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TITLE: Academy of Kidney Cancer Investigators Dean Award

PRINCIPAL INVESTIGATOR: Brian Rini

CONTRACTING ORGANIZATION: Vanderbilt University Medical Center, Nashville, TN

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The CDMRP/KCRP Academy of Kidney Cancer Investigators (ACKI) fosters the development and commitment of early career kidney cancer investigators through provision of the raw materials and structured mentorship for focused, sustainable, and ultimately independent success. A Dean and advisory panel of relevant experts has been established and the first class of mentor/mentee pairs has been admitted to the Academy. The annual in person meetings have been held including the most recent in-person at the AACR Special Conference on RCC in Austin, TX. Quarterly AKCI meetings were held virtually for project status updates, input from the entire group as to ongoing issues, barriers and how to overcome them and future directions. In addition, monthly didactics with relevant topic experts outside of AKCI are ongoing and have provided rich and complementary RCC translational topics. Significant academic output has already been realized through this structured virtual academy.

15. SUBJECT TERMS
AKCI, mentoring, renal cell carcinoma, mentor, mentees

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TABLE OF CONTENTS

1. **Introduction:**
   The CDMRP/KCRP Academy of Kidney Cancer Investigators (ACKI) was established as a non-traditional method to foster the development of early career investigators in renal cell carcinoma-focused research. The inaugural Dean's award and the corresponding awards to the mentor/mentee pairs established the foundation of this Academy. The first year saw a kick-off meeting to gather all relevant parties and focused on refining the submitted projects of the mentees. Significant improvements/changes were made to projects. My role of the Academy Dean has been to facilitate and enrich the provision of the raw materials and establish the framework to ensure continued progress towards the mutual goal of eliminating kidney cancer. I established a diverse advisory panel with broad expertise across laboratory and clinical RCC realms which has facilitated the career growth of the mentees through regular feedback. I have revised my advisory panel in response to the mentees projects and requirements to include more basic science/translational expertise with the addition of Drs. William Kim and Samra Turajlic. Significant cumulative accomplishments of this growing and robust academy are noted below.

2. **Keywords:** *AKCI, mentoring, renal cell carcinoma, mentor, mentees*

3. **Accomplishments**

	Accomplishments
Major Task 1: Establishment of SMART goals	
Initial virtual meetings to align AKCI members and provide feedback on scientific projects, goals and mentoring plan	Inaugural AKCI kick-off meeting held November 2020 with focused feedback to all mentees
First annual AKCI meeting held in conjunction with KCA meeting	Inaugural AKCI kick-off meeting held November 2020 with focused feedback to all mentees
Establishment of virtual mentoring platform (MentorcliQ)	Platform established and all AKCI members have access (this platform abandoned in 2022 due to lack of significant contribution)
Finalize goals for all AKCI participants	Mentees submitted revised SMART goals after meeting. This occurs annually with new mentees.
Major Task 2: Ongoing education, goals/progress	
Monthly virtual interactive meetings	Monthly didactics ongoing
Ongoing assessment of progress towards goals, barriers, strategies to overcome barriers and refinement of goals, including ongoing MentorcliQ use	Quarterly AKCI meetings with all members and advisory board held
Annual AKCI meeting	Held November 2020, November 2021, June 2023
Meeting including KCRP staff	Held November 2020, November 2021, June 2023
Major Task 3: Collaboration	
Assignment of advisory board member as secondary mentor to one AKCI early career investigator	Ongoing
Establishment of DUA/MTAs across AKCI institutions	Individual agreements are accomplished per specific projects.
Integration of AKCI members with CDMRP	Ongoing

Consortium Award institutions	
Major Task 4: Deliverables / SMART goals	
Abstract annually to at least one major relevant meeting	See below for accounting of deliverables
First author, peer-reviewed publications	
Peer-reviewed funding for laboratory-based investigators or industry funding for clinical trials/translational work	
Participation in multiple clinical trials and named Principal Investigator	
Establishment of a collaborative project with at least one AKCI member/institution	
Invitations to speak at other academic medical centers	
Membership and active participation/leadership in 1-2 national or international societies	

What was accomplished under these goals?

As noted above, all required meetings for the AKCI as intended have occurred. These meetings provided a forum for mentees to present their updated research plans and significant feedback and refinement of plans occurred. The table below outlines the suggested quantitative metrics for AKCI members and the achievements to date. All of the achievements listed below are at least partially attributable to the mentee involvement in AKCI.

Stated Goals	**Cumulative achievements of AKCI mentees**
Submission of least 1 abstract annually to at least one major relevant meeting (e.g. ASCO, AACR, GU symposium, KCA) annually	38 RCC abstracts submitted to major meetings
An average of 2-3 first author, peer-reviewed publications annually	36 total first- or last-author publications
At least one podium presentation at a national meeting annually	20 podium presentations at national meetings
Securing either peer-reviewed funding for laboratory-based investigators or industry funding for clinical trials/translational work	45 peer-reviewed grants submitted / 13 funded
Establishment of a collaborative project with at least one AKCI member/institution within the first two years, and 2-3 collaborative projects over the course of the award	4 collaborative projects initiated
Invitations to speak at other academic medical centers (e.g. Grand Rounds; average 1-2 invites/per year)	18 talks at other academic centers
Membership and active participation/leadership in 1-2 national or international society committees over the	Active participation in 8 societies

course of the award	

What opportunities for training and professional development has the project provided?
The didactic series offers mentees the ability to interact with recognized experts in the RCC field and hone relevant skills. Further, opportunities for presentation of their work (quarterly AKCI meetings, presentations at the annual KCA meeting) are critical to continued professional development. New AKCI members are integrated into the annual Kidney Cancer Association meeting to present their projects and network with established leaders in the RCC field.

How were the results disseminated to communities of interest?
The mentees report their findings through publications and presentations as above. Also, new mentees present their projects annually at the KCA meeting. Finally, an AKCI website (www.AKCI.org) and YouTube channel (https://www.youtube.com/@AcademyofKidneyCancerInvestiga/videos) house the academic accomplishments and didactic videos. Both are open to the general public to widely disseminate the knowledge generated.

What do you plan to do during the next reporting period to accomplish the goals?
The ACKI will continue its quarterly meetings and didactic series. Further growth of AKCI membership will also contribute to a more robust RCC community to refine projects and goals of the mentees.

4. Impact

What was the impact on the development of the principal discipline(s) of the project?
The AKCI has established the framework for a functional, virtual academy with high-level academic output. Most notably, this growing Academy will serve to draw more early career investigators into RCC-relevant research to benefit patients and the broader RCC community.

Early Career investigators were invited to the AKCI in-person June 2023 meeting to advertise the accomplishments of the AKCI with the intent of leading to more applications especially among URM investigators. AACR provided travel grants for URMs and other early career investigators to attend this meeting.

What was the impact on other disciplines?
Nothing to Report

What was the impact on technology transfer?
Nothing to Report

What was the impact on society beyond science and technology?
Nothing to Report

5. Changes/Problems

Changes in approach and reasons for change

Change in Advisory Board occurred in the 2022-2023 project year in response to the needs of the ECIs. Drs. David McDermott and Rob Uzzo rotated off and were replaced by more basic/translational investigators, Drs. William Kim and Samra Turajlic. I will continue to

consider refinement to advisory board membership to suit the needs of the mentees. No other change or problems were encountered.

Actual or anticipated problems or delays and actions or plans to resolve them

None

Changes that had a significant impact on expenditures: *None*

6. **Products:** *Nothing to report*

7. **Participants & Other Collaborating Organizations**

What individuals have worked on the project?
Please see below:

Name:	***Brian Rini, MD***
Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	***0000-0002-2212-080X***
Nearest person month worked:	*2.4*
Contribution to Project:	***Dr. Rini oversaw all aspects of operation for the Academy***
Funding Support:	*CDMRP, NCI*
Name	***Rebecca Renee Boster***
Project Role:	*Administrative Assistant*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	*3.0*
Contribution to Project:	*Rebecca Boster is responsible for administrative support for the AKCI. This includes interaction with mentor/ECI pairs for travel to annual meetings, webinar set-up and operation and interfacing with MentorcliQ for any issues with the digital platform.*
Funding Support:	*N/A*
Name:	***James Brugarolas, MD***
Project Role:	*Chair of the SAB*
Researcher Identifier (e.g. ORCID ID):	*https://orcid.org/0000-0002-8575-499X*
Nearest person month worked:	*0.6 month*
Contribution to Project:	*Dr. Brugarolas is working with Dr. Rini to brainstorm about the best use of additional funding that has been provided to the Academy to foster its mission. Beyond the AKCI meetings, Drs. Rini and Brugarolas make themselves available to mentees to address challenges in their research or academic progression that they may individually face. Finally, Dr. Brugarolas continues to*

	serve as a mentor to two successful AKCI applicants, including a minority faculty member, and as secondary mentor to another, which gives him a valuable perspective complementing his perspective as SAB Chair.
Funding Support:	*CDMRP, NCI*
Name:	William Y. Kim. MD
Project Role:	*Advisory Board Member*
Researcher Identifier (e.g. ORCID ID):	*0000-0001-7922-2156*
Nearest person month worked:	*0.36*
Contribution to Project:	*Dr. Kim advised Academy scholars on projects and career development.*
Funding Support:	*NCI, CDMRP*
Name:	***Sumanta Pal***
Project Role:	*Advisory Board Member*
Researcher Identifier (e.g. ORCID ID):	*https://orcid.org/0000-0002-1712-0848*
Nearest person month worked:	*1CM*
Contribution to Project:	*Dr. Pal has served as an advisory board member and has been involved in establishing goals for Early Career Investigators and provide opportunities for successful completion of those goals.*
Funding Support:	*NCI, CDMRP*
Name:	***M. Celeste Simon, MD***
Project Role	*Advisory Board Member*
Researcher Identifier:	*000-0001-9106-447X*
Nearest person month worked	*0.48*
Contribution to project	*Dr. Simon serves as an Advisory Board member, attending meetings, mentoring investigators and assessing progress*
Funding Support:	*NCI, LUDWIG INSTITUTE FOR CANCER RESEARCH*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
Yes, please see below Other support documents for the PI and key personnel with annotated changes since last reporting period.

