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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

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Regents of the University of Michigan
3003 S. State Street
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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 and Wayne State University Institutional Review Boards (IRB) was obtained (task 100% 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)

DNA and RNA was extracted from 50 urine specimens (task 10% complete).

Profile extracted RNA (months 19-24)

Targeted next-generation RNA sequencing (RNAseq) data was generated for 50 urine specimens (task 10% complete).

Analyze RNA sequencing data (months 25-30)

After standard quality control (QC) filtering, raw RNAseq data was normalized and analyzed as described previously (PMID: 33812851). ETS gene fusion (i.e., *TMPRSS2-ERG*, etc.) were identified in several samples (see example in Figure 1). The presence of high-grade prostate cancer [i.e., Gleason score 4 + 3 = 7 (Grade Group 3)] was predicted in approximately half of the samples and was positively associated with high expression of *ERG*, *HOXC6*, *PCA3*, and *SChLAP1* (see Figure 2 below).

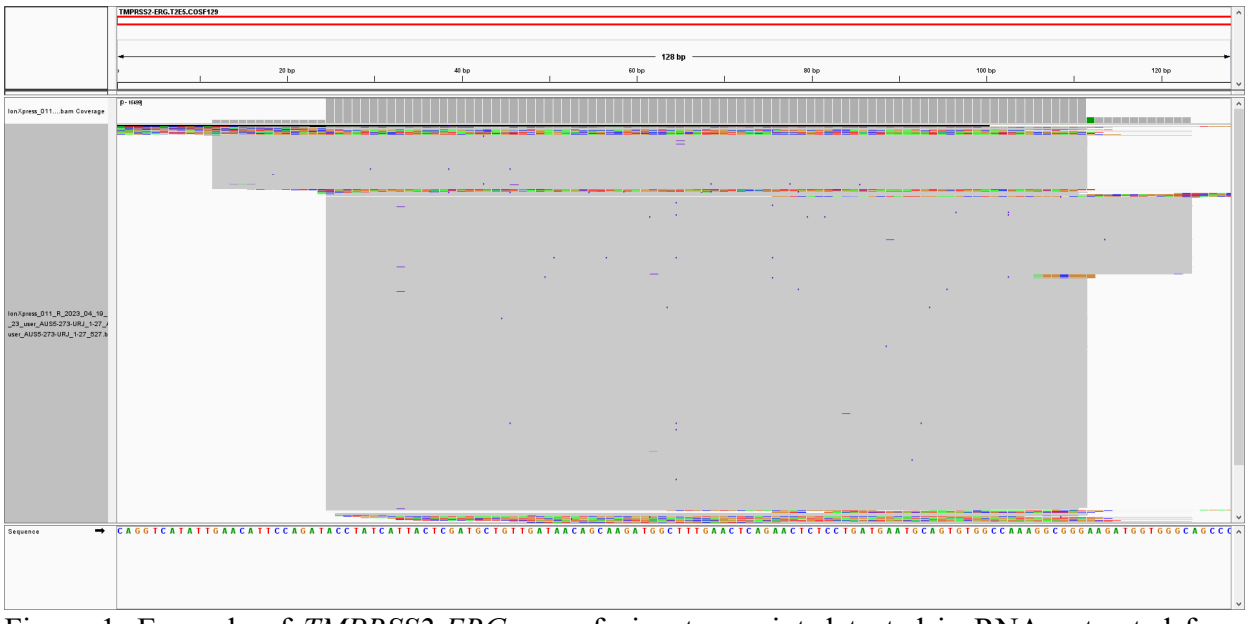

Figure 1. Example of *TMPRSS2-ERG* gene fusion transcript detected in RNA extracted from whole urine using targeted RNAseq.

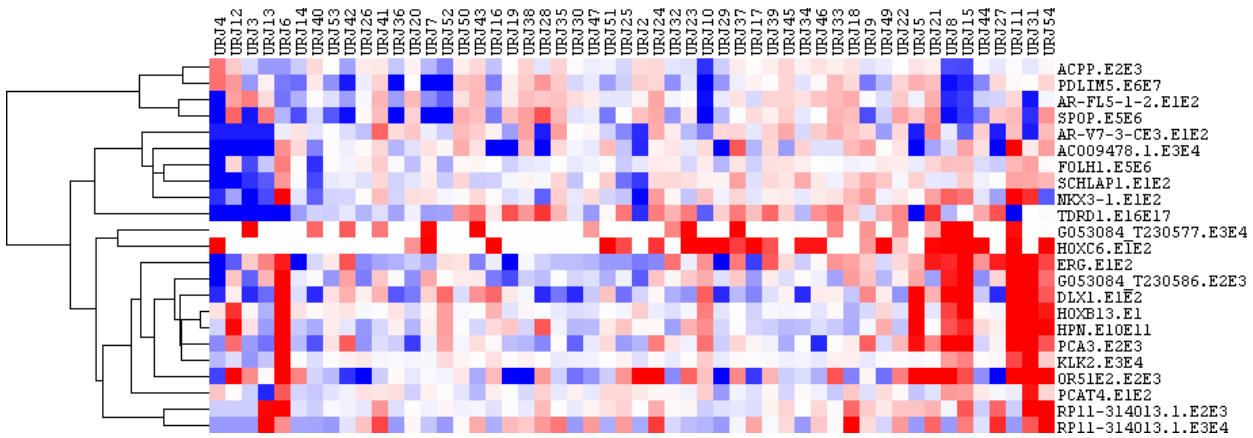

Figure 2. Heatmap of expression estimates derived from urine targeted RNAseq data ordered from left to right by likelihood of high-grade prostate cancer highlights significant positive correlation with several transcripts, including *ERG*, *HOXC6*, *PCA3*, and *SChLAP1* (adjusted p-value < 0.05).

