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TITLE: Integrative Molecular Profiling of Whole Urine in African American Men with Aggressive Prostate Cancer

PRINCIPAL INVESTIGATOR: Aaron M. Udager, M.D., Ph.D.

CONTRACTING ORGANIZATION: University of Michigan, Ann Arbor, MI

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6. AUTHOR(S)

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5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Regents of the University of Michigan
3003 S. State Street
Ann Arbor, MI 48109

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

African-American men have a high incidence of prostate cancer and experience higher mortality rates relative to other racial and ethnic populations. Early detection of aggressive disease is critical to reducing death and morbidity related to prostate cancer and, as such, is a major focus for multi-disciplinary efforts to reduce racial and ethnic health disparities. Recently, our group has developed and validated a new and innovative next-generation sequencing approach that is able to detect prostate cancer-associated germline variants, somatic alterations, and RNA biomarkers in urine, and we have demonstrated that this next-generation sequencing method is significantly better at identifying men with aggressive prostate cancer than serum PSA or other urine-based molecular tests. Thus, the goal of this proposed research is to determine whether a novel integrative NGS approach to urine-based prostate cancer testing can augment early detection of African-American men with aggressive disease.

15. SUBJECT TERMS

Next-generation sequencing, transcriptomic signatures, gene fusions, expressed somatic alterations, germline variants, genomic risk score

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1. INTRODUCTION:

African-American men have a high incidence of prostate cancer and experience higher mortality rates relative to other racial and ethnic populations. Early detection of aggressive disease is critical to reducing death and morbidity related to prostate cancer and, as such, is a major focus for multi-disciplinary efforts to reduce racial and ethnic health disparities. Recently, our group has developed and validated a new and innovative next-generation sequencing approach that is able to detect prostate cancer-associated germline variants, somatic alterations, and RNA biomarkers in urine, and we have demonstrated that this next-generation sequencing method is significantly better at identifying men with aggressive prostate cancer than serum PSA or other urine-based molecular tests. Thus, the goal of this proposed research is to determine whether a novel integrative NGS approach to urine-based prostate cancer testing can augment early detection of African-American men with aggressive disease.

2. KEYWORDS:

Next-generation sequencing (NGS), transcriptomic signatures, gene fusions, expressed somatic alterations, germline variants, genomic risk score

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Aim 1: Evaluate the performance of an established whole urine NGS assay for the detection of high-grade prostate cancer in African-American men.

Aim 2. Validate a high-throughput NGS-based germline genomic profiling method for whole urine and determine its impact on the detection of high-grade prostate cancer in African-American men.

What was accomplished under these goals?

Aim 1: Evaluate the performance of an established whole urine NGS assay for the detection of high-grade prostate cancer in African-American men.

Obtain local IRB approval (months 1-3)

Study approval from the University of Michigan Institutional Review Board (IRB) was obtained (task 75% complete).

Obtain HRPO approval (months 4-6)

Study approval from the Department of Defense Human Research Protection Office (HRPO) was obtained for the University of Michigan portion of the project (task 75% complete).

Identify and collect urine specimens from Caucasian and AA men (N = 480) (months 7-18)

Prospectively maintained prostate cancer urine biospecimen databases were queried, and 240 study specimens from Caucasian men were retrospectively identified (task 40% complete).

Extract DNA and RNA from urine specimens (months 15-20)

Nothing to report.

Profile extracted RNA (months 19-24)

Nothing to report.

Analyze RNA sequencing data (months 25-30)

Nothing to report.

Compare RNA sequencing data between Caucasian and AA men (months 31-36)

Nothing to report.

Aim 2. Validate a high-throughput NGS-based germline genomic profiling method for whole urine and determine its impact on the detection of high-grade prostate cancer in African-American men.

Design targeted NGS panel to detect germline variants (months 1-6)

The Ion AmpliSeq Designer tool was utilized to design a targeted NGS panel to detect known prostate cancer-associated single nucleotide polymorphisms (SNPs), additional validated prostate cancer-associated SNPs in African-American men, and the entire coding regions of commonly mutated DNA repair genes (task 100% complete).