PREVIOUS/CURRENT/PENDING SUPPORT – Brian Rini, MD, FASCO

CURRENT

5P30 CA068485-27 (Park)
Title: Vanderbilt-Ingram Cancer Center Support Grant
Agency: NIH/NCI
Grants Officer: Mike Steenstra,

Email: michael.steenstra@nih.gov

Address of Funding Agency: 9000 Rockville Pike, Bethesda, Maryland
Performance Period: 09/15/2020 – 08/31/2025
Funding level:
Project Goals: Vanderbilt-Ingram Cancer Center (VICC) is a matrix center that integrates all of Vanderbilt's cancer-related expertise and resources in order to deliver its mission of alleviating cancer death and suffering through pioneering research; innovative patient-centered care; and evidence-based prevention, education and community initiatives. This mission is accomplished through translation of exceptional cancer research into interventions for the prevention, diagnosis and treatment of cancer. The Cancer Center Support Grant provides infrastructure to facilitate multidisciplinary basic, clinical and population-based research, to advance VICC discoveries to cancer patients and the community, and to educate and train the next generation of cancer investigators and workforce.
Specific Aims:
Aim 1. To conduct, support and enhance state-of-the-art, multidisciplinary basic, clinical and population-based research.
Aim 2. To coordinate and integrate cancer-related research and activities across Vanderbilt and to collaborate with our local, regional, national and global partners on initiatives of the highest priority to the National Cancer Program.
Aim 3. To train and develop the next generation of cancer investigators, cancer leaders and the continuum of cancer care providers.
Aim 4. To assess and prioritize community needs and to leverage partnerships to address those needs through cancer research, care and control activities.
Role: Co-Investigator, Chief for Clinical Trials
PERSON MONTHS:

YYYY	Person Months
2023	1.2 calendar
2024	1.2 calendar
2025	1.2 calendar

Overlap: None

This Award Technical Progress Report - Effort increase from 2.4CM to 3.6CM/New effort not assigned yet
W81XWH2020046 (Rini)
Title: Academy of Kidney Cancer Investigators Dean Award
Agency: CDMRP
Grants Officer: Juan A. Rodriguez,

E-mail: juan.a.rodriguez236.civ@mail.mil
Address of Funding Agency: 820 Chandler St, Fort Detrick, MD 21702-50147
Performance Period: 09/02/2020 – 09/01/2025
Funding level:
Project Goals: The major goal of this project is to foster the development and commitment of early career kidney cancer investigators through provision of the raw materials and structured mentorship for focused, sustainable and ultimately independent success.
Specific Aims:
Aim 1. Establish renal cell carcinoma (RCC) mentor and Dean/advisory panel who devote regular, dedicated time to career advancement of the mentees.
Aim 2. Provide visibility and opportunities to interact with other members of the multidisciplinary academic RCC community and beyond.
Aim 3. Focuse on training across the spectrum of RCC research including relevant workshops and didactics;

Aim 4. Provide regular feedback through a virtual platform on progress towards the goal of becoming an independent RCC researcher.
Aim 5. Develop RCC mentors through structured mentorship guidance with feedback / monitoring of progress.
Aim 6. Organize an annual, in-person workshop to bring all relevant parties together to critically evaluate the mentoring plans, discuss ongoing research projects, identify barriers and strategies to overcome them, foster intra-Academy collaboration and provide a concrete roadmap for the next year.
Role: Principal Investigator
PERSON MONTHS:

YYYY	Person Months
2023	2.4 calendar
2024	3.6 calendar
2025	3.6 calendar

Overlap: None

W81XWH2120025 (Rini)
Title: Kidney Cancer Clinical Trials Consortium
Effort: 2.40 CM
Agency: Congressionally Directed Medical Research Programs
Grants Officer: Jennifer Shankle,
E-mail: jennifer.e.shankle.civ@mail.mil,

Address of Funding Agency: 820 Chandler St, Fort Detrick, MD 21702-5014
Performance Period: 09/15/2021 – 09/14/2024
Funding level:
Project Goals: The goal of the Vanderbilt-Ingram Cancer Center's (VICC) participation in the Kidney Cancer Research Consortium (KCRC) is to meaningfully contribute to Phase I and II clinical research in the context of this multi-institutional collaboration. VICC will contribute intellectual input and translational research expertise to the KCRC as well as robust patient accrual. Participation in the Consortium will provide a critical platform for the co-development of Renal Cell Carcinoma (RCC) clinical trials enhanced by the pooled expertise of the Consortium members.
Specific Aims:
Aim 1. Design innovative, mechanism-based translational clinical trials for the KCRC.
Aim 2. Accrue at least 15 patients per year to KCRC trials.
Aim 3. Perform translational research on samples obtained from KCRC trials.
Role: Principal Investigator
PERSON MONTHS:

YYYY	Person Months
2023	2.4 calendar
2024	2.4 calendar

Overlap: None

KC210158/ W81XWH-21-KCRP-IDA (Rini)
Title: RNAseq-Based Biomarkers Identify Targetable Biologic Drivers of Kidney Cancer
Effort: 1.20 CM
Agency: Congressionally Directed Medical Research Programs
Grants Officer: Medha Darshan,
E-mail: medha.s.darshan.civ@mail.mil,

Address of Funding Agency: 820 Chandler St, Fort Detrick, MD 21702-5014

Performance Period: 09/01/2022-08/31/2025
Funding level:
Project Goals: The central hypothesis that RNAseq can be used to identify biologic drivers of ccRCC in individual patients and improve outcomes.
Specific Aims:
Aim 1. Develop methods to prospectively assign individual tumors to IMmotion 151-derived RNAseq clusters inreal time.
Aim 2. Evaluate the RNAseq biomarker in a retrospective validation cohort.
Aim 3. Evaluate macrophage infiltration as a biologic driver of cluster 3/6 tumors.
Role: Principal Investigator
PERSON MONTHS:

YYYY	Person Months
2023	1.20 calendar
2024	1.20 calendar
2025	1.20 calendar

Overlap: None

New since last reporting period
KC210255/W81XWH-21-KCRP-CTA (Rini)
Title: OPtimal Treatment by Invoking biologic Clusters in Renal Cell Carcinoma (OPTIC RCC)
Effort: 1.20 CM
Agency: Congressionally Directed Medical Research Programs
Address of Funding Agency: 820 Chandler St, Fort Detrick, MD 21702-5014
Performance Period: 09/01/2022-08/31/2026
Funding level:
Project Goals: The purpose of this study is to test our hypothesis that a new tool that measures the genetic signature of kidney cancer tumors can precisely match a patient to a pure immunotherapy regimen or an immunotherapy/tumor blood vessel poison combination
Specific Aims: The current proposal will test this hypothesis by prospectively evaluating gene expression in patient tumors, assigning patient tumors to IMmotion 151 clusters, and using this cluster assignment to choose an FDA-approved first line therapy for patients with metastatic clear cell RCC.
Role: Principal Investigator
PERSON MONTHS:

YYYY	Person Months
2023	1.20 calendar
2024	1.20 calendar
2025	1.20 calendar
2026	1.20 calendar

Overlap: None

New - Awarded Effective Date 09.01.2023
KC220067/W81XWH-22-KCRP-IDA
Title: Peripheral Systemic Response Assessment in RCC
Effort: 0.00 calendar months
Principal Investigator: Kathryn E. Beckermann
Support Agency: CDMRP
Grant Officer: Medha Darshan,
E-mail: medha.s.darshan.civ@mail.mil,

Performance Period: 09/01/2023 – 08/31/2026

Level of Funding:
Project Goal: We hypothesize that the peripheral blood of patients with RCC have circulating T cells with high mitochondrial metabolism and exhaustion markers which reflect RCC TIL and expand during treatment with checkpoint inhibition.
Specific Aims:
Aim 1: To test if patients with RCC have circulating peripheral blood T cells with high mitochondrial metabolism that reflect RCC TIL metabolism and function.
Aim 2: To test the hypothesis that expansion of T cell subsets with high mitochondrial activity occurs
in the peripheral blood of patients undergoing systemic treatment with checkpoint inhibition.
Role: Co-Mentor
Person Months: 0.00CM
Overlap: None

PENDING: None

Summary of Effort commitment "Active" and "Pending -in incoming 90-days" proposals:

Grant	08/01/2023	Proposed adjustment	Final effort/Notes
5P30 CA068485-27 (Park)	1.2		1.2
W81XWH2120025 (Rini)	2.4		2.4
W81XWH2020046 (Rini)	2.4	+1.2	3.6
KC210158/W81XWH-21-KCRP-IDA (Rini)	1.2		1.2
KC210255/W81XWH-21-KCRP-CTA (Rini)	1.2		1.2
Total Active	8.4	+1.2	9.6
Pending	0.0		0.0
Total *Active* with incoming *Pending*	**8.4**	**+1.2**	**9.6**

