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14. ABSTRACT
Prostate cancer (PCa) is one of the leading causes of cancer-related death in men worldwide, but efforts to delineate patients with advanced disease has been marred by widespread inter- and intra-tumor heterogeneity. While a significant fraction of our work was stalled by the ongoing pandemic, we were still able to quantify tissue composition and heterogeneity by single-cell analysis. We found that all cells of the human prostate are present in the mouse prostate, but the mouse prostate bears hitherto known exceptional diversity of cell types, including multiple luminal epithelial cell sub-types. We find that gene signatures of neuroendocrine cells (NE) of the mouse prostate resembles that of NE cells of the mouse lung and NE prostate cancers (NEPCs). As single-cell RNA sequencing requires large amounts (1-10 g) of fresh tissues that are often not clinically accessible we developed a novel pipeline for single-nucleus RNA sequencing and single-nucleus ATAC sequencing from small amounts (0.1-1g) of archived (frozen) tissues from autopsies. We have now generated the cell atlas of benign prostates, localized prostate cancer of distinct grades, metastatic PCa from four different sites and NEPCs. We are currently correlating clinical information with our single cell data for prostate tumor stratification.

15. SUBJECT TERMS
Single cell analysis, mouse prostate, mouse lung, cell-of-origin, localized prostate cancer, Gleeson score, metastatic prostate cancer, neuroendocrine prostate cancer

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1. INTRODUCTION

Prostate cancer (PCa) is one of the leading causes of cancer-related death in men worldwide. Currently, a major challenge in PCa is to distinguish low-risk indolent cancers from aggressive ones that need immediate therapeutic intervention. Additional complexities arise in the veteran population, wherein wartime exposure to toxins not only increases PCa risk, but aggravates the disease with unknown mechanisms. Efforts to succinctly delineate these aspects and clinically stratify patients with advanced disease have been challenging owing to widespread inter- and intra-tumor pathological heterogeneity, resulting from variability in composition of the tumor and its microenvironment between and within patients. This heterogeneity is widely considered as one of the major reasons for the failure of local therapy in 30 - 40% of patients that bear homogeneous clinical risk parameters. Therefore, there is an urgent need to understand the extent and causalities of heterogeneity for resolving mechanisms of PCa progression and for the development of prognostic and predictive biomarkers that guide treatment decisions. We propose to uniquely address this gap using a novel single cell analysis (SCA) platform.

2. KEYWORDS

Single cell analysis, mouse prostate, mouse lung, cell-of-origin, localized prostate cancer, Gleeson score, metastatic prostate cancer, neuroendocrine prostate cancer

3. ACCOMPLISHMENTS

What were the major goals of the project?

The central hypothesis of the proposed research is that variability in the cellular composition of tumors and their microenvironment over time and between patients directly informs on tumor progression and disease heterogeneity. Therefore, we propose to dissect the variability in tumor composition through PCa progression and unravel patient-specific tumor and microenvironment compositional signatures for clinical stratification of the disease. The aims of our study are as follows;

Aim 1: Investigate the evolution of tumor microenvironment during PCa progression.

Major task 1: Identify variability in cellular composition of tumors through cancer progression using scRNAseq

Specific tasks:

A. Acquire IACUC and DoD ACURO approval (month 1-3)
B. Generate genetically engineered mouse models (GEMMs, months 3-7)
C. Acquire and process tissues for single cell RNA sequencing (scRNAseq) and analyze results (months 5-11)

Major task 2: Identify the spatial co-ordinates of distinct cell types through cancer progression using high-throughput single-molecule fluorescence in situ hybridization (HITSFISH)

Specific tasks:

A. Acquire and process tissues for HITSFISH using probes prioritized by scRNAseq (months 5-11)
B. HITSFISH image analysis to identify spatial co-ordinates of cells (months 8-12)
C. Immunohistochemistry (IHC) and In Situ Hybridization (ISH) for high priority genes to generate biomarker panel of disease progression (months 11-12)

Aim 2: Understand the impact of therapeutic intervention on tumor microenvironment.

Major task 1: Curate compositional changes of tumors and their microenvironment during therapeutic intervention.

Specific tasks:

A. Generate GEMMs and initiate MycCap allograft models (months 13-17)
B. Acquire and process tissues for scRNAseq and analyze results (months 14-21)

Major task 2: Spatially define compositional changes of tumors and their microenvironment during therapeutic intervention.

Specific tasks:

A. Acquire and process tissues for HITSFISH using probes prioritized by scRNAseq (months 21-24)
B. HITSFISH image analysis to identify spatial co-ordinates of cells (months 21-24)
C. IHC and ISH for high priority genes to generate theranostic biomarker panel for treatments (months 23-24)

Aim 3: Create a human prostate tumor cell atlas to stratify aggressive PCa subtypes in the general and veteran population.

Major task 1: Identify the variability in cell type composition of normal prostates and PCa tumors amongst patients.

Specific tasks:

A. Acquire IRB / HRPO approval (month 1-24)
B. Acquire tumor and normal samples from University of Michigan retrospective case series (n=42) and retrospective samples from the VA (n=12, months 24-28)
C. Fresh tissue acquisition from warm autopsies (n=6, months 24-28)
D. scRNAseq of human samples and analyze results (months 24-28)
E. HITSFISH using scRNAseq priorotized probes and image analysis to identify the spatial co-ordinates of cell types in each patient (months 28-32)

Major task 2: Integrative analysis of PCa exome, transcriptome and SCA data to identify biomarker panels for PCa stratification.

