** To determine whether amplified FGFR1 maintains an ER-dependent proliferation program by physical association with ER $\alpha$  in the nucleus of estrogen-deprived ER+/FGFR1-amp breast cancers., and to confirm and quantitate the FGFR1/ER association using imaging approaches.

**Aim 2:** To determine if FGFR1 amplification correlates with maintenance of proliferation in patients with early ER+/HER2– breast cancer treated with a short course of palbociclib and/or with a shorter PFS in patients with advanced ER+/HER2– breast cancer treated with fulvestrant ± the CDK4/6 inhibitor abemaciclib.

**Aim 3:** To determine the heterogeneity of breast cancer cell states in response to fulvestrant ± the FGFR TKI lucitanib by single cell transcriptomic analysis of ER+/FGFR1-amplified patient-derived xenografts (PDXs).

### **Completed Research Support**

**TBCRC (Johns Hopkins: Arteaga)**

**10/01/2006 – 08/31/2017**

Avon Foundation/Breast Cancer Research Foundation/Susan G. Komen for the Cure Foundation  
Translational Breast Cancer Research Consortium (TBCRC)

To implement and participate in clinical and translational investigator-initiated studies within the TBCRC

**CRP-07-234-06-COUN (Arteaga)**

**07/01/2012 – 06/30/2017**

American Cancer Society Clinical Research Professorship  
Combinations of anti-HER2 therapies to eliminate drug resistance

This grant provides the research protocol and technical support for the collection of tumor tissues as well as the equipment necessary for the analysis of drug resistant tumors

**PDF1229712 (Balco)**

**10/05/2012 - 10/14/2015**

Susan G. Komen Foundation

DUSP4: A Novel Tumor Suppressor that Represses MAPK Activity and CSCs

To demonstrate conclusively that loss of DUSP4 increases the number of cancer stem cells in breast tumors, causes resistance to treatment (CSC trait) and contributes to breast cancer progression.

Role: Co-Investigator

**PDF1227859 (Bhola)**

**11/19/2012 - 11/18/2015**

Susan G. Komen Foundation

Targeting the TGFβ Pathway in Breast Cancer Stem Cells

To identify a clinically relevant therapeutic strategy, prognostic signature and novel therapeutic targets that will improve TNBC therapy by eliminating TGFβ mediated enrichment of CSCs.

Role: Co-Investigator

**SAC100013 (Arteaga)**

**07/01/2010 – 01/31/2014**

Susan G. Komen for the Cure Foundation

Profiling breast cancer after neoadjuvant treatment: A platform for discovery of mechanisms of drug resistance

To profile breast cancers after chemotherapy or antiestrogens to identify mechanisms of drug resistance.

**U3 PHARMA GmbH (Arteaga)**

**01/01/2012 - 03/07/2014**

U3-Daiichi Sankyo

Inhibition of PI3K and TORC1/2 with DS-7423 in combination with HER3 (ERBB3) neutralizing monoclonal antibody U3-1287

To determine if the HER3 MAb U3-1287 delays or abrogates feedback upregulation of HER3 in human breast cancer cells treated with DS-7423; to determine if inhibition of HER3 with U3-1287 synergizes with the PI3K-TORC1/2 inhibitor DS-7423 against breast cancer xenografts *in vivo*

**R01 CA143126 (Cook)**

**12/01/2009 – 11/30/2014**

NIH/NCI

HER3 Signaling in Development and Cancer of the Breast

To provide a mechanistic understanding of how ErbB3 signaling influences complex biological events during mammary gland development and tumorigenesis using transgenic mouse models and breast cancer cell lines.

Role: Co-Investigator

**R01 CA080195 (Arteaga)**

**04/01/2010 – 01/31/2015**

NIH/NCI

ERBB2 targeted antitumor strategies in breast cancer

To determine if genetic and/or pharmacological inhibitors of PI3K reverse resistance to HER2 inhibitors in HER2-overexpressing breast cancer cells with *PIK3CA* mutations. To discover mechanisms of acquired resistance to HER2 kinase inhibitors in HER2-overexpressing human breast cancer cells and tumors.

## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.  
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME S. Gail Eckhardt, MD eRA COMMONS USER NAME (credential, e.g., agency login) Eckhardt.Gail	POSITION TITLE Professor of Medicine with Tenure		
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Stephen F. Austin State University, Nacogdoches, TX	BS	1981	Chemistry
University of Texas Medical Branch, Galveston, TX	MD	1985	Medicine

### A. Personal Statement

My background and area of expertise is in oncology drug development and gastrointestinal cancers. For the past 24 years I have been conducting preclinical and early clinical studies with novel targeted agents in conjunction with mentoring clinicians in patient-oriented research. My specific areas of focus are phase I trials, colorectal cancer (CRC), targeted therapies (particularly MEK inhibition), patient-derived tumor xenograft models, rational combination strategies, and predictive biomarker development for novel agents. My role at the Dell Medical School at the University of Texas at Austin is Chairman of the Department of Oncology, Director of the **LIVESTRONG** Cancer Institutes and Associate Dean for Cancer Programs. I have been charged with building a comprehensive cancer center that encompasses basic, translational, and clinical research, cancer care, and education. I served for 5 years on the NCI CCSG Parent IRG Committee and am a member of 10 NCI-designated Cancer Center EABs. My role as Chair on this SPORE EAB is to provide input into the development of research projects, particularly those involving developmental therapeutics as well as overall strategy and structure.

1. Tentler J, Weekes C, Leong S, Jimeno A, Messersmith W, Pitts T, Tan AC, Arcaroli J, Eckhardt SG. Patient-derived tumor explant models. *Nat. Rev. Clin. Oncol* 2012 9, 338–350. PMC3928688
2. Micel LN, Tentler JJ, Smith PG, Eckhardt SG. Role of Ubiquitin Ligases and the Proteasome in Oncogenesis: Novel Targets for Anticancer Therapies. *J Clin Oncol*. 2013 Mar 20;31(9):1231-8. PMC3807137
3. Lieu CH, Tan AC, Leong S, Diamond JR, Eckhardt SG. From Bench to Bedside: Lessons Learned in Translating Preclinical Studies in Cancer Drug Development. *J Natl Cancer Inst*. 2013 Oct 2;105(19):1441-56.
4. Wong KM, Capasso A, Eckhardt SG. The Changing Landscape of Phase I Trials in Oncology. *Nat Rev Clin Oncol*. 2015 Nov 10. doi: 10.1038/nrclinonc.2015.194. [Epub ahead of print]

### B. Positions and Honors

#### Positions and Employment

1985-1988	Medical Residency, Internal Medicine, University of Virginia Medical Center, Charlottesville VA
1988-1990	Postdoctoral Fellowship, Division of Experimental and Molecular Medicine, Scripps Clinic and Research Foundation, La Jolla CA
1990-1992	Medical Oncology Fellowship, University of California at San Diego, CA
1991-1992	Research Fellowship, Departments of Medicine and Biology, University of California at San Diego, CA
1992-1999	Clinical Faculty, Department of Medicine, Division of Medical Oncology, University of Texas Health Science Center at San Antonio TX
1992-1995	Assistant Member, Institute for Drug Development, Cancer Therapy and Research Center, San Antonio, TX
1995-1999	Associate Director, Clinical Research, Institute for Drug Development, Cancer Therapy and Research Center, San Antonio, TX
1994-1999	Director, Drug Development Fellowship Training Program, Cancer Therapy Research Center, Institute for Drug Development, San Antonio, TX

1999-2002 Associate Professor of Medicine, Director of Phase I and GI Malignancies Programs, Division of Medical Oncology, University of Colorado Health Sciences Center, Denver, CO

2002-2017 Professor of Medicine, University of Colorado Health Sciences Center, Denver, CO

2004-2017 Professor of Medicine with Tenure, University of Colorado Health Sciences Center, Denver, CO.

2004-2014 Co-Program Leader, Developmental Therapeutics, UCCC

2006-2014 Division Head, Medical Oncology

2011-2017 Associate Director for Translational Research, University of Colorado Cancer Center

2017-Present Professor and Chair, Department of Oncology, Associate Dean of Cancer Programs, and Director, **LIVESTRONG** Cancer Institutes; Dell Medical School at the University of Texas at Austin; Austin, TX

### **Other Experience and Professional Memberships**

Mentor, ASCO Leadership Development Program (2017-2019; Chair 2018); Member Case Western Cancer Center EAB (2018-present); Member, Yale Cancer Center EAB (2018-present); Member EAB for Cancer Moonshots Program MDACC (2018); Member, NCI Special Emphasis Panel for NCI Outstanding Investigator Awards (R35); Chair, Vanderbilt University GI SPORE EAB (2016-present); Member, Barbara Ann Karmanos Cancer Institute External Advisory Board (EAB)(2016-present); Member, University of Wisconsin Carbone Cancer Center External Advisory Board EAB (2015-present), Member, University of Michigan Cancer Center EAB (2015-present); Member, Indiana University Cancer Center EAB (2013-present); Member, Baylor Daniel L. Duncan Cancer Center EAB (2012-present); Member, OHSU Knight Cancer Center EAB (2012- present); Member Georgetown Lombardi Cancer Center EAB (2011-present); Standing Member, NCI Cancer Centers Parent Committee (2010-2015); Member TCGA CRC Working Group 2010-2012; Member NCI Colorectal Cancer Task Force 2010-present; Member, NCI Clinical Trials Working Group (CTWG) Evaluation Committee 2006-2007; Member, NCI GI Steering Committee 2006-2010; Member, NCI Investigational Drug Steering Committee 2006-2008 and 2014-present; Member (2005-2009), and Chair (2009-2010), FDA Oncology Drugs Advisory Committee (ODAC); Member, ASCO Board of Directors, 2004-2007; ASCO Board Liaison, Clinical Research Committee 2005-2007; Co-Chair ASCO Translational Research Task Force 2005-2006; Member, NCI Developmental Therapeutics Study Section 2005-2006; Steering Committee, ASCO GI Malignancies Symposium, 2006-2008; Co-Chair, ASCO GI Malignancies Symposium, 2004; Vice-Chair (2002) and Chair (2003) ASCO Program Committee; Member, ASCO Publications Committee, 2002-2005; Member, EORTC Early Clinical Trials Review Panel, 2002-present.; Member, ASCO Molecular Oncology Task Force, 2001-2003.; Member, GI Steering Committee, SWOG 2001-2004; Reviewer, ET-1 Study section, NCI/NIH, 2001.; Faculty, ASCO/AACR/MOG Pan-Asian Clinical Research Methods Workshop, Australia, 2004, 2006; Faculty, ASCO/AACR Clinical Research Methods Workshop, Vail, CO 2000-2003, and Course Director 2007-2009; Program Committee, FECS/ASCO/AACR Methods in Clinical Cancer Research, Flims, Switzerland, 2001-2003.; Member, Molecular Markers Study Section, NCI; Sept and Oct, 2000.; External Reviewer, Drug Development Group, National Cancer Institute, 2000- present; Co-Chair, Angiogenesis Symposium, American Association for Cancer Research 91<sup>st</sup> Annual Meeting, 2000.; Member, American Association for Cancer Research Cain Memorial Award Selection Committee, 2000.; Member, Angiogenesis Working Group, National Cancer Institute 1998-2000.; Member, RAID study section, National Cancer Institute 1998-2000.

### **Honors**

Alpha Chi, 1976; Gamma Sigma Epsilon, 1981; Alpha Omega Alpha, 1985; NCI FIRST Award, 1995; Midcareer Investigator Award in Patient-Oriented Research (K24), 2005; Fellow of the American Society of Clinical Oncology, 2008; University of Colorado Technology Transfer Office Business Advisor of the Year, 2011. Merrill J. Egorin Outstanding Mentor of the Year award, AACR/ASCO Methods in Clinical Cancer Research, Vail, CO, 2014 and 2015. Dr. Cheng Yu Tung Award for Drug Development, Hong Kong, China 2015.

### **C. Contribution to Science**

1. My early career was focused on the development of targeted therapy at a time when the bulk of drug development was focused on cytotoxic agents. While most of the agents in development were not particularly selective against their targets, my lab and clinical work focused on ensuring that biomarker studies were incorporated to assess biological effects.

a. Rowinsky, E., Hammond, L., Ayelsworth, C., Humphrey, R., Siu, L., Smith, L., Thurman, A., Rodriguez, G., Sorensen, M., Von Hoff, D., Eckhardt, S.G. Prolonged administration of BAY 12-9566, an oral non peptidic biphenyl matrix metalloproteinase (MMP) inhibitor: a phase I and pharmacokinetic (PK) study. *J Clin Oncol* 18:178-186, 2000.

b. Eckhardt SG, Rizzo J, Sweeney KR, Cropp G, Baker S, Kraynak M, Kuhn JG, Villalona-Calero MA, Hammond L, Weiss G, Thurman A, Smith L, Drengler R, Eckardt J, Moczygemba J, Hannah AL, Von Hoff DD, Rowinsky EK. A Phase I and Pharmacologic Study of the Tyrosine Kinase Inhibitor SU101 in Patients with Advanced Solid Tumors. *J Clin Oncol* 17(4), 1095-1104, 1999.

c. Alex A Adjei, Roger B Cohen, Wilbur Franklin, Clive Morris, David Wilson, Julian R Molina, Lorelei J Hanson, Lia Gore, Laura Chow, Stephen Leong, Lara Maloney, Gilad Gordon, Heidi Simmons, Allison Marlow, Kevin Litwiler, Suzy Brown, Gregory Poch, Katie Kane, Jerry Haney, and S. Gail Eckhardt. A Phase I Pharmacokinetic and Pharmacodynamic Study of the Oral, Small-Molecule MEK1/2 Inhibitor AZD6244 (ARRY-142886) in Patients with Advanced Cancers. *J Clin Oncol*; 26(13):2139-46, 2008

d. M. Pia Morelli, Amy M. Brown, Todd M. Pitts, John J. Tentler, Fortunato Ciardiello, Anderson Ryan, Juliane M. Jürgensmeier and S. Gail Eckhardt. Targeting Vascular Endothelial Growth Factor Receptor-1 and -3 With Cediranib (AZD2171): Effects on Migration and Invasion of GI Cancer Cell Lines. *Mol Cancer Ther* 2009 Sep;8(9):2546-58. Epub 2009 Sep 15.

2. As targeted agents became more selective within the context of genomic data, my group worked on ways in which we could utilize preclinical models, functional imaging, and genomics data to develop pharmacodynamic and predictive biomarkers. We were one of the initial groups in the country to establish a large bank of genomically annotated patient-derived xenografts and in some studies we assessed biological activity using functional imaging. Our preclinical work with a small molecule IGF1R inhibitor was translated to an investigator-initiated clinical trial (although unfortunately the development of the drug was halted prior to completion).

a. John J. Tentler, Erica L. Bradshaw-Pierce, Natalie J. Serkova, Kendra M. Hasebroock, Todd M. Pitts, Jennifer R. Diamond, Graham C. Fletcher, Mark R. Bray and S. Gail Eckhardt. Assessment of the *In Vivo* Antitumor Effects of ENMD-2076, A Novel Multi-Targeted Kinase Inhibitor, Against Primary and Cell Line-Derived Human Colorectal Cancer Xenograft Models. *Clin Cancer Res* 2010 Jun 1;16(11):2989-98.

b. Todd M. Pitts, Aik Choon Tan, Gillian N. Kulikowski, John J. Tentler, Amy M. Brown, Sara A. Flanigan, Stephen Leong, Christopher D. Coldren, Fred R. Hirsch, Marileila Varela-Garcia, Christopher Korch, and S. Gail Eckhardt. Development of an Integrated Genomic Classifier for a Novel Agent in Colorectal Cancer: Approach to Individualized Therapy in Early Development. *Clin Cancer Res*. 2010 Jun15;16(12):3193-204.

c. John J. Tentler, Aik Choon Tan, Sujatha Nallapareddy, Anna Spreafico, Todd M. Pitts, M. Pia Morelli Heather M. Selby, Maria I. Kachaeva, Sara A. Flanigan, Gillian N. Kulikowski, Stephen Leong, John J. Arcaroli, Wells A. Messersmith and S. Gail Eckhardt. Identification of Predictive Markers of Response to the MEK1/2 Inhibitor Selumetinib (AZD6244) in KRAS-Mutated Colorectal Cancer. *Mol Cancer Ther* 2010 Dec;9(12):3351-62. Epub 2010 Oct 5.

d. Pitts TM, Kulikowski GN, Tan AC, Murray BW, Arcaroli JJ, Tentler JJ, Spreafico A, Selby HM, Kachaeva MI, McPhillips KL, Britt BC, Bradshaw-Pierce EL, Messersmith WA, Varela-Garcia M, Eckhardt SG. Association of the epithelial-to-mesenchymal transition phenotype with responsiveness to the p21-activated kinase inhibitor, PF-3758309, in colon cancer models. *Front Pharmacol*. 2013;4:35.

3. More recently, we have been focusing on the MAPK pathway through MEK inhibition, utilizing our novel models, genomic data, and synthetic lethal screens to identify rational combination partners. For example, the paper by Spreafico et al. was the result of a synthetic lethal screen in colorectal cancer using colorectal cancer cell lines exposed to selumetinib, a MEK inhibitor, which revealed that WNT pathway genes were

upregulated in the presence of resistance to selumetinib. This preclinical work was then translated into an NCI/CTEP trial that led to an ASCO CDA and K23.

a. Spreafico A, Tentler JJ, Pitts TM, Tan AC, Gregory MA, Arcaroli JJ, Klauck PJ, McManus MC, Hansen RJ, Kim J, Micel LN, Selby HM, Newton TP, McPhillips KL, Gustafson DL, Degregori JV, Messersmith WA, Winn RA, Eckhardt SG. Rational Combination of a MEK Inhibitor, Selumetinib, and the Wnt/Calcium Pathway Modulator, Cyclosporin A, in Preclinical Models of Colorectal Cancer. Clin Cancer Res. 2013 Aug 1;19(15):4149-62. doi: 10.1158/1078-0432.CCR-12-3140. Epub 2013 Jun 11.

b. Morelli MP, Tentler JJ, Kulikowski GN, Tan AC, Bradshaw-Pierce EL, Pitts TM, Brown AM, Nallapareddy S, Arcaroli JJ, Serkova NJ, Hidalgo M, Ciardiello F, Eckhardt SG. Preclinical Activity of the Rational Combination of Selumetinib (AZD6244) in Combination with Vorinostat in KRAS-Mutant Colorectal Cancer Models. Clin Cancer Res 2011 18(4):1051-62.

c. Lieu CH, Klauck PJ, Henthorn PK, Tentler JJ, Tan AC, Spreafico A, Selby HM, Britt BC, Bagby SM, Arcaroli JJ, Messersmith WA, Pitts TM, Eckhardt SG. Antitumor activity of a potent MEK inhibitor, TAK-733, against colorectal cancer cell lines and patient derived xenografts. Oncotarget. 2015; 6(33):34561-72.

d. Davis SL, Robertson KM, Pitts TM, Tentler JJ, Bradshaw-Pierce EL, Klauck PJ, Bagby SM, Hyatt SL, Selby HM, Spreafico A, Ecsedy JA, Arcaroli JJ, Messersmith WA, Tan AC, Eckhardt SG. Combined inhibition of MEK and Aurora A kinase in KRAS/PIK3CA double-mutant colorectal cancer models. Front Pharmacol. 2015 Jun 16;6:120. doi: 10.3389/fphar.2015.00120. eCollection 2015.

Complete List of Published Work in

MyBibliography: <http://www.ncbi.nlm.nih.gov/sites/myncbi/16CjxExUy6r5u/bibliographay/41486623/public/?sort=date&direction=ascending>

## D. Research Support

### Ongoing Research Support

CPRIT Recruitment of Established Investigators Eckhardt (PI) 12/01/2016 to 11/30/2021

Title: Recruitment of Established Investigators Award

The overall goal of this proposal is to build a comprehensive preclinical and clinical platform for informed, rational, and patient-centered drug development in Austin.

Role: PI

1UM1CA186688 Eckhardt (PI) 03/14/2014 to 01/31/2019

Southwest Early Clinical Trials Consortium

The overall goal of this project is to participate as a site (with MDACC) in the NCI Experimental Therapeutics Clinical Trials Network for the development of novel agents.

Role: PI (Co-PIs at MDACC: Meric-Bernstam, Yao)

### Completed Research Support (last 3 years):

DOD/Collaborative Idea Award (Eckhardt) 09/15/11 to 09/29/15

CA1005172 Eckhardt (PI)

Collaborative Model for Acceleration of Individualized Therapy of Colon Cancer

The overall goal of this Idea Award is enhance the efficiency and speed of developing novel and individualized therapy for patients with KRAS mutant colorectal cancer (CRC) using a comprehensive bioinformatics approach and novel patient-derived preclinical models of human CRC.

Role: PI (Collaborating PI: AC Tan)

**BIOGRAPHICAL SKETCH**  
**DO NOT EXCEED FIVE PAGES.**

NAME: Mesa, Ruben A.

eRA COMMONS USER NAME (credential, e.g., agency login): RUBENMESA

POSITION TITLE: Director, Mays Cancer Center at UT Health San Antonio MD Anderson

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Illinois, Urbana, IL	BS	05/1991	Nuclear Engineering and Physiology
Mayo Medical School, Rochester, MN	MD	05/1995	Medicine
Mayo Graduate School of Medicine, Rochester, MN	Residency	06/1998	Internal Medicine
Mayo Graduate School of Medicine, Rochester, MN	Fellowship	06/2002	Hematology/Medical Oncology

**A. Personal Statement**

I began serving in 2017 as the Director of the Mays Cancer Center at UT Health San Antonio MD Anderson (formerly known as a Cancer Therapy & Research Center), an NCI- designated cancer center at the University of Texas Health Science Center at San Antonio (P30 CA054174). As the Director of the Mays Cancer Center, I am responsible for all scientific, clinical, and administrative issues related to cancer at UT Health San Antonio MD Anderson. I oversee the Mays Cancer Center membership, space, budget, clinical and research operations, as well as recruitment. My transition to the Mays Cancer Center brings my experience with almost 50 distinct clinical trials focusing on the spectrum of needs for patients with all MPNs including the global phase III clinical trial programs of ruxolitinib in myelofibrosis, ruxolitinib in polycythemia vera, pacritinib in myelofibrosis, momelotinib in myelofibrosis, and P1101 in essential thrombocythemia. As an investigator in novel therapeutics it became clear that MPN patients have many disease associated symptoms, these symptoms are tied to pathologically increased cytokines which correspond to symptoms, and that therapies frequently do not resolve these symptoms especially fatigue.