IN-KIND: None
Foreign Collaboration: None

PREVIOUS

3P30 CA068485-25S2 (Pietenpol)
Title: The COVID-19 and Cancer Consortium: NCI Administrative Supplement to P30 Cancer Center Support Grant (CCSG)
Effort: 1.8 calendar months
Agency: NIH/NCI
Grants Officer: Sonya Roberson, E-mail: robersos@mail.hih.gov
Address of Funding Agency: 9000 Rockville Pike, Bethesda, Maryland
Performance Period: 05/01/2021 – 08/31/2022
Funding level:
Project Goals: The driving goal of the consortium is to collect prospective, granular, uniformly organized information to help generate hypotheses for translational science, and to arm treating providers with the most complete data resource as rapidly as possible on cancer patients infected with COVID-19

Specific Aims:
Aim 1. Ensure a robust and sustained mechanism for collecting data at scale from existing institutions and future participating sites.
Aim 2. Collect detailed follow-up information on the currently accrued patients to understand longer-term outcomes.
Role: Co-Project Lead

***3*P30 CA068485-24S4 (Pietenpol)**
Title: COVID-19 and Cancer Consortium (CCC19)
Effort: 1.2 calendar months
Agency: NIH/NCI
Grants Officer: Matinson Owusu, E-mail: joyann.rohan@nih.gov
Address of Funding Agency: 820 Chandler St, Fort Detrick, MD 21702-50147
Performance Period: 04/30/2016 - 08/31/2020
Funding level:
Specific Aims: Rapidly expand **CCC19 Registry** activities by 1) enhancing infrastructure for data collection and storage of uniform COVID-19 cancer patient etiology, treatment and outcome data; 2) engaging expert epidemiologists and biostatisticians to analyze consortium data and define best practices, new therapeutic modalities, and/or outcomes of clinical trials**.**
Role: Co-Investigator
Overlap: None

P30-CA04370 (Gerson)
Title: Case Comprehensive Cancer Center Support Grant
Effort: 0.5 calendar months
Agency: NCI
Grants Officer: Cammie La, lac@mail.nih.gov
Address of Funding Agency: 8717 Grovemont Cir # 115, Bethesda, MD 20892
Performance Period: 08/01/1997 – 03/31/2019
Funding level:
Project Goals: To improve the prevention, diagnosis, and therapy of cancer through discovery, evaluation, and dissemination to reduce cancer morbidity and mortality in Northern Ohio and the Nation.
Specific Aims:
Aim 1. Improve the prevention, diagnosis, and therapy of cancer through research.
Aim 2. Stimulate and support innovative, coordinated, interdisciplinary research on cancer diagnosis, treatment,and control.
Aim 3. Develop clinical applications of research discoveries and to make these applications available.
Role: Co-Investigator
Overlap: None

R01-CA168488 (Finke)
Title: Regulation of MDSC Function and Trafficking
Effort: 0.36 calendar months
Agency: NCI
Grants Officer: Mohla, Suresh, mohlas@mail.nih.gov
Address of Funding Agency: 8717 Grovemont Cir # 115, Bethesda, MD 20892
Performance Period: 07/01/2012 – 01/31/2019
Funding level:
Project Goals: To test whether the prevalence of n-MDSCs in some patients correlates with an angiogenic gene expression profile driven by elevated proinflammatory cytokines (IL-1β), and if, by contrast, other patients with tumors infiltrated by largely linage-negative- and/or m-MDSC subsets

are characterized by a more immunosuppressive profile with distinct patterns of cytokine expressionn and clinical outcomes.
Specific Aims:
Aim 1. Define individual contributions of IL-1β, IL-6, GM-CSF, and G-CSF in modulating immunosuppressive and/or pro-angiogenic phenotypes of MDSC populations.
Aim 2. Define chemokine receptor expression and immunosuppressive and pro-angiogenic gene expression within select MDSC subsets.
Aim 3. Determine the impact of the cytokine/chemokine content of the tumor microenvironment on phenotypes of adoptively transferred BM-derived CD11b+Gr1+ cell populations by assessing patterns of functional gene expression within subsets before and after transfer.
Role: Co-Investigator
Overlap: None

CURRENT/PREVIOUS/PENDING OTHER SUPPORT - BRUGAROLAS, JAMES, M.D., PH.D.
Current

New since last reporting period

Title: University of Texas Southwestern Medical Center SPORE in Kidney Cancer
Time commitment: 2.4 calendar months
Supporting agency: NIH/NCI 2P50 CA196516
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Rogers Gross
Office of Grants Administration
National Cancer Institute, NIH
9609 Medical Center Drive Shady
Grove West Tower 2W524

Period of Performance: 08/01/2022 – 07/31/2027
Level of funding:
Brief Description of the project's goals: This is a specialized program of research excellence in kidney cancer to translate basic science discoveries into the clinic. Dr. Brugarolas is the contact PI. The SPORE contains 3 projects, 4 core facilities, a career enhancement program, and a developmental research program. Among the 3 projects, Dr. Brugarolas is PI of Project 1.
List of specific aims (Project 1): Aim 1. To develop a novel molecular imaging tool to monitor HIF2a in CCRCC patients; Aim 2. To execute a clinical trial of a tumor-directed HIF2a siRNA targeting both wild-type and drug-resistant HIF2a.
THERE IS NO OVERLAP.

Title: Dissecting the mechanism of cabozantinib anti-tumor effect in renal cancer
Time commitment: 0.1 calendar months
Supporting agency: NIH/NCI R21 CA263264
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Crystal Wolfrey 9000
Rockville Pike
Bethesda, MD 20892
wolfreyc@mail.nih.gov
Period of Performance: 07/01/2021 – 12/31/2023 (NCE)
Level of funding:
Brief Description of the project's goals: To determine how cabozantinib exerts its anti-tumor activity and explore the role of the tumor microenvironment in mediating the anti-tumor effects of cabozantinib. **This project is in a 6-month no cost extension.**

List of specific aims: Aim 1. To dissect the mechanism of cabozantinib anti-tumor activity by evaluating acquired resistance in tumor cells; Aim 2. To explore the role of the tumor microenvironment in mediating cabozantinib anti-tumor effects using an innovative mouse model. **There is no overlap.**

Title: Directing immunotherapy with iPET
Time commitment: 0.1 calendar months
Supporting agency: V Foundation Translational Award T2018-011
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

Contact Person: Carole Wegner
14600 Weston Parkway
Cary, NC. 27513

Period of Performance: 11/01/2018 – 11/01/2023 (NCE)
Level of funding:
Brief Description of the project's goals: This project funds a clinical trial of immunoPET (iPET) to measure PD-L1 expression in patients. **This project is in a no-cost extension.**
List of specific aims: Aim 1. To validate iPET in patients with RCC prior to surgery by coregistering iPET signal with PD-L1 expression on surgical specimens using 3D reconstruction and tumor-specific molds; Aim 2. To explore the predictive value of iPET in patients with metastatic RCC treated with immune checkpoint inhibitors.
THERE IS NO OVERLAP.

New since last reporting period
Title: PET imaging of HIF-2a in renal cancer (**Brugarolas and Sun**)
Time commitment: (Calendar/Academic/Summer): 0.60 calendar months **Supporting agency:** Department of Defense HT9425-23-1-0904
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

Contact Person: Michael D. Hall, Ph.D.
Science Officer | Congressionally Directed Medical Research Program
Lung Cancer Research Program
Kidney Cancer Research Program
Department of Defense
1077 Patchel Street
Fort Detrick, MD 21702-5024
michael.d.hall14.civ@mail.mil

Period of Performance: 09/01/2023 – 08/31/2026
Level of Funding:
Brief Description of the project's goals: This project seeks to develop a second-generation radiopharmaceutical, [^{18}F]PT2977, for positron emission tomography (PET) imaging of HIF2α in patients diagnosed with ccRCCs. **Dr. Brugarolas serves as co-PI.**
List of specific aims: Aim 1. To design and develop synthetic routes to the precursor of [^{18}F]PT2977 and accomplish automated radiosynthesis of [^{18}F]PT2977; Aim 2. To validate PET imaging of HIF2α with [^{18}F]PT2977 in RCC tumorgrafts (TGs); Aim 3. To complete the required pre-IND experiments for an FDA IND application and set everything in place to launch a clinical trial.
THERE IS NO OVERLAP BETWEEN THIS PROJECT AND THE SPORE PROJECT 1 SINCE THEY FOCUS ON COMPLETELY DIFFERENT STRUCTURES. WHEREAS THE SPORE PROJECT 1 FOCUSES ON EXPLORING THE POTENTIAL OF PT2385 AS A RADIOTRACER, THIS PROJECT FOCUSES INSTEAD ON EVALUATING PT2977, ALSO CALLED BELZUTIFAN.