Specific tasks:

A. Integrative analysis to identiy cell of origin (months 32-36)
B. IHC and ISH for high priority biomarkers that stratify patients (months 35-36)

With the advent of this award in Sep 2019 and per the statement of work (SOW), the first 4 months were spent on accruing the ACURO approval (on Jan 3) and necessary reagents (by Jan 21). We then initiated mouse models (Pten-/- and HiMyc) appropriate for Aim 1 in January, which typically take 4-5 months for generation of founder colonies. Unfortunately, the pandemic dawned upon us within 2 months, bringing these assays to a staggering halt, especially since the University mandated exclusive performance of COVID-related research. Even though we could not generate these GEMMs, per Aim 1 we extracted and performed single-cell analysis of normal prostates and lungs from control mice. These assays enabled us to initiate the cell-of-origin analysis pertaining to Aim 3, much ahead of schedule. Moreover, we had slotted the first 2 years for mouse-related work and accruing HRPO / cadaver use approvals, but fortuitously the cadaver use was approved in September. This enabled us to quickly pivot to Aim 3 (year 3 in SOW) well in advance and we generated the first-of-its kind cell atlas for benign prostates, localized prostate cancer of distinct grades, metastatic PCa from four different sites and neuroendocrine prostate tumors. We are currently correlating clinical information with our single cell data prostate tumor stratification.

What was accomplished under these goals?

The qualifications, skills, and experience of collaborators and personnel included in this application are paramount for the success of this interdisciplinary project, which integrates high-resolution imaging, bioinformatics, generation of mouse models and pathology. Our results (detailed below) about extensive cellular diversity in mouse prostates, the putative cell-of-origin of prostate tumors and the presence of exhaustive T-cells in metastatic PCa has paved the way for the initial preparation of a manuscript.

The overall goal of this award is to create a comprehensive cell atlas, a resource, that details prostatic tissue and tumor complexity and the extent of heterogeneity in cell composition across tissue/patient samples (Fig.1.).

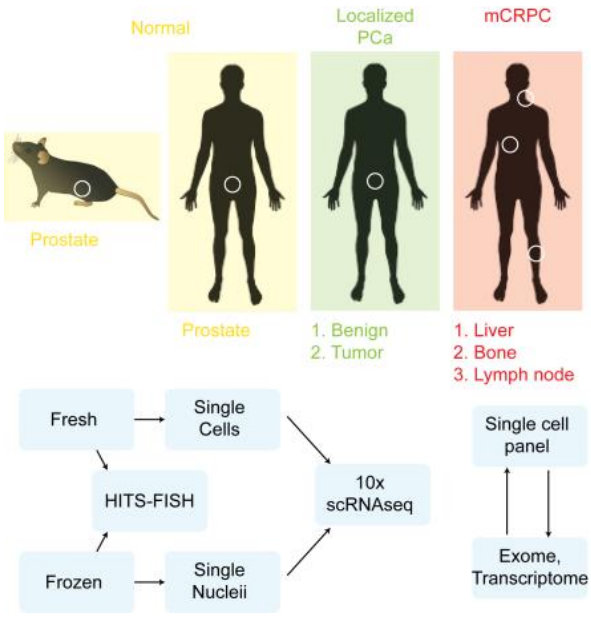

Figure 1. Schematic of workflow to create a prostate and PCa cell atlas.

To understand if the mouse prostate bears functionally similar cell types of the human prostate we have now generated a detailed cell atlas of the mouse prostate. To this end, we surgically removed prostates from ~23 FVB mice, pooled them, dissociated them and profiled them by single-cell RNA sequencing (scRNAseq). We identified all five major cell types expected to be present in the mouse and human prostate, namely basal epithelial cells, luminal epithelial (LE) cells, neuroendocrine (NE) cells, stromal cells and immune cells. In addition, we found exceptional diversity of cell types (28 overall), including novel LE cell sub-types (7), in the mouse prostate (Fig.2-6).

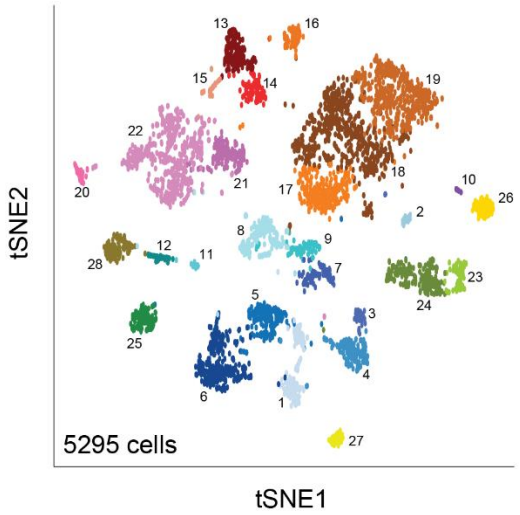

Figure 2. tSNE plot representing cells of the mouse prostate.

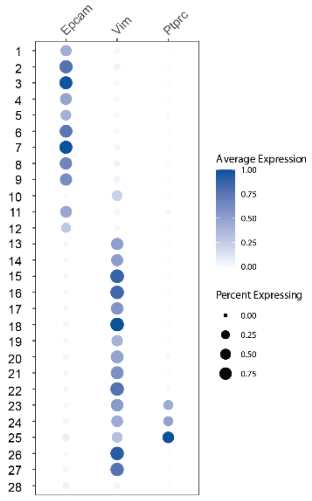

Figure 3. Bubble plot representing expression of canonical markers in epithelial cells, mesenchymal cells and immune cells.