Dr Huberty (Co-PI); ASU) and myself began engaging our research interests three years ago after she shared her work using online yoga to reduce PTSD symptoms in women after stillbirth with our Cancer Wellness Program as a potential strategy to improve the health of cancer patients. As a result, the development of a non-pharmacologic approach for symptom management, such as yoga, became a key area of focus for our collaborative work to further complement medical therapy in MPN patients.

Dr. Huberty and I have completed both a feasibility and pilot study to determine the feasibility and preliminary effects on symptoms and inflammation of online yoga in MPN patients. This work is published in *Haematologica* (feasibility study) and is in-review at *BMC Complementary and Alternative Medicine* (pilot study). We have had tremendous success not only with compliance to the interventions, data collection, and preliminary effects for the use of online yoga to improve MPN symptoms and inflammation but also as a team. Dr. Huberty and myself work quite well together with myself as the lead related to MPN symptomology, medical conduct, safety parameters, and disease-based therapy and Dr. Huberty as the lead related to delivering and managing the online yoga intervention. We communicate regularly (sometimes daily) via email and/or phone and attend in person meetings at least once a month.

With over 291 peer reviewed publications, extensive clinical trial leadership experience, co leadership of the NCI funded Myeloproliferative Disorders Consortium since 2009 (2P01 CA108671), leadership of the Mays Cancer Center at UT Health San Antonio MD Anderson (P30 CA054174) and federally funded clinical trial program (U10 CA180790) I have the expertise necessary to carry out this R01 with Co-I Huberty.

## B. Positions and Honors

### Positions and Employment

2000 – 2001	Instructor of Medicine, College of Medicine, Mayo Clinic
2001 – 2004	Assistant Professor of Medicine, College of Medicine, Mayo Clinic
2005 – 2009	Associate Professor of Medicine, College of Medicine, Mayo Clinic
2002 – 2009	Consultant, Division of Hematology, Mayo Clinic, Rochester, MN
2007 – 2009	Section Head, Division of Hematology, Mayo Clinic, Rochester, MN
2009 – 2017	Professor of Medicine, College of Medicine, Mayo Clinic
2009 – 2017	Consultant, Division of Hematology/Oncology, Mayo Clinic, Scottsdale, AZ
2010 – 2017	Chair, Division of Hematology/ Oncology Mayo Clinic, Scottsdale, AZ
2012 – 2017	Deputy Director, Mayo Clinic Cancer Center
2015 – Present	Panel Chair for MPNs, National Cancer Center Network (NCCN)
2017 – Present	Director, UT Health San Antonio Cancer Center
2017 – Present	Professor of Medicine, UT Health San Antonio

## C. Contribution to Science

### 1) Development of Ruxolitinib, and JAK inhibition, for myelofibrosis

I was integrally involved with the design and complete levels of testing for the development of ruxolitinib, the first oral JAK inhibitor therapy for patients with myelofibrosis first the phase I/II and subsequently the Phase III study known as the COMFORT I study of ruxolitinib vs. placebo. Additionally, I have been integrally involved with the entire JAK inhibitor program for patients with myelofibrosis (mometinib (Phase I-III), fedratinib (PH II-III), LY2784544 (PH II), and NS-018(PH II)). Finally, I was the principal investigator of the RELIEF Study and co-principal investigator of the RESPONSE Study, two studies of ruxolitinib in patients with polycythemia vera which led to the FDA approval of the agent or as second line for patients with polycythemia vera.

- A. Verstovsek S, Kantarjian H, **Mesa RA**, Pardanani AD, Cortes-Franco J, Thomas DA, Estrov Z, Fridman JS, Bradley EC, Erickson-Viitanen S, Vaddi K, Levy R, Tefferi A. Safety and efficacy of INCB018424, a JAK1 and JAK2 inhibitor, in myelofibrosis. *N Engl J Med.* 2010 Sep 16; 363(12):1117-27. PMID:20843246. PMCID: Not available. DOI:10.1056/NEJMoa1002028.
- B. Verstovsek S, **Mesa RA**, Gotlib J, Levy RS, Gupta V, DiPersio JF, Catalano JV, Deininger M, Miller C, Silver RT, Talpaz M, Winton EF, Harvey JH, Arcasoy MO, Hexner E, Lyons RM, Paquette R, Raza A, Vaddi K, Erickson-Viitanen S, Koumenis IL, Sun W, Sandor V, Kantarjian HM. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. *N Engl J Med.* 2012 Mar 1; 366(9):799-807. PMID:22375971. PMCID: Not available. DOI:10.1056/NEJMoa1110557.
- C. Vannucchi AM, Kiladjian JJ, Griesshammer M, Masszi T, Durrant S, Passamonti F, Harrison CN, Pane F, Zachee P, **Mesa R**, He S, Jones MM, Garrett W, Li J, Pirron U, Habr D, Verstovsek S. Ruxolitinib in polycythemia vera resistant to or intolerant of hydroxyurea. *N Eng J Med.* 2014.
- D. Komrokji RS, Seymour JF, Roberts AW, Wadleigh M, To LB, Scherber R, Turba E, Dorr A, Zhu J, Wang L, Granston T, Campbell MS, **Mesa RA**. Results of a phase 2 study of pacritinib (SB1518), a JAK2/JAK2(V617F) inhibitor, in patients with myelofibrosis. *Blood.* 2015 Apr 23; 125(17):2649-55. Epub 2015 Mar 11. PMID:25762180. PMCID: 4490373. DOI:10.1182/blood-2013-02-484832.

### 2) Defined the burden and spectrum of disease related symptoms in patients with myeloproliferative neoplasms

My team developed and validated the Myeloproliferative Neoplasm Symptom Assessment Form, a patient-reported outcome form that has helped to demonstrate the significant symptomatic burden for patients with myelofibrosis, polycythemia vera, and essential thrombocythemia. These instruments have subsequently gone on to be validated in 15 different languages and have been tested in over 40 countries with aggregate data in almost 5,000 patients, and have become standard for response assessment.

- A. Scherber R, Dueck AC, Johansson P, Barbui T, Barosi G, Vannucchi AM, Passamonti F, Andreasson B, Ferri ML, Rambaldi A, Samuelsson J, Birgegard G, Tefferi A, Harrison CN, Radia D, **Mesa RA**. The Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF): international prospective validation and reliability trial in 402 patients. *Blood.* 2011 Jul 14; 118(2):401-8. Epub 2011 May 02. PMID:21536863. PMCID: Not available. DOI:10.1182/blood-

2011-01-328955.

- B. **Mesa RA**, Gotlib J, Gupta V, Catalano JV, Deininger MW, Shields AL, Miller CB, Silver RT, Talpaz M, Winton EF, Harvey JH, Hare T, Erickson-Viitanen S, Sun W, Sandor V, Levy RS, Kantarjian HM, Verstovsek S. Effect of ruxolitinib therapy on myelofibrosis-related symptoms and other patient-reported outcomes in COMFORT-I: a randomized, double-blind, placebo-controlled trial. *J Clin Oncol*. 2013 Apr 1; 31(10):1285-92. Epub 2013 Feb 19. PMID:23423753. PMCID: 4979167 DOI:10.1200/JCO.2012.44.4489.
- C. Geyer HL, Scherber RM, Dueck AC, Kiladjian JJ, Xiao Z, Slot S, Zweegman S, Sackmann F, Fuentes AK, Hernandez-Maraver D, Dohner K, Harrison CN, Radia D, Muxi P, Besses C, Cervantes F, Johansson PL, Andreasson B, Rambaldi A, Barbui T, Vannucchi AM, Passamonti F, Samuelsson J, Birgegard G, **Mesa RA**. Distinct clustering of symptomatic burden among myeloproliferative neoplasm patients: retrospective assessment in 1470 patients. *Blood*. 2014 Jun 12; 123(24):3803-10. Epub 2014 Feb 19. PMID:24553173. PMCID:4067502. DOI:10.1182/blood-2013-09-527903.

### 3) **Defined role of aberrant apoptosis in patients with myelofibrosis**

Aberrant apoptosis was identified for patients with myelofibrosis during my time under mentorship of my K23 Award (K23-CA 96780) from 2002 through 2007 under the mentorship of Scott Kaufmann, M.D., Ph.D. We demonstrated prior to the discovery of the JAK2 mutation aberrant apoptosis in this population of patients as well as identified the linkage between JAK2 V617F stat3 and impaired neutrophil apoptosis in patients with myelofibrosis. Investigations of this pathway led to observations regarding inhibition of heat shock protein-90 sensitizing primary cells of patients from myelofibrosis who transform to acute myeloid leukemia could be sensitized to cytarabine. Additionally, we identified the role of farnesyl transferase inhibition overcoming apoptosis resistance which led to the CTEP-sponsored tipifarnib study which we conducted in myelofibrosis through the Phase II Consortium.

- A. **Mesa RA**, Loegering D, Powell HL, Flatten K, Arlander SJ, Dai NT, Heldebrant MP, Vroman BT, Smith BD, Karp JE, Eyck CJ, Erlichman C, Kaufmann SH, Karnitz LM. Heat shock protein 90 inhibition sensitizes acute myelogenous leukemia cells to cytarabine. *Blood*. 2005 Jul 1; 106(1):318-27. Epub 2005 Mar 22. PMID:15784732. PMCID:1895127. DOI:10.1182/blood-2004-09-3523.
- B. **Mesa RA**, Tefferi A, Lasho TS, Loegering D, McClure RF, Powell HL, Dai NT, Steensma DP, Kaufmann SH. Janus kinase 2 (V617F) mutation status, signal transducer and activator of transcription-3 phosphorylation and impaired neutrophil apoptosis in myelofibrosis with myeloid metaplasia. *Leukemia*. 2006 Oct; 20(10):1800-8. Epub 2006 Jul 27. PMID:16871275. PMCID: Not available. DOI:10.1038/sj.leu.2404338.
- C. **Mesa RA**, Camoriano JK, Geyer SM, Wu W, Kaufmann SH, Rivera CE, Erlichman C, Wright J, Pardanani A, Lasho T, Finke C, Li CY, Tefferi A. A phase II trial of tipifarnib in myelofibrosis: primary, post-polycythemia vera and post-essential thrombocythemia. *Leukemia*. 2007 Sep; 21(9):1964-70. Epub 2007 Jun 21. PMID:17581608. PMCID: Not available. DOI:10.1038/sj.leu.2404816.

### 4) **Defined the role of immunomodulatory therapy in patients with myelofibrosis**

I was the principal investigator or co-principal investigator in a suite a clinical trials focusing on the benefits of immunomodulatory therapy alone or in combination with corticosteroids to overcome the anemia of patients with myelofibrosis. These studies began with single agent thalidomide; thalidomide with prednisone; thalidomide with prednisone with etanercept; thalidomide with prednisone with cyclophosphamide; lenalidomide as single agent; lenalidomide combined with prednisone; and finally pomalidomide alone or in combination with corticosteroids. The results of these efforts have helped to identify immunomodulatory therapy as a globally utilized therapy to abrogate the anemia of patients with myelofibrosis and culminated in the phase III RESUME study of pomalidomide in patients with myelofibrosis.

- A. Tefferi A, Verstovsek S, Barosi G, Passamonti F, Roboz GJ, Gisslinger H, Paquette RL, Cervantes F, Rivera CE, Deeg HJ, Thiele J, Kvasnicka HM, Vardiman JW, Zhang Y, Bekele BN, **Mesa RA**, Gale RP, Kantarjian HM. Pomalidomide is active in the treatment of anemia associated with myelofibrosis. *J Clin Oncol*. 2009 Sep 20; 27(27):4563-9. Epub 2009 Aug 03. PMID:19652059. PMCID: 4979191. DOI:10.1200/JCO.2008.21.7356.
- B. **Mesa RA**, Yao X, Cripe LD, Li CY, Litzow M, Paietta E, Rowe JM, Tefferi A, Tallman MS.

Lenalidomide and prednisone for myelofibrosis: Eastern Cooperative Oncology Group (ECOG) phase 2 trial E4903. Blood. 2010 Nov 25; 116(22):4436-8. Epub 2010 Jul 22. PMID:20651074. PMCID:2996111. DOI:10.1182/blood-2010-05-287417.

#### 5) Development of international guidelines for diagnosis, response, and treatment of myeloproliferative neoplasms

I was a co-founding member of the International Working Group for Myelofibrosis in Treatments which helped to establish response criteria nomenclature and the first set of international guidelines specifically for myelofibrosis. Additionally, I have been an integral member of Working Party 9 of the European LeukemiaNet helping to establish response criteria for polycythemia vera, essential thrombocythemia, and myelofibrosis as well as resistance criteria for hydroxyurea use in patients with polycythemia vera. Subsequently, I have helped to initiate and founded the inaugural National Cancer Center Network (NCCN) Guideline Panel for MPNs, which is an ongoing effort.

- A. **Mesa R**, Jamieson C, Bhatia R, Deininger MW, Gerds AT, Gojo I, et al. Myeloproliferative Neoplasms, Version 2.2017, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2016;14(12):1572-611.
- B. Barosi G, **Mesa R**, Finazzi G, Harrison C, Kiladjian JJ, Lengfelder E, McMullin MF, Passamonti F, Vannucchi AM, Besses C, Gisslinger H, Samuelsson J, Verstovsek S, Hoffman R, Pardanani A, Cervantes F, Tefferi A, Barbui T. Revised response criteria for polycythemia vera and essential thrombocythemia: an ELN and IWG-MRT consensus project. Blood. 2013 Jun 6; 121(23):4778-81. Epub 2013Apr16. PMID:23591792.PMCID:3674675.DOI:10.1182/blood-2013-01-478891.

#### **Complete List of Published Work in MyBibliography: 291 Listed**

<https://www.ncbi.nlm.nih.gov/sites/myncbi/ruben.mesa.1/bibliography/48104467/public/?sort=date&direction=descending>

#### **D. Additional Information: Research Support and/or Scholastic Performance**

##### **Under Review**

2P01

CA108671

Hoffman

7/1/2017 –

6/30/2022

National Cancer Institute, NIH

MPD Research Consortium, Project 4

GOAL: The goals of Project 4 are to conduct, in patients with MPN, a series of hypothesis driven novel translational clinical trials, based on interactions with the core laboratory based projects (Projects 1-3) in order, to identify active new agents and approaches, including those based on individualized personal medicine, that act either alone or in combination, to change both the treatment paradigm and natural history of the disease leading to improve outcomes for patients.

Role: Co-Project Director

R01

CAxxxxxx

Huberty/Mesa

9/1/201

7 – 8/31/2022

National Cancer Institute, NIH

Can Online Yoga Improve Symptom Burden in MPN Patients? The Mindful Health for MPN Study

GOAL: The primary goal of this project is to determine the effectiveness of a 12-week *home-based, online-streamed* yoga intervention on fatigue and other symptoms (e.g., anxiety, depression, sleep disturbance, sexual dysfunction, pain intensity), overall symptom burden, QoL, and biomarkers associated with stress and inflammation in MPN patients as compared to a general health education podcast control group.

Role: Multi-PI

#### **Ongoing Research Support**

2P01 CA108671 Hoffman 7/1/2011 – 6/30/2017  
National Cancer Institute, NIH No Cost Extension  
MPD Research Consortium, Project 6  
GOAL: The goals of Project 6 are to conduct, in patients with MPN, a series of hypothesis driven novel translational clinical trials, based on interactions with the core laboratory based projects (Projects 1-5) in order, to identify active new agents and approaches, including those based on individualized personal medicine, that act either alone or in combination, to change both the treatment paradigm and natural history of the disease leading to improve outcomes for patients.

Role: Co-Project Director

P30 CA054174 Mesa 8/1/2017 – 7/31/2019  
National Cancer Institute, NIH  
UT Health San Antonio Cancer Center Support Grant  
GOAL: This cancer center support grant provides research core and program infrastructure support to members of the cancer center for the conduct of their cancer-related research.

Role: Director/ Principal Investigator  
50% Effort (6 Months)

### **Completed Research Support**

Foundation Mesa 1/1/2011 – 4/30/2014  
MPD Research Foundation  
Validation of use of the Myeloproliferative Neoplasm Symptom Assessment Form Diary to Assess Symptomatic Pains in Patients with Polycythemia Vera and Post Polycythemia Myelofibrosis. Funded by MPN Research Foundation  
GOAL: Validate a novel instrument of patient reported outcomes in myelofibrosis.

P30 CA015083 Diasio 3/1/2009 – 8/1/2017  
National Cancer Institute, NIH  
Mayo Comprehensive Cancer Center Grant, Data Safety and Monitoring System  
GOAL: Chair the protocol and clinical trial oversight committee for Cancer Center  
Role: Co-Investigator

U10 CA180790 Alberts 5/6/2014 – 8/1/2017  
National Cancer Institute  
National Clinical Trials Network  
GOAL: Coordinate federally funded clinical trials at Mayo Clinic Cancer Center open in Arizona.  
Role: Co-Investigator

13-007635  
Gilead Sciences. (GS-US-352-0101) Mesa 2/1/2014 – 8/1/2017  
A Phase 3, Randomized, Double-blind Active-controlled Study Evaluating Momelotinib vs. Ruxolitinib in Subjects with Primary Myelofibrosis (PMF) or Post-Polycythemia Vera or Post- Essential Thrombocythemia Myelofibrosis (Post-PV/ET MF) in: 13-007635: A Phase 3, Rand, Double-blind Active-controlled Study Eval Momelotinib vs. Ruxolitinib in Subjects w/ Primary Myelofibrosis (PMF) or Post-Polycythemia Vera or Post- Essential Thrombocythemia Myelofibrosis (Post-PV/ET MF).  
GOAL: Determine front line therapy for patients with myelofibrosis who have anemia.

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Reynolds, Charles Patrick

eRA COMMONS USER NAME): CPREYNOLDS

POSITION TITLE: Cancer Center Director TTUHSC School of Medicine

**EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Texas, Austin TX	BA	May 1974	Biology
Univ. of TX Southwestern Medical School Dallas TX	MD	Jun 1979	Medicine
University of Texas, Austin TX	PhD	Dec 1979	Cell Biology
Univ. of TX Southwestern Medical School Dallas TX	Postdoc	Jun 1980	Cancer Immunology
National Naval Medical Center, Bethesda MD	Resident	Jul 1981	Pediatrics

**A. Personal Statement** My major research interest is in cancer developmental therapeutics and includes research in molecular target discovery, preclinical drug development, and clinical trials. A major focus of my research in drug development is on retinoids for cancer therapy, both as differentiation inducers and as cytotoxic agents. We also conduct studies to identify mechanisms of drug resistance so as to identify novel approaches to overcome such resistance. My laboratory develops novel models for preclinical drug testing and establishes new cell lines and patient-derived mouse xenografts from both pediatric and adult cancers. We develop clinical trials based on our laboratory studies, and for some of these I am the IND sponsor for the novel agent. Our laboratory investigations consistently translate to clinical trials that demonstrate activity of the novel approach in patients.

**B. Positions and Honors****Positions and Employment**

1979-1980 Postdoctoral Fellow, Cancer Immunology, UT Southwestern Medical School, Dallas, TX.  
 1980-1981 Pediatric Intern, Dept. of Pediatrics, National Naval Medical Center, Bethesda, MD.  
 1981-1982 LT and Battalion Surgeon, HQ Battalion, 3rd Marine Division, Okinawa, Japan.  
 1982-1983 LT, Transplantation Research Pgm Center, Naval Medical Research Inst, Bethesda, MD.  
 1983-1986 LCDR and Chief, Immunotherapeutic Section, Naval Medical Research Institute  
 1987-1989 Assist. Professor, Pediatrics, UCLA School, Los Angeles, CA.  
 1989-2000 Assoc. Professor of Pediatrics and Pathology, Div. of Hematology-Oncology, Childrens Hospital of Los Angeles (CHLA) and USC School of Medicine, Los Angeles, CA.  
 1993-2008 Head, Developmental Therapeutics Section, Childrens Hospital Los Angeles  
 2000-2008 Professor of Pediatrics and Pathology, Div. of Hematology-Oncology, CHLA/USC.  
 2000-2008 Co-director, Developmental Therapeutics Pgm, Norris Comp. Cancer Center, USC  
 2003-2008 Director, Develop. Therapeutics Pgm, USC-CHLA Institute for Pediatric Clinical Research  
 2008-present Cancer Center Director, Professor of Cell Biology & Biochemistry, Pediatrics, Internal Medicine, School of Medicine, Texas Tech University Health Sciences Center, Lubbock, TX

**Other Experience and Professional Memberships**

1984-1986 Natl Naval Med Center Liaison to Presidential Protective Division, US Secret Service  
 1987-2000 Director, Childrens Cancer Group Neuroblastoma Bone Marrow Purging Laboratory  
 2001-present Childrens Oncology Group (COG) Neuroblastoma Steering Committee  
 2001-2005 COG: Neuroblastoma Disease Committee, Vice-Chair  
 2001-present COG: Developmental Therapeutics Committee, Neuroblastoma Liaison  
 2001-present COG: ABTR04B1 Cell Culture and Xenograft Model Banking Protocol, Chair  
 2001-present Director, COG Cell Culture + Xenograft Repository ([www.COGcell.org](http://www.COGcell.org))

2001-2007 Director COG Neuroblastoma Stem Cell Purging Laboratory  
 1999-2000 Reviewer, National Cancer Institute Rapid Access to Intervention Development Program  
 2000-present US Food & Drug Administration Special Government Employee  
 2000-2007 US FDA Pediatric Subcommittee of the Oncologic Drugs Advisory Committee  
 2003-present Editorial Board, *Clinical Cancer Research*  
 2007-2008 Natl. Cancer Inst. SBIR/STTR ZRG1 Cancer Drug Dev. + Therapeutics Study Section  
 2008-present Natl. Inst. Child Health and Development, Best Pharmaceuticals for Children Act Panel  
 2008-2013 Chartered member, Natl. Cancer Inst Drug Discovery + Molecular Pharm. Study Section  
 2008-present Director, South Plains Oncology Consortium ([www.SPONC.org](http://www.SPONC.org))  
 2008-present Chief Scientific Officer, CerRx, Inc.  
 2012-2014 University Advisory Committee, Cancer Prevention Research Inst of Texas (CPRIT)  
 2009-present Advisory Committee on Childhood Cancer, CPRIT  
 2010 ZRG1 NCI Stimulus Package Final Review Panel  
 2011-present Principal Investigator, Texas Cancer Cell Repository ([www.TXCCR.org](http://www.TXCCR.org))  
 2011-2015 Co-PI, Texas Cancer Research Biobank ([www.TXCRB.org](http://www.TXCRB.org))  
 2014-present Natl Cancer Inst ZRG1 OTC-W Cancer Therapeutics and Drug Development study section  
 2014-2015 Natl Cancer Inst Mouse Models Translational Research study section, co-chair.  
 2015-present Editorial Board, *Molecular Cancer Therapeutics*  
 2015-2018 NIH ZRG1 OTC-H Small Business: Cancer Diagnostics and Treatments Study Section  
 2017 NIH ZCA1-RTRB-E-A1 NCI PDX Network study section

Sponsor of Investigational Drug Applications with FDA for intravenous emulsion fenretinide (IND 70058) and buthionine sulfoximine (IND 69112)

### Honors

1988 Gold Medal for Research Achievement awarded by Nihon University, Tokyo, Japan  
 1992 Team Physician, 1992 USA Olympic Shooting Team, 25<sup>th</sup> Olympiad, Barcelona, Spain  
 2004 Eurand Prize for Novel Approaches in Oral Drug Delivery by the Controlled Release Society  
 2008 Best Clinical Paper Award, *Advances in Neuroblastoma Research*, Chiba, Japan  
 2011 Most cited paper in *Clinical Cancer Research*, 2009 (*Clin Cancer Res* 15:1126-1132, 2009)  
 2011 Texas Tech University System Chancellor's Council Research Award  
 2016 Texas Tech University Health Sciences Center Distinguished University Professor

### **C. Contribution to Science**

1. I have been actively developing laboratory models for understanding biological and preclinical therapeutic studies of neuroblastoma for > 40 years. We established the first sets of neuroblastoma cell lines obtained from patients prior to and at disease progression after therapy (a). Subsequent work with these and many additional cell lines established in my laboratory enabled us to define that a sustained and significant drug resistance is acquired by neuroblastomas that progress after chemotherapy and especially after intensive myeloablative chemotherapy and radiation (b). We have employed our neuroblastoma cell line panels to define the molecular mechanisms of drug resistance, such as loss of p53 function (c) and overexpression of glutathione, the latter leading to clinical trials with BSO (d).