Title: Epigenetic Modifications of Cytosines in Clear Cell Kidney Carcinogenesis and Survival (Salas, L.)
Time commitment: 0.6 calendar months
Supporting agency: Department of Defense W81XWH-20-1-0778
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Joshua D. McKean
US Army Medical Research Acquisition Activity 820
Chandler Street
Fort Detrick, MD 21702-50147
Period of Performance: 09/01/2020 – 08/31/2024
Level of funding (subcontract):
Brief Description of the project's goals: The proposed work is designed to better characterize cytosine modifications in ccRCC, and to fill current gaps in the knowledge about the epigenetic structure of ccRCC. **Dr. Brugarolas serves as a mentor to the applicant and receives some salary support.**
List of specific aims: Aim 1. To characterize the specific DNA methylation and DNA hydroxymethylation patterns between 200 ccRCC and 50 normal adjacent kidney samples from the Renal Tumor Tissue Bank at Dartmouth; Aim 2. To evaluate whether specific changes in DNA hydroxymethylation are related to changes in cancer survival; Aim 3. To examine whether the observed changes in DNA methylation and DNA hydroxymethylation alter the levels of mRNA and miRNA in the kidney cancer samples.
THERE IS NO OVERLAP.

This Award Technical Progress Report
Title: Academy of Kidney Cancer Investigators Dean Award (Rini, B.)
Time commitment: 0.88 calendar months
Supporting agency: Department of Defense W81XWH-20-2-0046
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Juan A. Rodriguez
US Army Medical Research Acquisition Activity 820
Chandler St.
Fort Detrick, MD 21702-50147
juan.a.rodriguez236.civ@mail.mil

Period of Performance: 09/02/2020 – 09/01/2025
Level of funding:
Brief Description of the project's goals: The major goal of this project is to foster the development and commitment of early career kidney cancer investigators through provision of raw materials and structured mentorship for focused, sustainable, and ultimately independent success. **Dr. Brugarolas serves as chair of the scientific advisory board and receives some salary support.**
List of specific aims: Aim 1. Establish renal cell carcinoma (RCC) mentor and Dean/advisory panel who devote regular, dedicated time to career advancement of the mentees; Aim 2. Provide visibility and opportunities to interact with other members of the multidisciplinary academic RCC community and beyond; Aim 3. Focus on training across the spectrum of RCC research including relevant workshops and didactics; Aim 4. Provide regular feedback through a virtual platform on

progress towards the goal of becoming an independent RCC researcher; Aim 5. Develop RCC mentors through structured mentorship guidance with feedback/monitoring of progress; Aim 6. Organize an annual, in-person workshop to bring all relevant parties together to critically evaluate the mentoring plans, discuss ongoing research projects, identify barriers and strategies to overcome them, foster intra-Academy collaboration and provide a concrete roadmap for the next year.
THERE IS NO OVERLAP.

Title: Leveraging digital pathology and deep learning to predict immunotherapy response (**Kapur, PI**)
Time commitment: 0.48 calendar months
Supporting agency: Department of Defense W81XWH-21-1-0630
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Joshua D. McKean
US Army Medical Research Acquisition Activity 820
Chandler Street
Fort Detrick, MD 21702-50147
Period of Performance: 09/01/2021 – 08/31/2024
Level of funding:
Brief Description of the project's goals: Leverage digital pathology and deep learning to probe features associated with transcriptomic signatures predictive of immunotherapy response. **Dr. Brugarolas serves as co-investigator and the budget includes funds to support his salary.**
List of specific aims: Aim 1. Validate identification of immune and vascular cells in H&E images from IMmotion150; Aim 2. Establish a deep learning pipeline to predict transcriptomic signatures on IMmotion150; Aim 3. Develop a deep learning pipeline to predict treatment response using IMmotion150 and validate on IMmotion151 clinical trial date.
THERE IS NO OVERLAP.

Title: Dissecting Intratumor Heterogeneity in Kidney Cancer Using Deep Learning (**Rajaram, PI**)
Time commitment: 0.6 calendar months
Supporting agency: CPRIT RP220294
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Patty Moore
Cancer Prevention and Research Institute of Texas
1701 North Congress Avenue
Suite 6-127
Austin, TX 78701
Period of Performance: 03/01/2022 – 02/28/2025
Level of funding:
Brief Description of the project's goals: To establish a morpho-genomic biomarker that considers intratumor heterogeneity to predict therapy response by applying deep learning approaches to the analysis of clinical trial datasets. **Dr. Brugarolas serves as collaborator and the budget includes funds to support his salary.**
List of specific aims (Project 1): Aim 1. Optimize a metric-learning approach to demarcate regions reflecting different molecular states; Aim 2. Identify morpho-genomic clades predictive of

response by leveraging clinical trial datasets; Aim 3. Deploy a morpho-genomic biomarker transcending ITH to predict therapy response using a real-world dataset.

THERE IS NO OVERLAP.

New since last reporting period

Title: Recurrent Genomic Alterations Driving Clear Cell Renal Cell Carcinoma Development (**Ly, PI**)
Time commitment: 0.6 calendar months
Supporting agency: Department of Defense W81XWH-22-1-0764
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Michael D. Hall, Ph.D.
Science Officer | Congressionally Directed Medical Research Program
Lung Cancer Research Program
Kidney Cancer Research Program
Department of Defense
1077 Patchel Street
Fort Detrick, MD 21702-5024
michael.d.hall14.civ@mail.mil

Period of Performance: 08/01/2022 – 07/31/2026
Level of funding:
Brief Description of the project's goals: The goal of this project is to identify how renal cell division errors initiate chromosome 3p/5q chromothripsis and reconstruct how oncogenic selection shapes the genomic rearrangement landscape of ccRCC. **Dr. Brugarolas serves as a mentor to the applicant and the budget includes funds to support his salary.**
List of specific aims (Project 1): Aim 1. Engineer experimental systems to induce chromosome 3p and 5q micronuclei and chromothripsis in non-transformed human renal epithelial cells; Aim
2. Determine whether 3p and 5q chromothripsis can partially or fully drive renal cell tumorigenesis; Aim 3. Identify recurrent signatures of genetic alterations emerging throughout oncogenic transformation.
There is no overlap.

New since last reporting period

Title: Multifunctional Immunotherapy Nanoparticle to Enable Innate Immunotherapy for Kidney Cancer (**Wang AZ, PI**)
Time commitment: (Calendar/Academic/Summer): 0.60 calendar months
Supporting agency: Department of Defense HT9425-23-1-0516
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Medha Darshan, M.S, MAT
Science Officer | Congressionally Directed Medical Research Programs
Kidney Cancer Research Program (KCRP)
Bone Marrow Failure Research Program (BMFRP)
Department of Defense
1077 Patchel Street
Fort Detrick, MD 21702-5024
medha.s.darshan.civ@health.mil

Period of Performance: 06/15/2023 – 06/14/2026
Level of Funding:
Brief Description of the project's goals: This project seeks to develop a novel therapeutic strategy based on NK-activating nanoparticles to improve treatment efficacy of kidney cancer. **Dr. Brugarolas serves as co-investigator and the budget includes funds to support his salary.**
List of specific aims: Aim 1. To engineer NK-activating MINPs that can target kidney cancer; Aim 2. To identify the most effective immune therapeutic combination for NK.
THERE IS NO OVERLAP.

New since last reporting period

Title: Leveraging SCARB1 Overexpression for the Treatment of ccRCC with Low-Density Lipoprotein Nanocarriers (**Corbin, PI**)
Time commitment: 0.36 calendar months
Supporting agency: Department of Defense HT9425-23-1-0866
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Michael D. Hall, Ph.D.
Science Officer | Congressionally Directed Medical Research Program
Lung Cancer Research Program
Kidney Cancer Research Program
Department of Defense
1077 Patchel Street
Fort Detrick, MD 21702-5024
michael.d.hall14.civ@mail.mil

Period of Performance: 08/15/2023 – 08/14/2026
Level of funding:
Brief Description of the project's goals: To investigate the therapeutic utility of LDL-DHA treatment for Renal Cell Carcinoma. **Dr. Brugarolas serves as collaborator and receives no salary support.**
List of specific aims: Aim 1. To investigate the binding, uptake, and cytotoxicity of the LDL-DHA formulation against a panel of normal and malignant kidney cells; Aim 2. To develop a rat model of kidney cancer to assess LDL-DHA drug delivery kinetics, safety, and short-term anticancer effects; Aim 3. To compare effectiveness of LDL-DHA vs current front-line treatment to provide sustained long term antitumor control in a rat kidney cancer model.
THERE IS NO OVERLAP.

New since last reporting period
Title: Leveraging Biophysicochemical Motifs in T Cell Receptor Antigen Binding Regions and Antigen Co-occurrence to Predict Response to Immune Checkpoint Inhibitors (**Kapur, PI**)
Time commitment: (Calendar/Academic/Summer): 0.30 calendar months
Supporting agency: Department of Defense HT9425-23-1-0794
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Medha Darshan, M.S, MAT
Science Officer | Congressionally Directed Medical Research Programs
Kidney Cancer Research Program (KCRP)
Bone Marrow Failure Research Program (BMFRP)
Department of Defense

1077 Patchel Street
Fort Detrick, MD 21702-5024
medha.s.darshan.civ@health.mil

Period of Performance: 09/01/2023 – 08/31/2026
Level of Funding:
Brief Description of the project's goals: To provide understanding of what drives differential ICI responsiveness by exploiting genomic differences associated with differential inflammatory states, TCR antigen binding region motifs and shared antigens. **Dr. Brugarolas serves as co-investigator and the budget includes funds to support his salary.**
List of specific aims: Aim 1. Elucidate the TCRB profile differences that distinguish B- and P-ccRCCs; Aim 2: Elucidate the TCRB antigen binding region motif and antigen co-occurrence patterns that distinguish B-and P-ccRCCs; Aim 3: Evaluation of model performance and predictive value for ICI response.
THERE IS NO OVERLAP.

