AWARD NUMBER: W81XWH-21-2-0025

TITLE: Kidney Cancer Clinical Trials Consortium

PRINCIPAL INVESTIGATOR: Brian Rini, MD

CONTRACTING ORGANIZATION: Vanderbilt University Medical Center

REPORT DATE: OCTOBER 2023

TYPE OF REPORT: ANNUAL

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

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4. TITLE AND SUBTITLE Kidney Cancer Clinical Trials Consortium		**5a. CONTRACT NUMBER** W81XWH-21-2-0025 **5b. GRANT NUMBER** **5c. PROGRAM ELEMENT NUMBER**
6. AUTHOR(S): **Brian I. Rini, MD** E-Mail: brian.rini@vumc.org		**5d. PROJECT NUMBER** **5e. TASK NUMBER** **5f. WORK UNIT NUMBER**
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Vanderbilt University Medical Center 1161 21st Ave S STE D3300 MCN Nashville, TN 37232-0011		**8. PERFORMING ORGANIZATION REPORT**
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development Command Fort Detrick, Maryland 21702-5012		**10. SPONSOR/MONITOR'S ACRONYM(S)** **11. SPONSOR/MONITOR'S NUMBER(S)**
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13. SUPPLEMENTARY NOTES		

14. ABSTRACT: Vanderbilt University Medical Center (VUMC) has been an active and engaged participant in the Kidney Cancer Clinical Trials Consortium over the course of the reporting period. VUMC has led the first protocol conducted through the Consortium (Haake, PI) looking at circulating tumor DNA (ctDNA) in advanced renal cell carcinoma (RCC) patients receiving immune-based systemic therapy. This trial has accrued 153 patients out of 160 planned and will generate preliminary data for future studies and extramural finding. Further, the first therapeutic study from the Consortium was proposed and is led by an VUMC investigator (Beckermann, PI) investigating the combination of ipilimumab/nivolumab plus a small molecule inhibitor of the adenosine signaling pathway. This trial is accruing patients at MD Anderson and other sites including VUMC are opening imminently. Drs. Beckermann and Rini are active participants at the monthly Consortium meetings providing critical feedback regarding new proposals and the general direction and governance of the Consortium.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION**	**18. NUMBER**	**19a. NAME OF RESPONSIBLE PERSON** USAMRDC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**	UU	19	**19b. TELEPHONE NUMBER** *(include area code)*
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1. **INTRODUCTION:** VUMC has long been home to a critical mass of RCC basic, translational, and clinical researchers. To amplify the impact of VUMC's efforts, RCC Consortium membership was sought and accomplished in the last funding cycle. Harnessing the expertise of VUMC members, two protocols have been accepted by the Consortium for execution as described below and two more RCC clinical trials have been accepted and are in development.

2. **KEYWORDS:** RENAL CELL CARCINOMA, CTDNA, CIFORADENANT

3. **ACCOMPLISHMENTS:** VUMC with Dr. Scott Haake has created the first translational study understanding novel techniques to measure ctDNA in patients with kidney cancer at time of diagnosis and while on therapy. This protocol accrued patients across most of the Consortium sites. Data is currently being analyzed and will lead to additional grant applications and efforts in the ctDNA arena in RCC.