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)

DNA was extracted from 50 blood specimens (task 50% complete).

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

Targeted next-generation DNA sequencing (DNAseq) data was generated for 50 matched pairs of urine and blood specimens (task 10% complete).

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

After standard QC filtering, raw DNAseq data was aligned to the human genome and germline variants were detected and annotated using Ion Torrent Suite software and custom in-house bioinformatics pipelines. A variety of pathogenic germline variants were identified in blood specimens – including *ATM* frameshift/stopgain mutations, *BRCA1* frameshift/stopgain mutations, *BRCA2* frameshift/stopgain/splicing mutations, *BRIP1* frameshift mutations, *MLH1* stopgain mutation, *MSH2* frameshift mutation, *MSH6* stopgain mutation, *NBN* frameshift mutation, *PALB2* stopgain mutation, *PMS2* missense mutation, and *TP53* missense/stopgain mutations – which were also detected in matched urine specimens (see example in Figure 3). These results provide initial validation of the targeted NGS approach for germline variant detection.

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?

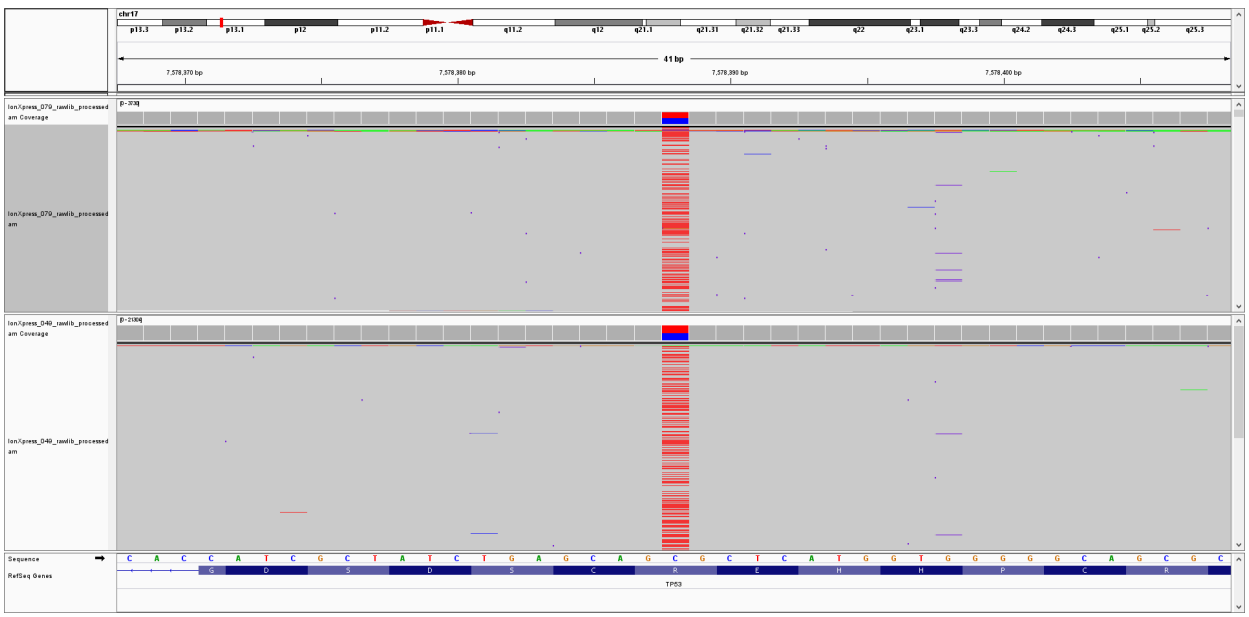

Figure 3. Example of a germline *TP53* missense mutation detected by targeted DNAseq in DNA extracted from a matched pair of blood (top) and urine (bottom) specimens.

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 HRPO approval for the Wayne State portion of the project. We will complete identification and collection of urine, blood, and/or tissue specimens from Caucasian and African-American men. After additional DNA and RNA extraction from urine, blood, and/or tissue specimens, we will continue 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

IRB approval at the University of Michigan and Wayne State University took longer than expected, but we are working to finalize HRPO approval for the Wayne State portion of the project. In the meantime, we designed and initially validated the targeted NGS panel for germline variant detection and have begun 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 delayed hiring a research technician to work on the study until the current 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

Name:	Chia-Jen Liu
Project Role:	Technician
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest Person Month Worked:	4
Contribution to Project:	Mr. Liu extracted DNA and RNA from urine and blood samples, prepared targeted NGS libraries, and performed sequencing of NGS libraries.
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.

