AWARD NUMBER: W81XWH-14-1-0476

TITLE: The Thoc1 Ribonucleoprotein as a Novel Biomarker for Prostate Cancer Treatment Assignment

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REPORT DATE: October 2017

TYPE OF REPORT: Annual

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

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2017	Annual	15 Sep 2016 - 14 Sep 2017

4. TITLE AND SUBTITLE
The Thoc1 Ribonucleoprotein as a Novel Biomarker for Prostate Cancer Treatment Assignment

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-14-1-0476

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
.
Health Research, Inc.
Buffalo,NY 14263

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT: Active surveillance (AS) is an option for men with low risk prostate cancer in order to reduce over treatment, but few men choose it because current prognostic indicators are imperfect. The objectives of this research are to test whether pThoc1 can improve the assignment of prostate cancer patients to therapy. We have made significant progress on the goals articulated in the Statement of Work. IRB/HRPO approval has been obtained for construction and use of new TMAs (PI Mohler and Goodrich). The TMAs from PCaP have been obtained (PI Mohler and Goodrich). Pathology analysis of 1146 patient specimens and construction of TMAs are completed and the TMA sections were requested, pending immunostaining (PI Mohler). Optimization of TMA staining is complete and staining of PCaP TMAs initiated (PI Goodrich). IRB/HRPO approval for active surveillance specimens has been obtained (PI Mohler, Goodrich).The PCaP Dx biopsy tissue sections were obtained for patients that would have qualified for active surveillance and they were immunostained (PI Mohler and Goodrich). Half of the RPCI Dx biopsies from active surveillance patients were pathology reviewed and obtained (PI Mohler). ELISA assays for measuring pThoc1 and pThoc1 autoantibodies have been successfully developed (PI Goodrich). Analysis of serum samples from a mouse model of prostate cancer has been performed, establishing feasibility (PI Goodrich). IRB/HRPO approval for serum samples has been obtained (PI Mohler, Goodrich). All preparative, optimization, and regulatory approval work has thus been completed, setting the stage for data gathering in year 2 of the grant. Over treatment is complicates the clinical management of prostate cancer. Improving the ability to distinguish aggressive from indolent disease is recognized as an unmet need by the 2013 PCRP Overarching Challenges. Identifying pThoc1 as a biomarker that can help meet this need will have significant impact.

15. SUBJECT TERMS
Prostate cancer, biomarker, active surveillance, prognostic indicator, tissue microarray, immunostaining, ribonucleoprotein

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	25	19b. TELEPHONE NUMBER *(include area code)*

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1. Introduction

Active surveillance (AS) has been proposed as an option for men with low risk prostate cancer in order to reduce over treatment. Only a fraction of eligible men choose AS, however, because current prognostic indicators are imperfect. Biomarkers that improve upon PSA levels, clinical stage and Gleason score to distinguish between prostate cancers that can be observed safely from those that require immediate treatment could help "right size" recommended treatment. The objectives of this proposal are to test whether pThoc1 can improve the assignment of prostate cancer patients to therapy, to test whether pThoc1 correlates with observed racial disparities in prostate cancer mortality, to determine whether pThoc1 can identify active surveillance patients whose prostate cancer will progress, and to develop methods to quantitate pThoc1 or pThoc1 autoantibody in serum. The general study design is to assay pThoc1 in independent cohorts of clinically annotated prostate cancer biospecimens for which clinical and follow up data is available using previously developed antibody reagents and immunostaining methods. Over treatment is a critical issue complicating the clinical management of prostate cancer. Improving the ability to distinguish aggressive from indolent disease in men newly diagnosed with prostate cancer is recognized as an unmet need by the 2013 PCRP Overarching Challenges. Identifying pThoc1 as a biomarker that can help meet this need will have significant impact.

2. Keywords

Prostate cancer, biomarker, active surveillance, prognostic indicator, tissue microarray, immunostaining, ribonucleoprotein

3. Accomplishments

The Years 1, 2 and 3 Tasks for the Mohler laboratory were copied from the Statement of Work and progress reported for each bullet under each task for each specific aim.

Specific Aim 1) Characterize pThoc1 levels in independent cohorts of human prostate cancer radical prostatectomy specimens.

Task 1- Construct prostate TMAs

- Finish construction of 1146 patient TMAs

A team of four pathologists completed the review of the H&E stained tissue sections from each of the 1146 patients. 828 patients' tissues were used for TMA construction. Construction of the new RPCI tissue microarray (TMA) set was completed and consists of 44 individual TMA blocks (Figure 1).

Figure 1. PrCa30-73 TMA blocks

TMA	Description	No. Patients
RPCI_PrCa30_	Prostatic adenocarcinoma cases that qualified to TCGA. Tumor and normal cores. Cases from 2007-2009.	20
RPCI_PrCa31_	Prostatic adenocarcinomacases that qualified to TCGA. Tumor and normal cores. Cases from 2009-2013.	22
RPCI_PrCa32_	African American prostatic adenocarcinoma cases not included in PrCa18. Tumor and normal cores. Cases from 2007-2012.	26
RPCI_PrCa33_	Prostatic adenocarcinoma cases from patients with biochemical persistence/recurrence. Tumor and normal cores. Cases from 2006-2007.	31
RPCI_PrCa34_	Prostatic adenocarcinoma cases from patients with biochemical persistence/recurrence. Tumor and normal cores. Cases from 2007-2008.	31
RPCI_PrCa35_	Prostatic adenocarcinoma cases from patients with biochemical persistence/recurrence. Tumor and normal cores. Cases from 2008-2009.	31
RPCI_PrCa36_	Prostatic adenocarcinoma cases from patients with biochemical persistence/recurrence. Tumor and normal cores. Cases from 2009-2010.	31
RPCI_PrCa37_	Prostatic adenocarcinoma cases from patients with biochemical persistence/recurrence. Tumor and normal cores. Cases from 2010-2011.	31
RPCI_PrCa38_	Prostatic adenocarcinoma cases from patients with biochemical persistence/recurrence. Tumor and normal cores. Cases from 2011-2012.	20
RPCI_PrCa39_	Prostatic adenocarcinoma cases from patients with biochemical persistence/recurrence. Tumor and normal cores. Cases from 2006-2012.	19
RPCI_PrCa40_	Extremes of grade cohort. Prostatic adenocarcinoma cases from patients with a gleason score of 6.Tumor and normal cores. Cases from 2005-2007.	31
RPCI_PrCa41_	Extremes of grade cohort. Prostatic adenocarcinoma cases from patients with a gleason score of 6.Tumor and normal cores. Cases from 2007-2008.	31
RPCI_PrCa42_	Extremes of grade cohort. Prostatic adenocarcinoma cases from patients with a gleason score of 6.Tumor and normal cores. Cases from 2008-2010.	31