New since last reporting period
Title: Characterization of epigenetic and metabolic vulnerability in VHL-deficient ccRCC and its therapeutic potential (**Luo, PI**)
Time commitment: (Calendar/Academic/Summer): 0.60 calendar months
Supporting agency: Department of Defense HT9425-23-1-0863
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Medha Darshan, M.S, MAT
Science Officer | Congressionally Directed Medical Research Programs
Kidney Cancer Research Program (KCRP)
Bone Marrow Failure Research Program (BMFRP)
Department of Defense
1077 Patchel Street
Fort Detrick, MD 21702-5024
medha.s.darshan.civ@health.mil

Period of Performance: 09/01/2023 – 08/31/2026
Level of Funding:
Brief Description of the project's goals: This study seeks to harness the synthetic lethality of SGI-1027 for the development of a novel therapeutic strategy in VHL-deficient ccRCC by using clinically relevant in vivo models. **Dr. Brugarolas serves as co-investigator and the budget includes funds to support his salary.**
List of specific aims: Aim 1. To dissect the mechanism underlying synthetic lethality of SGI-1027 in VHL-deficient ccRCC; Aim 2. To evaluate therapeutic potential of SGI-1027 in clinically relevant VHL-deficient ccRCC models in vivo
THERE IS NO OVERLAP.

New since last reporting period
Title: Targeting stem-like CD8 T cells in immunotherapy against kidney cancer (**Yao, PI**) **Time commitment:** 0.6 calendar months
Supporting agency: Department of Defense HT9425-23-1-0801
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

Contact Person: Michael D. Hall, Ph.D.
Science Officer | Congressionally Directed Medical Research Program
Lung Cancer Research Program
Kidney Cancer Research Program
Department of Defense
1077 Patchel Street
Fort Detrick, MD 21702-5024
michael.d.hall14.civ@mail.mil

Period of Performance: 09/01/2023 – 08/31/2027
Level of funding:
Brief Description of the project's goals: To understand whether generating antitumor stem-like CD8 T-cell and improving their fitness are critical for the efficacy of therapies against RCC. **Dr. Brugarolas serves as a mentor to the applicant and receives no salary support**
List of specific aims: Aim 1. To define the role of tumor-specific stem-like CD8 T cells in PD1 blockade therapy in RCC; Aim 2. To evaluate whether TKI treatment modulates the metabolism and microenvironment of stem-like CD8 T cells to potentiate the efficacy of PD1 blockade in RCC.
THERE IS NO OVERLAP.

New since last reporting period
Title: Identification of DCLK2-TBK1 signaling axis as a potential therapeutic target in kidney cancer (**Zhang, PI**)
Time commitment: 0.48 calendar months
Supporting agency: NIH/NCI RO1 CA284591
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: Venkatachalam, Sundaresan
sundarv@nih.gov

Period of Performance: 09/01/2023 – 08/31/2028
Level of funding:
Brief Description of the project's goals: To evaluate how DCLK2 regulates TBK1 activity in ccRCC and to determine the therapeutic potential of targeting this pathway. **Dr. Brugarolas serves as co-investigator and the budget includes funds to support his salary.**
List of specific aims: Aim 1. To characterize the functional significance of DCLK2 in kidney cancer; Aim 2. To delineate the molecular mechanism by which DCLK2 contributes to kidney tumorigenesis; Aim 3. To investigate the therapeutic potential of targeting DCLK2-TBK1 in kidney cancer orthotopic xenografts and patient derived xenografts (PDXs).
THERE IS NO OVERLAP.

Pending
Title: Dissecting TFE3 Mediated Tumorigenesis (**Brugarolas**)
Time commitment: (Calendar/Academic/Summer): 1.8 calendar months
Supporting agency: CPRIT

NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

TBD

Period of Performance: 03/01/2024 – 02/29/2028

Level of Funding:

Brief Description of the project's goals: This project proposes to leverage an innovative mouse model of tRCC developed in the laboratory and that faithfully recapitulates the human disease to investigate the molecular mechanisms of tRCC tumorigenesis. **Dr. Brugarolas will serve as PI. List of specific aims:** Aim 1. Structure/function analysis of ASPSCR1-TFE3 translocation driven tRCC *in vivo*; Aim 2. To understand how TFE3 translocations promote tumor growth; Aim 3. To explore oncogenic events cooperating with ASPSCR1-TFE3 translocation. THIS PROJECT OVERLAPS WITH THE NIH/NCI APPLICATION BELOW BUT ONLY IN THE PROPOSED AIM 2. AIM 1 DOES NOT OVERLAP AS IT EVALUATES DIFFERENT STRUCTURAL DOMAINS AND AIM 3 DOES NOT OVERLAP EITHER AS IT EXAMINES THE COOPERATIVITY WITH DIFFERENT TUMOR SUPPRESSOR GENES.

Title: Leveraging First Mouse Model Reproducing Human Translocation Renal Cell Carcinoma to Investigate Molecular Mechanisms (**Brugarolas**)

Time commitment: (Calendar/Academic/Summer): 1.8 calendar months

Supporting agency: NIH/NCI

NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

TBD

Period of Performance: 04/01/2024 – 03/31/2029

Level of Funding:

Brief Description of the project's goals: This project proposes to leverage an innovative mouse model of tRCC developed in the laboratory and that faithfully recapitulates the human disease to investigate the molecular mechanisms of tRCC tumorigenesis. **Dr. Brugarolas will serve as PI. List of specific aims:** Aim 1. To dissect the functional role of the N-terminal transactivation domain in tRCC tumorigenesis using gene editing in the mouse; Aim 2. To dissect how ASPSCR1- TFE3 promotes cell proliferation and in particular to assess the role of EPHA5 in tumorigenesis; Aim 3. To leverage the ASPSCR1-TFE3 mouse model to explore cooperative oncogenic events. **This project overlaps with the CPRIT application above but only in the proposed Aim 2. Aim 1 does not overlap as it evaluates different structural domains and Aim 3 does not overlap either as it examines the cooperativity with different tumor suppressor genes.**

Title: Tumor Extravasation in Zebrafish as a Prognostic Marker and a Therapeutic Target for Metastasis of Kidney Cancer (**Ariizumi, PI**)

Time commitment: 0.18 calendar months

Supporting agency: Department of Defense

NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

Contact Person: TBD

Period of Performance: 09/01/2023 – 08/31/2026

Level of funding:

Brief Description of the project's goals: To evaluate the potential of tumor extravasation in a zebrafish model as a biomarker for metastasis for kidney cancer. **Dr. Brugarolas will serve as co- investigator. This award provides salary funds corresponding to the effort.**

List of specific aims: Aim 1. Determine whether TC extravasation scores in zebrafish predict metastatic risk of RCC; Aim 2. Determine whether targeting rHS prevents metastasis in zebrafish and mouse xenograft models.
THERE IS NO OVERLAP.

Title: Targeting a Novel Carbohydrate as an Immune-Angiogenic Regulator for Kidney Cancer Treatment (**Ariizumi, PI**)
Time commitment: 0.12 calendar months
Supporting agency: CPRIT
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: TBD
Period of Performance: 03/01/2024 – 02/28/2027
Level of funding:
Brief Description of the project's goals: To explore the use of a carbohydrate as an immune-angiogenic regulator for the treatment of kidney cancer. **Dr. Brugarolas will serve as co-investigator. This award provides salary funds corresponding to the effort.**
List of specific aims: Aim 1. To evaluate the efficacy and safety of rHS-targeting to treat PDX of renal cell carcinoma (RCC) in humanized mouse model, in a comparison with ICIs; Aim 2. To characterize expression of HS/HSPG vs. PD1/PDL1 in TME during cancer progression; Aim 3. Identify distinct role of rHSPG in regulating T cell functions from PD1.
THERE IS NO OVERLAP.

Title: Roles of ISGF3 in ccRCC tumorigenesis and combination therapy with a STING agonist (**Yang, PI**)
Time commitment: 0.12 calendar months
Supporting agency: Thomas Jefferson University
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:
Contact Person: TBD
Period of Performance: 10/01/2024 – 09/30/2028
Level of funding (subcontract):
Brief Description of the project's goals: This study will examine the role of ISGF3 in RCC tumorigenesis, and if a STING agonist combined with PD-L1 therapy or an mTOR inhibitor are more effective in treating RCC tumors in murine models. **Dr. Brugarolas will serve as a consultant.**
List of specific aims: Aim 1: Determine if ISGF3 loss is sufficient to help VHL-deficient mice to develop ccRCC; Aim 2. Examine if the combination of a STING agonist and an mTOR inhibitor can overcome drug resistance; Aim 3. Understand how STING agonists upregulate PD-L1 expression, and whether the combination of a STING agonist and an anti-PD-L1 antibody boost therapeutic effect.
THERE IS NO OVERLAP.

Title: JMJD6-DGAT1 Signaling Axis Regulates Lipid Droplets and Tumorigenesis in ccRCC (**Zhang, PI**)
Time commitment: (Calendar/Academic/Summer): 0.60 calendar months
Supporting agency: CPRIT

NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

Contact Person: Patty Moore; pmoore@cprit.texas.gov
Period of Performance: 03/01/2024 – 02/28/2027
Level of Funding:
Brief Description of the project's goals: This project seeks to investigate how JMJD6 is essential for ccRCC tumorigenesis by regulating DGAT1 expression and lipid droplet formation. **Dr. Brugarolas will serve as co-investigator. This award provides salary funds corresponding to the effort.**
List of specific aims: Aim 1. Dissect the role of JMJD6 in ccRCC tumorigenesis; Aim 2. Elucidate the molecular mechanism by which the JMJD6-DGAT1 signaling axis contributes to ccRCC tumorigenesis. Aim 3: Determine the therapeutic potential of targeting JMJD6-DGAT1 in ccRCC.