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

Previous/Current/Pending SUPPORT

UDAGER, AARON

POSITIONS & SCIENTIFIC APPOINTMENTS

2021-	Co-Director, Liquid Biopsy Shared Resource, University of Michigan Rogel Cancer Center, Ann Arbor, MI
2021 -	Associate Director, Pathology Physician Scientist Training Pathway, University of Michigan Medical School, Ann Arbor, MI
2021 -	Clinical Associate Professor, University of Michigan Medical School, Ann Arbor, MI
2017-2021	Clinical Assistant Professor, University of Michigan Medical School, Ann Arbor, MI
2015-2016	Clinical Lecturer, University of Michigan Medical School, Ann Arbor, MI
2012-2015	Resident, Anatomic Pathology, Michigan Medicine, Ann Arbor, MI
2004-2012	Fellow, Medical Scientist Training Program, University of Michigan Medical School, Ann Arbor, MI

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

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 application

W81XWH-20-1-0405 — Alumkal (PI) — 0.48 CM (YR3)
Department of Defense — total award amount — 9/2020-8/2023
Tom Winter
Grants Management Specialist

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 application

R37 CA222829 Xu (PI) 0.24 CM
NIH/NCI 1/2019-12/2023
Jennifer Meininger
Grants Management Specialist

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 application

U01 CA232931 Hadjiyski/Alva (MPI) 0.24 CM
NIH/NCI 5/2019-4/2024
Jennifer Meininger
Grants Management Specialist j

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 application

P50 CA186786 Chinnaiyan/Palapattu/Heath (MPI) 0.36 CM
NIH/NCI 9/2019-8/2024
Jennifer Meininger
Grants Management Specialist

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 application

R01 CA186786 Alumkal (PI) 0.54 CM (YR2-5)
NIH/NCI 9/2020-8/2025
Elizabeth Bui

Grants Management Specialist

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 application

W81XWH-21-1-0238 Udager (PI) 1.08 CM
Department of Defense total award amount 6/2021-5/2024
Tom Winter
Grants Management Specialist

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.
No overlap with this application

W81XWH-21-1-0663 Udager (PI) 0.24 CM
Department of Defense total award amount 9/2021-8/2023 Robert Olekszak

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 application

R21 CA259763 Day (PI) 0.48 CM
NIH/NCI 12/2021-11/2023
Mimi Bui

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 application

AWD020538 Alumkal (PI) 0.48 CM (effort in yr 1 only)
NCCN Pfizer/Astellas 10/2021-9/30/2024 Nicole Kamienski

NCCN Pfizer/Astellas Enzalutamide: Clarifying Tumor and Microenvironmental Determinants of Enzalutamide Resistance
Goal(s): The goal of this proposal is to understand whether differences in the tumor architecture or tumor microenvironment are associated with the risk of enza resistance or NEPC development. We hypothesize that an integrative, multi-omics approach for studying tumor heterogeneity will not only allow us to gain insights into the biology of rare tumor cell populations and mechanisms that contribute to de novo enza resistance or NEPC development but also change the paradigm of using spatial profiling approaches to understand tumor architecture and how that architecture changes under the pressure of therapeutic agents. Completion of the proposed work is predicted to lead to better stratification of patients at greatest risk of specific enza resistance mechanisms so we may develop effective co-targeting strategies.
Role: Co-Investigator
No overlap with this application

R37 CA273138 Palmbos (PI) 0.36 CM
NIH/NCI 08/01/2022 – 07/31/2027
Mimi Bui

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. Aim 1 will utilize live cell imaging, 3D culture and live animal models of invasion. Aim 2 will leverage unique GEMM of bladder cancer to dissect the essential functions of TRIM29 in vivo. Aim 3 will use our multiple models to identify therapeutic strategies to target TRIM29-mediated invasion. This research is conceptually innovative in the characterization of a novel TRIM29-focal adhesion pathway of invasive progression and technically innovative in the development of novel bladder cancer murine models, advanced 3D tumor invasion assays and identification of novel therapeutic targeting strategies. The proposed research is significant because identification of the downstream drivers of TRIM29-mediated invasive progression will help to define the mechanism of bladder cancer invasive progression and allow identification of novel therapeutic targets and strategies to block these processes.
Role: Co-Investigator
No overlap with this application

PENDING GRANTS

Title: Biomarkers for AI Decision Support in Immunotherapy for Urinary Tract Cancer

Major Goals: The goal of this project is to develop and evaluate effective decision support tools that merge image-based and non-image-based biomarkers to assist radiologists and oncologists in assessment of cancer change as a result of immunotherapy treatment.
Status of Support: Pending
Project Number: R01 CA272781
PD/PI: Hadjiyski and Alva
Source of Support: NIH
Primary Place of Performance: University of Michigan
Project/Proposal Start and End Date: (MM/YYYY) (if available): 12/01/2023 – 11/30/2028
Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period. 1.08 CM

Title: Individualized Response Adaptive Radiation Therapy
Major Goals: In standard radiation therapy (RT), patients receive a dose that is chosen chiefly by the risk of causing toxicity in the most sensitive fraction of the population. We hypothesize that individualized, response adaptive RT that combines pre-treatment as well as intra-treatment markers predictive of both tumor response as well as normal tissue toxicities will produce superior tumor control, compared to standard dosing, with the same or lower risks of treatment-related toxicities. Furthermore, we hypothesize that advanced imaging and innovative statistical approaches will add additional biomarkers of response, further improving our ability to predict both response and toxicity. These hypotheses will be tested in 3 projects. 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). As the only group that has successfully adapted treatment to the individual patient response, we are uniquely positioned to carry out this work. We have chosen to focus on patients with poor prognosis HCC and high risk OPSCC, as these are common tumors that cause substantial morbidity and mortality, but the underlying hypothesis that adaptive RT is superior to standard population based RT is paradigm shifting and widely applicable.
Status of Support: Pending
Project Number: 23-PAF04121
PD/PI: Balter/Lawrence
Source of Support: NIH
Primary Place of Performance: University of Michigan
Project/Proposal Start and End Date: (MM/YYYY) (if available): 09/01/2023 – 08/31/2028
Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period. 0.84 CM