Identify matched blood or tissue specimens from Caucasian and AA men (N = 100) (months 7-18)

Prospectively maintained prostate cancer urine biospecimen databases were queried, and 50 study specimens from Caucasian men were retrospectively identified (task 40% complete).

Extract DNA from blood or tissue specimens (months 15-20)

Nothing to report.

Profile extracted DNA for germline variants (months 19-24)

Nothing to report.

Analyze DNA sequencing data from matched blood and urine specimens (months 25-32)

Nothing to report.

Compare urine DNA sequencing data between Caucasian and AA men (months 31-36)

Nothing to report.

What opportunities for training and professional development has the project provided?

Nothing to report.

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

During the next reporting period, we plan to finalize IRB approval at Wayne State University and, thereafter, HRPO approval for the entire project. We will complete identification and collection of urine, blood, and/or tissue specimens from Caucasian and African-American men. After DNA and RNA extraction from urine, blood, and/or tissue specimens, we will begin to profile RNA and DNA using our integrative NGS approach.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to report.

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

University of Michigan IRB and HRPO study approval took longer than expected, and we are still working to finalize IRB approval at Wayne State University. In the meantime, we were able to design the targeted NGS panel for germline variant detection and beging to identify study specimens from clinical databases.

Changes that had a significant impact on expenditures

Due to longer than expected time for IRB and HRPO study approval and continuing impacts of the COVID-19 pandemic, we have delayed hiring a research technician to work on the study; however, we plan to hire someone for this position in the next reporting period.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report.

6. PRODUCTS:

Publications, conference papers, and presentations

Nothing to report.

Website(s) or other Internet site(s)

Nothing to report.

Technologies or techniques

Nothing to report.

Inventions, patent applications, and/or licenses

Nothing to report.

Other Products

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Aaron Udager
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	0000-0002-8254-5404
Nearest Person Month Worked:	1
Contribution to Project:	Dr. Udager has led all aspects of the study, including: obtaining approval from the local IRB and Department of Defense HRPO; and, identifying study cases.
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?

Please see the Appendices for updated Other Support documents for Drs. Udager, Salami, and Powell. New and ended support is indicated for each investigator.

What other organizations were involved as partners?

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

N/A

QUAD CHARTS:

N/A

9. APPENDICES:

Updated Other Support for Dr. Aaron Udager
Updated Other Support for Dr. Simpa Salami
Updated Other Support for Dr. Isaac Powell

OTHER SUPPORT

UDAGER, AARON

CURRENT

W81XWH-19-1-0407 Udager (PI) 3.66 CM
Department of Defense total award amount 9/2019-8/2023
Tom Winter
Grants Management Specialist
sidney.t.winter.civ@mail.mil

Intratumoral heterogeneity of aggressive molecular biomarkers in lethal primary prostate cancer
Goal(s): The goal of this project is to utilize immunohistochemistry, in situ hybridization, and next-generation sequencing to establish the frequency and pattern of intratumoral biomarker heterogeneity in lethal prostate cancer and delineate the spectrum of associated molecular alterations in these spatially-distinct areas. Specific Aims: Aim 1. Determine the incidence and pattern of spatial intratumoral heterogeneity of aggressive molecular biomarkers in lethal primary prostate cancer. Aim 2. Compare the frequency and spectrum of genomic alterations across spatially-distinct areas of lethal prostate cancer with intratumoral biomarker heterogeneity. Aim 3. Evaluate transcriptomic alterations that accompany intratumoral biomarker heterogeneity in lethal prostate cancer.
No overlap with this project

W81XWH-20-1-0405 Alumkal (PI) 0.60 CM (YR3)
Department of Defense total award amount 9/2020-8/2023
Tom Winter
Grants Management Specialist
sidney.t.winter.civ@mail.mil