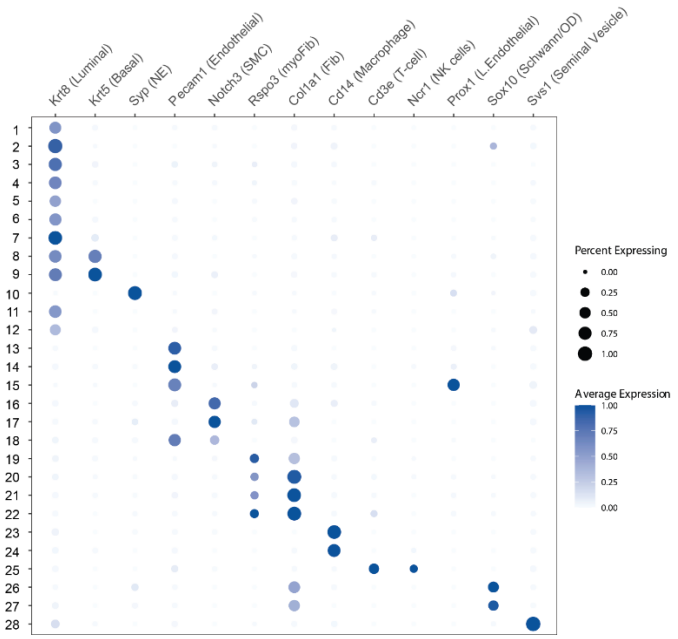

Figure 4. Bubble plot representing expression of prostate-specific canonical markers in various cell types.

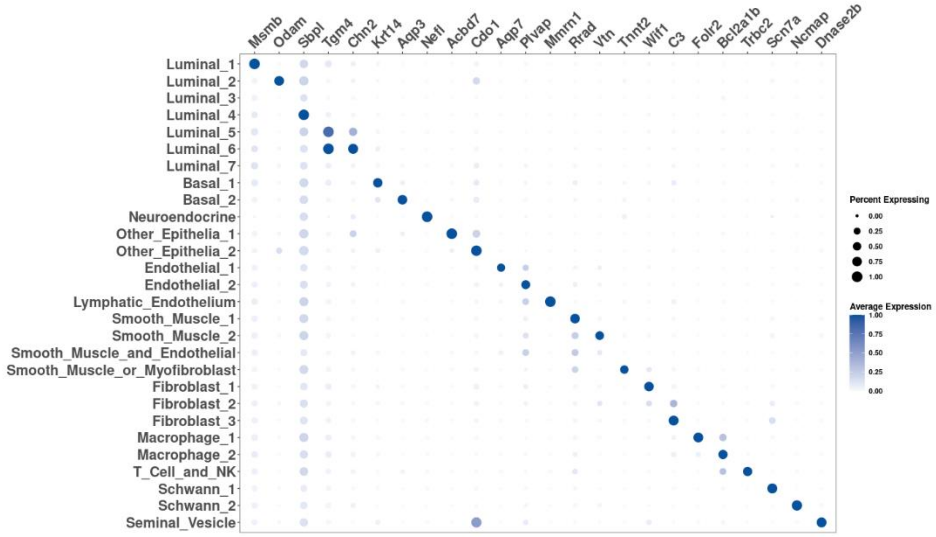

Figure 5. Bubble plot representing expression of novel markers of each cell type identified by this study.

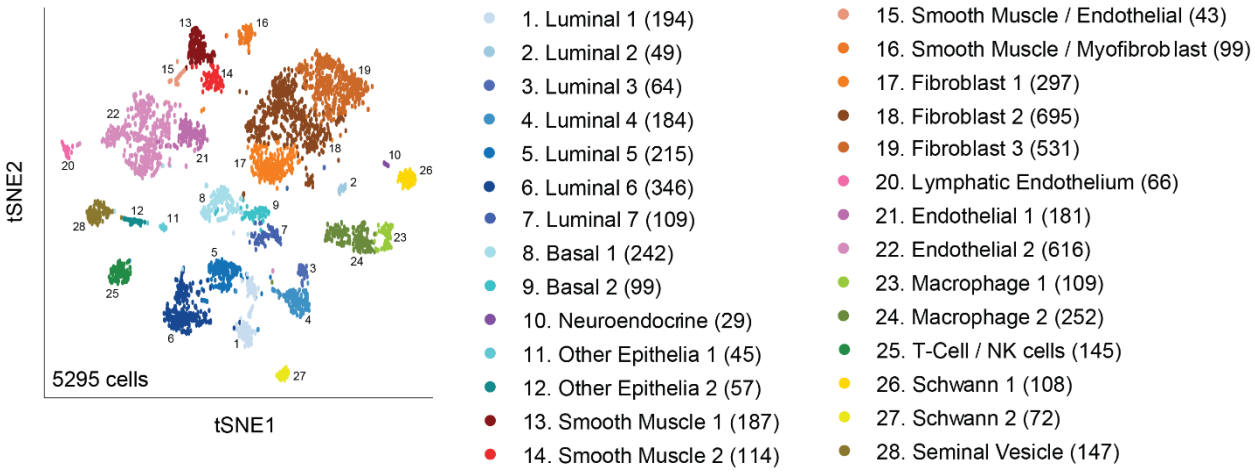

Figure 6. tSNE plot and corresponding cell type identification, based on Figures 2-5.

Unexpectedly, biomarkers corresponding to distinct sub classes of LE cells were each a component of the pathway for seminal fluid production, the prime function of the prostate (Fig.7). These data suggest that each luminal cell sub-type may have a distinct function in anatomically distinct locations of the prostate, effectively positing a division-of-labor model. Alternatively, each luminal cell sub-type we identified are present in all lobes and glands of the prostate, but corresponds to a temporally distinct state, wherein luminal cell plasticity is the prime reason for such heterogeneity.