THERE IS NO OVERLAP.

Previous (within the past 5 years)

Award ended/completed since last reporting period
Title: University of Texas Southwestern Medical Center SPORE in Kidney Cancer
Time commitment: 3.06 calendar months
Supporting agency: NIH/NCI 1P50CA196516
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

Contact Person: Rogers Gross
Office of Grants Administration
National Cancer Institute, NIH
9609 Medical Center Drive Shady
Grove West Tower, 2W524

Period of Performance: 08/01/2016 – 07/31/2022 (NCE)
Level of funding:
Brief Description of the project's goals: This is a specialized program of research excellence in kidney cancer to translate basic science discoveries at UT Southwestern into the clinic. Dr. Brugarolas is the overall PI. The SPORE contains 4 projects, 4 core facilities, a career enhancement program, and a developmental research program. Among the 4 projects, Dr. Brugarolas is PI of Project 1.
List of specific aims (Project 1): Aim 1. Identify biomarkers of HIF-2-dependency in ccRCC using tumorgrafts; Aim 2. Anticipate mechanisms of acquired resistance to HIF-2 inhibitor; Aim 3. Explore multiparametric magnetic resonance (MR) imaging as a pharmacodynamic marker in a first-in-human, phase I clinical trial of a HIF2-I in patients with advanced ccRCC.
THERE IS NO OVERLAP.

Title: Understanding TFE3-mediated tumorigenesis through analysis of a novel, clinically relevant mouse model of translocation renal cell carcinoma
Time commitment: 1.2 calendar months
Supporting agency: CPRIT RP180191
NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

Contact Person: Patty Moore

Cancer Prevention and Research Institute of Texas
1701 North Congress Avenue
Suite 6-127
Austin, TX 78701

Period of Performance: 03/01/2018 – 02/28/2022

Level of funding:

Brief Description of the project's goals: This project leverages a novel mouse model of translocation RCC to investigate TFE3 induced tumorigenesis and therapeutic response.

List of specific aims: Aim 1. Structure/function analysis of ASPSCR1-TFE3; Aim 2. To understand the molecular mechanisms by which TFE3 induces tumor development; Aim 3. To evaluate the potential of immunotherapy in our TRCC GEMM.

THERE IS NO OVERLAP.

Title: Targeting the undruggable: a first-in-class inhibitor of the HIF-2 transcription factor

Time commitment: 1.2 calendar months

Supporting agency: CPRIT RP160440

NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

Contact Person: Patty Moore
Cancer Prevention and Research Institute of Texas
1701 North Congress Avenue
Suite 6-127
Austin, TX 78701

Period of Performance: 03/01/2016 – 08/28/2019

Level of funding:

Brief Description of the project's goals: This project focuses on the evaluation of HIF-1 and HIF-2 in large cohort of RCCs, the evaluation of combination therapies in preclinical models and the dissection of molecular mechanisms of acquired resistance.

List of specific aims: Aim 1. To evaluate the clinical impact of ccRCC subtypes defined by HIF-1a / HIF-2a expression and HIF2-I sensitivity; Aim 2. To evaluate the potential of combination therapy against Type 2 tumors; Aim 3. To understand the molecular mechanism and implications of acquired resistance.

THERE IS NO OVERLAP.

Title: Evaluation of the BAP1 tumor suppressor gene in renal cell carcinoma

Time commitment: 1.2 calendar months

Supporting agency: NIH/NCI

NAME AND ADDRESS OF THE FUNDING AGENCY'S PROCURING CONTACTING/GRANTS OFFICER:

Contact Person: Ronald Johnson
9609 Medical Center Dr.
Bethesda, MD 20892

Period of Performance: 12/03/2013 – 11/30/2019

Level of funding:

Brief Description of the project's goals: The goal of this project is to investigate the role of BAP1 in RCC tumorigenesis.

List of specific aims: Aim 1. Identification of BAP1 complex components in ccRCC cell lines and tumorgrafts; Aim 2. Identification of genomic sites of BAP1 action by ChIP-Seq; Aim 3. Generation of a mouse model recapitulating the molecular genetics of human ccRCC; Aim 4. Synthetic lethal screen to identify compounds selectively targeting BAP1-deficient ccRCC cells **There is no overlap.**

FOREIGN AND DOMESTIC RESOURCES (not listed above)
Other Grants, Contracts, Cooperative Agreements & Funds Not to UTSW :None
Non-UTSW Appointments, Affiliations, and Consulting Activities Providing Support for Research at UTSW: None
Materials that are Not Freely Available to Others: None
Foreign Collaborations/Foreign Components (*not already included in the previously listed Grants*): None
Visiting Faculty/Scholars/Scientists/Post-docs/Students Receiving Financial Support from Another Institution (*not UTSW*): None

Previous/Current/Pending Support - Pal, Sumanta, MD

Current

Title: City of Hope Clinical Oncology Career Research Development Program
Time Commitments: 0.60 cal. mo.
Supporting Agency: NIH/NCI
Address: 9609 Medical Center Drive, West Tower, 2nd Floor, Rockville, MD 20850
Contracting/Grants Officer: Amy Bartosch
Performance Period: 08/01/2020-07/31/2025
Level of Funding:
Project Goal: The goal of this project is to provide advanced training in oncologic clinical investigation to oncologic surgeons, medical oncologists, hematologists, radiation oncologists, or pathologists at the junior faculty level consisting of formal didactic courses in biostatistics, clinical research, and basic science.
Specific Aims: 1. To provide a multidisciplinary curriculum with didactic, laboratory, and clinical experience components in basic, translational, and clinical research in cancer-related fields 2. To foster a mentoring program through which young investigators can develop into leaders in translational research 3. To provide K12 Scholars a career development program that is well-integrated into the Comprehensive Cancer Center, providing access to cancer center resources and expertise.
Overlap: None

This Award Technical Progress Report
Title: Academy of Kidney Cancer Investigator Dean Award
Time Commitments: 0.60 cal. mo.
Supporting Agency: DOD/USAMRAA
Address: 820 Chandler St., Fort Detrick, MD 21702
Contracting/Grants Officer: Juan Rodriguez, GMS
Performance Period: 09/02/2020-09/01/2025
Level of Funding:
Project Goal: The aim of this project is to establish the Academy of Kidney Cancer Investigators (AKCI) framework to ensure continued progress towards the goal of eliminating kidney cancer.
Specific Aims: The Academy will result in a cadre of RCC early career investigators and mentors. A ruthless focus and efficiency towards pursuing only those projects that are aligned with the goal of developing an RCC career and eliminating kidney cancer will be emphasized.
Overlap: None

New since last reporting period

Title: Cancer Center Support Grant
Time Commitments: 0.60 cal. mo.
Supporting Agency: NCI/NIH
Address: 10 Center Dr, Bethesda, MD 20814
Contracting/Grants Officer: Sonya Roberson
Performance Period: 04/2023-11/2027
Level of Funding:

Project Goal: The Cancer Center Support Grant provides support for administration and infrastructure for the City of Hope Comprehensive Cancer Center.
Specific Aims: 1) Identify, develop, produce, and advance first-in-field and first-in-human new treatments; 2) Implement four strategic initiatives: advancing precision medicine, expanding cellular therapeutics, promoting health equity, and enhancing clinical research in the clinical network; 3) Assess and address the cancer burden in the COHCCC Catchment Area, promoting early detection, prevention, novel treatments, aging, and survivorship; 4) Advance training and educational initiatives to support the next generation of cancer-focused scientists and clinicians; 5) Enact concrete policies to enhance diversity, equity, and inclusion in the COHCCC Membership and Leadership. During the next cycle, the COHCCC will expand on historic strengths and advance critical initiatives that will benefit the diverse population of the Catchment Area and the larger community of individuals at risk for or affected by cancer.
Overlap: None

New since last reporting period

Title: Optimal Treatment by Invoking Biologic Clusters in Renal Cell Carcinoma (OPTIC RCC)
Time Commitments: 0.60 cal. mo.
Supporting Agency: DOD/USAMRRA
Address: 820 Chandler St., Fort Detrick, MD 21702
Contracting/Grants Officer: Darrell Beaver, GMS
Performance Period: 09/2022-09/2026
Level of Funding:
Project Goal: The goal is review of the literature and preliminary data led to our central hypothesis that RNAseq can be used to identify biologic drivers of ccRCC in individual patients and improve outcomes. This project will test this hypothesis by prospectively evaluating gene expression in
patient tumors, assigning patient tumors to biologic clusters, and using this cluster assignment to choose an FDA approved first line therapy for patients with metastatic clear cell RCC.
Specific Aims: The current proposal will test this hypothesis by prospectively evaluating gene expression in patient tumors, assigning patient tumors to biologic clusters, and using this cluster assignment to choose an FDA-approved first line therapy for patients with metastatic clear cell RCC.
Overlap: None