RPCI_PrCa43_	Extremes of grade cohort. Prostatic adenocarcinoma cases from patients with a gleason score of 6.Tumor and normal cores. Cases from 2010-2012.	28
RPCI_PrCa44_	Extremes of grade cohort. Prostatic adenocarcinoma cases from patients with a gleason score of 6.Tumor and normal cores. Cases from 2006-2012.	24
RPCI_PrCa45_	Extremes of grade cohort. Prostatic adenocarcinoma cases from patients with a gleason score of 6.Tumor and normal cores. Cases from 2005-2011.	29
RPCI_PrCa46_	Extremes of grade cohort. Prostatic adenocarcinoma cases from patients with a gleason score of 8, 9, or 10.Tumor and normal cores. Cases from 2006-2009.	31
RPCI_PrCa47_	Extremes of grade cohort. Prostatic adenocarcinoma cases from patients with a gleason score of 8, 9, or 10.Tumor and normal cores. Cases from 2009-2011.	21
RPCI_PrCa48_	Extremes of grade cohort. Prostatic adenocarcinoma cases from patients with a gleason score of 8, 9, or 10.Tumor and normal cores. Cases from 2006-2012.	23
RPCI_PrCa49_	Extent of disease cohort; category 1 (worst). Prostatic adenocarcinoma cases from patients with LN/seminal vesicle invaded (margin irrelevant) status. Tumor and normal cores. Cases from 2006-2009.	31
RPCI_PrCa50_	Extent of disease cohort; category 1 (worst). Prostatic adenocarcinoma cases from patients with LN/seminal vesicle invaded (margin irrelevant)status. Tumor and normal cores. Cases from 2009-2011.	20
RPCI_PrCa51_	Extent of disease cohort; category 1 (worst). Prostatic adenocarcinoma cases from patients with LN/seminal vesicle invaded (margin irrelevant) status. Tumor and normal cores. Cases from 2007-2012.	19
RPCI_PrCa52_	Extent of disease cohort; category 2. Prostatic adenocarcinoma cases from patients with Margin positive, LN/seminal vesicle negative status. Tumor and normal cores. Cases from 2006-2007.	31
RPCI_PrCa53_	Extent of disease cohort; category 2. Prostatic adenocarcinoma cases from patients with Margin positive, LN/seminal vesicle negative status. Tumor and normal cores. Cases from 2007-2009.	31

RPCI_PrCa54_	Extent of disease cohort; category 2. Prostatic adenocarcinoma cases from patients with Margin positive, LN/seminal vesicle negative status. Tumor and normal cores. Cases from 2009-2010.	31
RPCI_PrCa55_	Extent of disease cohort; category 2. Prostatic adenocarcinoma cases from patients with Margin positive, LN/seminal vesicle negative status. Tumor and normal cores. Cases from 2010-2011.	31
RPCI_PrCa56_	Extent of disease cohort; category 2. Prostatic adenocarcinoma cases from patients with Margin positive, LN/seminal vesicle negative status. Tumor and normal cores. Cases from 2011-2012.	23
RPCI_PrCa57_	Extent of disease cohort; category 2. Prostatic adenocarcinoma cases from patients with Margin positive, LN/seminal vesicle negative status. Tumor and normal cores. Cases from 2007-2012.	23
RPCI_PrCa58_	Extent of disease cohort; category 3. Prostatic adenocarcinoma cases from patients with bladder neck invasion/extra-capsular extension, margin negative status. Tumor and normal cores. Cases from 2005-2007.	31
RPCI_PrCa59_	Extent of disease cohort; category 3. Prostatic adenocarcinoma cases from patients with bladder neck invasion/extra-capsular extension, margin negative status. Tumor and normal cores. Cases from 2007-2009.	31
RPCI_PrCa60_	Extent of disease cohort; category 3. Prostatic adenocarcinoma cases from patients with bladder neck invasion/extra-capsular extension, margin negative status. Tumor and normal cores. Cases from 2009-2011.	31
RPCI_PrCa61_	Extent of disease cohort; category 3. Prostatic adenocarcinoma cases from patients with bladder neck invasion/extra-capsular extension, margin negative status. Tumor and normal cores. Cases from 2011-2012.	22
RPCI_PrCa62_	Extent of disease cohort; category 3. Prostatic adenocarcinoma cases from patients with bladder neck invasion/extra-capsular extension, margin negative status. Tumor and normal cores. Cases from 2006-2012.	21

RPCI_PrCa63_	Extent of disease cohort; category 4 (best). Prostatic adenocarcinoma cases from patients with organ confined, margin negative status. Tumor and normal cores. Cases from 2006.	31
RPCI_PrCa64_	Extent of disease cohort; category 4 (best). Prostatic adenocarcinoma cases from patients with organ confined, margin negative status. Tumor and normal cores. Cases from 2006-2007.	31
RPCI_PrCa65_	Extent of disease cohort; category 4 (best). Prostatic adenocarcinoma cases from patients with organ confined, margin negative status. Tumor and normal cores. Cases from 2007.	31
RPCI_PrCa66_	Extent of disease cohort; category 4 (best). Prostatic adenocarcinoma cases from patients with organ confined, margin negative status. Tumor and normal cores. Cases from 2007-2008.	31
RPCI_PrCa67_	Extent of disease cohort; category 4 (best). Prostatic adenocarcinoma cases from patients with organ confined, margin negative status. Tumor and normal cores. Cases from 2008-2009.	31
RPCI_PrCa68_	Extent of disease cohort; category 4 (best). Prostatic adenocarcinoma cases from patients with organ confined, margin negative status. Tumor and normal cores. Cases from 2009-2010.	31
RPCI_PrCa69_	Extent of disease cohort; category 4 (best). Prostatic adenocarcinoma cases from patients with organ confined, margin negative status. Tumor and normal cores. Cases from 2010-2012.	31
RPCI_PrCa70_	Extent of disease cohort; category 4 (best). Prostatic adenocarcinoma cases from patients with organ confined, margin negative status. Tumor and normal cores. Cases from 2005-2012.	31
RPCI_PrCa71_	Extent of disease cohort; category 4 (best). Prostatic adenocarcinoma cases from patients with organ confined, margin negative status. Tumor and normal cores. Cases from 2006-2012.	22
RPCI_PrCa72_	Extent of disease cohort; category 4 (best). Prostatic adenocarcinoma cases from patients with organ confined, margin negative status. Tumor and normal cores. Cases from 2005-2012.	21

RPCI_PrCa73_	Prostatic adenocarcinoma; cases that did not fit any of the criteria to be included in TMAs PrCa30-PrCa72. Tumor and normal cores. Cases from 2010-2012.	21

- Obtain 328 AA and 361 CA patient TMAs from PCaP

The IRB protocol was reviewed and approved by the North Carolina – Louisiana Prostate Cancer Project (PCaP) Management Committee. Their approval was contingent on successful development of the ELISA assay to detect Thoc1 and Thoc1 autoantibodies in serum samples. PCaP tissue sections were released October 2, 2015 after Dr. Goodrich's laboratory completed the feasibility study and submitted the supporting documentation.

- Obtain HRPO approval, amend IRB protocol

The IRB protocol for this study was amended and reviewed and approved by the RPCI Genito-Urinary Disease Site Research Group (GU DSRG) and by the Office of Research Subject Protection (ORSP). The approval process took approximately 6 months. DoD PCRP approval required an additional 9 months when DOD PCRP questioned the PCaP and RPCI granted exemptions.