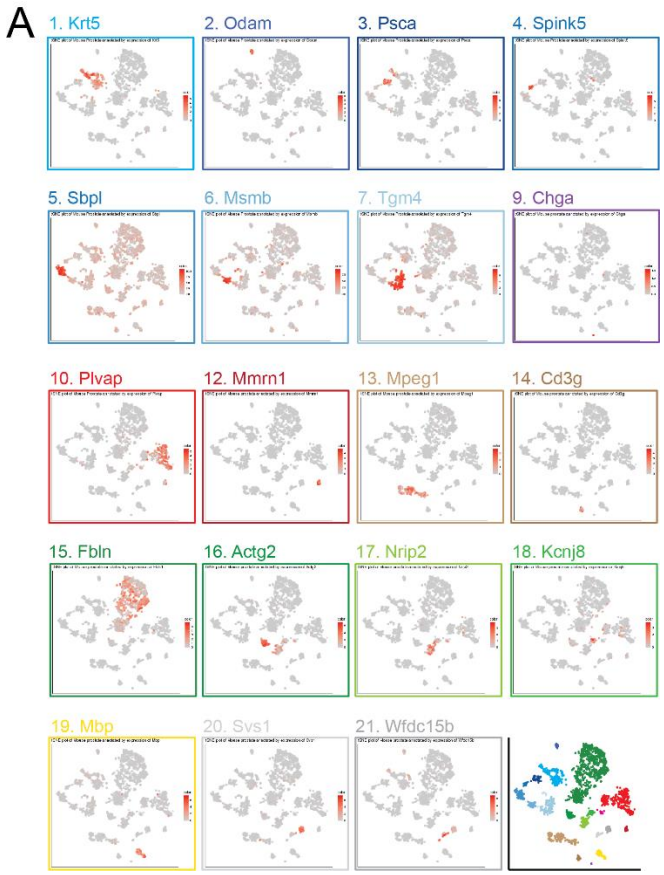

Figure 7. Markers of prostatic function expressed in distinct LE cells, as represented in tSNE plots

RNA-ISH of Spink1 and Pbsn (an androgen receptor / AR regulated gene), genes that are expressed in 2 distinct LE subtypes, are almost mutually exclusive, and that Spink1 expression is specific to one lobe of the prostate (Fig.8), thereby supporting our division of labor hypothesis.

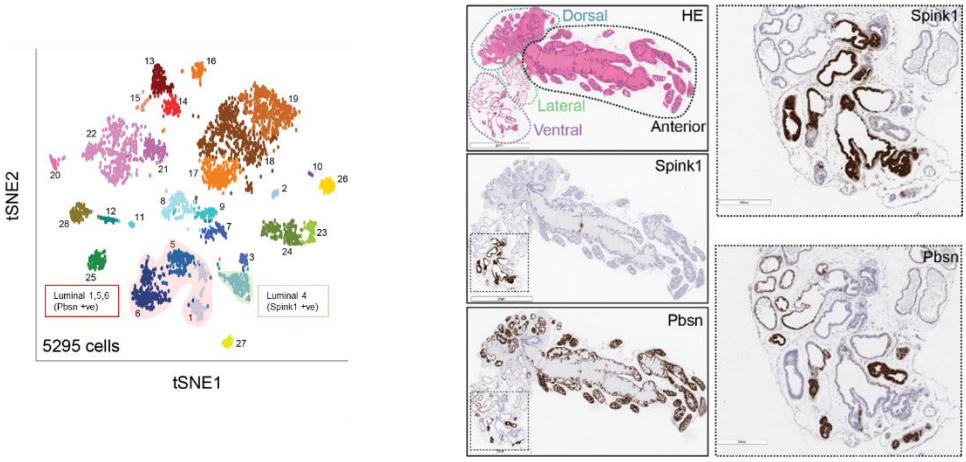

Figure 8. tSNE plot (left) highlighting Pbsn and Spink1 positive clusters. RNA-ISH image (right) of the prostate with Pbsn and Spink1.

Due to the enhanced depth of our sequencing pipeline, we were able to detect the elusive and rare NE cells in the prostate, which constituted 0.5% of all cells types we detected. These NE cells had a very similar gene expression program to NE cells, but not other epithelia (eg – alveolar or bronchial), of the lung, as expected if NE cells were from a distinct lineage. Unexpectedly, we found that the gene signature of prostate NE cells was similar to that in neuroendocrine prostate cancers (NEPC, Fig.9-10).