- a. **Reynolds CP**, Biedler JL, Spengler BA, Reynolds DA, Ross RA, Frenkel EP, Smith RG: Characterization of human neuroblastoma cell lines established before and after therapy. *J National Cancer Institute* 76:375-387, 1986. PMID:3456456
- b. Keshelava N, Seeger RC, Groshen S, **Reynolds CP**: Drug resistance patterns of human neuroblastoma cell lines derived from patients at different phases of therapy. *Cancer Research* 58:5396-5405, 1998. PMID: 9850071
- c. Keshelava N, Zuo JJ, Chen P, Waidyaratne SN, Luna MC, Gomer CJ, Triche TJ, **Reynolds CP**: Loss of p53 function confers high-level multi-drug resistance in neuroblastoma cell lines. *Cancer Research* 61:6185-6193, 2001. PMID:11507071
- d. Villablanca JG, Volchenbom SL, Cho H, Kang MH, Cohn SL, Anderson CP, Marachelian A, Groshen S, Tsao-Wei D, Matthay KK, Maris JM, Hasenauer CE, Czarnecki S, Lai H, Goodarzia F, Shimada S, **Reynolds CP**: A Phase I New Approaches to Neuroblastoma Therapy study of buthionine sulfoximine and melphalan with autologous stem cells for recurrent/refractory high-risk neuroblastoma. *Pediatr Blood Cancer* 63:1349-56, 2016. PMID: 27092812

2. An important aspect of preclinical drug development is having robust methods for assessing drug activity. My laboratory was the first to define the optimal approach to assessing subcutaneous tumors in mouse xenografts, a method cited > 900 times and used by many laboratories doing translational research with mouse models (a). Recognizing the need for a method to accurately assess drug response in cell culture that could measure > 2 logs of cytotoxicity I developed a novel digital image microscopy system for cytotoxicity testing in 96 well plates called DIMSCAN (b). Our laboratory and the DIMSCAN technology has been the *in vitro* testing system for the NCI Pediatric Preclinical Testing Program for 10 years, testing > 80 drugs and enabling multiple clinical trials (c). We have employed DIMSCAN to guide mouse model testing and also clinical trials, with a recent example being our work with nalIRI (MM-398) in preclinical (cell line and xenograft) models of pediatric solid tumors (d) that led to an ongoing phase I trial

- a. Tomayko MM and **Reynolds CP**: Determination of subcutaneous tumor size in athymic (nude) mice. *Cancer Chemotherapy and Pharmacology* 24:148-154, 1989. PMID: 2544306
- b. Frgala T, Kalous O, Proffitt RT, **Reynolds CP**: A novel cytotoxicity assay with a 4 log dynamic range that identifies synergistic drug combinations. *Molecular Cancer Therapeutics* 6:886-89, 2007. PMID: 17363483
- c. Kang MH, Smith MA, Morton CL, Nino Keshelava N, Houghton PJ, **Reynolds CP**: National Cancer Institute Pediatric Preclinical Testing Program: Model description for *in vitro* cytotoxicity testing. *Pediatr Blood Cancer* 56:239-49, 2011. PMCID:PMC30055
- d. Kang MH, Wang J, Makena M Lee JS Paz N, Hall CP, Song MM, Calderon RI, Cruz R Hindle A, Ko W, Fitzgerald J, Drummond DC, Triche TJ, **Reynolds CP**: Activity of MM-398, nanoliposomal irinotecan (nal-IRI), in Ewings family tumor xenografts is associated with high exposure of tumor to drug and high *SLFN11* expression. *Clinical Cancer Research* 21:1139-50, 2015. PMID: 25733708

3. A long-standing interest has been in utilizing induction of differentiation in neuroblastoma as a therapy. Working with colleagues at the NCI we demonstrated that the first molecular event in retinoic-acid induced differentiation of neuroblastoma was down-regulation of the key oncogene MYCN (a). My laboratory determined that the optimal differentiation inducer to employ clinically was 13-cis-retinoic acid and we designed a dose schedule that obtained desired drug exposures and demonstrated tolerability and anti-tumor activity in a phase I clinical trial (b). Combining our work on myeloablative therapy (including a novel approach to purging tumor from bone marrow) with our work on 13-cis-retinoic acid, my colleagues and I designed and carried out a randomized phase III study that established myeloablative therapy followed by 13-cis-retinoic acid as standard-of-care for treating high-risk neuroblastoma (c). We sought to build on our established paradigm of following myeloablative therapy with well-tolerated agents acting via novel mechanisms to attack minimal residual disease. I worked with colleagues in the COG to design a successful phase III study that achieved a further improvement in patient outcome (and defined current standard-of-care) by adding immunotherapy to the post-myeloablative therapy with 13-cis-retinoic acid. That phase III study led to the recent FDA approval of dinutuximab + GM-CSF + IL-2 + 13-cis-retinoic acid for treating neuroblastoma (d).

- a. Thiele CJ, **Reynolds CP**, Israel MA: Decreased expression of *N-myc* precedes retinoic acid induced morphological differentiation of human neuroblastoma. *Nature* 313:404-407, 1985. PMID: 3855502
- b. Villablanca JG, Avramis V, Khan A, Matthay KK, Ramsay NKC, Seeger RC, **Reynolds CP**: Phase I trial of 13-cis-retinoic acid (cRA) in neuroblastoma patients following bone marrow transplantation (BMT). *J Clinical Oncology* 13:894-901, 1995. PMID: 7707116
- c. Matthay KK, Villablanca JG, Seeger RC, Stram DO, Harris RE, Ramsay NK, Swift P, Shamada H, Black CG, Brodeur GM, Gerbing R, **Reynolds CP**: Treatment of high risk neuroblastoma with intensive chemotherapy, radiotherapy, autologous bone marrow transplantation, and 13-cis-retinoic acid. *New England J Medicine* 341:1165-1173, 1999. PMID: 10519894
- d. Yu AL, Gilman AL, Ozkaynak MF, London WB, Kreissman SG, Chen HX, Smith M, Anderson B, Villablanca JG, Matthay KK, Shimada H, Grupp SA, Seeger RC, **Reynolds CP**, Buxton A, Reisfeld RA, Gillies SD, Cohn SL, Maris JM, Sondel PM: Anti-GD2 antibody with GM-CSF, IL2 and isotretinoin for neuroblastoma: A Children's Oncology Group (COG) Phase III Study. *New England J Medicine* 363:22-32, 2010. PMCID: PMC3086629

4. We discovered that the retinoid fenretinide (4-HPR) was highly active against neuroblastoma cell lines resistant to retinoic acid and that it acted via a novel mechanism, stimulating over-production of dihydroceramides and demonstrated that combining the dihydroceramide-generating fenretinide with

sphingolipid agents achieved a highly synergistic cytotoxicity for a broad range of cancer cells with minimal normal cell toxicity (a). We developed novel oral and intravenous novel formulations of fenretinide. Our phase I trial of the LXS fenretinide oral powder formulation demonstrated successful translation of the approved bioavailability to patients and 4 complete responses in children with recurrent neuroblastoma (b). We are currently developing additional 4-HPR-based drug combinations (c). Our phase I trial of intravenous 4-HPR achieved multiple complete responses in peripheral T cell lymphomas (d). We have ongoing a phase II study of intravenous 4-HPR in PTCL and a phase I study combining intravenous 4-HPR with the sphingolipid agent safinol.

- a. Maurer BJ, Cabot MC, **Reynolds CP**: Synergistic cytotoxicity in solid tumor cell lines of N-(4-hydroxyphenyl)retinamide and modulators of ceramide metabolism. *J National Cancer Institute* 92:1897-1908, 2000. PMID: 11106681
  - b. Maurer BJ, Kang MH, Janeba J, Groshen S, Matthay KK, Sondel PM, Maris JM, Jackson HA, Goodarzi F, Shimada H, Villablanca JG, Czarnecki S, Beth Hasenauer B, **Reynolds CP**, Marachelian A: Phase I trial of fenretinide delivered orally in a novel organized lipid complex in patients with relapsed neuroblastoma: A report from the NANT consortium. *Pediatr Blood Cancer* 60:1801-8, 2013. PMID: 23813912
  - c. Chen NE, Maldonado V, Khankaldyyan V, Shimada H, Song MM, Maurer BJ, **Reynolds CP**: Reactive oxygen species mediates the synergistic activity of fenretinide combined with the microtubule inhibitor ABT-751 against multi-drug resistant recurrent neuroblastoma xenografts. *Molecular Cancer Therapeutics* 15:1-12, 2016. PMID: 27530131
  - d. Mohrbacher A, Yang AS, Groshen S, Kummar S, Gutierrez ME, Kang MH, Tsao-Wei D, **Reynolds CP**, Newman E, Maurer BJ: Phase I study of fenretinide delivered intravenously in patients with relapsed or refractory hematologic malignancies: a California Cancer Consortium Trial. *Clinical Cancer Res* 23: 4550-4555, 2017. PMID: 28420721
5. The Reynolds laboratory was the first to analyze telomerase gene expression in relationship to outcome in neuroblastoma (a) and the first to establish and characterize cell lines (and now PDXs) from ALT and EST neuroblastomas (b,c).
- a. Choi MR, Kim NW, Amshey S, Zuo JJ, Gerbing R, Stram D, Lukens JN, Matthay KK, Seeger RC, **Reynolds CP**: Telomerase activity by TRAP assay and telomerase RNA (hTR) expression are predictive of outcome in neuroblastoma. *Medical Pediatric Oncology* 35:647-650, 2000. PMID 11107138
  - b. Farooqi AS, Rebecca A, Dagg RA, Choi MR, Shay JW, **Reynolds CP**, Lau LMS: Alternative lengthening of telomeres in neuroblastoma cell lines is associated with a lack of *MYCN* genomic amplification and with p53/MDM2/p14(ARF) pathway aberrations. *J Neurocol* 119:17-26, 2014. PMID:24792489
  - c. Dagg RA, Pickett HA, Neumann AA, Napier CE, Henson JD, Teber ET, Arthur JW, **Reynolds CP**, Murray J, Haber M, Sobinoff AP, Lau LMS, Reddel RR. Extensive proliferation of human cancer cells with ever-shorter telomeres *Cell Rep*. 19:2544-2556, 2017. PMID: 28636942

### Complete List of Published Work in Public Databases

(> 225 peer-reviewed papers, >20,000 citations, H Index = 73)

NCBI My Bibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/charles.reynolds.2/bibliography/40489757/public/?sort=date&direction=ascending>

Google Scholar: <https://scholar.google.com/citations?user=Y2a9-dAAAAAJ&hl=en>

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## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

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NAME: Hong, David S

eRA COMMONS USER NAME (agency login): dshong

POSITION TITLE: Professor, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Yale University, New Haven, CT	BS	1/1993	Oncology
Albert Einstein College of Medicine, Bronx, NY	MD	1/1999	Medicine

### A. Personal Statement

I am a Professor, Deputy Chairman in the Department of Investigational Cancer Therapeutics (Phase I Program), Clinical Medical Director of the Clinical Center for Targeted Therapy (CCTT), and Associate Vice President of Clinical Research at The University of Texas MD Anderson Cancer Center. The approach of the department is unique with an emphasis on molecular characterization of each patients tumor and personalized therapy in the Phase I setting. Throughout my career I have developed an interest in studying the efficacy of novel drug combinations in patients with solid tumors. As a faculty member in the Department of Investigational Cancer Therapeutics I have an extensive track record of leading successful studies that involve a strong correlative component and collaborating with other investigators, from both basic science and clinical specialties, within MD Anderson and outside institutions. Currently, I am the Principal Investigator on 95 research protocols that involve a wide range of sponsors including the Cancer Therapy Evaluation Program (CTEP) at the National Cancer Institute. I have been an author or co-author on over 231 publications. Recently my research endeavors have focused on developing personalized therapies for patients, whose tumors bear specific genetic mutations and/or amplifications; also combining targeted therapies with immunotherapies; and developing novel RNA therapeutics. I have demonstrated the ability to successfully place patients on clinical trials, manage toxicities and oversee the correlative studies associated with various Phase I research projects.

### B. Positions and Honors

#### Positions and Employment

2005-2007	Assistant Professor, Department of Gastrointestinal (GI) Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX
2007-present	Clinical Medical Director, Clinical Center for Targeted Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX
2007-2012	Assistant Professor, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX
2010-2012	Committee Chair, Clinical Research Committee, The University of Texas MD Anderson Cancer Center, Houston, TX
2012-2017	Associate Professor, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX
2013-present	Deputy Chair, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX
2017-present	Professor, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX
2017-present	Associate Vice President of Clinical Research, The University of Texas MD Anderson Cancer Center, Houston, TX

#### Other Experience and Professional Memberships

1997-1998	Research Fellow, Howard Hughes Institute, Albert Einstein College of Medicine, Bronx, NY
1999-2001	Internal Medicine Residency, Thomas Jefferson University Hospital, Philadelphia, PA

- 2004 Chief Medical Oncology Fellow, The University of Texas MD Anderson Cancer Center, Houston, TX
- 2004 Rotation at the NCI-CTEP, National Cancer Institute, Bethesda, MD
- 2005-present Member, CRC 4 Committee, The University of Texas MD Anderson Cancer Center, Houston, TX
- 2013-present CCSG Targeted Therapy Program Co-Leader, The University of Texas MD Anderson Cancer Center, Houston, TX

**Honors**

- 1997 Howard Hughes Research Fellowship, Albert Einstein School of Medicine
- 1999 Special Diploma with Distinction in Research-Immunology, Albert Einstein School of Medicine
- 2004 ASCO Young Investigator Award, The University of Texas MD Anderson Cancer Center
- 2004 Jesse H. Jones Award, The University of Texas MD Anderson Cancer Center
- 2011 Best Boss Award 2011, The University of Texas MD Anderson Cancer Center
- 2012 Gerald P. Bodey Award, The University of Texas MD Anderson Cancer Center

**C. Contribution to Science**

1. NIH. I have been involved in the development of several molecules that have led to FDA approval and changes in the standard of care (e.g. dabrafenib, tremetani, cabazatinib, silutuximab, and levatinib). As the PI of a multicenter early phase trial with multi-kinase inhibitor lenvatinib, initial activity was seen in thyroid cancer which led to a fruitful collaboration with Steve Sherman and ultimately the FDA approval of levatinib in differentiated thyroid cancer. I have been an exceptionally collaborative clinical investigator. Several of the phase I protocols, that I wrote and developed tested first-in-human molecules developed by MD Anderson investigators. These include RTA-402, a NF-κB and cyclin D1 inhibitor (Michael Andreef, MD, PhD) and PBI-05204 an AKT, FGFR inhibitor (Robert A. Newman, PhD). RTA-402 (bardoxolene methyl) proved to be efficacious against cancer and improved patients' renal function. The combination of vemurafenib, cetuximab and irinotecan, which demonstrated encouraging activity in BRAF mutant colorectal cancer in early phase clinical trial designed by both myself and Dr. Scott Kopetz, has led to an R01 grant from NIH and will proceed to phase II trial supported by SWOG. I have developed a number of collaborations outside of MD Anderson including Dr. Dario Marchetti, the Jack L. Titus Professor and Director CTC Core Facility Baylor College of Medicine exploring the role of CTC in brain metastasis which has led to a DOD and CPRIT grant.

**D. Additional Information: Research Support and/or Scholastic Performance**

**Ongoing Research Support**

P30-CA 16672 DePinho (PI) 7/1/1978-6/30/2018  
NIH/NCI

Targeted Therapy Program Cancer Center Support (Core) Grant

This project supports 21 shared resources that facilitate core activities. This project also supports activities in Planning and Evaluation, Senior Leaders, Program Leaders and for Development to enhance faculty recruitment, to provide seed support for multi-investigator grants and to develop a limited number of new shared resources.

Role: Co-Program Leader (2013 - 2014)

1-R01-CA187238-01 Hong (PI) 8/4/2014-7/31/2019  
NIH/NCI

Therapeutic Strategies for Patients With BRAF Mutant Colorectal Cancer

To define the maximum tolerated dose (MTD) of vemurafenib when used in combination with cetuximab and Irinotecan.

Role: Principal Investigator

**Completed Research Support**

Translational Research Initiative Grant Hong (PI) 1/1/2004-1/1/2010  
NIH/NCI

Phase I study of Tipifarnib and Sorafenib in Advanced Biopsable Cancer

1) To define the phase II dose 2) To evaluate the safety and toxicity and to determine MTD of tipifarnib in combination with sorafenib.

Role: Principal Investigator

Goodwin Funding Award Hong (PI)

1/1/2007-9/6/2013

NIH/NCI

Phase I Clinical Trial Evaluating the Toxicity, Pharmacokinetics and Biological Effect of Intravenous Bevacizumab (Avastin) in Combination with Escalating Doses of Oral AZD2171 for Patients with Advanced Malignancies

1) To evaluate the safety and toxicity profile of intravenous bevacizumab (avastin□) administered in combination with oral AZD2171 for patients with advanced malignancies. 2) To determine the pharmacokinetic profile of oral AZD2171 in combination with bevacizumab (avastin□) administered to patients with advanced malignancies.

Role: Principal Investigator

RP110248 Hwu (PI)

12/1/2010-11/30/2013

Cancer Prevention & Research Institute of Texas (CPRIT)

Augmenting T Cell-based melanoma Immunotherapy by targeting oncogenic BRAF

To explore the potential of augmenting T Cell-based immunotherapies with the use of BRAF/(V600E) inhibitors

Role: Co-Investigator

RP140181

8/31/2014-8/30/2017

Cancer Prevention & Research Institute of Texas (CPRIT)

Mechanisms of CTC Biomarkers in Breast Cancer Brain Metastasis

Task: To determine the effects of therapeutic inhibition of Notch1 and HPSE CTC markers on BCBM onset

Task: To mechanistically link combinatorial Notch1/HPSE CTC subsets to clinical BCBM Task: To assess the regulation of Notch1/HPSE axis expression in CTC subsets affecting BCBM onset

Role: Co-Principal Investigator

## D. Research Support

### Ongoing Research Support

**RP170510** (Reynolds, PI) **12/01/2016-11/30/2020**  
**Cancer Prevention & Research Institute of Texas (CPRIT).** *Telomere Maintenance Mechanisms in Neuroblastoma.* Studies of mechanisms of telomere maintenance in neuroblastoma and the role of a lack of a telomere maintenance mechanism on regression of low-risk neuroblastomas. Role: PI

**Alex's Lemonade Stand Foundation (Reynolds, PI)** **01/01/18 – 12/31/23**  
*Childhood Cancer Repository Powered by Alex's Lemonade Stand Foundation*  
Supports establishing, banking, and distributing cell lines and PDXs of childhood cancer. Role: PI

**RO1 CA221957** **Reynolds CP and Kang MK (MPI)** **12/17-11/20**  
*Characterization of a panel of neuroblastoma patient-derived models for preclinical therapeutic studies.*  
Supports RNA sequencing, whole exome sequencing, proteomics, and defining responses to drugs for a panel of patient-derived neuroblastoma cell lines and xenografts. Role: MPI

**OC150083** (Reynolds, PI) **06/01/16-05/31/18**  
**Department of Defense (DOD)** "Novel Platinum/Taxane-Based Drug Combinations (Preclinical) for Ovarian Cancer". This grant supports preclinical xenograft studies on novel drug combinations in models of ovarian cancer. Role: PI

**R01 CA168699** (Kang, PI) **08/01/13-07/31/18**  
**National Cancer Institute (NCI)** *Pharmacokinetics and Pharmacogenomics of 13-cis retinoic acid in high-risk neuroblastoma* This grant supports pharmacology and pharmacogenomics studies of patients enrolled in phase III Children's Oncology Group studies of neuroblastoma so as to improve dosing of 13-cis-retinoic acid in patients with high-risk neuroblastoma. Role: Co-investigator

**St Baldrick's Foundation** (Reynolds, PI) **1/01/2015-12/31/2018**  
*Pediatric Oncology Infrastructure Grant.* This grant supports a clinical research associate for pediatric oncology trials here at TTUHSC Lubbock. Role: PI

**R44 CA183316** (Simpson, PI; CerRx, Inc.) **06/14/14-02/28//19**  
**National Cancer Institute (NCI)** *A Phase I trial combining IV fenretinide and IV safinol to target overproduction of cytotoxic dihydroceramides in malignant cells .* Grant provides partial support for conducting a first-in-man phase I trial of the combination of intravenous fenretinide and safinol. Role: Co-investigator

**RP150416** (Maurer, PI) **02/15-1/19**  
**Cancer Prevention and Research Institute of Texas (CPRIT)**  
*Translational investigations on fenretinide and safinol for pediatric cancer use.* Laboratory studies on mechanisms of fenretinide + sphingolipid modulators and a phase I clinical trial in neuroblastoma. Role: Co-investigator

### Completed Research Support

**R21CA161889** (Reynolds, PI) **07/08/11-07/07/16**  
**National Cancer Institute (NCI)** *Phase I trial of fenretinide + safinol*  
This grant supports conduct of a phase I study in adult solid tumors combining intravenous fenretinide with intravenous safinol. (Drug supplies are via a RAID grant, CP Reynolds, PI).