   Dr. Beckermann and Rini created the first therapeutic clinical trial conducted under Consortium auspices. Ciforadenant is an investigational immunotherapeutic small molecule that selectively and reversibly binds adenosine-2A receptors (A_{2A}Rs) on T lymphocytes and other cells of the immune system. Preclinical studies show that the addition of ciforadenant to CTLA4 and PD1 blockade shows enhanced efficacy and in some cases elimination of the established tumors (Willingham et al., 2018). Recently, in a first in human study, the A2AR antagonist ciforadenant was found to be safe and showed activity as monotherapy in RCC patients with refractory disease following multiple lines of therapy showing a median progression free survival (mPFS) of 4.1 months (Fong et al., 2019). INC is a Phase 1b/2 single-arm, multicenter study to assess safety and efficacy of the combination of ipilimumab, nivolumab, and ciforadenant in the frontline treatment of patients with advance clear cell renal cell carcinoma. The primary objective is to determine the safety and tolerability and to assess the depth of response (>50% by RECIST 1.1 Eisenhaur, 2009) based on a Bayesian design in patients with advanced RCC treated with ipilimumab, nivolumab, and ciforadenant. Secondary objectives will estimate the objective response rate (ORR), duration of response (DOR) progression free survival (PFS), progressive disease (PD) rate, and irAE rate of ipilimumab, nivolumab, and ciforadenant combination in untreated advanced RCC. Exploratory objectives include assessing gene expression signatures and pharmacodynamic parameters with outcome. This trial is actively accruing patients across multiple sites.

   In addition, two new clinical trials have been proposed by VUMC and are in active development in the Consortium. The first involves an ITK inhibitor which is an immunomodulatory compound that will be tested in the refractory RCC setting supported by Corvus. Also, the LAG-3 inhibitor, relatlimab, will be tested in a small phase 2 randomized trial in front-line RCC with ipilimumab/nivolumab. Both proposals build upon the strengths of the Consortium in translational immunotherapy trials in RCC and have potential to lead to larger, registration-intent studies.

4. **IMPACT:** The projects noted above have the potential to impact RCC therapeutics. ctDNA is emerging across cancers as a potentially effective way to monitor for disease recurrence and the effectiveness of systemic therapy. RCC has been considered a 'low shedding' tumor, and techniques developed through the Consortium ctDNA project will enable better ctDNA detection. This is a critical first step in applying the technology to the therapeutic setting.

Further, the clinical trial of Ipi/Nivo + ciforadent will represent one of the first all-immune triplets to be tested in advanced RCC. Adenosine signaling contributes to immune suppression by downregulating T cell activity and increasing myeloid suppressive activity with preclinical and early phase clinical data to support the use of ciforadenant an adenosine 2A receptor antagonist to block the pathway. The proposed phase 1/2 trial will have a lead in of 8 patients assessing safety in the novel combination with ipilimumab and nivolumab and then an expansion for a total of 51 patients to enroll will assess efficacy by asking if this combination increases the percentage of patients achieving a >50% shrinkage in tumor volume. The establishment of safety and a signal of clinical activity will lead to large-scale clinical trials that could impact the initial standard of care in advanced RCC.

5. CHANGES/PROBLEMS: NONE

6. PRODUCTS: NONE

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Name:	**Brian Rini, MD, FASCO**
Project Role:	Principal investigator
Researcher Identifier (e.g. ORCID ID):	0000-0002-2212-080X
Nearest person month worked:	2.4
Contribution to Project:	Dr. Rini is the PI of the VUMC Consortium grant. He oversees all aspects of VUMC's participation including coordination of proposal submission, concept review and execution of Consortium projects and clinical trials.
Funding Support:	CDMRP, NCI
Name:	**Kathryn E Beckermann, MD, PhD**
Project Role:	Sub PI
Researcher Identifier:	0000-0002-4616-6140
Nearest person month worked:	1.8
Contribution to Project:	Dr. Beckermann worked alongside Dr. Rini to present clinical trial concepts, attend meetings, and discuss scientific work related to the KCRC.
Funding support:	CDMRP/NCI
Name:	**Rebekah J. Caza**
Project Role:	Clinical Trials Manager
Researcher Identifier:	N/A