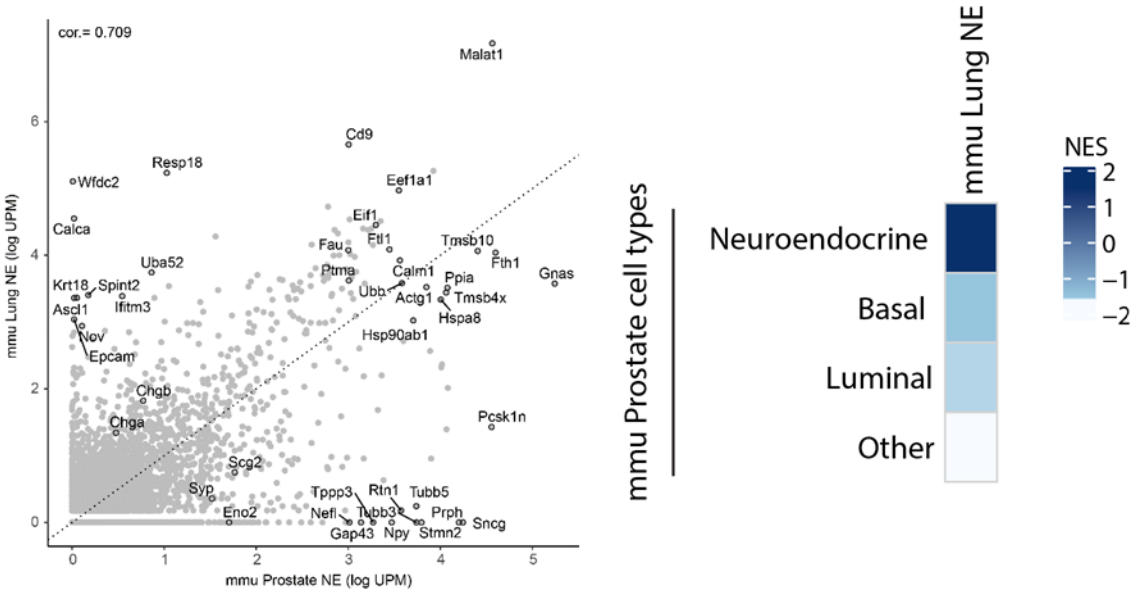

Figure 9. Correlation plot (left) and gene enrichment plot (right) comparing NE cells of the mouse lung and prostate.

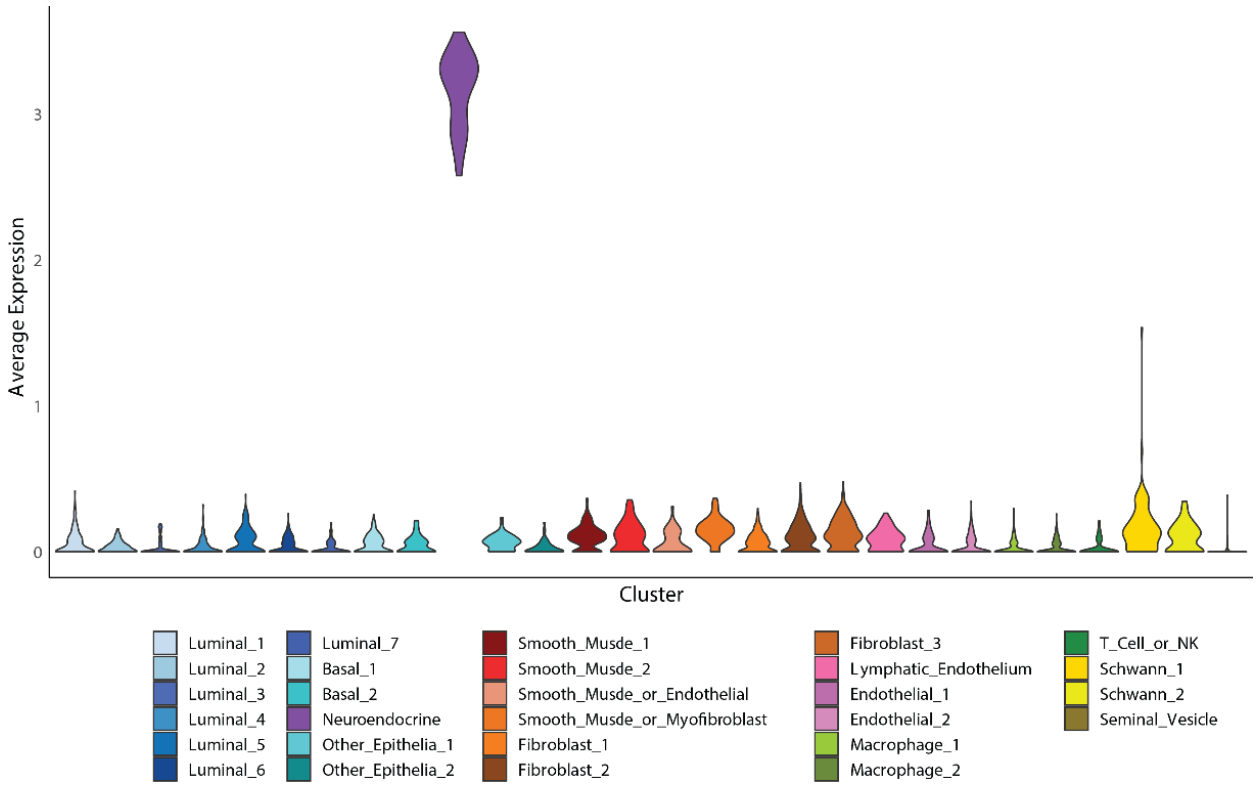

Figure 10. Violin plot representing the unique definition of a NE cell gene signature.

One among the seven LE cell sub-types expressed high levels of SPINK1, strongly suggesting that aberrations in these cells may mediate SPINK1 positive PCa. Comparative informatics analysis of our mouse prostate scRNAseq data with ensemble RNAseq data from TCGA showed that SPINK1 +ve LE cells are indeed more similar to SPOP mutant / SPINK1 positive PCa, supporting our thesis that these cells may serve as the cell of origin for SPOP mutant PCa (Fig.11). While our mouse NE cell signature is over-represented in NEPCs (Fig.12), better than NE cell signatures from published human prostate scRNAseq datasets (Henry et al, Cell reports, 2018), we are yet to find the distinction between *ab initio* and de-differentiated NEPCs.