Task 2- Immunostain TMAs

- Further optimization of immunostaining

The immunohistochemistry methods were optimized for immunostaining of Thoc1 and PMP22.

- Immunostain RPCI 92 AA and 92 CA patient TMAs
- Immunostain 328 AA and 361 CA patient TMAs
- Immunostain 1146 patient TMAs

Immunostaing of the PCaP TMAs, RPCI 92 AA and 92 CA and PrCa 30-73 TMA sets was completed.

Task 3- Analyze data

- Score pathology and immunostaining of TMA slides

Scoring of the acquired images, in collaboration with Dr. Azabdaftari was completed for the PCaP TMA sets and are in progress for the RPCI 92 AA and 92 CA and PrCa 30-73 TMA sets.

- Correlate immunostaining with clinical data

Clinical data were acquired from PCaP and the data analysis is in progress. The clinical data from RPCI will be requested once scoring is complete (to avoid bias).

Specific Aim 2) Characterize pThoc1 levels in a cohort of human prostate cancer patients on active surveillance.

Task 1- Immunostain active surveillance patient biopsies

- IRB/HRPO approval for active surveillance specimens

The IRB protocol for this study was amended, reviewed and approved by the RPCI Genito-Urinary

Disease Site Research Group (GU DSRG) and by the Office of Research Subject Protection (ORSP). The approval process took approximately 6 months. DoD PCRP approval required an additional 9 months when DOD PCRP questioned the PCaP and RPCI granted exemptions.

Task 2- Enroll ~50 prostate cancer patients per year on active surveillance

- Annotate clinical data

Patients continue to be recommended for and to select active surveillance at RPCI. Each has all demographic, clinical, pathological and oncological outcome data entered prospectively in a relational database by our clinical team and data managers [565 are enrolled as of October 8, 2017, which includes 130 new patients since October14, 2015, the date of the original progress report].

- Immunostain biopsy tissue sections

565 patients are enrolled on active surveillance at RPCI [as of October 8, 2017]. Diagnostic prostate biopsy tissue specimens are available for 115 patients. All other patients had prostate biopsies performed at other facilities. Obtaining them from individual pathology laboratories would be costly and time consuming, based on previous PCaP experience. The study group will be expanded to include diagnostic biopsy tissue sections from RPCI and PCaP patients who would have qualified for active surveillance (NCCN very low, low or favorable intermediate [T1c, Gleason grade 3+4, PSA < 10] prostate cancer). A search for RPCI performed prostate biopsies is in progress. That should add some of the 130 new active surveillance patients for future studies.

DSRG and ORSP approvals were obtained at RPCI and from the PCaP Management Committee. The approval process took approximately 6 months. DoD PCRP approval required an additional 9 months when DOD PCRP questioned the PCaP and RPCI granted exemptions.

PCaP provided diagnostic prostate biopsies from 183 men on October 2, 2015, which have been immunostained and visually scored. The RPCI diagnostic biopsy tissue sections are being prepared by the RPCI Pathology Resource Network (PRN). PRN has identified 115 cases that are enrolled on active surveillance at RPCI or qualify for active surveillance, per NCCN guidelines, but received a different treatment. All 115 cases were reviewed by Dr. Azabdaftari and and PRN delivered the unstained diagnostic biopsy tissue sections on October 1, 2017. Immunostaining is completed for 50 cases. Immunostaining for 65 cases is in progress.

Specific Aim 3) Test whether pThoc1 or autoantibodies against pThoc1 can be detected in the serum of prostate cancer patients.

Task 2- Assay serum pThoc1 or pThoc1 autoantibodies in human prostate cancer serum samples

- IRB/HRPO approval for serum samples

The protocol for this study was amended and reviewed and approved by the RPCI Genito-Urinary Disease Site Research Group (GU DSRG) and by the Office of Research Subject Protection (ORSP). The approval process took approximately 6 months. DoD PCRP approval required an additional 9 months when DOD PCRP questioned the PCaP and RPCI granted exemptions.

- Methods adaptation to human samples if necessary

The serum pThoc1 and pThoc1 autoantibodies assay was standardized previously for mouse serum. The assay optimization for human serum was completed.

- Assay serum pThoc1 concentrations in RPCI serum samples
- Assay serum pThoc1 autoantibody titers in RPCI serum samples

Serum from 50 normal cases, which were age and race matched with the PCaP cases, were acquired and the analysis is in progress. We are in process of obtaining and analyzing the RPCI serum samples from the same cases from which diagnostic prostate biopsies were obtained.

- Assay serum pThoc1 concentrations in PCaP serum samples
- Assay serum pThoc1 autoantibody titers in PCaP serum samples

The PCaP serum samples were obtained and analyzed.

Task 3 – Analyze data

- Correlate pThoc1 and autoantibody concentrations and RPCI clinical data

RPCI Clinical data will be requested once the serum analysis is complete (to avoid bias).

- Correlate pThoc1 and autoantibody concentrations and RPCI clinical data

Clinical data were obtained from PCaP and the data analysis is in progress.

4. Impact

None

5. Changes/Problems

None

6. Products

None

7. Participants & Other Collaborating Organizations

James L. Mohler, MD	Partnering PI	1 calendar months
Gissou Azabdaftari, MD	Co-Investigator	<1 calendar months
Elena Pop, MD	Co-Investigator	1 calendar months
Kristopher Attwood, PhD	Biostatistician	<1 calendar months
John Stocking	Lab technician	6 calendar months

No other organizations are involved in the research.

Changes in Other Support

James L. Mohler, MD

Completed
Title: Prostate Cancer: Transition to Androgen Independence, Project 1: Interference with the Androgen Receptor and Its Ligands in Recurrent Prostate Cancer (French - PI)
Time Commitments: 0.60 calendar months
Supporting Agency: National Cancer Institute P01-CA77739
Name and address of the Funding Agency's Procuring Contracting/Grants Officer:
Mark Kramer, Administrative Director, UNC Lineberger Comprehensive Cancer Center Campus Box 7295
102 Mason Farm Road, Chapel Hill, NC 27599-7295, Phone: (919) 966-0233, Fax: (919) 966-3015, mkramer@med.unc.edu
Performance Period: 04/01/2005-03/31/2017 (NCE)
Level of Funding: $2,292,618
Brief description of project's goals: Renewal of a project that tests the hypothesis that recurrence of prostate cancer during androgen deprivation therapy can be prevented or delayed by preventing the accumulation of tissue androgens and/or inhibiting the androgen receptor.
List of specific aims:
1. Prevent the changes in androgen metabolism that provide AR ligand(s) in the immediate post-castration period
2. Degrade AR ligand(s) formed in the immediate post-castration period
3. Diminish or eliminate AR in the immediate post-castration period