Title: University of Michigan Rogel Cancer Center Support Grant 2023-2028
Major Goals: The University of Michigan (U-M) Rogel Cancer Center (Rogel) has a distinguished history of scientific excellence, collaboration, and impact. Rogel's Mission is to reduce the burden of cancer and advance health equity through transdisciplinary collaboration in research, education, patient care and community outreach, and the Vision is to be a leader in prevention, early diagnosis, optimal treatment and care for all at risk of, or affected by, cancer. 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). The Center has 326 members representing 54 departments and nine schools and colleges across the University of Michigan.
Status of Support: Pending
Project Number: P30 CA046592
PD/PI: Fearon
Source of Support: NIH
Primary Place of Performance: University of Michigan
Project/Proposal Start and End Date: (MM/YYYY) (if available): 6/1/2023 – 5/31/2028
Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period. 0.36 CM

Title: Real time fine needle assessment of architectural heterogeneity in prostate cancer
Major Goals: The central hypothesis of this research is that a fine needle probe-based PA prostate pre-biopsy can guide prostate biopsy, improve the core yield, and decrease false negative rates. The objective of this study is to validate the correlation between the PA measurements and the PCa grading through an observational human subjects study. The specific aims include investigating the performance of the needle PA probe in accessing PCa using 1) biopsy tissue cores; 2) ex vivo human prostate samples procured through prostatectomy, and 3) in vivo human subjects. We will leverage the research team's extensive expertise in the clinical practice of PCa diagnosis and pathology as well as PA technology. The proposed prebiopsy procedure is designed within the framework of current clinical practice and is therefore highly translational. The knowledge gained in this study will prepare us to conduct a future clinical trial of the proposed diagnostic procedure in detecting PCa. Once successfully tested, the PA pre-biopsy will benefit PCa patients by facilitating accurately targeted needle biopsies for the early detection of clinically significant PCa..
Status of Support: Pending
Project Number: R37 CA222829
PD/PI: Xu
Source of Support: NIH
Primary Place of Performance: University of Michigan
Project/Proposal Start and End Date: (MM/YYYY) (if available): 1/1/2024 – 12/31/2025
Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period. 0.24 CM

Title: Defining the Biological Arc of Grade Group 1 Prostate Cancer
Major Goals: The long-term goal of this project is to further reduce the biological uncertainty associated with surveillance for favorable-risk prostate cancer. Although most men with favorable-risk disease are candidates for surveillance, its use varies widely and ranges from 20 to 90% across individual providers. A major barrier to implementation by providers, and acceptance by patients, relates to uncertainty around the biology of Grade Group 1 (GG1; Gleason 6) prostate cancer. Key unresolved questions include: Does GG1 prostate cancer progress over time? Does GG1 cancer share molecular origins with higher-grade disease and lymph node metastases? Are there molecular features of GG1 tumors that predict the presence of synchronous, but undetected, higher-grade disease elsewhere in the prostate? Is GG1 cancer more aggressive in African Americans? To be sure, the biological trajectory of GG1 prostate cancer represents a critical knowledge gap. We hypothesize that GG1 prostate cancer rarely undergoes clonal grade progression, and that molecular changes in GG1 cancer do not predict the presence of synchronous higher-grade disease. To test these hypotheses, we propose the following aims: 1) to determine if high-grade prostate cancer arises clonally from

GG1 prostate cancer in men on surveillance, 2) to interrogate primary multifocal prostate cancer for shared clonality between GG1 and higher-grade disease/lymph node or distant metastases, and 3) to molecularly dissect GG1 prostate cancer both within and without the context of synchronous grade discordant multifocality. The successful completion of the aims of this project will alter the way men with GG1 prostate cancer are clinically managed by further reducing uncertainty about the clinical and molecular arc of favorable-risk disease. Practically, these findings have the potential to provide confidence to providers and patients when selecting surveillance for GG1 prostate cancer by reducing concerns over clonal disease progression and by shedding light on the likelihood of co-existing higher-risk cancer that has yet to be detected—factors that play key roles in the selection and effective implementation of surveillance. Our research team composed of experts in prostate cancer management, molecular profiling, and bioinformatics, coupled with our distinctive and extensive access to relevant tissue resources, is uniquely poised to complete our research plan.
Status of Support: Pending
Project Number: GRANT13747951
PD/PI: Salami
Source of Support: NIH
Primary Place of Performance: University of Michigan
Project/Proposal Start and End Date: (MM/YYYY) (if available): 07/01/2023 – 06/30/2028
Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period. 0.60 CM