**CP130023** (Love, PI; CerRx, Inc.) **3/01/14-03/16/18**  
**Cancer Prevention & Research Institute of Texas (CPRIT).** *Targeted Ceramide-Based Therapeutics.* This support enables CerRx, Inc. to carry out a phase II study of intravenous fenretinide in peripheral T cell lymphoma. Role: Co-investigator





## **THE CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS CLINICAL TRIALS ADVISORY COMMITTEE CHARTER**

### **BACKGROUND**

Texas Health and Safety Code § 102.155 allows for the establishment of an ad hoc committee of experts to advise the Oversight Committee of the Cancer Prevention and Research Institute of Texas (“Oversight Committee”), and to advise the Cancer Prevention and Research Institute of Texas (“CPRIT” or “Institute”). The Clinical Trials Advisory Committee (“CTAC”) was created to advise the Oversight Committee regarding clinical trials. This Charter (“CTAC Charter”), adopted by the CTAC members and approved by the Oversight Committee on May 16, 2018, supersedes any other documents relating to the CTAC.

### **PURPOSE**

The primary purpose of the CTAC is to advise the Oversight Committee on important issues of the clinical trials. The CTAC shall give their expert opinion on the impact of current CPRIT mechanisms supporting clinical trials; give advice on opportunities to increase CPRIT’s impact on translating basic discoveries to clinical trials; and advise on mechanisms that would address barriers to patient enrollment in therapeutic clinical trials.

### **COMPOSITION**

The CTAC shall be composed of at least six members appointed by the Oversight Committee. CTAC members shall serve two-year terms, at the end of which the Oversight Committee may renew the appointment of the CTAC member or appoint a new member. The two-year terms of the CTAC already constituted at the time the CTAC Charter is approved shall begin on the day after approval of the charter.

If a CTAC member is unable to complete his or her term, the Oversight Committee shall appoint someone to fulfill the remainder of the term.

### **ELECTION OF OFFICERS**

The Institute’s Chief Executive Officer shall appoint the first CTAC Chairperson and Vice-Chairperson. Thereafter, the CTAC Chairperson and Vice Chairperson shall be elected to serve a two-year term by a majority of CTAC members present and able to vote at the first meeting

held on or after May 1, 2020, and thereafter for every even-numbered year. The term of an officer shall not extend longer than the officer's term on the CTAC.

### **MEETINGS AND QUORUM**

The CTAC shall meet as often as deemed necessary by the CTAC Chairperson. At a minimum, the CTAC shall meet annually to compose a report to send to the Oversight Committee and to conduct any other business required by this Charter, statutes, or administrative rules.

A meeting of the CTAC requires a quorum of members. Such meeting may take place in person or by teleconference. A quorum exists when at least a majority of appointed members of the CTAC is present or available via telephone. If there is an even number of currently appointed members, then half that number plus one member constitutes a quorum.

### **DUTIES AND RESPONSIBILITIES**

The CTAC shall submit a written report, at least annually, to the Oversight Committee regarding the work undertaken by the CTAC for the previous year and the CTAC's recommendations for the Institute. The CTAC shall submit the report by August of each calendar year to the Institute's Chief Executive Officer for distribution to the Oversight Committee.

The CTAC Chairperson shall present the report at the first regular meeting of the Oversight Committee following the submission of the written report. If the Chairperson is unable to attend, then the Vice-Chairperson or other designee may present the report.

The CTAC may provide on-going advice to the Oversight Committee regarding clinical trials.

### **OTHER DUTIES**

In addition to duties and responsibilities stated herein, the Oversight Committee's Presiding Officer may authorize additional, official duties of the CTAC.

### **AMENDING OR REPEALING THE CHARTER**

The CTAC retains the ability to make, alter, amend, or repeal the CTAC Charter. The CTAC shall make changes to the CTAC Charter pursuant to a majority vote of the CTAC members. Proposed changes are final once approved by a vote of the Oversight Committee.

**CHARTER APPROVAL**

As reflected by the signatures of the CTAC Chairperson and Oversight Committee’s Presiding Officer, the CTAC Charter was adopted and approved in compliance with the process specified herein on the dates stated below.

**Adopted by the CTAC**

**Approved by the Oversight Committee**

\_\_\_\_\_  
Chair, CTAC

\_\_\_\_\_  
Will Montgomery  
Presiding Officer, Oversight Committee

Date: \_\_\_\_\_

Date: May 16, 2018

**STATEMENT OF REVISIONS:** None

DRAFT



**May 2018 Oversight Committee  
Internal Audit Status Report  
As of April 30, 2018**

Weaver and Tidwell, LLP (Weaver) is the outsourced internal auditor of the Cancer Prevention Research Institute of Texas (CPRIT). The Weaver engagement team is led by Alyssa Martin, Partner and Daniel Graves, Partner.

**2018 Internal Audit Plan and Schedule**

The table below reflects the activity to date Weaver has completed for the 2018 Internal Audit Plan.

NEW INTERNAL AUDITS		
Internal Audit	Description	Timing
Post Award Grant Contracting and Monitoring	<p>Fieldwork for the Post Award Grant Contracting and Monitoring audit was completed on December 20, 2017. We issued the report on February 1, 2018. The audit resulted in an overall assessment of "Strong" with one finding.</p> <p>Moderate Risk Findings:</p> <ol style="list-style-type: none"> <li>1. Separated Employee User Access in the outsourced partner's grant monitoring portal</li> </ol> <p>Follow-up procedures on the remediation of the findings will be included in the proposed audit plan for fiscal year 2019.</p>	Complete
Communications	<p>Internal Audit included an evaluation of risks and internal controls in place related to CPRIT's Communications practices. Activities included Grantee Communications, Listserv, Website Content Compliance, Achievement Report, Media Relations, and Publicly Available Information.</p> <p>Fieldwork has been completed. An exit meeting with Management was held on April 30, 2018. The Findings and Observation Matrix will be delivered to CPRIT Management on May 4, 2018 outlining the preliminary results. Management Responses are expected by May 18, 2018 with a final report expected to be issued by the end of May.</p>	Fieldwork Complete
State Reporting	<p>Internal Audit will include an evaluation of risks and internal controls in place related to CPRIT's State Reporting practices. Activities to be evaluated will include Annual Reporting, Texas Cancer Plan, other Statutory State Reporting, and relevant Research and Analytical supportive data. Activities will also include responding to Public Information Act Requests.</p>	May 2018
Information Technology Services	<p>The Internal Audit was postponed to FY 2019 to allow Internal Audit to perform additional follow-up procedures over open Information Security findings.</p>	FY 2019

FOLLOW-UP PROCEDURES		
Follow-Up	Description	Timing
Training Follow-Up <ul style="list-style-type: none"> <li>• 2 Moderate Findings</li> </ul>	Fieldwork for these follow-up procedures was completed on January 19, 2018. The report was issued February 2, 2018. Both findings from the prior year's audit were remediated.	Complete
Internal Agency Compliance Follow-Up <ul style="list-style-type: none"> <li>• 1 Low Finding</li> </ul>	Fieldwork for these follow-up procedures was completed on January 19, 2018. The report was issued February 2, 2018. The one finding from the prior year's audit was remediated.	Complete
IT Security Follow-up	Fieldwork for initial follow-up procedures was completed on February 2, 2018. Additional follow-up procedures are scheduled to be performed in June 2018.	June 2018
Pre-Award Grant Management Follow-up <ul style="list-style-type: none"> <li>• 1 High Finding</li> <li>• 2 Moderate Findings</li> </ul>	Internal Audit performed follow-up procedures on the 3 findings from the 2017 Internal Audit to ensure corrective action was taken.  Fieldwork has been completed. An exit meeting with Management was held on April 30, 2018. The final report is expected to be issued by the end of May.	Fieldwork Complete
Procurement and P-Cards Follow-up <ul style="list-style-type: none"> <li>• 7 Moderate Findings</li> <li>• 2 Low Findings</li> </ul>	Internal Audit performed follow-up procedures on the 9 findings from the 2017 Internal Audit to ensure corrective action was taken.  Fieldwork has been completed. An exit meeting with Management was held on April 30, 2018. The final report is expected to be issued by the end of May.	Fieldwork Complete

We have prepared a summary schedule of audits, their status and a summary of the findings by risk rating. The schedule maps out the internal audit and follow-up procedures performed, by year, the report date, report rating, and the findings by risk rating. The summary schedule is attached.



Alyssa G. Martin, CPA, MBA, Internal Auditor  
 Executive Partner  
 Weaver and Tidwell L.L.P

**Cancer Prevention and Research Institute of Texas  
Internal Audit of Communications  
Internal Audit Risk Coverage  
March 2018**

**Scope:** The audit will focus on CPRIT's Communications processes. We evaluated the following sub-processes:

- External communication Strategy
- Grantee Communications
- Listserv
- Website Content Compliance
- Achievement Report
- Media Relations
- Publicly Available Information

**Monitored Risks**

Post-Award Grant Management and Grant Contracting		
Process Area	Risks Monitored	
External Communication Strategy	1	External communications are aligned with CPRIT's mission and goals
	2	Communication strategy determined by CPRIT management to be relevant and timely is reviewed and approved
	3	Communication strategy is updated on a periodic and as needed basis
	4	Communication strategy for each target audience is identified
	5	External communication effectiveness is tracked and monitored
Grantee Communications	6	Grantee communication is conducted by appropriate CPRIT staff
	7	Grantee contact information is accurate, timely, and up-to-date
	8	Grantee communications are adequately approved and documented
	9	Grantee communication is consistent with CPRIT's goals and mission
	10	Grantee communication is conducted via appropriate communication methods
Listserv	11	Listserv content is determined to be relevant and aligned with CPRIT's goals and mission
	12	Listserv content is reviewed and approved prior to release
	13	Listserv e-mail list is accurate and complete
	14	Listserv emails are analyzed for SPAM content prior to release
Website Content Compliance	15	Website content is reviewed and approved prior to posting
	16	Updates to website content are made in a timely manner
	17	Website content is in compliance with applicable State regulations
	18	Social media posts are reviewed and approved
	19	Information posted on social media is consistent with CPRIT's goals and mission
Achievement Report	20	Achievement Reports are reviewed and approved prior to release
	21	Report data sources are approved and validated
	22	Report content is determined by CPRIT to be relevant, accurate and complete
	23	Achievement Reports are prepared and released in a timely manner
Media Relations	24	Media inquiries are referred to appropriate CPRIT personnel
	25	All media communications initiated by CPRIT staff are adequately reviewed and approved prior to release
	26	Information provided via media outlets is accurate, complete, and timely
	27	Appropriate individuals are notified prior to CPRIT staff communicating with media
Publicly Available Information	28	News releases and supporting documentation are adequately maintained
	29	Information required to be publicly available is complete and accurate
	30	CPRIT is in compliance with State requirements for publicly available information
	31	Publicly available information is provided timely
	32	Publicly available information is reviewed and approved prior to release

**Cancer Prevention and Research Institute of Texas  
Schedule of Audits, Status, and Findings Summary  
As of April 30, 2018**

Audit	Fiscal Year	Status/Timing	Report Date	Report Rating	Open Findings			Closed Findings			Total Findings			Timing of Follow-Up Procedures by IA	
					High	Mod	Low	High	Mod	Low	High	Mod	Low		Total
<b>Fiscal Year 2015</b>															
Grant Management	2015	Complete	July 27, 2015	Satisfactory	-	8	1	9	-	-	-	-	8	1	9
Expenditures Internal Audit	2015	Complete	August 24, 2015	Strong	-	-	2	2	-	-	-	-	-	2	2
2014 Governance and IT Follow-Up	2015	Complete	August 14, 2015	Satisfactory	-	-	-	9	-	-	-	-	1	1	2
2014 Grantee Monitoring Follow-Up	2015	Complete	July 31, 2015	Satisfactory	-	-	-	14	-	-	-	-	11	1	2
<b>Fiscal Year 2015 Subtotal</b>					-	<b>8</b>	<b>3</b>	<b>34</b>	-	-	-	-	<b>18</b>	<b>1</b>	<b>6</b>
<b>Fiscal Year 2016</b>															
Commodity and Service Contracts Internal Audit	2016	Complete	May 13, 2016	Satisfactory	-	3	2	5	-	-	-	-	3	2	5
Revenue Internal Audit	2016	Complete	July 8, 2016	Strong	-	-	2	2	-	-	-	-	-	2	2
Information Security Internal Audit	2016	Complete	August 3, 2016												
Cash Management Internal Audit	2016	Complete	August 12, 2016	Strong	-	1	-	1	-	-	-	-	1	-	1
2015 Grant Management Follow-Up	2016	Complete	June 9, 2016	Strong	-	8	1	9	-	-	-	-	8	1	9
2015 Information Technology Follow-Up	2016	Complete	N/A	N/A	-	1	1	2	-	-	-	-	1	1	2
<b>Fiscal Year 2016 Subtotal</b>					-	<b>13</b>	<b>6</b>	<b>19</b>	-	-	-	-	<b>4</b>	<b>4</b>	<b>8</b>
<b>Fiscal Year 2017</b>															
Training Program Internal Audit	2017	Complete	March 10, 2017	Strong	-	2	-	2	-	-	-	-	2	-	2
Internal Agency Compliance	2017	Complete	April 17, 2017	Strong	-	1	-	1	-	-	-	-	1	-	1
Pre-Award Grant Management	2017	Complete	May 30, 2017	Satisfactory	1	2	-	3	-	-	-	-	1	2	3
Procurement and P-Card Internal Audit	2017	Complete	August 4, 2017	Satisfactory	-	7	2	9	-	-	-	-	7	2	9
2016 Information Security Follow-Up	2017	Complete	May 30, 2017												
2016 Commodity and Service Contracts Follow-Up	2017	Complete	July 13, 2017	Strong	-	3	2	5	-	-	-	-	3	2	5
2016 Revenue Follow-Up	2017	Complete	July 8, 2017	Strong	-	2	2	2	-	-	-	-	2	2	2
2016 Cash Management Follow-Up	2017	Complete	July 13, 2017	Strong	-	1	-	1	-	-	-	-	1	-	1
<b>Fiscal Year 2017 Subtotal</b>					<b>1</b>	<b>16</b>	<b>6</b>	<b>23</b>	-	-	-	-	<b>4</b>	<b>4</b>	<b>12</b>
<b>Fiscal Year 2018</b>															
Post Award Grant Monitoring Internal Audit	2018	Complete	February 1, 2018	Strong	-	1	-	1	-	-	-	-	1	-	1
Grant Contracting Internal Audit	2018	Fieldwork Complete	TBD	TBD	-	-	-	-	-	-	-	-	-	-	-
Communication Internal Audit	2018	May 2018	TBD	TBD	-	-	-	-	-	-	-	-	-	-	-
State Reporting Internal Audit	2018	FY 2019	TBD	TBD	-	-	-	-	-	-	-	-	-	-	-
Information Technology Services Internal Audit	2018	Fieldwork Complete	TBD	TBD	-	-	-	-	-	-	-	-	-	-	-
2016 Information Security Follow-Up	2018	Fieldwork Complete	February 2, 2018	Strong	-	2	-	2	-	-	-	-	2	-	2
2017 Training Program Follow-Up	2018	Complete	February 2, 2018	Strong	-	1	-	1	-	-	-	-	1	-	1
2017 Internal Agency Compliance Follow-Up	2018	Complete	February 2, 2018	Strong	1	2	-	3	-	-	-	-	1	2	3
2017 Pre-Award Grant Management Follow-Up	2018	Fieldwork Complete	TBD	TBD	-	7	2	9	-	-	-	-	7	2	9
2017 Procurement and P-Card Follow-Up	2018	Fieldwork Complete	TBD	TBD	-	13	2	16	-	-	-	-	3	1	10
<b>Fiscal Year 2018 Subtotal</b>					<b>1</b>	<b>13</b>	<b>2</b>	<b>16</b>	-	-	-	-	<b>3</b>	<b>1</b>	<b>13</b>
<b>FISCAL YEAR 2018 SUMMARY</b>															
Audit	Fiscal Year	Status/Timing	Report Date	Report Rating	Findings			Closed Findings			Total Open Findings			Timing of Follow-Up Procedures by IA	
					High	Mod	Low	High	Mod	Low	High	Mod	Low		Total
Post Award Grant Monitoring Internal Audit	2018	Complete	February 1, 2018	Strong	-	1	-	1	-	-	-	-	1	-	1
Grant Contracting Internal Audit	2018	Fieldwork Complete	May 2018	TBD	-	-	-	-	-	-	-	-	-	-	TBD
Communication Internal Audit	2018	May 2018	TBD	TBD	-	-	-	-	-	-	-	-	-	-	TBD
State Reporting Internal Audit	2018	FY 2019	TBD	TBD	-	-	-	-	-	-	-	-	-	-	TBD
Information Technology Services Internal Audit	2016	Fieldwork Complete	TBD	TBD	-	-	-	-	-	-	-	-	-	-	June 2018
Information Security Internal Audit	2017	Complete	February 2, 2018	Strong	-	2	-	2	-	-	-	-	2	-	-
Training Program Internal Audit	2017	Complete	February 2, 2018	Strong	-	1	-	1	-	-	-	-	1	-	-
Internal Agency Compliance	2017	Complete	May 2018	TBD	1	2	-	3	-	-	-	-	1	2	3
Pre-Award Grant Management	2017	Fieldwork Complete	May 2018	TBD	-	7	2	9	-	-	-	-	7	2	9
Procurement and P-Cards	2017	Fieldwork Complete	May 2018	TBD	-	13	2	16	-	-	-	-	3	1	10
<b>Total Findings For Internal Audit Follow-Up</b>					<b>1</b>	<b>13</b>	<b>2</b>	<b>16</b>	-	-	-	-	<b>3</b>	<b>1</b>	<b>10</b>



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** WAYNE R. ROBERTS, CHIEF EXECUTIVE OFFICER  
**SUBJECT:** SECTION 102.1062 WAIVER – REVIEW COUNCIL MEMBERS  
**DATE:** MAY 9, 2018

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**Waiver Request and Recommendation**

I request that the Oversight Committee approve a fiscal year 2018 conflict of interest waiver for review council members pursuant to Health & Safety Code § 102.1062 “Exceptional Circumstances Requiring Participation.” Unlike other conflict of interest waivers that the Oversight Committee has approved previously, this waiver is not granted for a specific conflict of interest or for a particular person. Instead, CPRIT intends to invoke this waiver as necessary to address the unusual scenario when a review council member has a conflict with a grant application that is part of the larger group of proposals that the review panel or review council must act upon (usually to recommend for awards). The waiver is necessary for a review council member to participate in the overall discussion and vote on the slate of award recommendations.

Although it would be ideal to consider each instance individually before granting the conflict of interest waiver, a prospective waiver is necessary in this scenario given the timing of the review process and scheduled Oversight Committee meetings. It is unlikely that review panel schedules will align with Oversight Committee meeting dates such that CPRIT will be able to secure a conflict of interest waiver in time for the review council member to participate in the review process. However, adequate protections are in place that, together with the waiver’s proposed limitations, mitigate the opportunity for review council members’ decisions regarding the award of grant funds to be influenced by anything other than merit and established criteria.

**Background**

Health & Safety Code § 102.1062 directs the Oversight Committee to adopt administrative rules governing the waiver of the conflict of interest requirements of the statute in exceptional circumstances. CPRIT’s administrative rule § 702.17(3) authorizes the Oversight Committee to approve a waiver that applies for all activities affected by the conflict during the fiscal year. The rules require that a majority of the Oversight Committee members must vote to approve the waiver. Any approved waiver must be reported to the lieutenant governor, speaker of the house of representatives, the governor, and the standing committees of each house of the legislature with primary jurisdiction over CPRIT matters.

The issue addressed by this waiver results from of the role review council members play in the review process. At the review panel level, the review council member chairs the review panel meeting. Occasionally, a review council member will identify a conflict of interest with an application assigned to the member's panel. If CPRIT is unable to reassign the application to a different panel, then the review council member follows the process set forth in CPRIT's conflict of interest rules and recuses himself or herself from any discussion, scoring, deliberation, or vote on the application. The proposed waiver will not change the review council member's responsibility to disclose the conflict or to recuse from the review of the application.

The difficulty arises when the review council member must lead the discussion, in his or her role as chair of the review panel, about the group of applications the panel recommends moving forward to the review council. If the application with which the review council member is in conflict advances as part of the group that scored well enough to move forward, the review council member's participation in the discussion on the group as a whole violates the member's agreement to not participate in "any discussion" of the conflicted application.

A similar challenge arises at the review council level. If the application with which the member is in conflict is part of the group considered by the review council, the conflict of interest rules prohibit the member from participating in the review council's discussion or vote on the group of awards. The review council member is unable to address questions about other applications heard by his or her panel due to his or her recusal from the process, potentially disadvantaging the other applications.

### **Exceptional Circumstances Requiring the Review Council Member's Participation**

In order to approve a conflict of interest waiver, the Oversight Committee must find that there are exceptional circumstances justifying the conflicted individual's participation in the review process. In this case, exceptional circumstances exist due to the necessity of the review council member's participation in the process to develop the overall award recommendation slates and the Oversight Committee should grant the proposed waiver. The limitations mitigate the potential for bias.