Targeting LSD1 in Neuroendocrine Prostate Cancer
Goal(s): The objectives of this proposal are to clarify mechanisms by which LSD1 promotes NEPC phenotypes and the anti-tumor activity of LSD1 inhibition so we may develop a new treatment strategy for NEPC patients and identify key companion biomarkers that indicate suppression of LSD1's critical function. Specific Aims: Aim 1: Identify an LSD1 inhibitor gene response signature and determine mechanisms by which LSD1 blocks gene expression in NEPC. Aim 2: Treat NEPC tumors in vivo with LSD1 inhibition and determine effect on tumor growth and differentiation. Aim 3: Determine mechanisms by which the LSD1+8a splice variant functions in NEPC.
Role: Co-Investigator
No overlap with this project

R37 CA222829 Xu (PI) 0.12 CM
NIH/NCI 1/2019-12/2023
Jennifer Meininger
Grants Management Specialist
jennifer.meininger@mail.nih.gov

Real time fine needle assessment of architectural heterogeneity in prostate cancer
Goal(s): The specific aims include: 1) examining label-free PCa aggressiveness assessments in ex vivo human tissues; and 2) examining contrast-enhanced PCa aggressiveness assessments in mouse models in vivo. Specific Aims: Aim 1. Test an all-optical fine needle PA probe for identifying aggressive PCa in biopsy cores. Aim 2. Practice and examine the PA pre-biopsy via simulated biopsy procedures with ex vivo human prostates. Aim 3.

Examine the correlation between the PA measurements and the pathology of the PCa via an observational human subjects study with 67 patients
Role: Co-Investigator
No overlap with this project

U01 CA232931 Hadjiyski/Alva (MPI) 0.24 CM
NIH/NCI 5/2019-4/2024
Jennifer Meininger
Grants Management Specialist
jennifer.meininger@mail.nih.gov

Biomarker-based tools for treatment response decision support of bladder cancer
Goal(s): The goal of this project is to validate the effectiveness of CDSS-T as an aid to the radiologists and the oncologists in assessment of bladder cancer change as a result of treatment through pilot clinical trials. Specific Aims: Aim 1. To perform a preparatory clinical trial with the clinicians at UM, which will simulate the real prospective clinical trial. Aim 2. To deploy the QIBC and CDSS-T tools at the three collaborating clinical sites. Aim 3. To use the QIBC and CDSS-T tools at the three clinical sites in the pilot clinical trial. Aim 4. To compare the clinicians' performance results with and without the QIBC and CDSST tools in the pilot clinical trial.
Role: Co-Investigator
No overlap with this project

P50 CA186786 Chinnaiyan/Palapattu/Heath (MPI) 0.60 CM
NIH/NCI 9/2019-8/2024
Jennifer Meininger
Grants Management Specialist
jennifer.meininger@mail.nih.gov

Michigan Prostate SPORE
Goal(s): The overall goal of this grant is the development of new approaches to the prevention, early detection, diagnosis and treatment of prostate cancer through translational research. Specific Aims: Project 1: Targeting Metastatic Prostate Cancer Patients with Biallelic Loss of CDK12. Project 2: Integrating a Novel MiPS-Based Next-Generation Sequencing Urine Assay for the Early Detection of Unfavorable Risk Prostate Cancer. Project 3: Exploring Ablation of the Androgen Receptor as a Therapeutic Approach for Castration-Resistant Prostate Cancer. Project 4: Targeting LSD1 in Neuroendocrine Prostate Cancer.
Role: Co-Investigator (Projects 2 and 4)
No overlap with this project

R01 CA186786 Alumkal (PI) 0.60 CM (YR2-5)
NIH/NCI 9/2020-8/2025
Elizabeth Bui
Grants Management Specialist
mimi.bui@mail.nih.gov

Targeting Prostate Cancer Lineage Plasticity with BET Bromodomain Inhibition
Goal(s): The goal of this project is to understand molecular mechanisms by which BET bromodomain proteins promote neuroendocrine prostate cancer progression so we can target those mechanisms. Specific Aims: Aim 1: Determine mechanisms by which E2F1 and BRD4 cooperate to promote expression of a t-NEPC lineage plasticity survival program. Aim 2: Treat t-NEPC patient tumors implanted in mice with BETi or BETd and measure anti-tumor activity and NEPC differentiation. Aim 3: Prevent castration-induced t-NEPC lineage switch with BETi or BETd using a patient tumor model of t-NEPC lineage switch implanted in mice.
Role: Co-Investigator
No overlap with this project