Overlap: None

Change in effort
Title: Cancer Center Support Grant (Johnson - PI)
Time Commitments: 2.70 calendar months
Supporting Agency: National Cancer Institute
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Kimberly Griffin, NCI Shady Grove, 9609 Medical Center Drive, West Tower, 2nd floor, Room 2W520, Rockville, MD 20850. 240-276-6315
Performance Period: 06/26/2014-04/30/2019
Level of Funding: $2,315,456
Brief description of project's goals:
Roswell Park Cancer Institute's Cancer Center Support Grant (CCSG) includes six programs and 13 cores resources. Support is provided for leadership, developmental funds, planning and evaluation and administration.
List of specific aims:
The resource provides a complete service from methods development and validation to sample handling and analysis to PK/PD modeling and simulation leading to informed decision-making about dosing, dose scheduling and drug combinations.
Overlap: None

Completed
Title: Diet changes among prostate cancer patients under expectant management (Marshall - PI)
Time Commitments: 0.60 calendar months
Supporting Agency: National Cancer Institute

Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Program Official: Howard L. Parnes, Email: hp24c@nih.gov Phone: 301-594-0920 Fax: 301-435-1564
Performance Period: 09/28/2009-01/31/2017 (NCE)
Level of Funding: $55,818
Brief description of project's goals: The focus of this study is to assess whether a diet emphasizing plant consumption decreases the probability that low grade, low-volume prostate cancer (LGLV)in expectant management(EM)patients progresses to a more aggressive form of cancer that merits active treatment. The intervention will be conducted through one of the leading cooperative oncology research groups: Cancer and Leukemia Group B (CALGB).
List of specific aims:
1. Assess the effect of a telephone-based dietary intervention on PSA, PSA doubling time, Gleason score and tumor extension in LGLV prostate cancer patients treated with EM.
2. Assess the effect of a telephone-based dietary intervention on treatment seeking, anxiety and coronary heart disease in prostate cancer patients treated with EM.

Overlap: None

Completed
Title: Defining intra- and intertumoral genomic heterogeneity in prostate cancer (Mohler - PI)
Time Commitments: 0.60 calendar months
Supporting Agency: Roswell Park Alliance Foundation
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Judith Epstein, Director Grants & Foundation Office, Elm & Carlton Streets, Research Studies Center Room 234, Buffalo, NY 14203, Judith.Epstein@RoswellPark.org
Performance Period: 12/10/2013-12/31/2016 (NCE)
Level of funding: $92,384
Brief description of project's goals:
Intra- and inter-tumoral CaP genomic heterogeneity necessitates extensive sampling of a radical prostatectomy specimen.
List of specific aims:
1. Determine intra- and inter-tumoral heterogeneity in CaP's mutational landscape using whole exome sequencing to determine heterogeneity within and among CaP foci derived from radical prostatectomy specimens from patients with high-risk disease who are expected to develop metastatic disease and require ADT
2. Define intra- and inter-tumoral CaP heterogeneity in structural gene rearrangement and gene expression patterns using RNA-Seq and RNA derived from the same CaP samples used in Aim 1

Overlap: None

No cost extension
Title: Cholesterol Lowering Intervention for Prostate Cancer Active Surveillance/Jr. Faculty Award to Alliance NCORP Research Base – Pilot Project (Kim/Mohler - PIs)
Time Commitments: 0.60 calendar months
Supporting Agency: Cedars/NCI
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Subcontract with Cedars Sinai. Cedars-Sinai Medical Center, Attention: Margaret Jenkins, Administrative Program Coordinator
Department of Surgery, Research Division, 8635 W. 3rd Street, Suite 973W, Los Angeles, CA 90048 margaret.jenkins@cshs.org
Performance Period: 04/01/2015 – 03/31/2017
Level of funding: $93,955 (sub contract)
Brief description of project's goals: The proposed research tests the hypothesis that intensive cholesterol lowering will decrease the growth rate of benign and malignant prostate epithelium. The proposed

research could provide the data necessary to justify a phase III clinical trial to address one of the major problems in urologic oncology how to prevent the progression of low risk prostate cancer to provide men higher levels of confidence for selection of active surveillance.
Overlap: None

No cost Extension
Title: Genetic variations in SLCO transporter genes contributing to racial disparity in aggressiveness of prostate cancer (Wu - PI)
Time Commitments: 0.12 calendar months
Supporting Agency: USAMRAA W81XWH-14-1-0453
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Mirlene Desir, Grant Specialist, Assistance Branch 4, MCMR-AAA-AD, USAMRAA, 820 Chandler Street, Fort Detrick, MD 21702, phone: 301-619-7733, fax: 301-619-9656, mirlene.desir@civ@mail.mil
Performance Period: 09/15/2014-08/31/2018 (NCE)
Level of funding: $764,100
Brief description of project's goals: The objective seeks to address how transporter-regulated androgen availability to cancer cells may contribute to the difference in prostate cancer aggressiveness between African American (AA) and European American (EA) men. The hypothesis is: Genetic variations in solute carrier family of organic anion transporting peptides (SLCO) androgen transporter genes and expression profiles of SLCO androgen transporters in prostate tissue are associated with aggressiveness of prostate cancer, and contribute to racial differences in prostate cancer aggressiveness. (Recommended for funding)
List of specific aims:
1. Examine genetic variations in SLCO transporters genes and to investigate the associations of the variations with prostate cancer aggressiveness in AA and EA.
2. Examine in situ expression profiles of SLCO transporters in prostate tissue and to investigate the associations of the expression profiles with prostate cancer aggressiveness in AA and EA.
3. Characterize the functions of candidate SLCO transporters in androgen uptake and to evaluate the biological effects on AR signaling in human prostate cancer cell lines.
Overlap: None

No cost Extension
Title: Deprive prostate cancer of DHEAS to prevent castration-recurrent prostate cancer (Wu – PI)
Time Commitments: 0.12 calendar months
Supporting Agency: NIH/NCI 1R21CA191895-01
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Viviana Knowles, 9609 Medical Center Drive, West Tower, Bethesda, MD 20892, phone: 240-276-5157, viviana.knowles@nih.gov
Performance Period: 09/17/2014-02/28/2018 (NCE)
Level of Funding: $419,884
Brief description of project's goals: This research seeks to address the racial differences in prostate cancer aggressiveness from a biological perspective.
List of specific aims:
1. Characterize the expression of STS and potential STS regulators in CRPC
2. Evaluate the value of targeting DHEAS usage by prostate cancer cells to prevent post-castration tumor growth
3. Identify DHEAS uptake mechanisms
Overlap: None

Prior pending, now active funding

Title: Genetic and Epigenetic Prostate Cancer Related alterations in early onset disease in African American Men (Woloszynska-Read)
Time Commitments: 1.20 calendar months
Supporting Agency: DoD
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Department of Defense, USA MED RESEARCH ACQ ACTIVITY 820 CHANDLER ST FORT DETRICK MD 21702-5014/ LYMOR BARNHARD
Performance Period: 04/01/2017-03/31/2020
Level of funding: $1,242,951
Brief description of project's goals: Proposed research aims to identify molecular alterations that distinguish aggressive forms of early onset prostate cancer commonly found in Afrinca American men will contribute to the development of African American tumor (epi)genetic signature(s) and ultimately will lead to personalized medicine strategies for this group of patients.
List of specific aims:
1. Determine the relative frequency of genetic lesions found in PCa in AAs and EAs.
2. Determine novel, clinically relevant methylomic and transcriptomic differences in PCa from AAs and EAsObtain and link vital status data and cause of death in PCaP research subjects