CPRIT's administrative rules require the Chief Compliance Officer to attend or designate an independent third party to attend peer review meetings and review council meetings when the panel discusses grant applications. The third-party observer must document that the reviewers follow CPRIT's grant review process consistently, including observing CPRIT's conflict of interest rules. The third-party observer will document any violation of this waiver in his or her written report, which CPRIT provides to the Oversight Committee prior to the vote on the award recommendations.

## **Proposed Waiver and Limitations**

In granting the conflict of interest waiver, I recommend that CPRIT permit the review council member to continue to perform the following activities and duties associated with CPRIT's review process subject to the stated limitations:

1. The review council member must disclose any conflict in writing pursuant to the electronic grant management process CPRIT has in place.
2. The review council member must recuse himself or herself from participation in the review, discussion, scoring, deliberation, and vote on the specific grant(s) identified as the conflict.
3. When the review panel or review council takes up the grant applications as a group, the review council member may participate in the discussion and vote on the proposed awards, so long as the review council member does not advocate for or against the application that the member has identified as a conflict.
4. Whenever CPRIT invokes this waiver, the Chief Compliance Officer will provide information about the use of the waiver, including the name of the review council member and the identified conflict, in the Chief Compliance Officer's Certification report. I will also include this information in the CEO affidavit I submit for the grant award mechanism.

Due to the nature of the conflict or the type of review process, this conflict of interest waiver will not apply to following:

- When the review council member's conflict of interest is a conflict described by T.A.C. § 702.13(c); or
- When the review council is acting as the only review panel in the review process (e.g. CPRIT recruitment awards and prevention dissemination awards.)

## **Important Information Regarding this Waiver and the Waiver Process**

- The Oversight Committee may amend, revoke, or revise this waiver, including but not limited to the list of approved activities and duties and the limitations on duties and activities. Approval for any change to the waiver granted shall be by a vote of the Oversight Committee in an open meeting.
- This waiver is limited to review council members operating under the circumstances specified in this request.





CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**To: OVERSIGHT COMMITTEE MEMBERS**  
**From: KRISTEN PAULING DOYLE, GENERAL COUNSEL**  
**CAMERON L. ECKEL, STAFF ATTORNEY**  
**Subject: CHAPTER 703 RULE CHANGES PROPOSED FOR FINAL**  
**ADOPTION**  
**Date: MAY 4, 2018**

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**Summary and Recommendation**

The Board Governance Subcommittee recommends that the Oversight Committee adopt the proposed administrative rule changes to §§ 703.13 and 703.21 as originally considered at the February meeting. Once the Oversight Committee approves the final order adopting the rule changes, CPRIT will submit the amendments to the Secretary of State and the changes will be effective 20 days later.

**Discussion**

State law requires an agency to set policy using a rulemaking process, which includes an opportunity for public comment on proposed rules and rule changes before the agency formally adopts the policy.

The Oversight Committee approved publication of proposed rule amendments to §§ 703.13 and 703.21 at the February meeting. CPRIT published the proposed rules in the *Texas Register* and made the rules available on the agency's website. CPRIT received no comments regarding the proposed changes.

The Board Governance Subcommittee met on May 3rd to review the final order with CPRIT's General Counsel. The Subcommittee recommends the Oversight Committee approve the final order adopting the proposed rule changes.

**Next Steps**

After the Oversight Committee adopts the proposed rule changes, CPRIT will submit the final order to the Secretary of State. The rule changes become effective 20 days after the date CPRIT files the order with the Secretary of State.



TITLE 25. HEALTH SERVICES

PART 11. CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS

CHAPTER 703. Grants for Cancer Prevention and Research

The Cancer Prevention and Research Institute of Texas (“CPRIT” or “the Institute”) adopts the amendments to §§ 703.13(b) and 703.21(b)(2)(B). The proposed amendments change the due date of the single audit determination form, which grant recipients are required to submit to the Institute annually. CPRIT published the proposed amendment in the March 9, 2018, issue of the *Texas Register* (43 TexReg 1380).

**Reasoned Justification**

The proposed amendment to § 703.13(b) changes the due date of the single audit determination form to 60 days after the close of the grant recipient’s fiscal year. CPRIT requires every grant recipient to submit the single audit determination form reporting whether the grant recipient has expended \$750,000 or more in state award funds. The amount of grant funds expended determines if the grant recipient must submit an audit. Changing the due date removes confusion regarding when single audit determination forms should be submitted and provides for a more streamlined submission process. The proposed change to § 703.21(b)(2)(B) ensures that the due date of the single audit determination form is consistently referenced within Chapter 703.

**Summary of Public Comments and Staff Recommendation**

CPRIT received no public comments regarding the proposed amendments to §§ 703.13 and 703.13.

The rule change is adopted under the authority of the Texas Health and Safety Code Annotated, § 102.108, which provides the Institute with broad rule-making authority to administer the chapter, including rules for awarding grants.

**Certification**

The Institute hereby certifies that Kristen Pauling Doyle, General Counsel, reviewed the adoption of the rules and found it to be a valid exercise of the agency’s legal authority.

To be filed with the Office of Secretary of State on May 18, 2018.

§ 703.13 Audits and Investigations

(a) Upon request and with reasonable notice, an entity receiving Grant Award funds directly under the Grant Contract or indirectly through a subcontract under the Grant Contract shall allow, or shall cause the entity that is maintaining such items to allow the Institute, or auditors or investigators working on behalf of the Institute, including the State Auditor and/or the Comptroller of Public Accounts for the State of Texas, to review, inspect, audit, copy or abstract its records pertaining to the specific Grant Contract during the term of the Grant Contract and for

the three year period following the date the last disbursement of funds is made by the Institute or all reports required pursuant to the Grant Contract are submitted and approved, whichever date is later.

(1) A Grant Recipient shall maintain its records pertaining to the specific Grant Contract for a period of three years following the date the last disbursement of funds is made by the Institute or all reports required pursuant to the Grant Contract are submitted and approved, whichever date is later.

(2) The Grant Recipient may maintain its records in either electronic or paper format.

(b) Notwithstanding the foregoing, the Grant Recipient shall submit a single audit determination form no later than 60 days following the close of the Grant Recipient's fiscal year. The Grant Recipient shall report whether the Grant Recipient has expended \$750,000 or more in state awards during the Grant Recipient's fiscal year. If the Grant Recipient has expended \$750,000 or more in state awards in its fiscal year, the Grant Recipient shall obtain either an annual single independent audit, a program specific independent audit, or an agreed upon procedures engagement as defined by the American Institute of Certified Public Accountants and pursuant to guidance provided in subsection (e).

(1) The audited time period is the Grant Recipient's fiscal year.

(2) The audit must be submitted to the Institute within 30 days of receipt by the Grant Recipient but no later than 270 days following the close of the Grant Recipient's fiscal year and shall include a corrective action plan that addresses any weaknesses, deficiencies, wrongdoings, or other concerns raised by the audit report and a summary of the action taken by the Grant Recipient to address the concerns, if any, raised by the audit report.

(A) The Grant Recipient may seek additional time to submit the required audit and corrective action plan by providing a written explanation for its failure to timely comply and providing an expected time for the submission.

(B) The Grant Recipient's request for additional time must be submitted on or before the due date of the required audit and corrective action plan. For purposes of this rule, the "due date of the required audit" is no later than the 270th day following the close of the Grant Recipient's fiscal year.

(C) Approval of the Grant Recipient's request for additional time is at the discretion of the Institute. Such approval must be granted by the Chief Executive Officer.

(c) No reimbursements or advances of Grant Award funds shall be made to the Grant Recipient if the Grant Recipient is delinquent in filing the required audit and corrective action plan. A Grant Recipient that has received approval from the Institute for additional time to file the required audit and corrective action plan may receive reimbursements or advances of Grant Award funds during the pendency of the delinquency unless the Institute's approval declines to permit reimbursements or advances of Grant Award funds until the delinquency is addressed.

(d) A Grant Recipient that is delinquent in submitting to the Institute the audit and corrective action plan required by this section is not eligible to be awarded a new Grant Award or a continuation Grant Award until the required audit and corrective action plan are submitted. A Grant Recipient that has received approval from the Institute for additional time to file the required audit and corrective action plan may remain eligible to be awarded a new Grant Award or a continuation Grant Award unless the Institute's approval declines to continue eligibility during the pendency of the delinquency.

(e) For purposes of this rule, an agreed upon procedures engagement is one in which an independent certified public accountant is hired by the Grant Recipient to issue a report of findings based on specific procedures to be performed on a subject matter.

(1) The option to perform an agreed upon procedures engagement is intended for a non-profit or for-profit Grant Recipient that is not subject to Generally Accepted Government Audit Standards (also known as the Yellow Book) published by the U.S. Government Accountability Office.

(2) The agreed upon procedures engagement will be conducted in accordance with attestation standards established by the American Institute of Certified Public Accountants.

(3) The certified public accountant is to perform procedures prescribed by the Institute and to report his or her findings attesting to whether the Grant Recipient records is in agreement with stated criteria.

(4) The agreed upon procedures apply to all current year expenditures for Grant Awards received by the Grant Recipient. Nothing herein prohibits the use of a statistical sample consistent with the American Institute of Certified Public Accountants' guidance regarding government auditing standards and 2 CFR Part 200, Subpart F, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards."

(5) At a minimum, the agreed upon procedures report should address:

(A) Processes and controls;

(B) The Grant Contract;

(C) Indirect Costs;

(D) Matching Funds, if appropriate;

(E) Grant Award expenditures (payroll and non-payroll related transactions);

(F) Equipment;

(G) Revenue Sharing and Program Income;

(H) Reporting; and

(I) Grant Award closeout.

(6) The certified public accountant should consider the specific Grant Mechanism and update or modify the procedures accordingly to meet the requirements of each Grant Award and the Grant Contract reviewed.

#### § 703.21 Monitoring Grant Award Performance and Expenditures

(a) The Institute, under the direction of the Chief Compliance Officer, shall monitor Grant Awards to ensure that Grant Recipients comply with applicable financial, administrative, and programmatic terms and conditions and exercise proper stewardship over Grant Award funds. Such terms and conditions include requirements set forth in statute, administrative rules, and the Grant Contract.

(b) Methods used by the Institute to monitor a Grant Recipient's performance and expenditures may include:

(1) Financial Status Reports Review - The Institute shall review Grant Award expenditures reported by Grant Recipients on the quarterly Financial Status Reports and supporting documents to determine whether expenses charged to the Grant Award are:

(A) Allowable, allocable, reasonable, necessary, and consistently applied regardless of the source of funds; and

(B) Adequately supported with documentation such as cost reports, receipts, third party invoices for expenses, or payroll information.

(2) Timely submission of Grant Award Reports - The Institute shall monitor the submission of all required reports and implement a process to ensure that Grant Award funds are not disbursed to a Grant Recipient with one or more delinquent reports.

(3) Grant Progress Reports - The Institute shall review Grant Progress Reports to determine whether sufficient progress is made consistent with the scope of work and timeline set forth in the Grant Contract.

(A) The Grant Progress Reports shall be submitted at least annually, but may be required more frequently pursuant to Grant Contract terms or upon request and reasonable notice of the Institute.

(B) Unless specifically stated otherwise herein, the annual Grant Progress Report shall be submitted within sixty (60) days after the anniversary of the effective date of the Grant Contract. The annual Grant Progress Report shall include at least the following information:

(i) An affirmative verification by the Grant Recipient of compliance with the terms and conditions of the Grant Contract;

(ii) A description of the Grant Recipient's progress made toward completing the scope of work specified by the Grant Contract, including information, data, and program metrics regarding the achievement of project goals and timelines;

(iii) The number of new jobs created and the number of jobs maintained for the preceding twelve month period as a result of Grant Award funds awarded to the Grant Recipient for the project;

(iv) An inventory of the equipment purchased for the project in the preceding twelve month period using Grant Award funds;

(v) A verification of the Grant Recipient's efforts to purchase from suppliers in this state more than 50 percent goods and services purchased for the project with grant funds;

(vi) A Historically Underutilized Businesses report;

(vii) Scholarly articles, presentations, and educational materials produced for the public addressing the project funded by the Institute;

(viii) The number of patents applied for or issued addressing discoveries resulting from the research project funded by the Institute;

(ix) A statement of the identities of the funding sources, including amounts and dates for all funding sources supporting the project;

(x) A verification of the amounts of Matching Funds dedicated to the research that is the subject of the Grant Award for the period covered by the annual report, which shall be submitted pursuant to the timeline in §703.11. In order to receive disbursement of grant funds, the most recently due verification of the amount of Matching Funds must be approved by CPRIT;

(xi) All financial information necessary to support the calculation of the Institute's share of revenues, if any, received by the Grant Recipient resulting from the project; and

(xii) A single audit determination form, which shall be submitted pursuant to the timeline in § 703.13.

(C) Notwithstanding subparagraph (B) of this paragraph, in the event that the Grant Recipient and Institute execute the Grant Contract after the effective date of the Grant Contract, the Chief Program Officer may approve additional time for the Grant Recipient to prepare and submit the outstanding reports. The approval shall be in writing and maintained in the Institute's electronic Grants Management System. The Chief Program Officer's approval may cover more than one report and more than one fiscal quarter.

(D) In addition to annual Grant Progress Reports, a final Grant Progress Report shall be filed no more than ninety (90) days after the termination date of the Grant Contract. The final Grant Progress Report shall include a comprehensive description of the Grant Recipient's progress made toward completing the scope of work specified by the Grant Contract, as well as other information specified by the Institute.

(E) The Grant Progress Report will be evaluated pursuant to criteria established by the Institute. The evaluation shall be conducted under the direction of the Chief Prevention Officer, the Chief Product Development Officer, or the Chief Scientific Officer, as may be appropriate. Required financial reports associated with the Grant Progress Report will be reviewed by the

Institute's financial staff. In order to receive disbursement of grant funds, the final progress report must be approved by CPRIT.

(F) If the Grant Progress Report evaluation indicates that the Grant Recipient has not demonstrated progress in accordance with the Grant Contract, then the Chief Program Officer shall notify the Chief Executive Officer and the General Counsel for further action.

(i) The Chief Program Officer shall submit written recommendations to the Chief Executive Officer and General Counsel for actions to be taken, if any, to address the issue.

(ii) The recommended action may include termination of the Grant Award pursuant to the process described in §703.14 of this chapter (relating to Termination, Extension, and Close Out of Grant Contracts).

(G) If the Grant Recipient fails to submit required financial reports associated with the Grant Progress Report, then the Institute financial staff shall notify the Chief Executive Officer and the General Counsel for further action.

(H) In order to receive disbursement of grant funds, the most recently due progress report must be approved by CPRIT.

(I) If a Grant Recipient fails to submit the Grant Progress Report within 60 days of the anniversary of the effective date of the Grant Contract, then the Institute shall not disburse any Grant Award funds as reimbursement or advancement of Grant Award funds until such time that the delinquent Grant Progress Report is approved.

(J) In addition to annual Grant Progress Reports, Product Development Grant Recipients shall submit a Grant Progress Report at the completion of specific tranches of funding specified in the Award Contract. For the purpose of this subsection, a Grant Progress Report submitted at the completion of a tranche of funding shall be known as "Tranche Grant Progress Report."

(i) The Institute may specify other required reports, if any, that are required to be submitted at the time of the Tranche Grant Progress Report.

(ii) Grant Funds for the next tranche of funding specified in the Grant Contract shall not be disbursed until the Tranche Grant Progress Report has been reviewed and approved pursuant to the process described in this section.

(4) Desk Reviews - The Institute may conduct a desk review for a Grant Award to review and compare individual source documentation and materials to summary data provided during the Financial Status Report review for compliance with financial requirements set forth in the statute, administrative rules, and the Grant Contract.

(5) Site Visits and Inspection Reviews - The Institute may conduct a scheduled site visit to a Grant Recipient's place of business to review Grant Contract compliance and Grant Award performance issues. Such site visits may be comprehensive or limited in scope.

(6) Audit Reports - The Institute shall review audit reports submitted pursuant to §703.13 of this chapter (relating to Audits and Investigations).

(A) If the audit report findings indicate action to be taken related to the Grant Award funds expended by the Grant Recipient or for the Grant Recipient's fiscal processes that may impact Grant Award expenditures, the Institute and the Grant Recipient shall develop a written plan and timeline to address identified deficiencies, including any necessary Grant Contract amendments.

(B) The written plan shall be retained by the Institute as part of the Grant Contract record.

(c) All required Grant Recipient reports and submissions described in this section shall be made via an electronic grant portal designated by the Institute, unless specifically directed to the contrary in writing by the Institute.

(d) The Institute shall document the actions taken to monitor Grant Award performance and expenditures, including the review, approvals, and necessary remedial steps, if any.

(1) To the extent that the methods described in subsection (b) of this section are applied to a sample of the Grant Recipients or Grant Awards, then the Institute shall document the Grant Contracts reviewed and the selection criteria for the sample reviewed.

(2) Records will be maintained in the electronic Grant Management System as described in §703.4 of this chapter (relating to Grants Management System).

(e) The Chief Compliance Officer shall be engaged in the Institute's Grant Award monitoring activities and shall notify the General Counsel and Oversight Committee if a Grant Recipient fails to meaningfully comply with the Grant Contract reporting requirements and deadlines, including Matching Funds requirements.

(f) The Chief Executive Officer shall report to the Oversight Committee at least annually on the progress and continued merit of each Grant Program funded by the Institute. The written report shall also be included in the Annual Public Report. The report should be presented to the Oversight Committee at the first meeting following the publication of the Annual Public Report.

(g) The Institute may rely upon third parties to conduct Grant Award monitoring services independently or in conjunction with Institute staff





CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**To: OVERSIGHT COMMITTEE MEMBERS**  
**From: KRISTEN PAULING DOYLE, GENERAL COUNSEL**  
**CAMERON L. ECKEL, STAFF ATTORNEY**  
**Subject: CHAPTERS 701 AND 703 PROPOSED RULE CHANGES**  
**Date: MAY 4, 2018**

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**Summary and Recommendation**

The Board Governance Subcommittee recommends that the Oversight Committee approve the proposed administrative rule changes for publication in the *Texas Register* for public comment. The proposed changes affect Texas Administrative Code Chapters 701 and 703.

**Discussion**

CPRIT's administrative rules set policy guiding CPRIT's grant review and grant contracting processes as well as administering other requirements of Texas Health and Safety Code Chapter 102. State law requires agencies to use a rulemaking process, which includes an opportunity for the public to comment on proposed rules and rule changes before the agency adopts the final policy.

The Board Governance subcommittee met on May 3rd to discuss the proposed rule changes to §§ 701.3, 701.27, and 703.11 with legal staff. The proposed amendment to § 701.3 clarifies the definition of "Request for Application" (RFA) includes any associated instructions released with the RFA. CPRIT proposes to amend Section 701.27 by deleting the requirement that CPRIT post Oversight Committee members' political contributions. The change is consistent with a recent legislative change to CPRIT's statute that removed political contribution reporting requirements for Oversight Committee members. The final proposed amendment to § 703.11 changes the time frame when a grantee may use a new federal indirect cost rate (FICR) towards their matching funds requirement. Currently, if the FICR changes less than six months following the anniversary of the effective date of the grant contract, the grant recipient may use the new rate. The proposed amendment changes the time from the effective date to "six months or less" for a grant recipient to use a new FICR. The subcommittee voted to recommend approval and publication of the proposed rule changes to the Oversight Committee.

## **Next Steps**

CPRIT will publish the proposed rule changes in the *Texas Register*. The publication date begins the 30-day period soliciting public comment. CPRIT will post the proposed rule on CPRIT's website and announce the opportunity for public comment via the CPRIT electronic list serve. CPRIT legal staff will summarize all public comments for the Oversight Committee's consideration when approving the final rule changes in August.

TITLE 25. HEALTH SERVICES

PART 11. CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS

CHAPTER 701. Policies and Procedures

The Cancer Prevention and Research Institute of Texas (CPRIT or the Institute) proposes amendments to §§ 701.3 and 701.27. The proposed amendments clarify the definition of Request for Applications and remove political contributions of Oversight Committee members as part of the Institute website.

**Background and Justification**

The proposed amendment to § 701.3 clarifies that the defined term, Request for Applications, includes any associated instructions released with the Request for Applications. The proposed amendment to § 701.27 makes the administrative rule consistent with a change to CPRIT's statute made during the 2017 Texas Legislature regular session. The Legislature amended Texas Health & Safety Code Chapter 102 to remove the requirements that Oversight Committee members report political contributions over \$1,000 and that CPRIT posts the reported information on its website. Consistent with those changes, the amendment to § 701.17 removes the report of Oversight Committee members' political contributions from the list of items the Institute is required to post on its website.

**Fiscal Note**

Kristen Pauling Doyle, Deputy Executive Officer and General Counsel for the Cancer Prevention and Research Institute of Texas, has determined that for the first five-year period the rule change is in effect, there will be no foreseeable implications relating to costs or revenues for state or local government due to enforcing or administering the rules.

**Public Benefit and Costs**

Ms. Doyle has determined that for each year of the first five years the rule change is in effect the public benefit anticipated due to enforcing the rule will be the clarification of a defined term and consistency with state law.

**Small Business, Micro-Business, and Rural Communities Impact Analysis**

Ms. Doyle has determined that the rule change will not affect small businesses, micro businesses or rural communities.

**Government Growth Impact Statement**

The Institute, in accordance with 34 Texas Administrative Code §11.1, has determined that during the first five years that the section will be in effect:

- (1) the proposed rule changes will not create or eliminate a government program;
- (2) implementation of the proposed rule changes will not affect the number of employee positions;

- (3) implementation of the proposed rule changes will not require an increase or decrease in future legislative appropriations;
- (4) the proposed rule changes will not affect fees paid to the agency;
- (5) the proposed rule changes will not create new rules;
- (6) the proposed rule changes will expand existing rules;
- (7) the proposed rule changes will not change the number of individuals subject to the rules; and
- (8) The rule changes are unlikely to have a significant impact on the state's economy. Although these changes are likely to have neutral impact on the state's economy, the Institute lacks sufficient data to predict the impact with certainty.