W81XWH-21-1-0238 | Udager (PI) | 1.20 CM
Department of Defense | total award amount | 6/2021-5/2024
Tom Winter
Grants Management Specialist
sidney.t.winter.civ@mail.mil

Integrative molecular profiling of whole urine in African-American men with aggressive prostate cancer
Goal(s): The goals of this project are: 1) evaluate the performance of a novel whole urine NGS assay for the detection of high-grade prostate cancer in African-American men; and, 2) validate and apply a high-throughput NGS genomic profiling method for whole urine to identify African-American men with aggressive prostate cancer. Specific Aims: Aim 1. Evaluate the performance of an established whole urine NGS assay for the detection of highgrade prostate cancer in African-American men. Aim 2. Validate a high-throughput NGS-based germline genomic profiling method for whole urine and determine its impact on the detection of high-grade prostate cancer in African-American men.
This project

W81XWH-21-1-0663 | Udager (PI) | 0.9 CM
Department of Defense | total award amount | 9/2021-8/2022
Judi Sgambato
judi.a.sgambato.civ@mail.mil

Targeting FOXA1-Mediated Epigenetic Reprogramming in Aggressive Salivary Gland Cancer
Goal(s): The goal of this proposed research is to characterize the FOXA1 cistrome in salivary duct carcinoma and determine the efficacy of the LSD1 inhibitor GSK2879552 for disrupting FOXA1-mediated epigenetic reprogramming and tumor growth in ex vivo organoid cultures. Specific Aims: Aim 1. Define the FOXA1 cistrome in salivary duct carcinoma. Aim 2. Determine molecular and cellular responses to LSD1 inhibition in salivary duct carcinoma.
No overlap with this project
****New support****

NCCN Pfizer/Astellas Enzalutamide | Alumkal (PI) | 0.60 CM (YR1)
award amount | 10/2021-9/2024

Clarifying Tumor and Microenvironmental Determinants of Enzalutamide Resistance
Goal(s): To provide positive impact by identifying cellular and molecular signatures of distinct cellular populations driving invasive progression. These findings could then lead to examination of candidate gene networks that will serve as the basis for biological function, potential biomarker identification and new therapeutic targets that are needed for bladder cancer patients who have been diagnosed with or have relapsed with muscle invasive disease. Specific Aims: Specific aim 1. To determine the transcriptomic signature of tumor cells and adjacent stroma isolated from the invasive interface of MIBC. Aim 2: To determine the cellular and transcriptomic signature of infiltrating immune cells in the invasive microenvironment of human bladder cancer. Aim 3: To analyze transcriptomic signatures from tumor, stromal and immune populations to identify gene regulatory programs unique to the invasive micro-environment of MIBC.
Role: Co-Investigator
No overlap with this project
****New support****

R21 CA259763 | Day (PI) | 0.40 CM
NIH/NCI | | 12/2021-11/2023
Sudhir B. Kondapaka
kondapas@mail.nih.gov

Delineation of tumor, stromal and immune transcriptomes at the infiltrating interface of muscle invasive bladder cancer
Goal(s): To provide positive impact by identifying cellular and molecular signatures of distinct cellular populations driving invasive progression. These findings could then lead to examination of candidate gene networks that will serve as the basis for biological function, potential biomarker identification and new therapeutic targets that are needed for bladder cancer patients who have been diagnosed with or have relapsed with muscle invasive disease. Specific Aims: Specific aim 1. To determine the transcriptomic signature of tumor cells and adjacent stroma isolated from the invasive interface of MIBC. Aim 2: To determine the cellular and transcriptomic signature of infiltrating immune cells in the invasive microenvironment of human bladder cancer. Aim 3: To analyze transcriptomic signatures from tumor, stromal and immune populations to identify gene regulatory programs unique to the invasive micro-environment of MIBC.
Role: Co-Investigator
No overlap with this project
****New support****