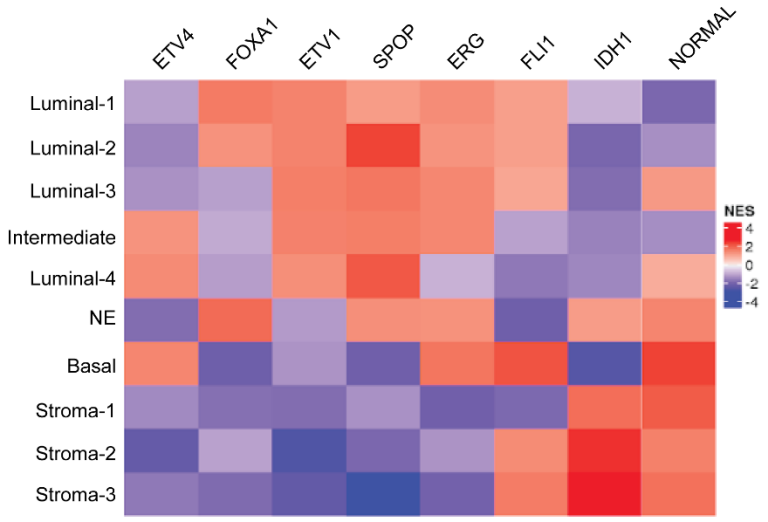

Figure 11. Gene signature enrichment analysis compared between the mouse prostate and distinct classes of PCa as described in TCGA.

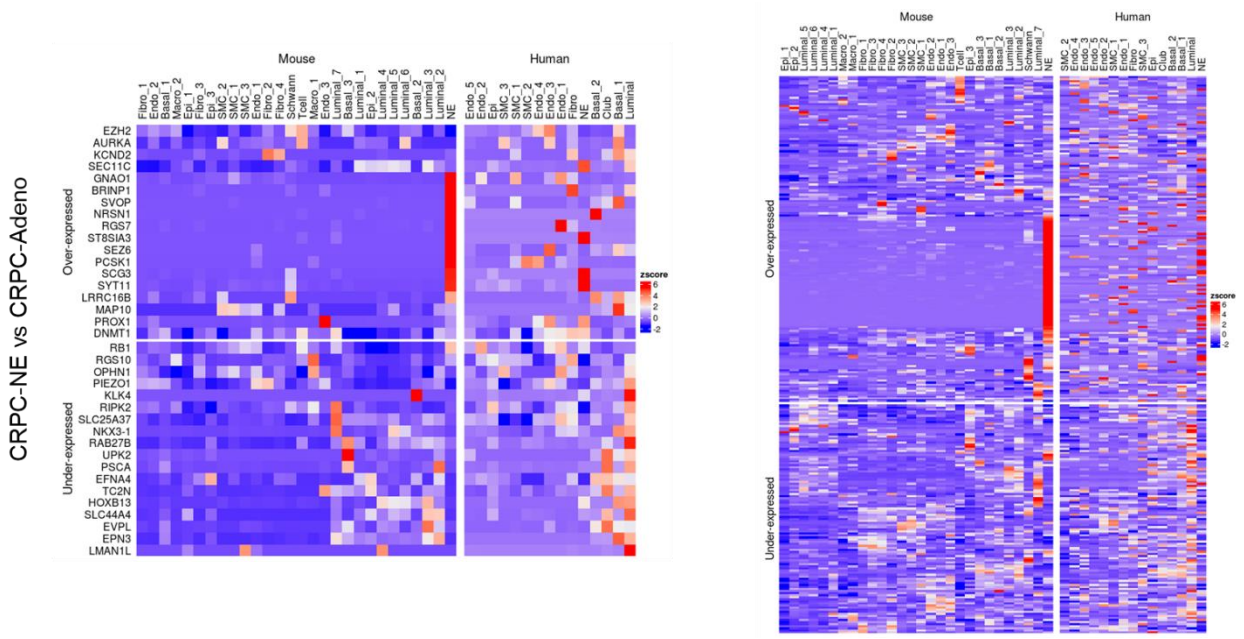

Figure 12. Correlation analysis of cell type specific gene signatures from our scRNAseq data, as compared to published bulk transcriptomics data from NEPCs.

Large volumes of fresh human prostates or prostate tumors are required for scRNAseq, but such samples are difficult and sometimes impractical to obtain at the clinic. To overcome this limitation, we have developed a pipeline for single-nucleus RNA sequencing (snRNAseq) from small

amounts (< 1 g) of fresh biopsies, and fresh-frozen or cryoprotected archived samples, which provides concordant results to scRNAseq (Fig.13).