Title: IRB 20076 - COH RP03 – TARDIS RCC Bladder
Time Commitments: 0.66 cal. mo.
Supporting Agency: Exact Sciences Corp.
Address: 5505 Endeavor Lane, Madison, WI 53719
Contracting/Grants Officer: Jake Orville, General Manager
Performance Period: 04/2022 – 06/2025
Level of Funding:
Project Goal: Provide patient samples and data to TGen for analysis as described herein for the Parties to review TARDIS as an investigational tool for monitoring minimal residual disease (MRD) in patients with advanced bladder or renal cell cancer receiving immunotherapy for the purposes of:
Specific Aims: Primary Objective: determining if patients with advanced renal and bladder cancer who have a durable response (CR, PR, or SD in excess of 6 months) have a lower ctDNA burden than patients who have primary progressive disease and Secondary Objective: demonstrating the range of ctDNA levels in subgroups of patients characterized by the degree of response to immunotherapy. In particular, we are interested in the range of ctDNA in patients who have a durable complete response to therapy. These findings will inform the design of a planned study which randomizes patients to either continue or discontinue immunotherapy in the context of a durable response.
Overlap: None

Pending - None

Previous

Effort ended since last reporting period

Title: Phase 1 and 2 Molecular and Clinical Pharmacodynamic Trials ET-CTN
Time Commitments: 0.60 cal. mo.
Supporting Agency: NIH/NCI
Address: 10 Center Dr, Bethesda, MD 20814
Contracting/Grants Officer: Joy Kearse, Grants Management Specialist
Performance Period: 04/22/2020-02/28/2026
Level of funding:
Project Goals: The goals are to use the existing relevant capabilities and scientific leadership of the California Cancer Consortium (CCC) to enhance the ETCTN program; to leverage the combined breadth of the clinical programs at COH, USC, UCD, and SCI NCI-Designated Comprehensive Cancer Centers to support the rapid completion of ETCTN trials; to use the central Data Coordinating Center (DCC) and Biostatistics Core (BC) at COH to facilitate frequent communication within the CCC and with the NCI and ETCTN, provide rapid development and effective oversight of trials, and ensure adherence to policies and procedures; and to optimize information gained from ETCTN clinical trials by including molecular characterization of patients' malignancies and incorporating molecular pharmacodynamic endpoints and investigational imaging.
Specific Aims: Specific Aims: (Aim 1) to use the existing relevant capabilities and scientific leadership of the CCC to enhance the ETCTN program; (Aim 2) to leverage the combined breadth of the clinical programs at COH, USC, UCD, and SCI NCI-Designated Comprehensive Cancer Centers to support the rapid completion of ETCTN trials; (Aim 3) to use the central Data Coordinating Center (DCC) and Biostatistics Core (BC) at COH to facilitate frequent communication within the CCC and with the NCI and ETCTN, provide rapid development and effective oversight of trials, and ensure adherence to policies and procedures; and (Aim 4) to optimize information gained from ETCTN clinical trials by including molecular characterization of patients' malignancies and incorporating molecular pharmacodynamic endpoints and investigational imaging.
Overlap: None

Award ended since last reporting period

Title: Pilot study to evaluate the biologic effect of CBM588 in combination with nivolumab/ipilimumab for patients with metastatic renal cell carcinoma
Time commitments: 0.60 cal. mo.
Supporting agency: Gateway for Cancer Research (Pal)
Address: 500 E. Remington Road, Schaumburg, IL 60173
Contracting/ Grants Officer: Delora Senft
Performance period: 06/01/2020-05/31/2023
Level of funding:
Project's goals: This is a phase 1 study to assess CBM588, a probiotic that has been shown to have immunomodulatory and anti-inflammatory effects on the lining of the intestines and can restore certain bacterial species such as Bifidobacterium spp and Lactobacillus spp to the gut.
Specific Aims: The primary objective of this study is to determine the effect of CBM588 in combination with nivolumab/ipilimumab in modulation of the gut microbiome in patients with mRCC. Secondary objective include evaluating the effect of CBM588 on the clinical efficacy of the nivolumab/ ipilimumab combination and determining the effect of CBM588 on systemic immodulation of the nivolumab/ ipilumab combination in patients with mRCC.
Overlap: None

Award ended since last reporting period

Title: Dual-Function CpG-STAT3Antisense Oligonucleotides for Immunotherapy of Metastatic Prostate Cancer
Time commitments: 0.36 cal. mo.
Supporting agency: Department of Defense W81XWH1910852 (Kortylewski)
Address: 9609 Medical Center Drive, Bethesda, MD 20892-9760
Contracting/Grants Officer: Nicholas E. Simon, PhD
Performance period:09/29/2019 – 09/28/2022
Level of funding:
Project's goals: We have optimized and validated the new CpG-STAT3ASO as an effective immunotherapy against bone-localized prostate tumors in mice, regardless of cancer cell genetics and sensitivity to STAT3 inhibition. Thus, we propose IND-enabling studies to characterize immunostimulatory effects, biomarkers of

response to CpG-STAT3ASO in human immune cells and to assess safety and toxicokinetic properties in mice and non-human primates. Our goal is to submit IND application to FDA and to initiate the first-in-human, phase I CpG-STAT3ASO trial in patients with metastatic prostate cancers within a year from the end of this award. We anticipate that, within 5 years after completion, clinical results from phase I/II studies will have a transformative effect on the treatment strategies for prostate tumors and potentially other immunologically "cold" human cancers.
Specific Aims: Aim 1: Characterize pharmacokinetic (PK) and pharmacodynamic (PD) properties of the selected lead CpG-STAT3 antisense oligonucleotide.
Aim 2: Evaluate efficacy and safety of intravenous administration of CpG-STAT3ASO in humanized mice and in standard animal models
Overlap: None

Title: Immunotherapy for Metastatic Castrate-Resistant Prostate Cancer Using CAR-Engineered T Cells Targeting Prostate Stem Cell Antigen
Time commitments: 0.60 cal. mo.
Supporting agency: Prostate Cancer Foundation (Priceman)
Address: 1250 Fourth Street, Santa Monica, CA 90401
Contracting/Grants Officer: Jonathan W. Simons
Performance period: 03/31/2016-03/31/2021
Level of funding:
Project's goals: The goal of this proposal is to initiate a phase I trial using PSCA-specific CAR T cells for the treatment of castration-resistant metastatic prostate cancer.
Specific Aims: Aim 1: Perform IND-enabling studies with cGMP-grade PSCA-CAR T cells
Aim 2: A Phase I clinical trial to evaluate PSCA-targeted T-cells for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC).
Overlap: None

Title*:* Predevelopment of VV2003, a Novel CRAC Channel Inhibitor, to Improve Outcomes Associated with Checkpoint Inhibitor Immunotherapy
Time commitments: 0.24 cal. mo.
Supporting agency: National Cancer Institute, NIH 2R44CA224454 (Greenberg)
Address: 9609 Medical Center Drive, West Tower, 2W464, Rockville MD, 20850-9710
Contracting/Grants Officer: Dawn M. Mitchum
Performance period: 09/01/2019-05/30/2020
Level of funding:
Project's goals: This is a pilot study to assess the effect of VV2003, an Orai1 blocker, on fresh biopsy specimens of patients with immune checkpoint inhibitor induced colitis.
Specific Aims: Aim 1. To determine inflammatory cytokine production with and without the Orai1 blocker VV2003 in fresh biopsy specimens of patients with immune checkpoint inhibitor induced colitis. Aim 2: To gather evidence about presence of Orai1 antibody in fresh biopsy specimens of patients with immune checkpoint inhibitor induced colitis. Aim 3: To determine clinical correlates of immune cytokine production in fresh biopsy specimens of patients with immune checkpoint inhibitor induced colitis with and without the Orai1 blocker VV2003.
Overlap: None

Curent/Pending/Previous Other support – Celeste Simon, PhD

ACTIVE
This Award Technical Progress Report
Title: Academy of Kidney Cancer Investigators Dean Award (Rini)
Time Commitment: 0.48 Calendar Months
Supporting Agency: DOD (W81XWH2020046)
Contracting Grant Officer:
Brad Jones, MA PHR
General Contracts Analyst
VUMC Office of Contracts Management Email: bradford.jones@vumc.org
Performance Period: 09/2020 – 09/2025

Level of Funding:
Project Goals: The objective for the CDMRP/KCRP Academy of Kidney Cancer Investigators (AKCI) is to foster the development and commitment of early career kidney cancer investigators through provision of the raw materials and structured mentorship for focused, sustainable, and ultimately independent success.
Role: Collaborator
Aims:
Task1: Establish SMART goals for Advisory Board members.
Task2: Attend meetings to assess ongoing education, goals and progress.
Task3: Collaboration – secondary mentor assignments, integration with CDMRP consortium award institutions, active participation in national or international societies
Overlap: None

Title: Abramson Cancer Center Support Grant (Vonderheide)
Time Commitment: 1.92 Calendar Months
Supporting Agency: NIH/NCI (P30 CA016520)
Contracting Grant Officer:
Henry Ciolino
Email: ciolinoh@mail.nih.gov
Performance Period: 01/01/21–11/30/25
Level of Funding:
Project Goals: This grant supports the cancer research infrastructure and mission of the Abramson Cancer Center at the University of Pennsylvania.
Role: Associate Director, Shared Resources
Aims: This funding mechanism does not have specific aims.
Overlap: None

Title: Exploiting Limited Arginine Availability in Liver Cancer Tumor Microenvironments
Time Commitment: .24 Calendar Months
Supporting Agency: Ludwig Institute for Cancer Research (Simon) Princeton University
Contracting Grant Officer:
Panina Zaurov
Ludwig Princeton Branch
127 Frick Chemistry Laboratory Washington Road
Princeton, New Jersey 08544
Email: pzaurov@princeton.edu
Performance Period: 07/2022 – 12/2024
Level of Funding:
Project Goals: The goal of this grant is to investigate the effects of urea cycle suppression on tumor progression and functionality of infiltrating immune cells in spontaneous mouse HCC models, based on hepatocyte specific Ass1 deletion. This funding is for multiple investigators and the Simon component is