PENDING

R01 Rege (PI) 0.60 CM
NIH/NCI 9/2022-8/2027
Grant Information
grantsinfo@nih.gov

Adrenal genetic causes of cortisol excess
Goal(s): Specific Aim 1 will define novel genetic causes and the prevalence of cortisol-driver somatic mutations in CPA as well as the role of molecular mechanisms leading to autonomous adrenal cortisol production. Specific Aim 2 will develop biomarker panels capable of diagnosing and subtyping adrenal CS.
Role: Co-Investigator
No overlap with this project

R01 Palmbos (PI) 0.60 CM
NIH/NCI 7/2022-6/2027
Grant Information
grantsinfo@nih.gov

Mechanism and Therapeutic Targeting of TRIM29-mediated Invasion in Bladder Cancer
Goal(s): The central hypothesis will be tested in the following specific aims: 1) To determine the mechanism of TRIM29 regulation of intermediate filament and focal adhesion in invasive progression. 2) To determine the genetic requirements for TRIM29-mediated invasive progression in preclinical models. 3) To develop and evaluate novel therapeutic strategies to target TRIM29-mediated invasion in bladder cancer.
Role: Co-Investigator
No overlap with this project

P01 Balter (PI) 0.84 CM
NIH/NCI 9/2022-8/2027
Grant Information
grantsinfo@nih.gov

Individualized Response Adaptive Radiation Therapy
Goal(s): Project 1, Individualized Response Adaptive RT for Hepatocellular Carcinoma (HCC), will use biological imaging and blood biomarkers obtained before and during the course of treatment together with advanced modeling and utility optimization to individualize RT for patients with poor prognosis HCC. Project 2, Individualized Response Adaptive RT for Oropharyngeal Squamous Cell Cancer (OPSCC), will use biological

imaging and blood biomarkers obtained before and during the course of treatment together with advanced modeling to individualize RT for patients with high risk (with or without oligometastases) p16 positive OPSCC. Project 3, Advanced MRI for Individualized Response Adaptive RT, will investigate improved imaging of tissue microstructure as a biomarker of response to therapy, with the goal of applying this new imaging approach to Projects 1 and 2 in the later years of the application. Project 3 will also develop increased sampling efficiency of imaging, and motion-corrected image reconstruction and biomarker mapping for patients with HCC and OPSCC. These projects will be supported by four cores supporting: 1) Administration; 2) Quantitative Imaging (Core A); 3) In Vivo Biomarkers (Core B); and 4) Statistics and Advanced Treatment Planning (Core C).
Role: Co-Investigator
No overlap with this project

P30 CA046592 Fearon (PI) 0.36 CM
NIH/NCI 6/2023-5/2028
Grant Information
grantsinfo@nih.gov

University of Michigan Rogel Cancer Center Support Grant 2023-2028
Goal(s): The Center provides an organizational framework to promote transdisciplinary cancer research through the development of well-funded basic, translational, clinical, and prevention programs and the development of shared resources. The Cancer Center's six Research Programs includes three basic programs – Signaling and Tumor Microenvironment; Cancer Genetics, and Developmental Therapeutics; one basic/clinical/translational program - Cancer Hematopoiesis and Immunology; one clinical/translational program - Translational and Clinical Research; and Cancer Control and Population Science. Rogel supports 13 Shared Resources and two developing Shared Resources: Cancer Data Science; Cell and Tissue Imaging; Experimental Irradiation; Flow Cytometry; Health Communications; Immune Monitoring; Pharmacokinetics; Preclinical Molecular Imaging; Structure and Drug Screening; Tissue and Molecular Pathology; Transgenic Animal Models; Proteomics; Single Cell Spatial Analysis; Epigenetics and Epigenomics (developing); and Liquid Biopsy (developing).
Role: Co-Investigator
No overlap with this project