Overlap: None

Prior pending, now active funding
Title: Racial differences in financial impact of prostate cancer treatment and outcome
Time Commitments: 1.44 calendar months Y1, 1.8 calendar months Y2, 2.40 calendar months Y3
Supporting Agency: DoD
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Not assigned
Performance Period: 04/01/2017-03/31/2020
Level of funding: $445,328
Brief description of project's goals: Recurrence of advanced CaP during androgen deprivation therapy leads to a variety of new FDA-approved treatments, which may include immunotherapy, androgen metabolism inhibitors, small molecule anti-androgens, radio-pharmaceuticals, and docetaxel, cabazitaxel or cisplatin, all of which can extend survival but cause side effects and are expensive. Complexities of insurance coverage and Medicare reimbursement, a trend toward increasing co-pays for covered medications and differences in availability of financial assistance from pharmaceutical companies for new agents makes challenging the anticipation of the amount of financial burden posed by advanced CaP. If cured of localized CaP, costs may result from treatment of side effects, such as incontinence and impotence. CaP has been reported to produce the highest level of financial distress among 7 common cancers studied. Patients and their family members have suffered loss of their home, had to quit or decrease job hours or intensity, or forego expensive treatments shown to prolong life. AAs compared to Caucasian Americans (CAs) have been reported to benefit from higher religiosity and "caregiverness" but suffer from lower socioeconomic reserve and medical sophistication. The central hypothesis is that the financial impact of CaP treatment and oncologic outcome differs between AAs and CAs newly diagnosed with CaP.
List of specific aims:
1. Locate and contact PCaP research subjects to update CaP status, CaP treatments received and comorbidities, repeat the QoL assessments performed at baseline and follow-up, and administer new surveys on financial burdens and stress and caregiver QoL and support
2. Locate and contact PCaP research subjects' treating physicians to update treatments received and oncologic outcome data
3. Obtain and link vital status data and cause of death in PCaP research subjects
4. Examine the role financial burden and stress have on CaP survival and QoL and whether this relationship was modified by race.

Overlap: None

OVERLAP STATEMENT

The DoD Idea Development Award PC150326P2 does not overlap with any current or pending grants. The NCI P01 is in Year 16 and no cost extension. The no cost extension does not provide funds for generation of new data but allows completion of 3 manuscripts. The NIH R21 grant application (CURRENT SUPPORT) seeks to develop a small molecule inhibitor of the catalytic site common to the 3α-oxidoreductases that would require additional funding for preclinical testing prior to translation to the clinic as a potential treatment for castration-recurrent prostate cancer. The DoD Idea Development Award PC150326P2 seeks to identify the key pathways and reveal new targets in the androgen pathway or pathways that allow prostate cancer to escape acutely the effects of initiation of androgen deprivation therapy. No other funded grants appear related. Hence, the research activities of the Mohler laboratory are complimentary but the P01, R21 and DoD IDEA Development Award do not overlap.

Kristopher Attwood, PhD

ACTIVE:

Change in effort

Title: Assessing the impact of differing pharmacy tobacco retail displays on smokers awareness, perceptions, and intentions to quit (1 R21 CA198824-01A1)
Time Commitments: 0.225 calendar (PI-Bansal Travers)
Supporting Agency: NIH
Grants Officer: Phone: Annette Kaufman; Annette.kaufman@nih.gov; (240) 276-6706
Performance Period: 6/1/16-5/31/18
Level of Funding: $471,625
Brief description of project's goals: The goal of this timely project is to take advantage of the ongoing natural experiment in the three largest U.S. pharmacy chains to better understand consumer perceptions of differences in point-of-sale advertising for using and quitting tobacco, particularly how it is received, understood, and acted on by young adult cigarette smokers.
List of specific aims:

1. To determine consumer attention to current point-of-sale retail displays, the factors associated with different amounts and areas of attention, and whether attention to these displays influences consumer perceptions of the appeal and perceived relative risks of smoking cigarettes.
2. To determine consumer attention to current smoking cessation messages at point-of-sale retail displays, the factors associated with different amounts and areas of attention, and whether attention to these displays influences consumer perceptions of the perceived benefits of quitting.
3. To determine changes in quit intentions as a function of differences between pharmacy PoS retail displays.
4. To determine if consumer attention to cessation messages at the point-of-sale are associated with changes in intention to quit smoking.

Overlap: NONE

Moved to completed

Title: Novel Mouse Models to Define Genetic Drivers of Aggressive Prostate Cancer (1R21 CA205627-01)
Time Commitments: 0.225 calendar (PI-Ellis)
Supporting Agency: NIH
Grants Officer: Grace Ault; grace.alt@nih.gov; Phone: (240) 276-6201
Performance Period: 04/15/16-03/31/17
Level of Funding: $471,625

Brief description of project's goals: Our principle objective is to characterize our genetically engineered mouse models to discover genetic switches which drive aggressive prostate cancer. Overall, our proposed studies will significantly impact prostate cancer research and how patients are clinically assessed to determine stratification of indolent from aggressive disease.
List of specific aims:

1. Specifically, aim 1 will determine if the retinoblastoma protein (Rb) is a suppressor of PCa metastasis.
2. Specific aim 2 will utilize a sleeping beauty mutagenesis screen to identify novel candidate genetic drivers of PCa metastasis.

Overlap: NONE

Increase in effort
Title: Cancer Center Support Grant – Biostatistical Core (RPCI subcontract) (5 P30 CA16056-39)
Time Commitment: 0.60 calendar (PIs-Johnson/Brady)
Supporting Agency: NIH
Funding Agency's Procuring Contracting/Grants Officer: Wooddill, Joseph; Phone: (301) 496-8635
Performance Period: 05/01/97-04/30/19
Level of Funding: $2,392,072
Project Goals: The major goal of this project is to provide biostatistical support for cancer clinical trials.
Specific Aims:

1. Facilities: Physical facilities dedicated to the conduct of cancer focused research, and to the center's shared resources, administration, and research dissemination efforts, should be appropriate and adequate to the task.
2. Organizational Capabilities: The center should be organized to take maximum advantage of institutional capabilities in cancer research, and to appropriately plan and evaluate center strategies and activities.
3. Transdisciplinary Collaboration and Coordination: Substantial coordination, interaction, and collaboration among center members from a variety of disciplines should enhance and add value to the productivity and quality of research in the center.
4. Cancer Focus: A defined scientific focus on cancer research should be clear from the center members' grants and contracts, and from the structure and objectives of its formal Programs.
5. Institutional Commitment: The center should be recognized as a formal organizational component with sufficient space, positions, and discretionary resources to insure its stability and fulfill the center's objectives.
6. Center Director: The director should be a highly qualified scientist and administrator with leadership experience and institutional authority appropriate to manage the center and further its scientific mission and objectives.