Title: Genetic mechanisms underlying adrenal cortisol excess
Major Goals: Adrenal masses are found in roughly 3-10% of the population, and most are benign tumors. Adrenocorticotropic hormone (ACTH)-independent autonomous cortisol secretion of various degrees is associated with 20% to 30% of the benign adrenal tumors – these tumors are referred to as cortisol-producing adenomas (CPAs) and occur more commonly in women than men. Cushing syndrome (CS) represents the signs and symptoms resulting from hypercortisolism such as visceral obesity, dyslipidemia, hypertension, type 2 diabetes, and osteoporosis. Contrary to the understanding that adrenal androgen precursors, such as DHEA and DHEAS, are suppressed in ACTH-independent hypercortisolism, a subset of women with CS shows signs of hyperandrogenism. Interestingly, our preliminary findings indicate that ~10% of women with adrenal hypercortisolism have elevated levels of adrenal-specific 11-oxyandrogens, suggesting their co-secretion with cortisol. While overt CS (OCS) is rare, mild autonomous cortisol secretion (MACS) affects a substantial 0.2–2% of the adult population and also is associated with an increased risk of adverse cardiovascular, bone, and metabolic complications. Adrenalectomy is the treatment of choice for OCS; nevertheless, the best approach to manage MACS remains uncertain. Somatic gene mutations are the primary cause of adrenal hypercortisolism. We recently applied an immunohistochemistry (IHC)-guided gene-targeted sequencing approach on formalin-fixed paraffin-embedded (FFPE) tissue that significantly improved the detection rate of known somatic mutations to over 70%. This approach has positioned our group to define the remaining disease-causing mutations and their molecular mechanisms causing dysregulated cortisol production. The overall goal of our study is to identify novel cortisol-driver somatic mutations in CPAs, and to define the role of the adrenal-specific 11-oxyandrogens in CPA-related morbidities. ●Specific Aim 1 will probe the working hypothesis that CPAs present with a unique spectrum of known and novel somatic mutations in cortisol-driver genes. We will use FFPE tissue for IHC-guided DNA capture of CPAs to identify novel cortisol-driver somatic mutations by whole exome sequencing. Adrenal cell models will be used to define the molecular mechanisms for newly identified CPA somatic mutations. ●Specific Aim 2 will test the working hypothesis that CPA production of 11-oxyandrogens results from aberrant tumor expression of steroidogenic enzymes and cofactors. Mass spectrometry will be used to quantify 11-oxyandrogens in patients with OCS and MACS. In parallel, CPA IHC, genetic analysis, and adrenal cell studies will be performed to dissect the juxtaposition and the cooperation between somatic mutations and expression of key steroid-producing players which enhances the ability of CPAs to produce 11-oxyandrogens. Overall significance and clinical impact: Completion of study goals will provide the foundational knowledge required to understand the pathogenesis of adrenal hypercortisolism which could, in turn, improve personalized diagnostic and therapeutic approaches for patients (especially MACS) with cortisol-producing adrenal tumors.

Status of Support: Pending
Project Number: GRANT13786376
PD/PI: Rege
Source of Support: NIH
Primary Place of Performance: University of Michigan
Project/Proposal Start and End Date: (MM/YYYY) (if available): 09/01/23 – 08/31/28
Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period. 0.60 CM

Title: Genetic Causes of Endocrine Hypertension in Black Americans
Major Goals: Primary aldosteronism (PA) is the most common cause of endocrine hypertension, accounting for 5-8% of hypertension and 11-20% of resistant hypertension. PA is characterized clinically by hypertension, increased plasma aldosterone, and suppressed renin levels. There is considerable evidence that chronic inappropriate elevation in circulating aldosterone levels causes cardiovascular, renal, and cerebrovascular damage as well as other pathologic conditions. Over the past decades, it has become clear that PA results, in part, from the disruption of adrenal cell calcium homeostasis leading to increased aldosterone synthase (CYP11B2) expression and aldosterone production.
Aldosterone-producing adenomas (APAs) are a major cause of PA. The introduction of next-generation sequencing (NGS) has provided important clues to the pathogenesis of PA. NGS assessment of APAs has defined a series of somatic mutations in genes that encode proteins impacting intracellular calcium levels, including KCNJ5, ATP1A1, ATP2B3, CACNA1D, CACNA1H, CLCN2 and SLC30A1 (aldosterone-driver gene mutations). Previous studies using grossly dissected snap frozen tumor tissue were not able to identify aldosterone-driver mutations in more than 45% of APAs. We applied a first-in-field sequencing approach by utilizing formalin fixed paraffin embedded (FFPE) tissue for CYP11B2 immunohistochemistry– guided DNA capture of APAs. This was followed by targeted NGS on genes frequently mutated in APAs. This strategy greatly bolstered the detection rate of somatic gene mutations to 90-96%, depending on the population studied. Multiple mutation analyses have been performed on APAs from Europeans, White Americans and East Asians, and have indicated ethnic and sex differences in genetic causes of APAs. However, the number of APA studies in Black Americans (BAs) is limited. Importantly, BAs are known to have higher rates of hypertension than White Americans and appear vulnerable to the effects of excess aldosterone production.
The proposed research will establish the novel somatic mutations causing aldosterone excess in APAs from BAs, define the molecular mechanisms driving aberrant aldosterone production in PA, and determine the impact of sex on the prevalence of BA aldosterone-driver APA mutations. In addition, completion of the project goals will help expansion of studies elucidating the major cause of endocrine hypertension in underrepresented populations.
Status of Support: Pending
Project Number: 23-PAF03808
PD/PI: Rege
Source of Support: American Heart Association, Inc.
Primary Place of Performance: University of Michigan
Project/Proposal Start and End Date: (MM/YYYY) (if available): 07/01/23 – 06/30/26
Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period. 0.60 CM