Nearest person month worked:	10.2
Contribution to Project:	Ms. Caza manages the portfolio of RCC clinical trials at VUMC including the Consortium projects noted here. She oversees all aspects of clinical protocol execution including scientific/IRB submissions, budget and contract negotiations, protocol-specific requirements, and protocol execution. She is responsible for managing clinical trials from pre-selection through study closure including acting as the primary liaison between trial sponsor and the site; working with team leadership and staff to address the dynamic needs of a trial throughout its life cycle; and facilitating regular team business meetings to maintain oversight of the trial portfolio in its entirety.
Funding support:	NIH/CDMRP
Name:	**Brittany Morelli**
Project Role:	Data management Specialist
Researcher Identifier:	N/A
Nearest person month worked:	4.5
Contribution to Project:	Ms. Morelli oversees all aspects of data management as it relates to VUMC's participation in Consortium-related projects. responsible for the data on all trials in the KCRC and VICC. This includes timely and accurate submission of treatment data entered into the agreed upon KCRC database, follow up reports, and query responses.
Funding support:	N/A

Name:	**Amanda Nolen**
Project Role:	Research Nurse Specialist
Researcher Identifier:	N/A
Nearest person month worked:	5.75
Contribution to Project:	Ms. Nolen is GU research nurse has extensive oncology research nursing experience. She provides nursing supervision, review trials to assure they have appropriate patient care support and are practical from a research nursing standpoint. Ms. Nolan is also involved in the screening, consenting, clinical care, follow-up, and data entry for patients on clinical trials in the KCRC.
Funding support:	N/A

- *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:
Dr. Brian Rini, MD, (PI),
Dr. Kathryn E. Beckermann, MD, PhD (Co-I),
with annotated changes since the last time this information has been submitted.

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
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

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 **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

This Award Technical Progress report
W81XWH2120025 (Rini)
Title: Kidney Cancer Clinical Trials Consortium
Effort: 2.40 CM
Agency: Congressionally Directed Medical Research Programs
Grants Officer: Jennifer Shankle
Address of Funding Agency: 820 Chandler St, Fort Detrick, MD 21702-5014
Performance Period: 09/15/2021 – 09/14/2024 (NCE)
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
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

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
KC220067/W81XWH-22-KCRP-IDA (Beckermann, K.)
Title: Peripheral Systemic Response Assessment in RCC
Principal Investigator: Kathryn E. Beckermann
Support Agency: CDMRP
Grant Officer: Medha Darshan **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:

KC230168 (Haake, S.)
Title: Gene Expression Analysis of Circulating Tumor Cells: A Next Generation Biomarker to Predict Immunotherapy Response in Metastatic Clear Cell Renal Cell Carcinoma
Principal Investigator: Scott Haake
Support Agency: CDMRP
Grant Officer: N/A
Performance Period: 09/30/2024 – 09/29/2028
Level of Funding:
Project Goal: Identify and develop new strategies for screening, early-stage detection, and accurate diagnosis and prognosis prediction of kidney cancers, with examples including biomarkers and imaging.
Specific Aims:
Aim 1: Quantify transcriptional alterations that drive tumor dissemination.
A*im 2:* Interrogate CTC gene expression signatures as biomarkers of response to immunotherapy.
Role: Co-Investigator
Person Months: 0.12CM
Overlap: None

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

Grant	10/01/2023	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
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
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
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
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

PREVIOUS/CURRENT/PENDING SUPPORT - Kathryn Eby Beckermann, MD, PhD

PREVIOUS

Grant ID: N/A
Title: *Metabolic Barriers to T cell Function and Immunotherapy in Renal Cell Carcinoma*
Time Commitments: 9.6 calendar months
Role: Principal Investigator
Supporting Agency: Merck-Cancer Research Institute
Grant Officer: Ryan Godfrey, Cancer Research Institute, 29 Broadway, 4th Floor
New York, NY 10006-3111
Performance Period: 03/01/2016-07/01/2018
Level of Funding:
Project Goals: To evaluate how the metabolic driven nature of renal cell carcinoma may alter tumor infiltrating CD8 T cell function.
Specific aims:
Aim 1: Test if RCC TIL have impaired mitophagy which alter metabolic pathways including fatty acid oxidation and reactive oxygen species.
Aim 2: Determine if RCC IDO1 expression and activity impairs TIL metabolism and effector function.