Overlap: None

Moved to completed
Title: Metabotropic Glutamate Receptor 1 in African American Prostate Cancer (5 R21 CA183892-01)
Time Commitments: 0.30 calendar (PI-Koochekpour)
Supporting Agency: NIH
Grants Officer: Elizabeth Woodhouse; elizabeth.woodhouse@nih.gov; Phone: (240) 276-6205
Performance Period: 04/01/14-03/31/17
Level of Funding: $466,950
Brief description of project's goals: Data generated from this exploratory study will define biological and/or clinicohistopathological significance or relevance of GRM1 expression in African American prostate cancer and may prove useful in discriminating clinically or biologically aggressive tumors from indolent (non-aggressive) tumors and minimizing prostate cancer disparity in African Americans.
List of specific aims:

1) Determine the association between tissue expression of GRM1 and clinicohistopathological predictors or prognosticators of prostate cancer progression or aggressiveness in African Americans.
2) Determine the association between GRM1 expression levels and invasive and metastatic phenotypes in African American prostate cancer cells.

Overlap: NONE

Moved to completed

Title: Therapeutic Efficacy of Riluzole in Prostate Cancer (5 R21 CA181152-02)
Time Commitments: 0.30 calendar (PI-Koochekpour)
Supporting Agency: NIH
Grants Officer: Michael Alley; michael.alley@nih.gov; Phone: (301) 624-1246
Performance Period: 07/01/14-06/31/16
Level of Funding: $221,589
Brief description of project's goals: This is a translational prostate cancer research aimed at determining the effect of glutamate receptor antagonist on tumor growth and metastatic ability, fatty acid synthase (FAS) expression and apoptotic markers in prostate cancer. This study will investigate the underlying mechanisms by which glutamate receptor antagonist down regulates FAS expression in prostate cancer cell lines.
List of specific aims:

1) Determine the therapeutic efficacy of Riluzole in in-vivo tumorigenesis assays.
2) Determine the association between Riluzole treatment and androgen receptor expression in tumor xenografts and prostate cancer cell lines.

Overlap: NONE

No cost extension

Title: Deprive Prostate Cancer of DHEAS to Prevent Castration-Recurrent Prostate Cancer (5 R21 CA191895-02)
Time Commitments: 0.30 calendar (PI-Wu)
Supporting Agency: NIH
Grants Officer: Neeraja Sathyamoorthy; neeraja.sathyamoorthy@nih.gov; Phone: (240) 276-6220
Performance Period: 09/01/15-02/28/2018 (NCE)
Level of Funding: $446,950
Brief description of project's goals: The proposed studies are required to validate the concept that DHEAS is an important source of precursors for intracrine production of T and DHT by prostate cancer cells. In addition, the transporters, STS, and STS regulators provide potential targets for therapy.
List of specific aims:

1) Characterize the expression of STS and potential STS regulators in CRPC.
2) Evaluate the value of targeting DHEAS usage by prostate cancer cells to prevent post-castration tumor growth.
3) Identify DHEAS uptake mechanisms.

Overlap: NONE

Pending to active

Title: Genetic and Epigenetic Prostate Cancer Related alterations in early onset disease in African America
Time Commitments: 0.60 calendar (PI- Woloszynska-Read)
Supporting Agency: DOD
Grants Officer: pending
Performance Period: 5/1/2017-4/30/2020
Level of Funding: $1,243,760

Brief description of project's goals: The objective of the proposal is to identify clinically relevant genomic and epigenomic events characteristic for prostate cancer (PCa) in African American (AA) men and compare/contrast those with/to PCa in European American (EA) men. These findings will be annotated with DNA methylation, gene expression, and demographic, environmental exposures, clinical, pathological and oncological outcomes.
List of specific aims:

1. Determine the relative frequency of genetic lesions found in PCa in AAs and EAs.
2. Determine novel, clinically relevant methylomic and transcriptomic differences in PCa from AAs and EAs.

Overlap: NONE

Pending
Title: CD27/CD70 mediated negative regulation of inflammatory T cell responses
Time Commitments: 0.24 calendar (PI-Cao)
Supporting Agency: NIH
Grants Officer: Pending
Performance Period: 4/1/2018-3/31/2023
Level of Funding: $3,357,088
Brief description of project's goals: For this project, we have used established murine models to study the roles of CD27/CD70 in allo-HCT. Our results reveal a novel inhibitory role played by this pathway in GVHD as specified in 2 aspects: 1) both CD27-/- and CD70-/- donor T cells caused more severe GVHD than WT donor T cells, suggesting that CD27/CD70 signaling in donor T cells inhibits alloreactive T cell response; 2) when used as hosts, both CD27-/- and CD70-/- mice exhibited more severe GVHD compared to WT hosts, suggesting that CD27/CD70 signaling in the host inhibits alloreactive T cell response.
List of specific aims:
1. Aim 1 will define the mechanisms by which donor T cell-derived CD27/CD70 suppresses GVHD.
2. Aim 2 will define the mechanisms by which host-derived CD27/CD70 signaling inhibits GVHD.
3. Aim 3 will define the clinical relevance of CD27/CD70 signaling in GVHD.

Overlap: NONE

Pending
Title: Selective Chemokine Modulation to Sensitize "Cold" Epithelial Tumors to Atezolizumab
Time Commitments: 0.30 calendar (PI- Kalinski)
Supporting Agency: NCI/NIH
Grants Officer: Pending
Performance Period: 12/1/2017-11/30/2020
Level of Funding: $3,000,000
Brief description of project's goals: Our cumulative clinical and preclinical data provide strong rationale to use CKM to sensitize "cold tumors" to checkpoint blockade.
List of specific aims:
1. Perform phase I portion of the clinical to apply atezolizuab combined with two increasing concentration of rintatolimod (200 mg and 400 mg: Cohorts 1 and 2) and two increasing dose levels of IFNalpha (Cohorts 3 and 4) in a mixed cohort of patients with breast, colon, urothelial or ovarian cancers, to evaluate safety of treatment and identify the phase II dose (Ph2D).
2. Perform phase II component of the trial in these 4 cancer types (12 pts with each tumor type) comparing the ability of the Ph2D CKM to modify TME, enhance intratumoral CTL infiltration and modify the PD-1/PD-L1/L2 system (pre- and post-CKM biopsies) in patients receiving atezolizumab, and obtain preliminary insight in the correlation between the individual CKM-induced chances in TME and the clinical responsiveness to atezolizumab in each of the studied patient groups.