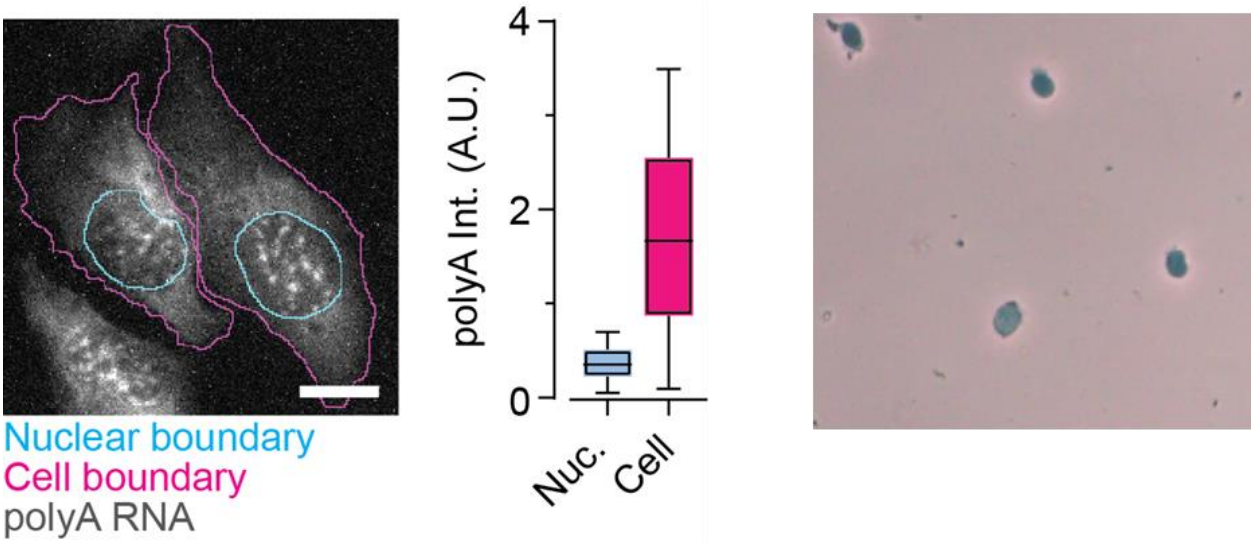

Figure 13. Nucleus and cell-boundary segmentation of cultured cells stained for polyA RNA (left). Middle panel depicts quantification of signal. Right panel is an image of nuclei extracted from archived, frozen tissues.

We first tested this pipeline on cultured cells, prior to venturing into precious tissue samples. To this end, we sequenced samples consisting of a mixture of prostate (normal and cancer) cell lines, as whole cells or from nuclei extracted from them, and found high concordance between scRNAseq and snRNAseq data (Fig.14).

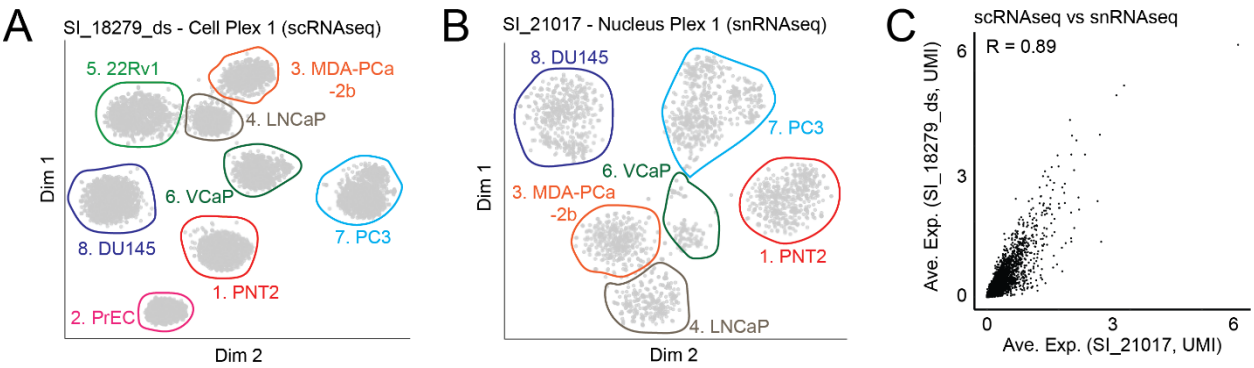

Figure 14. Concordance of scRNAseq and snRNAseq. (A) tSNE plot representing different cell types in the whole cell micture. (B) tSNE plot representing different clusters from nuclei of cells

represented in A. PrECs were not used in this mixture. (C) Correlation plot of scRNAseq vs snRNAseq.

We then tested this pipeline on small amounts of frozen benign tissues and found that snRNAseq identifies all basic cell types expected to be present in the normal prostate (Fig.15).

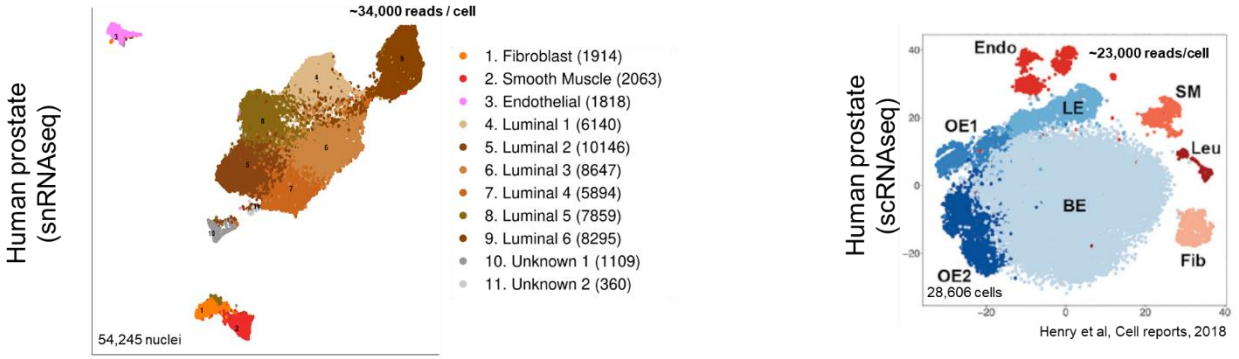

Figure 15. tSNE plot of benign human prostates from frozen tissues (left) and fresh tissues (right, published).

As many archived samples had poor RNA quality, we posited that chromosome accessibility as measured by ATACseq (Assay for Transposase-Accessible Chromatin followed by sequencing) of the more stable nuclear DNA will correlate with snRNAseq, especially since open-chromatin typically implies transcription. We then tested snATACseq on small amounts of frozen benign tissues and found that snRNAseq and snATACseq are highly correlated (Fig.16).