PREVIOUS

None

OVERLAP FOR ALL CURRENT AND PENDING GRANTS

None

OTHER SUPPORT

SALAMI, SIMPA

CURRENT

Joint Institute for Translational and Clinical Research Amy Huang Director yanhuang@umich.edu	Salami/Palapattu/Morgan/Gong (PI) total award amount	0.60 CM 10/2017-6/2023

Comprehensive Molecular Profiling of Renal Cell Carcinoma
Goal(s): The goal of this project is to characterize the genomic landscape of clear cell renal cell carcinoma and identify predictive biomarkers of recurrence.
No overlap with this project

W81XWH-18-1-0219 Department of Defense Grants.Gov Customer Support support@grants.gov	Salami (PI) total award amount	4.80 CM 10/2018-09/2022

Radiogenomic Characterization of Prostate Cancer: Distinguishing Aggressive from Indolent Disease
Goal(s): The successful completion of the proposed project will improve our understanding of the molecular basis of PCa visibility on mpMRI and guide treatment decisions based on mpMRI findings. This project will also identify an optimal paradigm for utilizing mpMRI, tissue-based and urinary biomarkers to reliably and accurately identify men with aggressive PCa, thus ensuring timely and appropriate treatment. Additionally, the results from the proposed research may lead to the rapid development of new biomarkers, imaging and therapeutic targets for aggressive disease.
No overlap with this project

P50 CA186786 NIH/NCI Jennifer Meininger Jennifer.meininger@mail.nih.gov	Chinnaiyan (PI)	1.80 CM 9/2019-8/2024

Michigan Prostate SPORE
Goal(s): The overall goal of this grant is the development of new approaches to the prevention, early detection, diagnosis and treatment of prostate cancer through translational research.
Role: Co-Lead (Project 2)
No overlap with this project

PENDING

None

PREVIOUS

Urology Care Foundation — Salami (PI) — 07/2016-6/2017
American Urological Association
info@UrologyCareFoundation.org

Molecular Profiling of Targeted Biopsy Tissue to Predict Progression on Active Surveillance
Goal(s): The goal of this proposal is to evaluate the possibility of using MRI/US fusion biopsy to serially track clones of cancer and determine the molecular profile of Gleason 6 cancers that are destined to progress.

P50 CA186786 — Chinnaiyan (PI) — 1/2017-12/2018
NIH/NCI
Jennifer Meininger
Grants Management Specialist
Jennifer.meininger@mail.nih.gov

Genomic Profiling to Characterize the Biologically Dominant Nodule in Multifocal Prostate Cancer with Lymph Node Metastasis
Goal(s): To characterize the biologically dominant nodule in multifocal PCa with lymph node metastasis and evaluate the prognostic accuracy of Oncotype DX™, Prolaris™ and Decipher™ scores in predicting lymph node metastasis
Role: Recipient of Michigan Prostate SPORE Career Enhancement Program Sub-Award

16YOUN17 — Salami (PI) — 7/2016-6/2019
Howard Soule
hsoule@pcf.org

Molecular Characterization of the Biologically Dominant Nodule in Multifocal Prostate Cancer with N1 Disease
Goal(s): The successful completion of our study will provide novel insights into the biology of multifocal prostate cancer. A better understanding of the biologically dominant nodule in multifocal disease holds promise for providing more accurate prognostic information for men with advanced disease. Further, our findings may lead to the identification of prioritized genes that can be targeted for therapy in patients with prostate cancer and LN metastasis. And finally, our study will compare the accuracy of existing expression-based genomic tests to predict LN metastasis in multifocal prostate cancer.

Massachusetts/Partners Healthcare — Salami (PI) — 10/2019-6/2021
Prostate Cancer Research Program
Jaclyn Rescigno
jrescigno@partners.org

Prostate Cancer Research Program, Integrated with Education and Awareness
Goal(s): This study looking at the role of MRI and genetic testing in prostate cancer care. All MRIs are performed at BWH. Samples will then be sent to the University of Michigan where they will run the assays and perform Genetic testing. The University of Michigan will look at all three platforms (Decipher, Oncotype, and Polaris) and identify the usefulness of MRIs. Additionally, will look at the targeted lesion on MRI and compare to the standard 12 core lesion.
****Support ended****

OVERLAP

There is no scientific or budgetary overlap.