3. Perform correlative studies to identify potential baseline- and treatment-associated correlates of clinical activity, identify potential secondary resistance mechanisms (such as immune-induced COX2, IL-10, TGFbeta, VEGF) and disease-specific differences, and develop optimized strategies with uniform effectiveness against epithelial cancers.
Overlap: NONE

Pending
Title: Surgeon-Authoring of Virtual Reality Training for Advanced Minimally Invasive Surgery
Time Commitments: 0.12 calendar (PI- Kurenov)
Supporting Agency: NIH
Grants Officer: Pending
Performance Period: 10/1/2017-9/30/2021
Level of Funding: $178,000
Brief description of project's goals: Building on state-of-the-art solutions of tissue simulation, parallel and high-end graphics computing for interactive 3D surgery simulation with force-feedback, this proposal breaks new ground by (a) enabling rapid prototyping of new scenarios with minimal computer or mathematics expertise, and (b) empowering surgeon-educators to be the primary authors who determine and fine-tune content, delivery and trainee feedback.
List of specific aims:
1. Building consensus on proficiency for advanced laparoscopic procedures using an interactive online interface, a module's lead surgeon-author will input the step-by-step list of tasks and associated safety issues of a procedure in the format: action, anatomy, tool, safety, comment. The task-safety list is reviewed by three or more experienced surgeon-educators, at least two from outside the author's institution and blinded to the author's identity. The goal is to reach consensus or to highlight disagreement and generate competing task-safety lists. We will deliver anatomic and pathological variants of three high risk procedures, Colectomy, Gastric Bypass and Nissen Fundoplication that are technically challenging both for surgeons and VR-tools. Hypothesis: The task-safety lists of laparoscopic tasks represent specialists' consensus, or competing approaches.
2. Rapid prototyping of new VR-training modules Geometry and physics of the VR simulation will leverage two actively supported, large open source projects (Blender and SOFA) and upload vetted simulations to a shared database as modular pieces of anatomy (organs, veins, connecting tissue, etc.) with their behavior (simlets). Hypothesis: The TIPS environment enables surgeon-educators to efficiently initialize and fine-tune advanced force-feedback VR lap-training modules.
3. Validating the VR-modules. Each training module is honed and validated by four feedback cycles: task-safety list review (by peer surgeons), module review (by peer surgeons), training (to proficiency) and Kirkpatrick level 3 (K3) study of trainees (by peer surgeons). Hypothesis: Surgeon-controlled VR-training improves competency and safety-awareness in the OR.
4. Building a VR-authoring community. Hypothesis: VR-training units can be developed and shared, decoupled in time and space.
Overlap: NONE

Pending
Title: Serum microRNA as a predictor of prostate cancer among patients with high-grade prostatic intraepith
Time Commitments: 0.30 calendar (PI-Marshall)
Supporting Agency: NCI/NIH
Grants Officer: Pending
Performance Period: 04/01/18-03/31/20
Level of Funding: $472,450
Brief description of project's goals: Can we use a non-invasive blood test of serum microRNAs to diagnose or predict prostate cancer (PC) development in a person with what is believed to be a

premalignant lesion, high-grade prostatic intra-epithelial neoplasia (HGPIN)? We are proposing to answer this with a study led by two principal investigators with significant expertise in PC epidemiology and microRNA biomarkers.
List of specific aims:
1. Identify diagnostic serum microRNA biomarkers for presence of PC in HGPIN using serum samples drawn 0-3 months before prostate biopsy for PC diagnosis.
2. Identify predictive serum microRNA biomarkers for likelihood of PC diagnosis in HGPIN patients, using serum samples drawn 18-24 months before biopsy.
Overlap: NONE

Title: Deprive prostate cancer of DHEAS to prevent castration-recurrent prostate cancer (5 R21 CA191895-02)
Time Commitments: 0.30 calendar (PI-Wu)
Supporting Agency: NCI/NIH
Grants Officer: Neeraja Sathyamoorthy; neeraja.sathyamoorthy@nih.gov; Phone: (240) 276-6220
Performance Period: 09/17/14-02/28/18 (NCE)
Level of Funding: $446,950
Brief description of project's goals: The proposed studies are required to validate the concept that DHEAS is an important source of precursors for intracrine production of T and DHT by prostate cancer cells. In addition, the transporters, STS, and STS regulators provide potential targets for therapy.
List of specific aims:
1) Characterize the expression of STS and potential STS regulators in CRPC.
2) Evaluate the value of targeting DHEAS usage by prostate cancer cells to prevent post-castration tumor growth.
3) Identify DHEAS uptake mechanisms.
Overlap: NONE

Gissou Azabdaftari

Moved to completed
Title: Defining intra- and intertumoral genomic heterogeneity in prostate cancer (62-2576-01)
Time Commitment: 0.60 Calendar Months (PI, Mohler)
Supporting Agency: Roswell Park Alliance Foundation
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Judith Epstein
Performance Period: 12/10/2013 – 12/31/2016
Funding: $50,000
Brief description of project's goals: Determine the intra- and inter-tumoral prostate cancer genomic heterogeneity and establish the best Method to sample a radical prostatectomy specimen
Specific Aims:
1. Determine intra- and inter-tumoral heterogeneity in CaP's mutational landscape using whole exome sequencing to determine heterogeneity within and among CaP foci derived from radical prostatectomy specimens from patients with high-risk disease who are expected to develop metastatic disease and require ADT.
2. Define intra- and inter-tumoral CaP heterogeneity in structural gene rearrangement and gene expression patterns using RNA-Seq and RNA derived from the same CaP samples used in Aim 1.

Role: Co-Investigator (Pathologist)

Overlap: None

Moved to completed
Title: Therapeutic Efficacy of Riluzole in Prostate Cancer (1R21CA181152-01A1)
Time Commitment: 0.30 Calendar Months (PI, Koochekpour)
Supporting Agency: NCI
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Michael C. Alley
Performance Period: 07/01/2014 – 06/30/2017
Funding: $221,589
Brief description of project's goals: This is a translational prostate cancer research aimed at determining the effect of glutamate receptor antagonist on tumor growth and metastatic ability, fatty acid synthase (FAS) expression and apoptotic markers in prostate cancer. This study will investigate the underlying mechanisms by which glutamate receptor antagonist down regulates FAS expression in prostate cancer cell lines.
Role: Co-Investigator (Pathologist)
Overlap: None

No cost extension
Title: Deprive Prostate Cancer of DHEAS to Prevent Castration-Recurrent Prostate Cancer (1R21CA191895-01)
Time Commitment: 0.60 Calendar Months (PI, Wu)
Supporting Agency: NIH
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Neeraja Sathyamoorthy
Performance Period: 09/17/2014 – 02/28/2018 (nce)
Funding: $229,028
Brief description of project's goals: To investigate the role of dehydroepiandrosterone sulfate (DHEAS) in the progression of prostate cancer to castration-recurrent prostate cancer. The goals are to identify the molecular mechanisms underlying the uptake, metabolism, ad biological functions of DHEAS, and to identify potential targets to deprive prostate cancer cells of DHEAS to prevent the progression tc astration-recurrent prostate cancer.
Specific Aims:
1. Characterize the expression of STS and potential STS regulators in CRPC.
2. Evaluate the value of targeting DHEAS usage by prostate cancer cells to prevent post-castration tumor growth.
3. Identify DHEAS uptake mechanisms.
Role: Co-Investigator (Pathologist)
Overlap: None