Title: Advancing in vivo Microstructure Imaging in Oral Cancers for Adaptive RT
Major Goals: Aim 1. Develop, optimize and evaluate a clinically applicable acquisition protocol and quantification models of MR-based in vivo microstructural imaging as a new means for oral/oropharyngeal cancer imaging. Aim 2. Validate in vivo modeled microstructural parameters with digital pathology of tissue samples from resected oral/oropharyngeal cancers. Aim 3. Assess clinical values of the in vivo microstructural parameters for early prediction of tumor progression during definitive chemoradiation therapy (CRT) in patients with oropharyngeal cancers.
Status of Support: Pending

Project Number: 23-PAF04550
PD/PI: Cao
Source of Support: NIH
Primary Place of Performance: University of Michigan
Project/Proposal Start and End Date: (MM/YYYY) (if available): 09/01/23 – 08/31/28
Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period. 0.60 CM

Title: Mechanisms of low-risk human papillomavirus (HPV)-driven sinonasal cancer
Major Goals: The overall goal of this project is to delineate the intrinsic and extrinsic mechanisms associated with malignant progression of low-risk human papillomavirus (HPV)-driven sinonasal squamous cell carcinomas. To accomplish this goal, we will utilize cutting-edge molecular techniques and bioinformatic approaches to: 1) determine host and viral genomic and transcriptomic alterations associated with malignant progression; and 2) comprehensively characterize and compare the tumor microenvironment of pre-malignant and malignant lesions.
Status of Support: Pending
Project Number: GRANT13900578
PD/PI: Udager
Source of Support: NIH
Primary Place of Performance: University of Michigan
Project/Proposal Start and End Date: (MM/YYYY) (if available): 04/01/2024 – 03/31/2029
Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period. 3.60 CM

Title: Targeting PROX1 in Prostate Cancer Lineage Plasticity
Major Goals: Define biomarkers of PROX1 function and identify targeting approaches.
Status of Support: Pending
Project Number: #23-PAF06169
PD/PI: Alumkal
Source of Support: Prostate Cancer Foundation
Primary Place of Performance: University of Michigan
Project/Proposal Start and End Date: (MM/YYYY) (if available): 09/01/2023 – 08/31/2025
Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period. 0.60 CM

PREVIOUS (ENDED WITHIN THE LAST 5 YEARS)

U01 CA179106 Hadjiyski (PI) 0.60 CM (YR4)
NIH/NCI 5/2014-4/2019
Jennifer Meininger
Grants Management Specialist

Biomarkers for staging and treatment response monitoring of bladder cancer
Goal(s): The goal of this project is to develop effective decision support tools that merge image-based and non-image-based biomarkers to assist radiologists and oncologists in assessment of cancer stage and change as a result of treatment. Specific Aims: Aim 1. Develop a quantitative image analysis tool (QIBC) for bladder GTV estimation on multi- modality (MM) images. Aim 2. Develop a computer decision support system (CDSS-S) to assist clinicians in cancer staging. Aim 3. Develop a computer decision support system (CDSS-T) to assist clinicians in evaluation of the change in the tumor characteristics as a result of neoadjuvant treatment. Aim 4. Evaluate the effects of QIBC and CDSS-T on inter-clinician variability and efficiency in estimation of GTV and treatment response. Aim 5. Evaluate CDSS-S and CDSS-T as decision support tools in pilot clinical studies.

Role: Co-Investigator

I, PD/PI or other senior/key personnel confirm that I:

Certify that the current and pending support provided on the application is current, accurate and complete; Agree to update such disclosure at the request of the agency prior to the award of support and at any subsequent time the agency determines appropriate during the term of the award; and Have been made aware of the requirements under Section 223(a)(1) of the William M. (Mac) Thornberry National Defense Authorization Act. Understand that false, fictitious, or fraudulent statements or claims may result in criminal, civil, or administrative penalties (U.S. Code, Title 18, Section 1001).

Signature and Date: Aaron M Udager

06/23/2023

PHS OTHER SUPPORT
For All Application Types – DO NOT SUBMIT UNLESS REQUESTED

There is no "form page" for reporting Other Support. Information on Other Support should be provided in the format shown below.

*Name of Individual: Simpa Salami
Commons ID: SIMPAS

Other Support – Project/Proposal

*Title: Radiogenomic Characterization of Prostate Cancer: Distinguishing Aggressive from Indolent Disease

*Major Goals: 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.

*Status of Support: Active

Project Number: W81XWH1810219

Name of PD/PI: Salami, Simpa

*Source of Support: DOD

*Primary Place of Performance: USA

Project/Proposal Start and End Date: (MM/YYYY) (if available): 09/30/2018-09/29/2023

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. [2018]	1.80 calendar
2. [2019]	1.80 calendar
3. [2020]	1.80 calendar
4. [2021]	1.80 calendar
5. [2022]	0.60 calendar

*Title: SPORE Project 2: Michigan Prostate SPORE

*Major Goals: 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.