Grant ID: K12CA090625-21
Title: *Vanderbilt Clinical Oncology Research Career Development Award Supplement Directed towards immuno-oncology research*
Time Commitments: 9.0 calendar months/effort ended June 2021
Role: Scholar
Principal Investigator: W. Kimryn Rathmell
Supporting Agency: National Cancer Institute
Grant Officer: Romy Reis, National Cancer Institute, 9609 Medical Center Drive
Bethesda, MD 20892-9760
Performance Period: 07/01/2016-06/30/2022 (NCE)
Level of Funding:

Project Goals: To target T cell metabolic dysfunction found in tumor infiltrating lymphocytes of renal cell carcinoma.
Specific aims:
Aim 1: Test if rescuing lack of TIL glycolytic capacity improves effector function through enhanced mitochondrial structure and function.
Aim 2: Determine if targeting co-stimulatory and inhibitory cell surface receptors of RCC TIL can rescue effector function because of alterations in fatty acid oxidation and glycolysis.
Aim 3: Test metabolic effects of treatment with checkpoint inhibitor therapy from patient peripheral blood using single cell analysis.
Overlap: None

Grant ID: VUMC87276 (W81XWH191082) Subaward Rutgers Cancer Institute
Title: *Endogenous retrovirus expression, chromatin abnormalities and response to immune checkpoint blockade in clear cell renal cell cancer*
Role: Co-Investigator
Principal Investigator: Shridar Ganesan
Time Commitments: .6 calendar months
Support Agency: CDMRP/ Rutgers Cancer Institute
Grant Officer: Richelle Dalere, Rutgers Cancer Institute of New Jersey
Division of Pre-Award Grant Support Services (DGSS)
120 Albany Street, Tower 1, 3rd Floor
New Brunswick, NJ 08901

Performance Period: 09/30/2019- 09/29/2022 (NCE)
Level of Funding:
Project Goal: This project seeks to investigate the role of endogenous retroviral virus mediated response to immunotherapy in patients with renal cell carcinoma. We will plan to collect patient samples, process, and perform biologic assays including RNA sequencing and DNA sequencing to further elucidate the mechanism behind this biology.
Specific aims:
Aim 1. Determine the relationship between ERV expression and perturbations in DNA methylation, histone modification and mutations in chromatin remodeling genes in ccRCC.
Aim 2. Determine relationships between ERV expression and the immune microenvironment in ccRCC.
Aim 3. Examine the relationship between expression of ERV3.2 and response to oimmune checkpoint blockade in ccRCC.

CURRENT/ACTIVE

Grant ID: LCFA-IASLC-BMS
Title: *Single cell analysis to understand the biology of response to immunotherapy in Lung Cancer*
Time Commitments: 0.48 calendar months
Role: Principal Investigator
Support Agency: Bristol-Myers Squibb, Lung Cancer Foundation of America, and International Association for the Study of Lung Cancer Young Investigator Immuno-Oncology Scholarship Fund
Grant Officer: Emily Petoskey
13100 E. Cotton Ave, Suite 10
Aurora, Colorado 80011
Performance Period: 04/01/2018-09/01/2023 (2nd NCE in progress)
Level of Funding:
Project Goals: To test if novel immunotherapy combination using PD-1 blockade and VEGF inhibition correlates with clinical response due to changes in the tumor microenvironment and immune milieu.

Specific aims:
Aim 1. To identify if changes in Ki67+ Tcells and MDSC measured by mass cytometry in the peripheral blood, correlates with response to combination therapy with vorolanib and nivolumab.
Aim 2. Using untargeted single cell genomic analysis, we will assess if systemic changes in immune cell populations corresponds with patient response to therapy.
Overlap: None

This Award Technical Progress Report
Grant ID: KC200245
Title: *Kidney Cancer Clinical Trials Consortium*
Role: Co-PI
Principal Investigator: Brian Rini
Time Commitments: 1.80 calendar months
Support Agency: Congressionally Directed Medical Research Programs
Grant Officer: Jennifer Shankle
820 CHANDLER STREET
FORT DETRICK, MD 21702-5014
Performance Period: 09/15/2021 - 09/14/2024 (NCE)
Level of Funding:
Project Goal: 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.