Submit written comments on the proposed rule changes to Ms. Kristen Pauling Doyle, General Counsel, Cancer Prevention and Research Institute of Texas, P. O. Box 12097, Austin, Texas 78711, no later than July 2, 2018. The Institute asks parties filing comments to indicate whether they support the rule revisions proposed by the Institute and, if a change is requested, to provide specific text proposed to be included in the rule. Comments may be submitted electronically to [kdoyle@cprit.texas.gov](mailto:kdoyle@cprit.texas.gov). Comments may be submitted by facsimile transmission to 512/475-2563.

### **Statutory Authority**

The Institute proposes the rule changes under the authority of the Texas Health and Safety Code Annotated, § 102.108, which provides the Institute with broad rule-making authority to administer the chapter. Ms. Doyle has reviewed the proposed amendments and certifies the proposal to be within the Institute's authority to adopt.

There is no other statute, article, or code affected by these rules.

### **§ 701.3**

The following words and terms, when used in this chapter, shall have the following meanings, unless the context clearly indicates otherwise.

(1) **Advisory Committee**--a committee of experts, including practitioners and patient advocates, created by the Oversight Committee to advise the Oversight Committee on issues related to cancer.

(2) **Allowable Cost**--a cost that is reasonable, necessary for the proper and efficient performance and administration of the project, and allocable to the project.

(3) **Annual Public Report**--the report issued by the Institute pursuant to Texas Health and Safety Code §102.052 outlining Institute activities, including Grant Awards, research accomplishments, future Program directions, compliance, and Conflicts of Interest actions.

(4) Authorized Expense--cost items including honoraria, salaries and benefits, consumable supplies, other operating expenses, contracted research and development, capital equipment, construction or renovation of state or private facilities, travel, and conference fees and expenses.

(5) Approved Budget--the financial expenditure plan for the Grant Award, including revisions approved by the Institute and permissible revisions made by the Grant Recipient. The Approved Budget may be shown by Project Year and detailed budget categories.

(6) Authorized Signing Official (ASO)--the individual, including designated alternates, named by the Grant Applicant, who is authorized to act for the Grant Applicant or Grant Recipient in submitting the Grant Application and executing the Grant Contract and associated documents or requests.

(7) Bylaws--the rules established by the Oversight Committee to provide a framework for its operation, management, and governance.

(8) Cancer Prevention--a reduction in the risk of developing cancer, including early detection, control and/or mitigation of the incidence, disability, mortality, or post-diagnosis effects of cancer.

(9) Cancer Prevention and Control Program--effective strategies and interventions for preventing and controlling cancer designed to reduce the incidence and mortality of cancer and to enhance the quality of life of those affected by cancer.

(10) Cancer Prevention and Research Fund--the dedicated account in the general revenue fund consisting of legislative appropriations, gifts, grants, other donations, and earned interest.

(11) Cancer Research--research into the prevention, causes, detection, treatments, and cures for all types of cancer in humans, including basic mechanistic studies, pre-clinical studies, animal model studies, translational research, and clinical research to develop preventative measures, therapies, protocols, medical pharmaceuticals, medical devices or procedures for the detection, treatment, cure or substantial mitigation of all types of cancer and its effects in humans.

(12) Chief Compliance Officer--the individual employed by the Institute to monitor and report to the Oversight Committee regarding compliance with the Institute's statute and administrative rules. The term may also apply to an individual designated by the Chief Compliance Officer to fulfill the duty or duties described herein, unless the context clearly indicates otherwise.

(13) Chief Executive Officer--the individual hired by the Oversight Committee to perform duties required by the Institute's Statute or designated by the Oversight Committee. The term may apply to an individual designated by the Chief Executive Officer to fulfill the duty or duties described herein, unless the context clearly indicates otherwise.

(14) Chief Prevention Officer--the individual hired by the Chief Executive Officer to oversee the Institute's Cancer Prevention program, including the Grant Review Process, and to assist the Chief Executive Officer in collaborative outreach to further Cancer Research and Cancer Prevention. The term may also apply to an individual designated by the Chief Prevention Officer to fulfill the duty or duties described herein, unless the context clearly indicates otherwise.

(15) Chief Product Development Officer--the individual hired by Chief Executive Officer to oversee the Institute's Product Development program for drugs, biologicals, diagnostics, or devices arising from Cancer Research, including the Grant Review Process, and to assist the Chief Executive Officer in collaborative outreach to further Cancer Research and Cancer Prevention. The term may apply to an individual designated by the Chief Product Development Officer to fulfill the duty or duties described herein, unless the context clearly indicates otherwise.

(16) Chief Scientific Officer--the individual hired by the Chief Executive Officer to oversee the Institute's Cancer Research program, including the Grant Review Process, and to assist the Chief Executive Officer in collaborative outreach to further Cancer Research and Cancer Prevention. The term may apply to an individual designated by the Chief Scientific Officer to fulfill the duty or duties described herein, unless the context clearly indicates otherwise.

(17) Code of Conduct and Ethics--the code adopted by the Oversight Committee pursuant to Texas Health and Safety Code §102.109 to provide guidance related to the ethical conduct expected of Oversight Committee Members, Program Integration Committee Members, and Institute Employees.

(18) Compliance Program--a process to assess and ensure compliance by the Oversight Committee Members and Institute Employees with applicable laws, rules, and policies, including matters of ethics and standards of conduct, financial reporting, internal accounting controls, and auditing.

(19) Conflict(s) of Interest--a financial, professional, or personal interest held by the individual or the individual's Relative that is contrary to the individual's obligation and duty to act for the benefit of the Institute.

(20) Encumbered Funds--funds that are designated by a Grant Recipient for a specific purpose.

(21) Financial Status Report--form used to report all Grant Award related financial expenditures incurred in implementation of the Grant Award. This form may also be referred to as "FSR" or "Form 269-A."

(22) Grant Applicant--the public or private institution of higher education, as defined by §61.003, Texas Education Code, research institution, government organization, non-governmental organization, non-profit organization, other public entity, private company, individual, or consortia, including any combination of the aforementioned, that submits a Grant Application to the Institute. Unless otherwise indicated, this term includes the Principal Investigator or Program Director.

(23) Grant Application--the written proposal submitted by a Grant Applicant to the Institute in the form required by the Institute that, if successful, will result in a Grant Award.

(24) Grant Award--funding, including a direct company investment, awarded by the Institute pursuant to a Grant Contract providing money to the Grant Recipient to carry out the Cancer Research or Cancer Prevention project in accordance with rules, regulations, and guidance provided by the Institute.

(25) Grant Contract--the legal agreement executed by the Grant Recipient and the Institute setting forth the terms and conditions for the Cancer Research or Cancer Prevention Grant Award approved by the Oversight Committee.

(26) Grant Management System--the electronic interactive system used by the Institute to exchange, record, and store Grant Application and Grant Award information.

(27) Grant Mechanism--the specific Grant Award type.

(28) Grant Program--the functional area in which the Institute makes Grant Awards, including research, prevention and product development.

(29) Grant Progress Report--the required report submitted by the Grant Recipient at least annually and at the close of the grant award describing the activities undertaken to achieve the goals and objectives of the funded project and including information, data and program metrics. Unless the context clearly indicates otherwise, the Grant Progress Report also includes other required reports such as a Historically Underutilized Business and Texas Supplier form, a single audit determination form, an inventory report, a single audit determination form, a revenue sharing form, and any other reports or forms designated by the Institute.

(30) Grant Recipient--the entire legal entity responsible for the performance or administration of the Grant Award pursuant to the Grant Contract. Unless otherwise indicated, this term includes the Principal Investigator, Program Director, or Company Representative.

(31) Grant Review Cycle--the period that begins on the day that the Request for Applications is released for a particular Grant Mechanism and ends on the day that the Oversight Committee takes action on the Grant Award recommendations.

(32) Grant Review Process--the Institute's processes for Peer Review, Program Review and Oversight Committee approval of Grant Applications.

(33) Indirect Costs--the expenses of doing business that are not readily identified with a particular Grant Award, Grant Contract, project, function, or activity, but are necessary for the general operation of the Grant Recipient or the performance of the Grant Recipient's activities.

(34) Institute--the Cancer Prevention and Research Institute of Texas or CPRIT.

(35) Institute Employee--any individual employed by the Institute, including any individual performing duties for the Institute pursuant to a contract of employment. Unless otherwise indicated, the term does not include an individual providing services to the Institute pursuant to a services contract.

(36) Intellectual Property Rights--any and all of the following and all rights in, arising out of, or associated therewith, but only to the extent resulting from the Grant Award:

(A) The United States and foreign patents and utility models and applications therefore and all reissues, divisions, re-examinations, renewals, extensions, provisionals, continuations and such claims of continuations-in-part as are entitled to claim priority to the aforesaid patents or patent

applications, and equivalent or similar rights anywhere in the world in Inventions and discoveries;

(B) All trade secrets and rights in know-how and proprietary information;

(C) All copyrights, whether registered or unregistered, and applications therefore, and all other rights corresponding thereto throughout the world excluding scholarly and academic works such as professional articles and presentations, lab notebooks, and original medical records; and

(D) All mask works, mask work registrations and applications therefore, and any equivalent or similar rights in semiconductor masks, layouts, architectures or topography.

(37) Invention--any method, device, process or discovery that is conceived and/or reduced to practice, whether patentable or not, by the Grant Recipient in the performance of work funded by the Grant Award.

(38) License Agreement--an understanding by which an owner of Technology and associated Intellectual Property Rights grants any right to make, use, develop, sell, offer to sell, import, or otherwise exploit the Technology or Intellectual Property Rights in exchange for consideration.

(39) Matching Funds--the Grant Recipient's Encumbered Funds equal to one-half of the Grant Award available and not yet expended that are dedicated to the research that is the subject of the Grant Award. For public and private institutions of higher education, this includes the dollar amount equivalent to the difference between the indirect cost rate authorized by the federal government for research grants awarded to the Grant Recipient and the five percent (5%) Indirect Cost limit imposed by §102.203(c), Texas Health and Safety Code.

(40) Numerical Ranking Score--the score given to a Grant Application by the Review Council that is substantially based on the final Overall Evaluation Score submitted by the Peer Review Panel, but also signifies the Review Council's view related to how well the Grant Application achieves program priorities set by the Oversight Committee, the overall Program portfolio balance, and any other criteria described in the Request for Applications.

(41) Overall Evaluation Score--the score given to a Grant Application during the Peer Review Panel review that signifies the reviewers' overall impression of the Grant Application. Typically it is the average of the scores assigned by two or more Peer Review Panel members.

(42) Oversight Committee--the Institute's governing body, composed of the nine individuals appointed by the Governor, Lieutenant Governor, and the Speaker of the House of Representatives.

(43) Oversight Committee Member--any person appointed to and serving on the Oversight Committee.

(44) Patient Advocate--a trained individual who meets the qualifications set by the Institute and is appointed to a Scientific Research and Prevention Programs Committee to specifically represent the interests of cancer patients as part of the Peer Review of Grant Applications assigned to the individual's committee.

(45) Peer Review--the review process performed by Scientific Research and Prevention Programs Committee members and used by the Institute to provide guidance and recommendations to the Program Integration Committee and the Oversight Committee in making decisions for Grant Awards. The process involves the consistent application of standards and procedures to produce a fair, equitable, and objective evaluation of scientific and technical merit, as well as other relevant aspects of the Grant Application. When used herein, the term applies individually or collectively, as the context may indicate, to the following review process(es): Preliminary Evaluation, Individual Evaluation by Primary Reviewers, Peer Review Panel discussion and Review Council prioritization.

(46) Peer Review Panel--a group of Scientific Research and Prevention Programs Committee members conducting Peer Review of assigned Grant Applications.

(47) Prevention Review Council--the group of Scientific Research and Prevention Programs Committee members designated as the chairpersons of the Peer Review Panels that review Cancer Prevention program Grant Applications. This group includes the Review Council chairperson.

(48) Primary Reviewer--a Scientific Research and Prevention Programs Committee member responsible for individually evaluating all components of the Grant Application, critiquing the merits according to explicit criteria published in the Request for Applications, and providing an individual Overall Evaluation Score that conveys the general impression of the Grant Application's merit.

(49) Principal Investigator, Program Director, or Company Representative--the single individual designated by the Grant Applicant or Grant Recipient to have the appropriate level of authority and responsibility to direct the project to be supported by the Grant Award.

(50) Product Development Review Council--the group of Scientific Research and Prevention Programs Committee Members designated as the chairpersons of the Peer Review Panels that review Grant Applications for the development of drugs, biologics, diagnostics, or devices arising from earlier-stage Cancer Research. This group includes the Review Council chairperson.

(51) Product Development Prospects--the potential for development of products, services, or infrastructure to support Cancer Research efforts, including but not limited to pre-clinical, clinical, manufacturing, and scale up activities.

(52) Program Income--income from fees for services performed, from the use or rental of real or personal property acquired with Grant Award funds, and from the sale of commodities or items fabricated under the Grant Contract. Except as otherwise provided, Program Income does not include rebates, credits, discounts, refunds, etc. or the interest earned on any of these items. Interest otherwise earned in excess of \$250 on Grant Award funds is considered Program Income.

(53) Program Integration Committee--the group composed of the Chief Executive Officer, the Chief Scientific Officer, the Chief Product Development Officer, the Commissioner of State

Health Services, and the Chief Prevention Officer that is responsible for submitting to the Oversight Committee the list of Grant Applications the Program Integration Committee recommends for Grant Awards.

(54) Project Results--all outcomes of a Grant Award, including publications, knowledge gained, additional funding generated, and any and all Technology and associated Intellectual Property Rights.

(55) Project Year--the intervals of time (usually 12 months each) into which a Grant Award is divided for budgetary, funding, and reporting purposes. The effective date of the Grant Contract is the first day of the first Project Year.

(56) Real Property--land, including land improvements, structures and appurtenances thereto, excluding movable machinery and equipment.

(57) Relative--a person related within the second degree by consanguinity or affinity determined in accordance with §§573.021 - 573.025, Texas Government Code. For purposes of this definition:

(A) examples of an individual within the second degree by consanguinity are a child, grandchild, parent, grandparent, brother, sister;

(B) a husband and wife are related to each other in the first degree of affinity. For other relationship by affinity, the degree of relationship is the same as the degree of the underlying relationship by consanguinity;

(C) an individual adopted into a family is considered a Relative on the same basis as a natural born family member; and

(D) an individual is considered a spouse even if the marriage has been dissolved by death or divorce if there are surviving children of that marriage.

(58) Request for Applications--the invitation released by the Institute seeking the submission of Grant Applications for a particular Grant Mechanism. It provides information relevant to the Grant Award to be funded, including funding amount, Grant Review Process information, evaluation criteria, and required Grant Application components. [The Request for Applications includes any associated written instructions provided by the Institute and available to all Grant Applicants.](#)

(59) Review Council--the term used to generally refer to one or more of the Prevention Review Council, the Product Development Review Council, or Scientific Review Council.

(60) Scientific Research and Prevention Programs Committee--a group of experts in the field of Cancer Research, Cancer Prevention or Product Development, including trained Patient Advocates, appointed by the Chief Executive Officer and approved by the Oversight Committee for the purpose of conducting Peer Review of Grants Applications and recommending Grant Awards. A Peer Review Panel is a Scientific Research and Prevention Programs Committee, as is a Review Council.

(61) Scientific Research and Prevention Programs Committee Member--an individual appointed by the Chief Executive Officer and approved by the Oversight Committee to serve on a Scientific Research and Prevention Programs Committee. Peer Review Panel Members are Scientific Research and Prevention Programs Committee Members, as are Review Council Members.

(62) Scientific Review Council--the group of Scientific Research and Prevention Programs Committee Members designated as the chairpersons of the Peer Review Panels that review Cancer Research Grant Applications. This group includes the Review Council chairperson.

(63) Scope of Work--the goals and objectives of the Cancer Research or Cancer Prevention project, including the timeline and milestones to be achieved.

(64) Senior Member or Key Personnel--the Principal Investigator, Project Director or Company Representative and other individuals who contribute to the scientific development or execution of a project in a substantive, measurable way, whether or not the individuals receive salary or compensation under the Grant Award.

(65) Technology--any and all of the following resulting or arising from work funded by the Grant Award:

(A) Inventions;

(B) Third-Party Information, including but not limited to data, trade secrets and know-how;

(C) databases, compilations and collections of data;

(D) tools, methods and processes; and

(E) works of authorship, excluding all scholarly works, but including, without limitation, computer programs, source code and executable code, whether embodied in software, firmware or otherwise, documentation, files, records, data and mask works; and all instantiations of the foregoing in any form and embodied in any form, including but not limited to therapeutics, drugs, drug delivery systems, drug formulations, devices, diagnostics, biomarkers, reagents and research tools.

(66) Texas Cancer Plan--a coordinated, prioritized, and actionable framework that helps to guide statewide efforts to fight the human and economic burden of cancer in Texas.

(67) Third-Party Information--generally, all trade secrets, proprietary information, know-how and non-public business information disclosed to the Institute by Grant Applicant, Grant Recipient, or other individual external to the Institute.

(68) Tobacco--all forms of tobacco products, including but not limited to cigarettes, cigars, pipes, water pipes (hookah), bidis, kreteks, electronic cigarettes, smokeless tobacco, snuff and chewing tobacco.

## § 701.27

To promote transparency in its activities, the Institute maintains the information described in this section and makes such information publicly available through the Institute's Internet website or upon request.

- (1) The Texas Cancer Plan;
- (2) The Institute's Annual Public Report;
- (3) The Conflict of Interest information described in this paragraph for the previous 12 months:
  - (A) A list of disclosed Conflicts of Interest requiring recusal.
  - (B) Any unreported Conflicts of Interest confirmed by an Institute investigation and actions taken by the Institute regarding same.
  - (C) Any Conflict of Interest waivers granted.

~~(4) An annual report of political contributions exceeding \$1,000 made to candidates for state or federal office by Oversight Committee Members for the five years preceding the Member's appointment and each year after the Member's appointment until the Member's term expires;~~

- ~~(4) [(5)]~~ The annual Grant Program priorities set by the Oversight Committee;
- ~~(5) [(6)]~~ Oversight Committee Bylaws;
- ~~(6) [(7)]~~ Code of Conduct and Ethics;
- ~~(7) [(8)]~~ A list, separated by Grant Program and Peer Review Panel, of the Scientific Research and Prevention Programs Committee Members provisionally appointed or approved by the Oversight Committee;
- ~~(8) [(9)]~~ The Institute's honoraria policy for Scientific Research and Prevention Programs Committee Members;
- ~~(9) [(10)]~~ The supporting documentation regarding the Institute's implementation of its Conflict of Interest policy and actions taken to exclude a conflicted Oversight Committee Member, Program Integration Committee Member, Scientific Research and Prevention Programs Committee Member or Institute Employee from participating in the review, discussion, deliberation and vote on the Grant Application;
- ~~(10) [(11)]~~ The Chief Executive Officer's annual report to the Oversight Committee on the progress and continued merit of each research Program funded by the Institute;
- ~~(11) [(12)]~~ Grant Applicant information:
  - (A) Name and address;
  - (B) Amount of funding applied for;
  - (C) Type of cancer addressed by the Grant Application; and

(D) A high-level summary of work proposed to be funded by the Grant Award;

(12) ~~(13)~~ Information related to Grant Awards, including the name of the Grant Recipient, the amount of the Grant Award approved by the Oversight Committee, the type of cancer addressed, and a high-level summary of the work funded by the Grant Award;

(13) ~~(14)~~ Records of a nonprofit organization established to provide support to the Institute;

(14) ~~(15)~~ Except as excluded by 702.7(f) of this Title, information related to any gift, grant, or other consideration provided to the Institute, Institute Employee, or a member of an Institute committee. Such information shall state:

(A) Donor's name;

(B) Amount of donation; and

(C) Date of donation;

(15) ~~(16)~~ A list of the Institute's Advisory Committees and the reports presented to the Oversight Committee by each Advisory Committee;

(16) ~~(17)~~ The Institute's approved internal audit annual report and the internal audit plan posted no later than thirty (30) days after approval by the Oversight Committee, or the Chief Executive Officer if the Oversight Committee is unable to meet;

(17) ~~(18)~~ A detailed summary of the weaknesses, deficiencies, wrongdoings, or other concerns raised by the audit plan or annual report and a summary of the action taken by the Institute to the address concerns, if any, that are raised by the audit plan or annual report;

(18) ~~(19)~~ Information regarding staff compensation in compliance with §659.026, Texas Government Code.



703.TITLE 25. HEALTH SERVICES

PART 11. CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS

CHAPTER 703. Grants for Cancer Prevention and Research

The Cancer Prevention and Research Institute of Texas (Institute or CPRIT) proposes an amendment to § 703.11. The proposed amendment changes the timeframe when a grant recipient may use a new federal indirect cost rate from “less than six months” to “six months or less.”

**Background and Justification**

The proposed amendment to § 703.11(b)(4) revises the starting date when a grant recipient may use a new federal indirect cost rate (FICR) to calculate the matching funds requirement. A grant recipient that is a public or private institution, as defined by § 61.003, Texas Education Code, may use their FICR as a credit when calculating the grant recipient’s matching funds requirement. Currently, if the FICR changes less than six months following the anniversary date of the effective date of the grant contract, the grant recipient may use the new rate. The proposed amendment changes the time to “six months or less” for a grant recipient to use a new FICR. This change clarifies the timeframe calculation and gives grant recipients more time to use an updated FICR.

**Fiscal Note**

Kristen Pauling Doyle, Deputy Executive Officer and General Counsel for the Cancer Prevention and Research Institute of Texas, has determined that for the first five-year period the rule change is in effect, there will be no foreseeable implications relating to costs or revenues for state or local government due to enforcing or administering the rules.

**Public Benefit and Costs**

Ms. Doyle has determined that for each year of the first five years the rule change is in effect the public benefit anticipated due to enforcing the rule will be the clarification of the time that a grant recipient may use a new FICR when calculating required matching funds.

**Small Business, Micro-Business, and Rural Communities Impact Analysis**

Ms. Doyle has determined that the rule change will not affect small businesses, micro businesses or rural communities.

**Government Growth Impact Statement**

The Institute, in accordance with 34 Texas Administrative Code §11.1, has determined that during the first five years that the section will be in effect:

- (1) the proposed rule changes will not create or eliminate a government program;
- (2) implementation of the proposed rule changes will not affect the number of employee positions;

- (3) implementation of the proposed rule changes will not require an increase or decrease in future legislative appropriations;
- (4) the proposed rule changes will not affect fees paid to the agency;
- (5) the proposed rule changes will not create new rules;
- (6) the proposed rule changes will expand existing rules;
- (7) the proposed rule changes will not change the number of individuals subject to the rules; and
- (8) The rule changes are unlikely to have a significant impact on the state's economy. Although these changes are likely to have neutral impact on the state's economy, the Institute lacks sufficient data to predict the impact with certainty.