*Status of Support: Active

Project Number: P50CA186786

Name of PD/PI: Chinnaiyan, Arul

*Source of Support: NIH/NCI

*Primary Place of Performance: USA

Name of Individual: Simpa Salami
Commons ID: SIMPAS

Project/Proposal Start and End Date: (MM/YYYY) (if available): 09/01/2019-08/31/2024

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. [2019]	1.80 calendar
2. [2020]	1.80 calendar
3. [2021]	1.80 calendar
4. [2022]	1.80 calendar
5. [2023]	1.80 calendar

*Title: Evolution of Kidney Cancer Metastases: Implications for Surveillance and Targeted Therapy

*Major Goals: The goals of this project will define the molecular profile of the kidney cancer clone most likely to metastasize and develop a molecular signature for RCC associated with recurrence/metastasis and/or mortality.

*Status of Support: Active

Project Number: AWD017037

Name of PD/PI: Salami, Simpa

*Source of Support: Robert Wood Johnson Foundation

*Primary Place of Performance: USA

Project/Proposal Start and End Date: (MM/YYYY) (if available): 01/01/2021-12/31/2024

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. [2021]	4.38 calendar
2. [2022]	4.38 calendar
3. [2023]	4.38 calendar

*Title: Integrative molecular profiling of whole urine in African-American men with aggressive prostate cancer

*Major Goals: The goal of this project is to: 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.

*Status of Support: Active

Project Number: W81XWH-21-1-0238

Name of PD/PI: Udager, Aaron

Name of Individual: Simpa Salami
Commons ID: SIMPAS

*Source of Support: DOD

*Primary Place of Performance: USA

Project/Proposal Start and End Date: (MM/YYYY) (if available): 06/01/2021-05/31/2024

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. [2021]	0.60 calendar
2. [2022]	0.60 calendar
3. [2023]	0.60 calendar

*Title: Molecular Characterization of the Biologically Dominant Nodule in Multifocal Prostate Cancer with N1 disease

*Major Goals: To determine and compare the molecular profile of each cancer focus in multifocal prostate cancer; ii) To characterize the biologically dominant nodule or index tumor in multifocal prostate cancer with lymph node (LN) metastasis; and iii) To evaluate the prognostic accuracy of Oncotype DX™, Prolaris™ and Decipher™ scores in predicting LN metastasis.

*Status of Support: Active

Project Number: 16YOUN17

Name of PD/PI: Salami, Simpa

*Source of Support: Prostate Cancer Foundation

*Primary Place of Performance: USA

Project/Proposal Start and End Date: (MM/YYYY) (if available): 06/27/2016-06/27/2024

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. [2016]	1.62 calendar
2. [2017]	3.00 calendar
3. [2018]	3.00 calendar
4. [2019]	0.01 calendar
5. [2020]	0.01 calendar
6. [2021]	0.01 calendar
7. [2022]	0.01 calendar
8. [2023]	0.01 calendar

*Title: Clinical translation of dual-modality transrectal ultrasound and photoacoustic imaging for detecting aggressive human prostate cancer

Name of Individual: Simpa Salami
Commons ID: SIMPAS

*Major Goals: develop the transrectal ultrasound and photoacoustic (TRUSPA) imaging platform and understand its performance and limitations for detection and characterization of human proposed cancer (PCa)

*Status of Support: Pending

Project Number: 23-PAF05372

Name of PD/PI: Wang, Xueding

*Source of Support: Pennsylvania State University/NIH

*Primary Place of Performance: USA

Project/Proposal Start and End Date: (MM/YYYY) (if available): 12/01/2023-11/30/2028

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. [2023]	0.00 calendar
2. [2024]	0.00 calendar
3. [2025]	1.20 calendar
4. [2026]	1.20 calendar
5. [2027]	1.20 calendar

*Title: Defining the Biological Arc of Grade Group 1 Prostate Cancer

*Major Goals: The long-term goal of this project is to further reduce the biological uncertainty associated with surveillance for favorable-risk prostate cancer

*Status of Support: Pending

Project Number: 23-PAF02381

Name of PD/PI: Salami, Simpa

*Source of Support: NIH

*Primary Place of Performance: USA

Project/Proposal Start and End Date: (MM/YYYY) (if available): 07/01/2023-06/30/2028

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. [2023]	1.80 calendar
2. [2024]	1.80 calendar
3. [2025]	1.80 calendar
4. [2026]	1.80 calendar
5. [2027]	1.80 calendar

Name of Individual: Simpa Salami
Commons ID: SIMPAS

*Title: Testing the Personal Patient Profile-Prostate (P3P) in Black Men

*Major Goals: The purpose of this study is to is to test P3P efficacy in a sample of Black men at geographically distinct research sites in hope of reducing decisional regret and increasing equitable outcomes

*Status of Support: Pending

Project Number: 23-PAF04431

Name of PD/PI: Salami, Simpa

*Source of Support: University of Washington/NIH

*Primary Place of Performance: USA

Project/Proposal Start and End Date: (MM/YYYY) (if available): 12/01/2023-11/30/2028

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. [2023]	0.60 calendar
2. [2024]	0.60 calendar
3. [2025]	0.60 calendar
4. [2026]	0.60 calendar
5. [2027]	0.60 calendar

*Title: University of Michigan Rogel Cancer Center Support Grant 2023-2028

*Major Goals: Reduce the burden of cancer and advance health equity through transdisciplinary collaboration in research, education, patient care and community outreach, and the Vision is to be a leader in prevention, early diagnosis, optimal treatment and care for all at risk of, or affected by, cancer.