Role: PI
Aims:
1. Characterize Arg competition between UC deficient murine and human HCC cells and immune cells, (T cells, monocytes, and macrophages) based on in vitro coculture experiments with 13C- and 15N- labeled Arg and define underlying mechanisms for unequal Arg uptake by HCC cells versus immune cells.
2. Investigate the effects of UC suppression on tumor progression and functionality of infiltrating immune cells in spontaneous mouse HCC models, based on hepatocyte specific Ass1 deletion, tumor burden assays, flow cytometry, single cell RNAseq, etc.
3. Perform in vivo 13C-Arg and 15N-Arg labeling to define Arg partitioning in HCC tumor microenvironments by cell type fractionation7 and also perform spatial metabolomics.
4. Determine which downstream pathways incorporate labeled Arg in HCC cells in vitro and in vivo.
5. Assess the impact of GCN2 inhibition on HCC tumor progression and immune cell functionality in spontaneous HCC models.
Overlap: None

New
Title: Stromal and vascular inputs into pancreatic cancer tumor neighborhoods (Stanger, Simon)

Time Commitment: 1.2 Calendar Months
Supporting Agency: NIH/NCI (R01 CA276512)
Contracting Grant Officer:
Program Official: Mercer, Natalie
Email: natalia.mercer@nih.gov
Performance Period: 7/1/23 – 6/30/28
Level of Funding:
Project Goals: The overall goal of this project is to gain a better understanding of the stromal components – vasculature and cancer associated fibroblasts – by which pancreatic cancer cells acquire essential nutrients, or through which they metastasize.
Role: PI
Aims:
Aim 1: Determine the causes and consequences of vascular heterogeneity in PDAC
Aim 2: Delineate molecular mechanisms and therapeutic opportunities underlying stromal support of lipid metabolism in PDAC
Aim 3: Evaluate routes of PDAC cell egress during tumor cell intravasation
Overlap: None

New
Title: Targeting Branched Chain Amino Acids in Kidney Cancer (Simon)
Time Commitment: 1.2 Calendar Months
Supporting Agency: US Department of Defense (HT94252310859)
Contracting Grant Officer:
Grants Management Specialist (GMS): Tiffany Lantz
Email: tiffany.r.lantz5.civ@health.mil
Performance Period: 08/15/23 – 08/14/26
Level of Funding:
Project Goals: A major risk factor of clear cell renal cell carcinoma (ccRCC) is obesity; obese individuals have elevated branched chain amino acids in their circulation. In this grant we propose to interrogate the BCAA pathway in ccRCC which we believe is downregulated to support ccRCC cell growth.
Role: PI
Aims:
Aim 1: Determine the role of reduced BCAA catabolism in contributing to ccRCC cell growth in vitro.
Aim 2: Determine the role of reduced BCAA catabolism in promoting ccRCC tumorigenesis in vivo.
Overlap: None

New
Title: Role of glutamine metabolism in Dendritic Cell Development (Haldar)
Time Commitment: 0.6 Calendar Months
Supporting Agency: NIH (1-R01- DK-138827-01A1)
Contracting Grant Officer:
Kenley, Charlette
Email: kenleyc@extra.niddk.nih.gov
Performance Period: 07/1/23 – 06/30/*26*
Level of Funding:
Project Goals: The major goal of the proposal is to understand which steps of cDC1 (conventional dendritic cells) differentiation are regulated by glutamate and its underlying molecular mechanisms. We will focus on epigenetic regulation of gene expression and oxidative stress as potential pathways by which glutamate mediates this effect.
Role: Co-Investigator
Aims:
Aim 1: Understanding how glutamate affects CDC1 lineage.
N.B.: There is a single Aim in this NIDDK funding mechanism.
Overlap: None

New
Title: Metabolic Influences on Complex Tumor Neighborhoods (Simon)
Time Commitment: 6 Calendar Months

Supporting Agency: NIH/DHHS (2-R35-CA-220483-08)
Contracting Grant Officer:
Ruffin, Daijsha Chevon
Email: daijsha.ruffin@nih.gov
Performance Period: 08/1/23 – 07/31/30
Level of Funding:
Project Goals: The objective of the proposed studies is to define how gluconeogenic, urea cycle, and lipogenic metabolic enzymes impart common metabolic adaptations to genetically diverse carcinomas of the GI system.
Role: PI
Aims:
There are no Specific Aims in this NCI R35 granting mechanism.
Overlap: Concerning the R35 CA220483, project dates will be amended to accommodate the pending renewal.

IN-KIND

Summary of In-Kind contribution: Visiting Student, Yizheng Xue, who conducts research activities in the Simon lab. Salary supported by Shanghai Jiao Tong University
Time Commitment: N/A
Supporting Agency: Shanghai Jiao Tong University
Performance Period: 07/5/23 – 07/4/24
Level of Funding:

PENDING: None.

PREVIOUS

Completed since last reporting period
Title: HIF-1alpha and FBP2 in sarcoma metabolism, progression, and metastasis (Simon and Yoon)
Time Commitment: 0.12 calendar months
Supporting Agency: NIH/NCI (R01CA158301)
Contracting Grant Officer:
Watson, Joanna M.
Email: watsonjo@mail.nih.gov
Performance Period: 2/1/17 – 1/31/23 (NCE)
Level of Funding:
Project Goals: The objective of the proposed studies is to explore the inter-related effects of these two factors in tumor cell heterogeneity, metastasis, and therapy resistance in the setting of soft tissue sarcomas.
Role: PI
Aims:
Aim 1. Define the role of FBP2 in sarcoma metabolism, progression, and metastasis.
Aim 2. Determine the role of HIF-1a in sarcoma stem-like metastasis and chemotherapy.
Overlap: None

Completed since last reporting period
Title: Exploiting Cholesterol Metabolism to Treat Primary and Metastatic Renal Carcinoma
Time Commitment: 1.2 Calendar Months
Supporting Agency: DOD KCRP IDA (W81XWH2010856)
Contracting Grant Officer:
Thomas Winter
Email: sidney.t.winter.civ@mail.mil
Performance Period: 09/01/20 – 09/29/22
Level of Funding:
Project Goals: The goal of this grant is to target cholesterol import and metabolism in clear cell renal cell carcinoma as a new means of treating primary and metastatic kidney cancer.

Role: PI
Aims:
Aim 1A: Evaluation of SCARB1 effects on orthotopic and metastatic ccRCC
Aim 1B: Translating SCARB1 inhibition into future ccRCC treatments
Aim 1C: Defining the mechanistic basis of SCARB1 effects on ccRCC cell growth
Aim 2A: Evaluation of HSD3B7 effects on orthotopic and metastatic ccRCC
Aim 2B: Defining the mechanistic basis of HSD3B7 inhibition-mediated ccRCC cell death
Overlap: None

Title: Combined HIF deficiency in Inflammation – Associated Colorectal Tumorigenesis
Supporting Agency: NIH 4R01 HL066310
Contracting Grant Officer:
Yu-Chung Yang yu-chung.yang@nih.gov
Performance Period: 5/1/16-4/30/18
Level of Funding:
Project Goals: Test the impact of inhibiting multiple HIFs simultaneously use a mouse model of cancer.
Role: PI
Overlap: None

Title: Cancer Cell Adaptation to Metabolic Stress
Supporting Agency: NIH P01CA104838
Contracting Grant Officer:
Willis Kristine kristine.willis@nih.gov
Performance Period: 9/1/14 – 8/31/21
Level of Funding:
Project Goals: Investigates the role of unsaturated lipids in cancer cell metabolism and survival, and how this influences stress responses with the endoplasmic reticulum
Role: PI
Aims:
Aim 1 Determine the molecular mechanisms whereby TXNIP promotes IRE1-mediated cell death under tumor-like stress.
Aim 2 Determine the functional role of HIF-2□ and ADRP in regulating lipid storage, ER stress responses, and fatty acid synthesis in ccRCC.
Overlap: None

Title: The effect of Oxygen Gradients on Sarcoma Invasiveness through Dynamic Collagen Modification
Supporting Agency: NIH U01CA210185
(Gerecht) **Performance Period:** 8/29/16 – 7/31/22
Contracting Grant Officer:
Zahir Nastaran nas.zahir@nih.gov
Level of Funding:
Project Goals: Identify the molecular and physical mechanisms underlying the initial steps of metastasis, invasion and migration, and develop predictive models for these mechanisms**.**
Role: PI
Aims:
Aim 1: To determine sarcoma cell and tumor graft responses to spatial oxygen gradients;
Aim 2: To characterize collagen remodeling during sarcoma invasion under hypoxic gradients; Aim 3: To determine how collagen fiber organization regulates hypoxic invasion and migration. **Overlap:** None

Title: Regulatory Role and Targetability of UFDI in MYC-driven Leukemia (Feng)
Supporting Agency: American Cancer Society
Performance Period: 7/1/2019 – 6/30/2020
Level of Funding:
Role: Collaborator
Overlap: None

Current/Previous/Pending – Samra Turajlic, MD

No any changes compare to previous reporting period and for this reason Other support document for Dr. Turajlic is not inclueded.

8. **Special Reporting Requirements** *None.*

9. **Appendices** *None.*