Submit written comments on the proposed rule changes to Ms. Kristen Pauling Doyle, General Counsel, Cancer Prevention and Research Institute of Texas, P. O. Box 12097, Austin, Texas 78711, no later than July 2, 2018. The Institute asks parties filing comments to indicate whether they support the rule revisions proposed by the Institute and, if a change is requested, to provide specific text proposed to be included in the rule. Comments may be submitted electronically to [kdoyle@cprit.texas.gov](mailto:kdoyle@cprit.texas.gov). Comments may be submitted by facsimile transmission to 512/475-2563.

### **Statutory Authority**

The Institute proposes the rule changes under the authority of the Texas Health and Safety Code Annotated, § 102.108, which provides the Institute with broad rule-making authority to administer the chapter. Ms. Doyle has reviewed the proposed amendment, and certifies the proposal to be within the Institute's authority to adopt.

There is no other statute, article, or code affected by these rules.

### **§ 703.11**

(a) Prior to the disbursement of Grant Award funds, the Grant Recipient of a Cancer Research Grant Award shall demonstrate that the Grant Recipient has an amount of Encumbered Funds equal to at least one-half of the Grant Award available and not yet expended that are dedicated to the research that is the subject of the Grant Award.

(1) The Grant Recipient's written certification of Matching Funds, as described in this section, shall be included in the Grant Contract.

(2) A Grant Recipient of a multiyear Grant Award may certify Matching Funds on a year-by-year basis for the amount of Award Funds to be distributed for the Project Year based upon the Approved Budget.

(3) A Grant Recipient receiving multiple Grant Awards may provide certification at the institutional level.

(4) Nothing herein restricts the Institute from requiring the Grant Recipient to demonstrate an amount of Encumbered Funds greater than one-half of the Grant Award available and not yet expended that are dedicated to the research that is the subject of the Grant Award. To the extent that a greater Matching Funds amount will be required, the Institute shall include the requirement in the Request for Applications and in the Grant Contract.

(b) For purposes of the certification required by subsection (a) of this section, a Grant Recipient that is a public or private institution of higher education, as defined by §61.003, Texas Education Code, may credit toward the Grant Recipient's Matching Funds obligation the dollar amount equivalent to the difference between the indirect cost rate authorized by the federal government for research grants awarded to the Grant Recipient and the five percent (5%) Indirect Cost limit imposed by §102.203(c), Texas Health and Safety Code, subject to the following requirements:

(1) The Grant Recipient shall file certification with the Institute documenting the federal indirect cost rate authorized for research grants awarded to the Grant Recipient;

(2) To the extent that the Grant Recipient's Matching Funds credit does not equal or exceed one-half of the Grant Award funds to be distributed for the Project Year, then the Grant Recipient's Matching Funds certification shall demonstrate that a combination of the dollar amount equivalent credit and the funds to be dedicated to the Grant Award project as described in subsection (c) of this section is available and sufficient to meet or exceed the Matching Fund requirement;

(3) Calculation of the portion of federal indirect cost rate credit associated with subcontracted work performed for the Grant Recipient shall be in accordance with the Grant Recipient's established internal policy; and

(4) If the Grant Recipient's federal indirect cost rate changes ~~less than~~ six months or less following the anniversary of the Effective Date of the Grant Contract, then the Grant Recipient may use the new federal indirect cost rate for the purpose of calculating the Grant Recipient's Matching Funds credit for the entirety of the Project Year.

(c) For purposes of the certification required by subsection (a) of this section, Encumbered Funds must be spent directly on the Grant Project or spent on closely related work that supports, extends, or facilitates the Grant Project and may include:

(1) Federal funds, including, but not limited to, American Recovery and Reinvestment Act of 2009 funds, and the fair market value of drug development support provided to the recipient by the National Cancer Institute or other similar programs;

(2) State of Texas funds;

(3) funds of other states;

(4) Non-governmental funds, including private funds, foundation grants, gifts and donations;

(5) Unrecovered Indirect Costs not to exceed ten percent (10%) of the Grant Award amount, subject to the following conditions:

(A) These costs are not otherwise charged against the Grant Award as the five percent (5%) indirect funds amount allowed under §703.12(c) of this chapter (relating to Limitation on Use of Funds);

(B) The Grant Recipient must have a documented federal indirect cost rate or an indirect cost rate certified by an independent accounting firm; and

(C) The Grant Recipient is not a public or private institution of higher education as defined by §61.003 of the Texas Education Code.

(6) Funds contributed by a subcontractor or subawardee and spent on the Grant Project, so long as the subcontractor's or subawardee's portion of otherwise allowable Matching Funds for a Project Year may not exceed the percentage of the total Grant Funds paid to the subcontractor or subawardee for the same Project Year.

(d) For purposes of the certification required by subsection (a) of this section, the following items do not qualify as Encumbered Funds:

(1) In-kind costs;

(2) Volunteer services furnished to the Grant Recipient;

(3) Noncash contributions;

(4) Income earned by the Grant Recipient that is not available at the time of Grant Award;

(5) Pre-existing real estate of the Grant Recipient including building, facilities and land;

(6) Deferred giving such as a charitable remainder annuity trust, a charitable remainder unitrust, or a pooled income fund; or

(7) Other items as may be determined by the Oversight Committee.

(e) To the extent that a Grant Recipient of a multiyear Grant Award elects to certify Matching Funds on a Project Year basis, the failure to provide certification of Encumbered Funds at the appropriate time for each Project Year may serve as grounds for suspending reimbursement or advancement of Grant Funds for project costs or terminating the Grant Contract.

(f) In no event shall Grant Award funds for a Project Year be advanced or reimbursed, as may be appropriate for the Grant Award and specified in the Grant Contract, until the certification required by subsection (a) of this section is filed and approved by the Institute.

(g) No later than 30 days following the due date of the FSR reflecting expenses incurred during the last quarter of the Grant Recipient's Project Year, the Grant Recipient shall file a form with the Institute reporting the amount of Matching Funds spent for the preceding Project Year.

(h) If the Grant Recipient failed to expend Matching Funds equal to one-half of the actual amount of Grant Award funds distributed to the Grant Recipient for the same Project Year the Institute shall:

(1) Carry forward and add to the Matching Fund requirement for the next Project Year the dollar amount equal to the deficiency between the actual amount of Grant Award funds distributed and the actual Matching Funds expended, so long as the deficiency is equal to or less than twenty percent (20%) of the total Matching Funds required for the same period and the Grant Recipient has not previously had a Matching Funds deficiency for the project;

(2) Suspend distributing Grant Award funds for the project to the Grant Recipient if the deficiency between the actual amount of Grant Funds distributed and the Matching Funds expended is greater than twenty percent (20%) but less than fifty percent (50%) of the total Matching Funds required for the period.

(A) The Grant Recipient will have no less than eight months from the anniversary of the Grant Contract's effective date to demonstrate that it has expended Encumbered Funds sufficient to fulfill the Matching Funds deficiency for the project.

(B) If the Grant Recipient fails to fulfill the Matching Funds deficiency within the specified period, then the Grant Contract shall be considered in default and the Institute may proceed with terminating the Grant Award pursuant to the process established in the Grant Contract;

(3) Declare the Grant Contract in default if the deficiency between the actual amount of Grant Award funds distributed and the Matching Funds expended is greater than fifty percent (50%) of the total Matching Funds required for the period. The Institute may proceed with terminating the Grant Award pursuant to the process established in the Grant Contract; or

(4) Take appropriate action, including withholding reimbursement, requiring repayment of the deficiency, or terminating the Grant Contract if a deficiency exists between the actual amount of Grant Award funds distributed and the Matching Funds expended and it is the last year of the Grant Contract;

(i) Nothing herein shall preclude the Institute from taking action other than described in subsection (h) of this section based upon the specific reasons for the deficiency. To the extent that other action not described herein is taken by the Institute, such action shall be documented in writing and included in Grant Contract records. The options described in subsection (h)(1) and (2) of this section may be used by the Grant Recipient only one time for the particular project. A second deficiency of any amount shall be considered an event of default and the Institute may proceed with terminating the Grant Award pursuant to the process established in the Grant Contract.

(j) The Grant Recipient shall maintain adequate documentation supporting the source and use of the Matching Funds reported in the certification required by subsection (a) of this section. The Institute shall conduct an annual review of the documentation supporting the source and use of Matching Funds reported in the required certification for a risk-identified sample of Grant Recipients. Based upon the results of the sample, the Institute may elect to expand the review of supporting documentation to other Grant Recipients. Nothing herein restricts the authority of the Institute to review supporting documentation for one or more Grant Recipients or to conduct a review of Matching Funds documentation more frequently 703.12. Limitation on Use of Funds





CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**To: OVERSIGHT COMMITTEE**  
**From: HEIDI MCCONNELL, CHIEF OPERATING OFFICER**  
**Subject: FY 2019 REQUEST FOR FINANCING OF CPRIT BONDS**  
**Date: MAY 7, 2018**

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**Recommendation**

CPRIT staff recommends that the Oversight Committee approve the attached resolution for a request for financing to the Texas Public Finance Authority (TPFA) to issue debt on behalf of CPRIT in fiscal year 2019. The amount to be financed is \$300 million in bond proceeds appropriated to CPRIT for its operations and prevention and research grant awards. I estimate that CPRIT will request TPFA issue \$207.7 million in commercial paper notes four times during fiscal year 2019 to pay for CPRIT administrative operations and grant reimbursements or authorized advances related to awards made in fiscal years 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018 and 2019.

**Background**

Through the Texas Public Finance Authority (TPFA), CPRIT has issued \$167.2 million in commercial paper notes in fiscal year 2018 for agency operations and to pay expenses for grant awards. In addition, TPFA has fixed out approximately \$1.3 billion in long-term general obligation bonds for debt CPRIT incurred from fiscal year 2010 through fiscal year 2017.





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CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

**A RESOLUTION  
AUTHORIZING A REQUEST FOR FINANCING  
AND THE EXECUTION AND DELIVERY OF DOCUMENTS  
REQUIRED TO EFFECT SUCH FINANCING**

**Whereas**, the Texas Public Finance Authority (the "Authority") is authorized to issue general obligation bonds to finance the grant program for cancer research and prevention and control for the use and benefit of the Cancer Prevention & Research Institute of Texas (the "Agency") pursuant to Article III, Section 67, Texas Constitution; Texas Health & Safety Code, Chapter 102, as amended; and Texas Government Code, Chapter 1232, as amended, (collectively, the "Authorizing Law");

**Whereas**, the Agency desires and intends to request the Authority to finance the costs of the program as permitted by the Authorizing Law; and

**Whereas**, the Agency recognizes that in order to finance the cost of the program, the Authority may issue short term obligations, general obligation bonds, either or both ("Obligations") in an aggregate principal amount sufficient to finance program costs in the estimated amount of \$300,000,000, plus the costs of issuance and related administrative costs, if any, which will be determined at the time of issuance; and

**Whereas**, the form of a Request for Financing, dated as of May 16, 2018, (the "Request for Financing") from the Agency to the Authority, which includes a detailed description of the program to be financed for the Agency ("program" herein) and a proposed expenditure schedule is presently before the CPRIT Oversight Committee.

**NOW THEREFORE BE IT RESOLVED** by the CPRIT Oversight Committee that:

Section 1. The purpose of the financing is to provide funds sufficient to make grant awards for cancer research and prevention and control and for the operations of the Agency, and the financing thereof is appropriate at this time. Accordingly, the execution and delivery of the Request for Financing to the Authority pursuant to the Authorizing Law is hereby ratified, approved and confirmed.

Section 2. The Chief Executive Officer of the Agency is hereby empowered, authorized and directed to:

- a. sign and deliver any and all documents necessary or desirable to effect the financing and provide the projects, which may include but not be limited to a Memorandum of Understanding and a Financing Agreement between the Agency and the Authority;

- b. cooperate with the Authority and its consultants to prepare an Official Statement in connection with the sale of the Obligations;
- c. and to take any other action necessary to assist in such sale.

Section 3. All actions not inconsistent with provisions of this Resolution heretofore taken by the Institute and the Chief Executive Officer or designee thereof and the other officers of, or consultants to the Institute, directed toward the financing of the Program, and the issuance of the Obligations are hereby ratified, approved and confirmed.

Section 4. The officers and employees of the Agency shall take all action in conformity with the Authorizing Law and the provisions of the General Appropriations Act, 85<sup>th</sup> Legislature, R.S. (2017) to effect the issuance of the Obligations and complete the Program as provided in the Agreement and take all action necessary or desirable or in conformity with the Authorizing Law for carrying out, giving effect to, and consummating the transactions contemplated by the Memorandum of Understanding, the Agreement, the Obligations, and this Request for Financing, including without limitation, the execution and delivery of any closing documents in connection with the closing of the Obligations.

Section 5. This Resolution was adopted at a meeting open to the public, and public notice of the time, place and purpose of said meeting was given, all as required by Ch. 551, Texas Government Code.

Adopted by the affirmative vote of a majority of the Cancer Prevention and Research Institute of Texas Oversight Committee present and voting on this 16<sup>th</sup> day of May, 2018.

Cancer Prevention and Research Institute  
of Texas Oversight Committee

Attested:

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Chairman

\_\_\_\_\_  
Secretary



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## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

### **Fiscal Year 2019 Request for Financing Program Description**

#### **Purpose**

The Cancer Prevention and Research Institute of Texas (CPRIT) is the state agency mandated to:

- 1) create and expedite innovation in the area of cancer research and in enhancing the potential for a medical or scientific breakthrough in the prevention of cancer and cures for cancer;
- 2) attract, create, or expand research capabilities of public or private institutions of higher education and other public or private entities that will promote a substantial increase in cancer research and in the creation of high-quality new jobs in this state; and
- 3) develop and implement the Texas Cancer Plan.

#### **Powers and Duties**

CPRIT will make grants to provide funds to public or private persons to implement the Texas Cancer Plan, and make grants to institutions of learning and to advanced medical research facilities and collaborations in this state for:

- 1) research into the causes of and cures for all types of cancer in humans;
- 2) facilities for use in research into the causes of and cures for cancer;
- 3) research, including translational research, to develop therapies, protocols, medical pharmaceuticals, or procedures for the cure or substantial mitigation of all types of cancer in humans; and
- 4) cancer prevention and control programs in this state to mitigate the incidence of all types of cancer in humans.

#### **Implementation Plan**

CPRIT estimates that \$207.7 million in bonds proceeds must be issued on an as-needed basis consistent with Texas Government Code, Chapter 1232 to cover grant award obligations from fiscal years 2011, 2012, 2013, 2014, 2015, 2016, 2017, and 2018; new grant award obligations made during fiscal year 2019; and operating costs for general agency administration and pre- and post-award grants management processes. During fiscal year 2019, CPRIT will use the bond proceeds to disburse grant funds for grants awarded by CPRIT during fiscal years 2012, 2013, 2014, 2015, 2016, 2017, 2018, and 2019. CPRIT is currently authorized to obligate approximately \$280 million for cancer prevention and research grant awards in fiscal year 2019.

CPRIT announces grant awards for cancer prevention education and service programs and academic and product development cancer research programs four times per year. CPRIT

anticipates that it will obligate all of the available \$280 million for cancer prevention, product development research, and academic research.

Grant funds are generally disbursed quarterly on a reimbursement basis to grant recipients. For certain types of grant awards, limited to product development, CPRIT advances funds in order to provide those specific types of recipients with working capital to meet their research milestones or objectives.

CPRIT is authorized to use bond proceeds to fund its grant review and award operations and indirect administration costs. At this time, the total budgeted amount of these two categories is \$16.7 million in bond proceeds for fiscal year 2019 based on the authorized appropriations in General Appropriation Act, 85<sup>th</sup> Legislature. CPRIT must transfer \$2.9 million in bond proceeds to the Texas Department of State Health Services (DSHS) for the operating costs associated with the Texas Cancer Registry. From the total of all of the agency's operating costs, CPRIT requires half of the proceeds to be available at the beginning of the state fiscal year to be able to cover the operating expenses for six months. CPRIT also requires proceeds at the beginning of each state fiscal quarter to pay for award costs reimbursed to grant recipients for the previous state fiscal quarter.

The scientific research program provides awards in the following areas: cancer biology, cancer genetics, immunology, imaging, therapeutics, prevention/epidemiology, and informatics/computation. The product development research program focuses awards on the development of cancer drugs, diagnostics, and devices based on discoveries made in one of the seven areas described above. Prevention program grants are awarded for cancer prevention information and services, early detection and treatment, professional education and practice, cancer data acquisition and utilization, or survivorship (the areas of the Texas Cancer Plan). Awards for all programs are issued for multiple years, ranging from two to five years.

CPRIT has established a grant process that allows grant proposals for cancer prevention, scientific research, and product development research to be submitted through requests for applications (RFA) issued throughout each fiscal year. All proposals are reviewed by multiple experts in the appropriate area. CPRIT has approximately 200 national experts in cancer prevention, research and product development to review proposals and provide funding recommendations to CPRIT.

The award recommendations developed by the peer review committees are forwarded to the Program Integration Committee (PIC) for consideration. The five members of the PIC are statutorily defined as the Chief Executive Officer (CEO), Chief Scientific Officer, Chief Prevention Officer, Chief Product Development Officer, and DSHS Commissioner. The PIC finalizes award recommendations across all programs prior to every Oversight Committee meeting. When those proposed awards are forwarded to the Oversight Committee, each recommended award is accompanied by an affidavit signed by the CEO to affirm that the award followed all required pre-award grant procedures. The Oversight Committee considers these recommendations and votes to approve the awards.

# Cancer Prevention and Research Institute of Texas

Estimated Expenditure Schedule, Fiscal Year 2019

<b>Fiscal Year 2019</b>	<b>September</b>	<b>October</b>	<b>November</b>	<b>December</b>	<b>January</b>	<b>February</b>	<b>March</b>	<b>April</b>	<b>May</b>	<b>June</b>	<b>July</b>	<b>August</b>	<b>Total</b>
Bond proceeds for Indirect Administration	\$ 1,515,326	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 1,515,326	\$ -	\$ -		\$ -	\$ -	\$ 3,030,652
Bond proceeds for Grant Review and Award Operations	\$ 6,844,550	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 6,804,550	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 13,649,100
Bond proceeds for Texas Cancer Registry (GAA 2018-19, Art. I, CPRIT Rider 5)	\$ 1,484,777	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 1,484,777	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 2,969,554
Bond proceeds for Prevention and Research Grants	\$ 45,155,347	\$ -	\$ -	\$ 44,700,000	\$ -	\$ -	\$ 44,195,347	\$ -	\$ -	\$ 54,000,000	\$ -	\$ -	\$ 188,050,694
<b>Debt Issuance Subtotal, Fiscal Year 2019</b>	<b>\$ 55,000,000</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ 44,700,000</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ 54,000,000</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ 54,000,000</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ 207,700,000</b>
<b>Cumulative Debt Total, Fiscal Year 2019</b>	<b>\$ 55,000,000</b>	<b>\$ 55,000,000</b>	<b>\$ 55,000,000</b>	<b>\$ 99,700,000</b>	<b>\$ 99,700,000</b>	<b>\$ 99,700,000</b>	<b>\$ 153,700,000</b>	<b>\$ 153,700,000</b>	<b>\$ 153,700,000</b>	<b>\$ 207,700,000</b>	<b>\$ 207,700,000</b>	<b>\$ 207,700,000</b>	<b>\$ 207,700,000</b>





CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**To: OVERSIGHT COMMITTEE MEMBERS**  
**From: HEIDI MCCONNELL, CHIEF OPERATING OFFICER**  
**Subject: CHIEF OPERATING OFFICER REPORT**  
**Date: MAY 7, 2018**

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**CPRIT Financial Overview for FY 2018, Quarter 2**

**FY 2018, Quarter 2 Operating Budget**

The agency expended approximately \$2.3 million, or 50%, in Indirect Administration and approximately \$2.9 million, or 25%, in Grant Review and Award Operations. These expenditures together with service contracts and salary obligations account for 92% of the overall administrative budget for the fiscal year. The budget also includes \$277,230 in conference fee revenue for CPRIT's 2017 conference held in November 2017.

During the second quarter, the agency received \$21,969 in revenue sharing payments. Total revenue sharing payments to date for FY 2018 are \$90,628.

**FY 2018, Quarter 2 Performance Measure Report**

In March 2018, CPRIT reported second quarter performance to the LBB on the two output measures that have quarterly reporting requirements:

- 1) Number of People Served by Institute Funded Prevention and Control Activities and
- 2) Number of Entities Relocating to Texas for Cancer Research Related Projects.

**Debt Issuance History**

In March 2018, the Texas Public Finance Authority issued \$99.0 million in general obligation bonds on CPRIT's behalf. This brings the total issued for the FY 2018 to \$167.2 million, and the total issued since CPRIT's inception to slightly less than \$1.5 billion.

**State Strategic Planning for the 2018-19 Biennium**

On March 7, 2018, the Governor's Office and Legislative Budget Board (LBB) jointly issued instructions about preparing and submitted agency strategic plans covering fiscal years 2019 through 2023. The required elements in the agency strategic plan have been greatly reduced from prior years which will streamline the plan to be submitted. All agency strategic plans are due by June 8, 2018, to the Governor's Office, LBB and other legislative oversight offices. The agency strategic plan does not require action by the Oversight Committee but will require the Oversight Committee Presiding Officer's signature. We will forward the CPRIT Strategic Plan for 2019 to 2023 to the Oversight Committee when complete.

Each agency strategic plan must include the agency mission and the agency goals and action plan. The other elements that will be included in CPRIT's strategic plan are the:

- 1) Budget structure,
- 2) List of measure definitions,
- 3) Historically Underutilized Business Plan, and
- 4) Agency workforce plan, report on customer service.

As part of strategic planning, agencies may address issues with their budget structures and performance measures. No changes to performance measures or the budget structure were requested, so the structure remains the following four strategies:

- 1) Award Cancer Research Grants (include academic and product development research)
- 2) Award Cancer Prevention Grants
- 3) Grant Review and Award Operations
- 4) Indirect Administration

This structure will be used in the preparation of the agency's Legislative Appropriations Request (LAR) which is the next step in preparing the state budget for the 2020-21 biennium.