*Status of Support: Pending

Project Number: P30CA046592

Name of PD/PI: Fearon, Eric

*Source of Support: NIH

*Primary Place of Performance: USA

Project/Proposal Start and End Date: (MM/YYYY) (if available): 06/01/2023-05/31/2028

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. [2023]	0.36 calendar
2. [2024]	0.36 calendar
3. [2025]	0.36 calendar

Name of Individual: Simpa Salami
Commons ID: SIMPAS

Year (YYYY)	Person Months (##.##)
4. [2026]	0.36 calendar
5. [2027]	0.36 calendar

*Title: Biology of Cancer Case-Control Study

*Major Goals: to validate a blood-based cancer screening test

*Status of Support: Pending

Project Number: 23-PAF05720

Name of PD/PI: Vaishampayan, Ulka

*Source of Support: Roche Molecular Systems, Inc.

*Primary Place of Performance: USA

Project/Proposal Start and End Date: (MM/YYYY) (if available): 05/01/2023-04/30/2028

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. [2023]	1.20 calendar
2. [2024]	1.20 calendar
3. [2025]	1.20 calendar
4. [2026]	1.20 calendar
5. [2027]	1.20 calendar

*Title: The Vallania Study: Multi-Cancer and Comorbidity Blood Sample and Clinical Data Collection for a Multiomics Screening Test Development

*Major Goals: To compare blood samples from cancer case and non-cancer control subjects in order to develop and characterize blood-based multiomics tests in specific cancer types or in a combination of multiple cancers & to evaluate blood-based multiomics tests in specific non cancer diseases or conditions

*Status of Support: Pending

*Project Number: 23-PAF04208

Name of PD/PI: Salami, Simpa

*Source of Support: Freenome, Inc.

*Primary Place of Performance: USA

Project/Proposal Start and End Date: (MM/YYYY) (if available): 03/01/2023-02/28/2026

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Name of Individual: Simpa Salami
Commons ID: SIMPAS

Year (YYYY)	Person Months (##.##)
1. [2023]	1.80 calendar
2. [2024]	1.80 calendar
3. [2025]	1.80 calendar

IN-KIND

*Estimated Dollar Value of In-Kind Information: None

***Overlap** (summarized for each individual): There is no scientific overlap

I, PD/PI or other senior/key personnel, certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SignNow e-signature ID: 8ba919e7d6...
06/27/2023 14:49:19 UTC

PHS OTHER SUPPORT
For All Application Types – DO NOT SUBMIT UNLESS REQUESTED

*Name of Individual: Powell, Isaac
Commons ID: AC4913

Other Support – Project/Proposal

*Title: Michigan Prostate SPORE

Major Goals: The Michigan Prostate SPORE seeks to decrease the morbidity and mortality associated with prostate cancer by making scientific advances that address critical questions in prostate cancer tumorigenesis and treatment.

*Status of Support: Active (THIS AWARD)

Project Number: 5P50CA186786-09

Name of PD/PI: Chinnaiyan/Palapattu/Heath

*Source of Support: NIH:NCI

*Primary Place of Performance: University of Michigan

Project/Proposal Start and End Date: (MM/YYYY) (if available): 09/03/2019-08/31/2024

*Total Award Amount (including Indirect Costs):

*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2019-2020	0.35 calendar
2. 2020-2021	0.35 calendar
3. 2021-2022	0.35 calendar
4. 2022-2023	0.34 calendar
5. 2023-2024	0.34 calendar

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

Major Goals: To test the hypothesis that an integrative molecular profiling approach to assay relevant transcriptomic biomarkers, somatic alterations, and germline variants in whole urine will improve the detection of aggressive prostate cancer in African-American men.

*Status of Support: Active

Project Number: W81XWH-21-1-0238

Name of PD/PI: Udager

*Source of Support: DOD

*Primary Place of Performance: University of Michigan

Project/Proposal Start and End Date: (MM/YYYY) (if available): 6/1/2021-5/31/2024

Name of Individual: Powell, Isaac
Commons ID: AC4913

* Total Award Amount (including Indirect Costs):

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2021-2022	0.35 calendar
2. 2022-2023	0.54 calendar
3. 2023-2024	0.54 calendar

*Title: Prostate Cancer Research Program, Clinical Consortium Research Site Award

Major Goals: The primary objective of the Clinical Consortium Award is to provide our site the support to develop and enhance collaborations necessary to rapidly execute Phase I and II prostate cancer clinical trials within the PCCTC.

*Status of Support: Completed

Project Number: W81XWH-17-2-0022

Name of PD/PI: Heath

*Source of Support: DOD

*Primary Place of Performance: Wayne State University

Project/Proposal Start and End Date: (MM/YYYY) (if available): 09/29/2017-09/29/2022

*Total Award Amount (including Indirect Costs):

*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2018	0.24 calendar
2. 2019	0.24 calendar
3. 2020	0.24 calendar
4. 2021	0.24 calendar
5. 2022	0.24 calendar

Name of Individual: Powell, Isaac
Commons ID: AC4913

IN-KIND

None

***Overlap** (summarized for each individual): None

I, PD/PI or other senior/key personnel, certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

*Signature: Dr. Isaac J. Powell, M.D.

Date: 6/13/2023