Grant ID: N/A
Title: Vanderbilt-Arsenal Bio Collaboration
Role: Principal Investigator
Principal Investigator: Kathryn Beckermann
Time Commitments: 0.24 calendar months
Support Agency: Arsenal Biosciences, Inc.
Two Tower Place, Suite 700,
South San Francisco, CA 94080
Grant Officer: Randy Reyes
Performance Period: 06/01/2022 - 05/30/2024
Level of Funding:
Project Goal: Understand the antigencitiy of primary kidney cancer cells.
Specific Aims:
Aim 1. Leverage complementary expertise at Vanderbilt U and ArsenalBio to assess functionality of engineered T cells in patient-derived tumor models of clear cell renal cell carcinoma (ccRCC).
Aim 2. Identify novel mechanisms of tumor-mediated T cell suppression in ccRCC and engineer resistant T cells for future therapeutic applications.
Overlap: None

Grant ID: N/A
Title: Vanderbilt-Aravive Research Collaboration
Role: Principal Investigator

Principal Investigator: Kathryn Beckermann
Time Commitments: 0.24 calendar months
Support Agency: Aravive Inc.
3730 Kirby Drive, Suite 1200
Houston, Texas 77098
Grant Officer: Amy Franke
Performance Period: 08/01/2022 - 07/31/2023 (Pending extension)
Level of Funding:
Project Goal: Understand if a soluble GAS6/AXL peripheral blood liquid biopsy correlates with response on cabozantinib.
Specific Aims:
Aim 1. Collect peripheral blood prior to treatment with cabozantinib in patients with metastatic RCC and measure soluble Gas6 and AXL.
Aim 2. Correlate levels of gas6 and axl with response to cabozantinib.
Overlap: None

Grant ID: W81XWH-21-KCRP-CA
Title: ***Artificial intelligence analysis of histopathology slides to develop biomarkers of response to immunotherapy in kidney cancer***
Role: Co-I
Principal Investigator: Anupama Reddy
Time Commitments: 0.12 calendar months
Support Agency: Congressionally Directed Medical Research Programs
Grant Officer: Jennifer Shankle
820 CHANDLER STREET
FORT DETRICK, MD 21702-5014
Performance Period: 09/30/2022 - 12/29/2023 (NCE)
Level of Funding:
Project Goal: The goal of this project is to develop biomarkers of immunotherapy response using AI models from H&E-stained histology images
Specific Aims:
Aim 1. AI-based modeling of immune cell types on histological images using mIF data as training labels.
Aim 2. Interpretation of latent features in the AI model.
Overlap: None

Grant ID: W81XWH-21-KCRP-CTA
Title: ***OPtimal Treatment by Invoking biologic Clusters in Renal Cell Carcinoma (OPTIC RCC)***
Role: Co-I
Principal Investigator: Brian Rini
Time Commitments: 1.20 calendar months
Support Agency: Congressionally Directed Medical Research Programs
Grant Officer: Medha Darshan
Performance Period: 09/01/2022 - 08/31/2026
Level of Funding:
Project Goal: 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.
Overlap: None

Grant ID: W81XWH-21-KCRP-IDA/KC210158
Title: ***RNAseq-Based Biomarkers Identify Targetable Biologic Drivers of Kidney Cancer***
Role: Co-I
Principal Investigator: Brian Rini
Time Commitments: 0.96 calendar months
Support Agency: Congressionally Directed Medical Research Programs
Grant Officer: Medha Darshan
Address of Funding Agency: 820 Chandler St, Fort Detrick, MD 21702-5014
Performance Period: 09/30/2022 - 09/29/2025
Level of Funding:
Project Goal: 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 in real 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.
Overlap: None