**Cancer Prevention and Research Institute of Texas**  
**Quarterly Financial Report**  
As of February 28, 2018

**Indirect Administration (B.1.1.)**

	2018 Appropriated	2018 Budgeted	% of Total Budget	Actual Expenditures & Grant Encumbrances (FYTD)	Remaining Budget	Percent Expended	Estimated Expenditures (YTD)	Lapse/Overspent
1001 Salaries and Wages	\$ 1,617,425	\$ 1,530,924		\$ 600,170	930,755	39%	\$ 600,170	\$ 930,755
1002 Other Personnel Costs	52,785	38,785		16,782	22,003	43%	16,782	22,003
2001 Professional Fees and Services	826,175	995,830		895,118	100,711	90%	895,118	100,711
2003 Consumable Supplies	27,584	27,584		12,733	14,851	46%	12,733	14,851
2004 Utilities	58,577	58,577		35,602	22,975	61%	35,602	22,975
2005 Travel	45,000	45,000		24,068	20,932	53%	24,068	20,932
2006 Rent-Building	-	32,673		29,955	2,718	0%	29,955	2,718
2007 Rent-Machine and Other	32,172	32,172		12,524	19,648	39%	12,524	19,648
2009 Other Operating Expenses	370,934	406,465		297,341	109,125	73%	297,341	109,125
<b>Subtotal - Indirect Administration (B.1.1.)</b>	<b>\$ 3,030,652</b>	<b>\$ 3,168,010</b>	<b>1.06%</b>	<b>\$ 1,924,292</b>	<b>\$ 1,243,719</b>	<b>61%</b>	<b>\$ 1,924,292</b>	<b>\$ 1,243,719</b>

**Grant Review and Award Operations (A.1.3.)**

	2018 Appropriated	2018 Budgeted	% of Total Budget	Actual Expenditures & Grant Encumbrances (FYTD)	Remaining Budget	Percent Expended	Estimated Expenditures (YTD)	Lapse/Overspent
1001 Salaries and Wages	\$ 2,991,208	2,949,626		\$ 1,624,490	\$ 1,325,136	55%	\$ 1,624,490	\$ 1,325,136
1002 Other Personnel Costs	3,856	3,856		29,970	(26,114)	0%	29,970	(26,114)
2001 Professional Fees and Services	10,443,893	11,138,507		10,254,984	883,523	92%	10,254,984	883,523
2003 Consumable Supplies	-	-		-	-	0%	-	-
2004 Utilities	1,628	4,203		5,303	(1,100)	126%	5,303	(1,100)
2005 Travel	87,500	87,500		18,931	68,569	22%	18,931	68,569
2009 Other Operating Expenses	218,997	159,539		18,668	140,871	12%	18,668	140,871
Conference		277,229		234,922	42,307	85%	234,922	42,307
<b>Subtotal - Grant Operations (A.1.3.)</b>	<b>\$ 13,747,082</b>	<b>\$ 14,620,461</b>	<b>4.90%</b>	<b>\$ 12,187,269</b>	<b>\$ 2,433,192</b>	<b>83%</b>	<b>\$ 12,187,269</b>	<b>\$ 2,433,192</b>

**Grants**

	2018 Appropriated	2018 Budgeted	% of Total Budget	Actual Expenditures & Grant Encumbrances (FYTD)	Remaining Budget	Percent Expended	Estimated Expenditures (YTD)	Lapse/Overspent
4000 Grants - Prevention (A.1.2)	\$ 28,037,956	\$ 28,037,956		\$ -	\$ 28,037,956	0%	\$ -	\$ 28,037,956
4000 Grants - Research (A.1.1.)	255,239,310	\$ 252,269,756		-	\$ 252,269,756	0%	-	252,269,756
<b>Subtotal - Grants</b>	<b>\$ 283,277,266</b>	<b>\$ 280,307,712</b>	<b>94.03%</b>	<b>\$ -</b>	<b>\$ 280,307,712</b>	<b>0%</b>	<b>\$ -</b>	<b>\$ 280,307,712</b>
<b>Grand Totals</b>	<b>\$ 300,055,000</b>	<b>\$ 298,096,183</b>	<b>100.00%</b>	<b>\$ 14,111,561</b>	<b>\$ 283,984,622</b>	<b>5%</b>	<b>\$ 14,111,561</b>	<b>\$ 283,984,622</b>

**Cancer Prevention and Research Institute of Texas  
Cancer Prevention and Research Institute Fund Account - 5136  
As of February 28, 2018**

	<b>02/01/2018- 02/28/2018</b>	<b>AY 18 Year to Date as of 02/28/2018</b>
<b>Beginning Balance : 02/01/2018</b>		<b>\$ 600,506</b>
<b>Increases:</b>		
(1)	\$ -	\$ -
(2)	-	
<b>Total Increases</b>	<b>\$ -</b>	<b>\$ 600,506.00</b>
<b>Reductions:</b>		
Expenditures - Appropriated	\$ -	\$ -
	\$ -	\$ -
	\$ -	\$ -
<b>Total Reductions</b>	<b>\$ -</b>	<b>\$ -</b>
<b>Ending Balance, 02/28/2018</b>		<b>\$ 600,506.00</b>

Note: (1) The Institute received a settlement from the Texas Cancer Coalition (TCC). This amount represents the final distribution and transfer of all funds (\$303,877) from the TCC which ceased operations in May 2013. These funds are in the State Treasury but are not appropriated to CPRIT. The beginning balance reflects the transfer of all TCC funds.

**Cancer Prevention and Research Institute of Texas**  
**License Plate Trust Fund Account - 0802**  
**As of February 28, 2018**

	<b>02/01/2018- 02/28/2018</b>	<b>AY 18 Year to Date as of 02/28/2018</b>
<b>Beginning Balance : 02/01/2018</b>		\$ -
<b>Increases:</b>		
(1) License Plate Revenue Received	\$ 938.65	\$ 5,162.54
<b>Total Increases</b>	<b>\$ 938.65</b>	<b>\$ 5,162.54</b>
<b>Reductions:</b>		
Expenditures - Appropriated	\$ -	\$ -
	-	-
<b>Total Reductions</b>	<b>\$ -</b>	<b>\$ -</b>
<b>Ending Balance, 02/28/2018</b>		<b>\$ 5,162.54</b>

Note:

**Cancer Prevention and Research Institute of Texas**

**Appropriated Receipts - 666**

**As of February 28, 2018**

	<u>02/01/2018- 02/28/2018</u>	<u>AY 18 Year to Date as of 02/28/2018</u>
<b><u>Beginning Balance : 02/01/2018</u></b>		<b>\$ 126,079.19</b>
<b>Increases:</b>		
(1) Product Development Application Fees Received	\$ -	\$ 5,000.00
(2) Appropriated Receipts applied to payments	\$ -	\$ -
(3) Conference Registration Fees	\$ -	\$ 213,697.96
(4) Conference Registration Fees-Credit Card	\$ -	\$ 5,452.71
<b>Total Increases</b>	<b><u>\$ -</u></b>	<b><u>\$ 224,150.67</u></b>
<b>Reductions:</b>		
Conference Expenditures - Appropriated	\$ -	\$ -
Credit Card Fees Expended	\$ -	\$ (5,452.71)
Legal Services Expenses (Application Fees)	\$ -	\$ -
<b>Total Reductions</b>	<b><u>\$ -</u></b>	<b><u>\$ (5,452.71)</u></b>
<b><u>Ending Balance, 02/28/2018</u></b>		<b><u><u>\$ 344,777.15</u></u></b>

Begin balance is \$68,000.00 for application fees and \$58,079.19  
(\$583.57 CC fees + \$37,079.13 + 20,416.49 registration + \$64.51 interest) for conference fees

**Cancer Prevention and Research Institute of Texas**  
**Interest & Sinking Fund Account - 5168**  
**As of February 28, 2018**

	<b>02/01/2018- 02/28/2018</b>	<b>AY 18 Year to Date as of 02/28/2018</b>
<b>Beginning Balance : 02/01/2018</b>		<b>\$ 38,695.04</b>
<b>Increases:</b>		
(1) Revenue Sharing / Royalties	\$ 111.31	\$ 66,603.88
<b>Total Increases</b>	<b>\$ 111.31</b>	<b>\$ 105,298.92</b>
<b>Reductions:</b>		
Expenditures - Appropriated	\$ -	\$ -
	\$ -	\$ -
	\$ -	\$ -
<b>Total Reductions</b>	<b>\$ -</b>	<b>\$ -</b>
<b>Ending Balance, 02/28/2018</b>		<b>\$ 105,298.92</b>

Note: Beginning  
Balance  
\$38,695.04



**Cancer Prevention and Research Institute of Texas  
FY 2018, Quarter 2 Performance Measure Report**

<b>Measure</b>	<b>Targeted Performance</b>	<b>QTR 1</b>	<b>QTR 2</b>	<b>QTR 3</b>	<b>QTR 4</b>	<b>Sum of QTRs</b>	<b>% of Mandate Attained</b>
<b>Number of People Served by Institute Funded Prevention and Control Activities</b>	500,000	282,167	218,357			500,524	100.10%
<b>Number of Entities Relocating to TX for Cancer Research Related Projects</b>	2	0	0			0	0.00%
<b>Annual Age-adjusted Cancer Mortality Rate</b>	156.8	N/A	N/A	N/A	N/A		0.00%
<b>Number of Published Articles on CPRIT-Funded Research Projects</b>	900	N/A	N/A	N/A	N/A		0.00%
<b>Number of New Jobs Created and Maintained</b>	1,325	N/A	N/A	N/A	N/A		0.00%

**Variance Explanations**

<b>Number of People Served by Institute Funded Prevention and Control Activities</b>
CPRIT grantees deliver these education and clinical services throughout the year, so the reported number of people served is not allocated evenly for each fiscal quarter.
<b>Number of Entities Relocating to TX for Cancer Research Related Projects</b>
This output is dependent on the number of companies applying for CPRIT Company Relocation Awards that can successfully advance through CPRIT's rigorous review and evaluation process, receive an award and actually relocate operations to Texas.



**CPRIT Commercial Paper and G.O. Bond Issuance**

Fiscal Year	Amount Appropriated	Dated Issued	Amount Issued	Amount Issued for Fiscal Year	Commercial Paper or GO Bond Issuance	Series	Comments	Interest Rate
2010	\$ 225,000,000	September 9, 2009	\$ 9,100,000		Commercial Paper Notes	Series A, Taxable		
2010		September 9, 2009	\$ 3,600,000		Commercial Paper Notes	Series B, Tax-Exempt	Defeased with cash July 2011	
2010		March 12, 2010	\$ 63,800,000		Commercial Paper Notes	Series A, Taxable		
2010		August 26, 2010	\$ 148,500,000		Commercial Paper Notes	Series A, Taxable		
				\$ 225,000,000				
2011	\$ 225,000,000	September 7, 2010	\$ 11,800,000		Commercial Paper Notes	Series A, Taxable		
2011		August 10, 2011	\$ 51,000,000		G.O. Bonds	Taxable Series 2011	Par amount of new money	Fixed Rate Bonds All-In-True Interest Cost 4.0144%
2011		August 10, 2011	\$ 232,045,000		G.O. Bonds (Refunding Bonds)	Taxable Series 2011	Par amount of refunding; Refunded \$233.2M of GOCP CPRIT Series A (9/9/09, 3/12/09, 8/26/09, 9/7/10)	Fixed Rate Bonds All-In-True Interest Cost 4.0144%
				\$ 62,800,000				
2012	\$ 300,000,000	September 7, 2011	\$ 3,200,000		Commercial Paper Notes	Series A, Taxable		
2012		December 8, 2011	\$ 3,200,000		Commercial Paper Notes	Series A, Taxable		
2012		March 2, 2012	\$ 12,300,000		Commercial Paper Notes	Series A, Taxable		
2012		June 21, 2012	\$ 15,000,000		Commercial Paper Notes	Series A, Taxable		
2012		August 16, 2012	\$ 42,000,000		Commercial Paper Notes	Series A, Taxable		
				\$ 75,700,000				
2013	\$ 300,000,000	September 6, 2012	\$ 9,600,000		Commercial Paper Notes	Series A, Taxable		
2013		May 16, 2013	\$ 13,400,000		Commercial Paper Notes	Series A, Taxable		
				\$ 23,000,000				
2014	\$ 300,000,000	November 25, 2013	\$ 55,200,000		Commercial Paper Notes	Series A, Taxable		
2014		March 13, 2014	\$ 47,000,000		Commercial Paper Notes	Series A, Taxable		
2014		June 17, 2014	\$ 60,300,000		Commercial Paper Notes	Series A, Taxable		
2014		July 8, 2014	\$ 233,280,000		G.O. Bonds (Refunding Bonds)	Taxable Series 2014	Par amount of refunding; Refunded \$237.88M of GOCP CPRIT Series A	Fixed Rate Bonds All-In-True Interest Cost 3.327184%
				\$ 162,500,000				
2015	\$ 300,000,000	November 5, 2014	\$ 57,600,000		Commercial Paper Notes	Series A, Taxable		
2015		April 29, 2014	\$ 112,000,000		Commercial Paper Notes	Series A, Taxable		
2015		June 26, 2015	\$ 75,000,000		Commercial Paper Notes	Series A, Taxable		
				\$ 244,600,000				





CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**To: OVERSIGHT COMMITTEE MEMBERS**  
**From: HEIDI MCCONNELL, CHIEF OPERATING OFFICER**  
**Subject: PROVISIONAL APPROVAL OF THE LEGISLATIVE  
APPROPRIATIONS REQUEST ITEMS FOR 2020-21 BUDGET**  
**Date: MAY 8, 2018**

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**Recommendation**

CPRIT staff recommends that the Oversight Committee provisionally approve the items to be requested (attachment) in the agency's Legislative Appropriations Request (LAR) for the 2020-21 biennium. The LAR will not be in a final form for approval at the Oversight Committee meeting because state agencies have just begun the strategic planning process which must be completed before work on the LAR can begin. Based on the LAR submission schedule in previous years, staff believes that CPRIT's LAR will be due to the Governor's Office and Legislative Budget Board (LBB) in early August prior to the Oversight Committee meeting scheduled that month.

As part of this provisional approval, CPRIT staff must present the drafted LAR to the Audit Subcommittee at a to-be-scheduled mid-summer meeting. The Audit Subcommittee will review the LAR to confirm that the content is consistent with the list of LAR request items provisionally approved by the Oversight Committee in May. After the Audit Subcommittee affirms that the content is consistent with items approved by the Oversight Committee, staff would send the LAR to the presiding officer for his signature and then submit the LAR to the Governor's Office, LBB, and other required legislative oversight offices.

Note that if the Audit Subcommittee determines that the LAR is inconsistent with the list of LAR request items provisionally approved by the Oversight Committee, CPRIT will convene a special meeting of the Oversight Committee to approve the LAR before the submission deadline.

**Background**

On March 7, the Governor's Office and LBB jointly issued instructions to state agencies for preparing and submitting their strategic plans for fiscal years 2019 through 2023. The submission of the agency's strategic plan is the first step in developing the state budget for the 2020-21 biennium which will be considered by the Texas Legislature when they convene for the 86<sup>th</sup> Regular Session on January 8, 2019. CPRIT's strategic plan is due by June 8, 2018.

LAR instructions for state agencies have not yet been issued by the Governor's Office and LBB.

**Potential Items for Inclusion in the  
2020-21 Legislative Appropriations Request to the 86<sup>th</sup> Texas Legislature**

REQUEST	EXPLANATION
Request \$124 million in General Revenue fund appropriation	Provides \$62 million in each year of the biennium for grant awards, bringing total grant funding to historic levels of \$280 million per year exclusive of \$20 million for operating expenses and the transfer to DSHS for the Cancer Registry.
Strike Rider 5, Transfer to DSHS for Cancer Registry	Transfer reduces CPRIT’s available G.O. Bond funds for grants by \$6 million over a biennium to fund an activity not managed by CPRIT. <i>If no transfer is required, CPRIT would have another \$6 million for grant awards and reduce the supplemental GR request to \$118 million for the biennium.</i>
Request FTE increase	1 additional FTE to provide additional IT support. Currently, CPRIT has a 35 FTE cap
Modify Rider 4, Transfer Authority, to allow CEO to report transfers within the limitations of Art. IX, Sec. 14.01 Appropriations Transfers allowed other state agencies	CEO notification to the LBB and Governor provides CPRIT the same authority given to other agencies to transfer up to 20% from one budget line item to another, excluding indirect administration, without requiring approval of those two offices and maximizes operational efficiency. <i>Requested in 2017.</i>
Request an increase in the CEO Exempt Salary amount in the Administrator’s Statement	Enhances the agency’s ability to pay a competitive salary in the event there is a need to hire a new CEO and provides room for a merit incentive to CEO.



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

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**MEMORANDUM**

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**To: OVERSIGHT COMMITTEE MEMBERS**  
**From: HEIDI MCCONNELL, CHIEF OPERATING OFFICER**  
**Subject: FY 2019 DUE DILIGENCE SUPPORT SERVICES CONTRACT APPROVAL**  
**Date: MAY 7, 2018**

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**Recommendation**

CPRIT staff recommends that the agency award a contract to ICON Clinical Research (ICON) for due diligence evaluation services at a not to exceed amount of \$212,200 in FY 2019. The contract cost is based on the estimated diligence evaluations completed by ICON during the year. At this time, Michael Lang projects up to eight diligence reports may be needed. CPRIT pays only for completed reports at a per report unit cost of \$26,525.

**Background**

Each year CPRIT receives approximately 50 product development grant applications. These applications are evaluated by peer review panels which evaluate submitted applications to select a subset of applications for due diligence.

Due diligence is a comprehensive assessment of the company prior to investment. ICON assesses diligence topics to assess likelihood of program success including:

- Discovery Science
- Preclinical Research
- Manufacturing
- Clinical Research
- Regulatory Approval
- Management and Financial
- Commercial

The Product Development Review Council provides a fund / not fund recommendation based largely on the diligence reports addressing these key issues.

CPRIT 's current contract is with ICON for these same services. ICON increased the diligence evaluation report unit cost by \$775 from a per report unit cost of \$25,750 in its current contract.





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**MEMORANDUM**

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**To: OVERSIGHT COMMITTEE**  
**From: HEIDI MCCONNELL, CHIEF OPERATING OFFICER**  
**Subject: FY 2019 GRANT MANAGEMENT SUPPORT SERVICES  
CONTRACT RENEWAL APPROVAL**  
**Date: MAY 7, 2018**

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**Recommendation**

CPRIT staff recommends that the agency exercise the second renewal option on our contract with SRA International, Inc., a CSRA Company (currently in transition in a merger with General Dynamics Information Technology) for a not to exceed amount of \$8,400,443 in FY 2019. The contract is based on time and materials provided by CSRA so CPRIT only pays for actual services received from CSRA up to the contracted amount.

**Background**

CSRA provides:

- Logistical support for in-person and virtual peer review meetings;
- Summarized evaluation reports for each grant application including peer review chair consensus statements, budget recommendations, and noted issues in clinical trials with human subjects or animal research;
- Scientific expertise for the evaluation of the annual and final progress reports for academic research grants;
- A Software as a Service (SaaS) subscription to their Grants Management Platform (GMP) software including the application receipt module, program and peer review module, and grant management module;
- Enhancements to their GMP grants management module to increase protections over the data in that module as well as provide CPRIT the ability to reset workflows for certain reports when they are incorrectly submitted;
- Enhancements to their GMP program and peer review module to increase protections over the data in that module
- Incorporation of grant request for application requirements in the GMP application receipt module for electronic application submission; and
- Administration of electronic grant pedigrees.

CSRA has subcontracts with two Texas-based Historically Underutilized Business (HUB) vendors for some support services. One subcontractor, Innovation Event Management, provides meeting support services for the in-person peer review meetings held in Dallas or Houston. The other, The Alamo Travel Group, makes air travel arrangements for peer reviewers attending in-person meetings.

This renewal will require approval from the Legislative Budget Board (LBB) for CPRIT to finalize the FY 2019 contract.

CPRIT awarded a new contract to CSRA beginning in FY 2017 with a cost of \$8,265,446 and exercised the first renewal option in FY 2018 at a cost of \$8,995,852.



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**MEMORANDUM**

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**TO:** OVERSIGHT COMMITTEE MEMBERS  
**FROM:** HEIDI MCCONNELL, CHIEF OPERATING OFFICER  
**SUBJECT:** FY 2019 OUTSIDE COUNSEL CONTRACTS APPROVAL  
**DATE:** MAY 7, 2018

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**Recommendation**

CPRIT staff recommends approval of outside counsel contract extensions for FY 2019 for Vinson & Elkins, LLP (\$125,000), Baker Botts, LLP (\$125,000), and Yudell Isidore, PLLC (\$125,000). These firms will provide legal advice and evaluation services regarding the intellectual property (IP) and revenue sharing agreements associated with CPRIT grants during FY 2019. The Office of the Attorney General must approve all outside counsel agreements and contract extensions prior to contract execution.

**Discussion**

CPRIT relies on outside legal counsel with IP expertise to conduct a review of companies' IP estate as part of the due diligence process. The IP due diligence is not a re-review of the grant application but serves as an independent analysis of the IP and associated licenses underlying the company's planned drug, device, diagnostic, technology, or service proposed for CPRIT funding. The Product Development Review Council uses information gained through the IP due diligence process to finalize their grant award recommendations.

These contract extensions and new contract are the result of CPRIT's request for proposals issued in September 2017 and FY 2018 Needs Assessment. The request for proposals included an option to renew the three outside counsel contracts for up to four additional one-year periods. The option to extend the contract(s) provides service continuity, particularly when review cycles cross fiscal years. The Office of the Attorney General must also approve outside counsel contracts and contract extensions.

CPRIT pays each firm based solely on the number of hours worked; there is no guaranteed minimum payment. Generally, the price per IP due diligence company project ranges from \$10,000 - \$20,000. The cost of each assessment varies based upon the complexity of the IP information and issues presented, as well as the volume of documents counsel must review. The outside counsel contracts use an hourly rate, which the Attorney General caps at \$525/hour. Contracting with multiple firms allows CPRIT to balance the workload and avoid potential conflicts of interest between the firms and the companies under review.