No cost extension
Title: Genetic Variations in SLCO Transporter Genes Contributing to Racial Disparity in Aggressiveness of Prostate Cancer (W81XWH-14-1-0453)
Time Commitment: 0.60 Calendar Months (PI, Wu)
Supporting Agency: DOD
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Mirlene Desir
Performance Period: 09/15/2014 – 09/14/2018 (nce)

Funding: $764,100
Brief description of project's goals: To investigate the role of genetic variations of SLCO transporters in racial disparity in aggressiveness of prostate cancer, with the focus on how genetic variations of the transporters may affect the availability of androgens to prostate cancer.
Specific Aims:
1. To examine genetic variations in SLCO transporters genes and to investigate the associations of the variations with prostate cancer aggressiveness in AA and EA.
2. To examine in situ expression profiles of SLCO transporters in prostate tissue and to investigate the associations of the expression profiles with prostate cancer aggressiveness in AA and EA.
3. To characterize the functions of candidate SLCO transporters in androgen uptake and to evaluate the biological effects on AR signaling in human prostate cancer cell lines.

Role: Co-Investigator (Pathologist)
Overlap: None

No cost extension
Title: The Prognostic Role of Circulating Tumor Cells in Clinically Localized Clear Cell Renal Cell Carcinoma (57-2626-01)
Time Commitment: 0.24 Calendar Months (PI, Kauffman)
Supporting Agency: Roswell Park Alliance Foundation
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Judith Epstein
Performance Period: 09/24/2015 – 09/23/2018 (nce)
Funding: $50,000
Brief description of project's goals: In this exploratory proposal, we intend to examine the prognostic value of AR heterogeneity in a case-nested pilot study of African American patients with AR mutation and sporadic prostate cancer.
Specific Aims:
1. To validate a multimarker 'cocktail' strategy and image-based flow-cytometry platform for detection and enumeration of CTC in ccRCC patients.
2. To determine the relation of perioperative CTC levels to ccRCC tumor histopathology and metastatic relapse.

Role: Co-Investigator (Pathologist)
Overlap: None

Completed
Title: Metabotropic Glutamate Receptor 1 in African American Prostate Cancer (1R21CA183892-01)
Time Commitment: 0.30 Calendar Months (PI, Koochekpour)
Supporting Agency: NCI
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Elizabeth Woodhouse
Performance Period: 04/01/2014 – 03/31/2017
Funding: $184,658

Brief description of project's goals: The objective of this project is to investigate the expression of metabotropic glutamate receptor and its association with clinical progression in a large cohort of African Americans with PCa.
Specific Aims:
1. To determine the association between tissue expression of GRM1 and clinicohistopathological predictors or prognosticators of PCa progression or aggressiveness in AAs.
2. To determine the association between GRM1 expression levels and invasive and metastatic phenotypes in AA-PCa cells. Data generated from this exploratory study will define biological and/or clinicohistopathological significance or relevance of GRM1 expression in AA-PCa and may prove useful in discriminating clinically or biologically aggressive tumors from indolent (non-aggressive) tumors and minimizing PCa disparity in AAs.

Role: Co-Investigator (Pathologist)
Overlap: None

Elena Pop

No cost extension
Title: Genetic variations in SLCO transporter genes contributing to racial disparity in aggressiveness of prostate cancer (Wu)
Time Commitments: 0.60 calendar months
Supporting Agency: CDMRP (W81XWH-14-1-0453)
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Mirlene Desir, Grant Specialist, Assistance Branch 4, MCMR-AAA-AD, USAMRAA, 820 Chandler Street, Fort Detrick, MD 21702, phone: 301-619-7733, fax: 301-619-9656, mirlene.desir@civ@mail.mil
Performance Period: 09/15/2014-09/14/2017
Level of funding: $764,100
Brief description of project's goals: The objective seeks to address how transporter-regulated androgen availability to cancer cells may contribute to the difference in prostate cancer aggressiveness between African American (AA) and European American (EA) men. The hypothesis is: Genetic variations in solute carrier family of organic anion transporting peptides (SLCO) androgen transporter genes and expression profiles of SLCO androgen transporters in prostate tissue are associated with aggressiveness of prostate cancer, and contribute to racial differences in prostate cancer aggressiveness.
List of specific aims:
Aim 1. Examine genetic variations in SLCO transporters genes and to investigate the associations of the variations with prostate cancer aggressiveness in AA and EA.
Aim 2. Examine *in situ* expression profiles of SLCO transporters in prostate tissue and to investigate the associations of the expression profiles with prostate cancer aggressiveness in AA and EA.
Aim 3. Characterize the functions of candidate SLCO transporters in androgen uptake and to evaluate the biological effects on AR signaling in human prostate cancer cell lines.
Overlap: None

No cost extension

Title: Deprive prostate cancer of DHEAS to prevent castration-recurrent prostate cancer (Wu)
Time Commitments: 1.80 calendar months
Supporting Agency: NIH/NCI 1R21CA191895-01
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Viviana Knowles, 9609 Medical Center Drive, West Tower, Bethesda, MD 20892, phone: 240-276-5157, viviana.knowles@nih.gov
Performance Period: 09/17/2014-08/31/2017 (NCE)
Level of Funding: $466,950
Brief description of project's goals: This research seeks to address the racial differences in prostate cancer aggressiveness from a biological perspective.
List of specific aims:
Aim 1. Characterize the expression of STS and potential STS regulators in CRPC
Aim 2. Evaluate the value of targeting DHEAS usage by prostate cancer cells to prevent post-castration tumor growth
Aim 3. Identify DHEAS uptake mechanisms
Overlap: None

Moved to current
Title: Understanding the Relative Contributions of and Critical Enzymes for the 3 Pathways for Intracrine Metabolism (Mohler)
Time Commitments: 0.90 calendar months
Supporting Agency: DoD Idea Development Award
Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Tom Winter Grants Specialist, Assistance Agreements Branch 4 U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick, MD 21702 Cell 240-357-1590 Office 301-619-2665 Thomas.s.winter2.civ@mail.mil
Performance Period: 09/30/2016 – 09/29/2019
Level of funding: $660,315
Brief description of project's goals:
Better understanding of intracrine androgen metabolism during ADT will identify new targets to reduce T and DHT production.
List of specific aims:
1. Determine the relative use of the 3 pathways for intracrine androgen metabolism in vitro, in vivo and in clinical specimens.
2. Identify the principal androgen metabolism enzymes (ie. 3a-oxidoreductases) responsible for primary backdoor DHT synthesis from androstanediol.
3. Determine the requirements for SRD5A1-3 in the frontdoor pathway of DHT synthesis from T and its precursors and of SRD5A1 and HSD17B3 in the secondary backdoor pathway of DHT synthesis from androstanedione.

Overlap: None

8. Special Reporting Requirements

This grant funds a Synergistic Idea Development Award in collaboration with Dr. David Goodrich (Partnering PI, Roswell Park Cancer Institute). Dr. Goodrich will be submitting an independent annual report describing his aspect of the work.