New
Grant ID: 2R01CA217987-06
Title: Metabolic barriers to T cell activation in clear cell renal cell carcinoma
Role: Co-I
Principal Investigator: Jeffrey Rathmell (Contact), W. Kimryn Rathmell
Time Commitments: 1.2 calendar months
Support Agency: NCI
Grant Officer: Ashley Utter
Performance Period: 04/01/2023 - 03/31/2028
Level of Funding:
Project Goal: These studies will establish mechanisms by which glutamine impairs T cell differentiation and test new potential targets to overcome metabolic immune suppression in the TME to improve anti-tumor immunity.
Specific Aims:
Aim 1: Test how nutrients in the ccRCC TME and tumor genetics influence TIL function and metabolism.
Aim 2: Determine how glucose and glutamine metabolism in the TME promote or suppress anti-tumor immunity.
Overlap: None

New
Grant ID: KC220067/W81XWH-22-KCRP-IDA
Title: Peripheral Systemic Response Assessment in RCC
Role: PI
Principal Investigator: Kathryn E. Beckermann
Time Commitments: 3.0 calendar months
Support Agency: CDMRP
Grant Officer: Medha Darshan
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.
Overlap: None

New
Grant ID: N/A
Title: Inflammatory Drivers of The Obesity-Cancer Connection
Role: Co-I
Principal Investigator: Jeffrey Rathmell
Time Commitments: 0.6 calendar months
Support Agency: The Mark Foundation for Cancer Research
1350 6th Ave, New York, NY 10019
Grant Officer: Ian Lesser

Performance Period: 10/01/2023 – 9/30/2026
Level of Funding:
Project Goal: We propose a collaborative program of cancer, metabolism, and immunology researchers to test the hypothesis that obesity increases risk for multiple cancer types while potentially augmenting responses to checkpoint blockade therapies through indirect effects on inflammation and active immune communication between adipose and tumor tissues.
Specific Aims:
Aim 1: Develop TABS and IMA cores and the team-led CAIR initiative.
Aim 2: Define fundamental mechanisms that drive the obesity-cancer connection and immunemediated links between adipose and tumor tissues.
Overlap: None

PENDING

KC230168 (Haake, S.)
Title: Gene Expression Analysis of Circulating Tumor Cells: A Next Generation Biomarker to Predict Immunotherapy Response in Metastatic Clear Cell Renal Cell Carcinoma
Principal Investigator: Scott Haake
Support Agency: CDMRP
Grant Officer: N/A
Performance Period: 09/30/2024 – 09/29/2028
Level of Funding:
Project Goal: Identify and develop new strategies for screening, early-stage detection, and accurate diagnosis and prognosis prediction of kidney cancers, with examples including biomarkers and imaging.
Specific Aims:
Aim 1: Quantify transcriptional alterations that drive tumor dissemination.
Aim 2: Interrogate CTC gene expression signatures as biomarkers of response to immunotherapy.
Role: Co-Investigator
Person Months: 0.12CM
Overlap: None

KC230214P1 (Beckermann, K.)
predictive biomarkersg with AI to understand the complex RCC tumor microenvironment and identify
Principal Investigator: Beckermann, K.

Support Agency: CDMRP
Grant Officer: N/A
Performance Period: 09/30/2024 – 09/29/2028
Level of Funding:
Project Goal: Oversight of this project including design, coordinating, oversight and conducting experiments, analyzing data, and preparation of manuscripts and future grants.
Role: Partnering PI
Person Months: 1.2CM
Overlap: None

IN-KIND: None

Foreign Collaboration: None

8. **SPECIAL REPORTING REQUIREMENTS - NONE**

9. **APPENDICES - NONE**