OTHER SUPPORT

POWELL, ISAAC

CURRENT

Title: Michigan Prostate SPORE, P50CA186786
PI: Arul Chinnaiyan, Ganesh Palapattu, Elizabeth Heath
Percentage of applicant's time: 4.5%
Supporting agency: NCI/NIH
Performance period: 09/03/2019-08/31/2024
Amount of funding:
Brief description of the project's goals and List of the specific aims: The Prostate SPORE supports an interactive group of basic and clinical investigators in a translational research program that has led to major discoveries in the diagnosis, prevention and treatment of prostate cancer. This application consists of four multidisciplinary projects: Project 1: Targeting Metastatic Prostate Cancer Patients with Biallelic Loss of CDK12; Project 2: Integrating a Novel MiPS-Based Next-Generation Sequencing Urine Assay for the Early Detection of Unfavorable Risk Prostate Cancer; Project 3: Exploring Ablation of the Androgen Receptor as a Therapeutic Approach for Castration-Resistant Prostate Cancer; Project 4: Targeting Autophagy in the Treatment of Metastatic Prostate Cancer. These projects are complemented by ongoing, successful Career Development and Developmental Research Programs. The projects and programs are supported by a strong ongoing institutional commitment of money and space as well as three cores: Administration, Biostatistics, and Biospecimen/Pathology (previously Tissue/Informatics). The Prostate SPORE program continues to place premiums on rigorous scientific review of its translational research programs, pairing of basic and clinical investigators, drawing on expertise of scientists from within and from outside the prostate cancer field, and utilizing flexibility to fund promising new research approaches.
Role: Co-Investigator (Project 2)
No overlap with this project

PENDING

None

PREVIOUS

Title: Prostate Cancer Susceptibility: The ICPCG Study (U01CA089600)
PI: Stephen Thibodeau
Supporting Agency: NIH/NCI
Performance Period: 9/30/2002-8/31/2018
Brief description of the project's goals: First, we will identify candidate PC susceptibility genes from whole-exome sequencing data derived from 763 familial cases (from 458 independent families) and prioritize those genes with variants that are most damaging (e.g., nonsense, frame-shift, splice site variants and selected other variants), co-segregate with PC within the tested families, and are rare in the general population (Aim 1). Second, we will further analyze the top 1000 candidate genes identified in Aim 1 by re-sequencing the coding regions in an independent set of 500 hereditary PC cases and 500 controls, looking specifically for genes with multiple damaging variants and variants that are found to be significantly more frequent among our cases compared to control data (Aim 2). Third, we will identify the most likely PC susceptibility loci by end-to-end re-sequencing of the top 100 genes identified in Aim 2 in an independent set of 1000 hereditary PC cases and 1000 controls (Aim 3). Our long-term goal is to identify genes associated with increased PC risk and aggressiveness that may be used to better screen men for PC and reduce the significant morbidity and mortality associated with this disease.
Role: Co-Investigator

Title: Prostate Cancer Research Program, Clinical Consortium Research Site Award, W81XWH-17-2-0022
PI: Elisabeth Heath
Supporting agency: Department of Defense
Performance period: 09/30/17-09/29/21
Brief description of the project's goals: To create a clinical trials instrument dedicated to early phase prostate cancer studies.
Specific aims: The types of clinical trials that we intend to propose to the Consortium have emerged from our focus on developing effective treatments and addressing mechanisms of resistance in men with high-risk or metastatic prostate cancer. For example, we have expertise in clinical trials that (1) evaluate novel agents as a single or combination therapy or modality and (2) evaluate the impact of therapy in African American men by assessing biologic factors that influence their response to therapy, such as inflammation, genetic makeup, and immune responsiveness. We will design prospective studies of racial differences in disease type, physiologic factors, and response to treatment, aiming at more precise personalized medicine.
Role: Co-Investigator
****Support ended****

OVERLAP

There is no scientific or budgetary overlap.