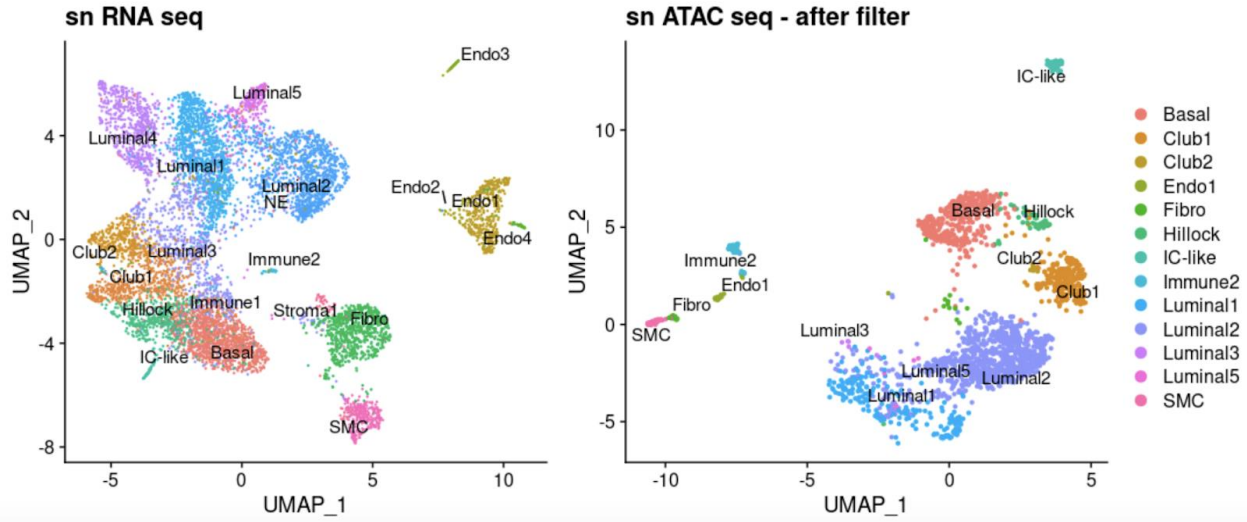

Figure 16. tSNE plot of benign human prostates from frozen tissues with cell types gleaned from snRNAseq (left) or snATACseq (right).

Using this novel pipeline, we identified cellular composition of the benign human prostate, cell-type specific differences across distinct grades (Gleeson-scores) of PCa (from treatment naïve patients) and niches of metastatic PCa from four distinct sites (adrenal gland, lung, liver and bone). To understand the cellular composition of prostate tumors and to uncover differences in microenvironment complexity between distinct stages of PCa, we performed snRNAseq and scRNAseq of localized and metastatic (lymph node) prostate tumors respectively (Fig.1.). We found that distinct grades of localized PCa, in treatment naïve patients with no known metastasis, had a distinct microenvironment from metastatic PCa. We additionally found that the T cell population in localized tumors were canonical regulatory T cells, whereas those in the metastatic cases were GZMB –ve / PD-1 +ve, exhausted T cells (Fig.17-21).

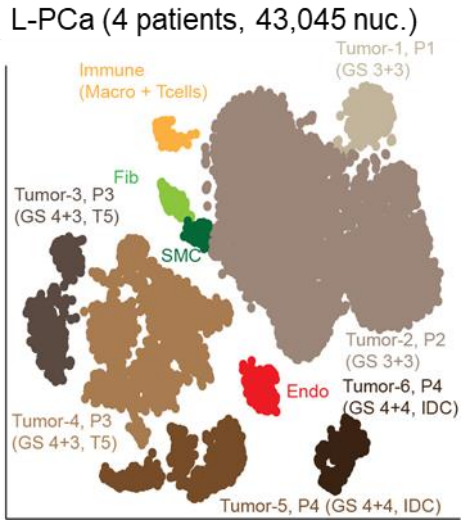

Figure 17. tSNE plot depicting cell types in localized prostate tumors of distinct Gleeson grades.

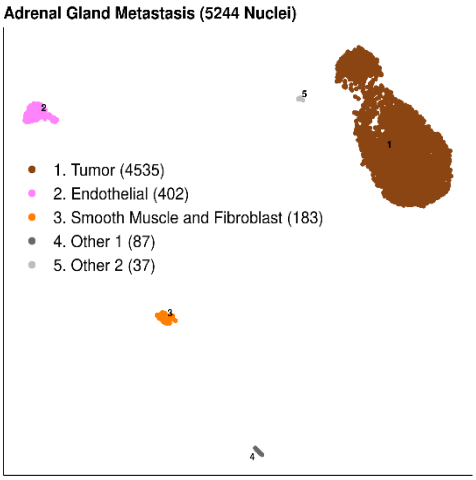

Figure 18. tSNE plot depicting cell types in metastatic prostate tumors (adrenal gland).

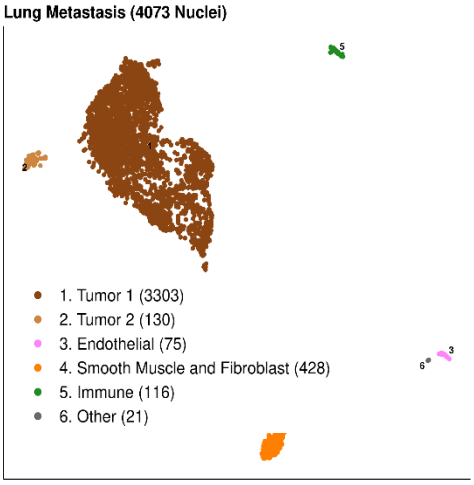

Figure 19. tSNE plot depicting cell types in metastatic prostate tumors (lung).

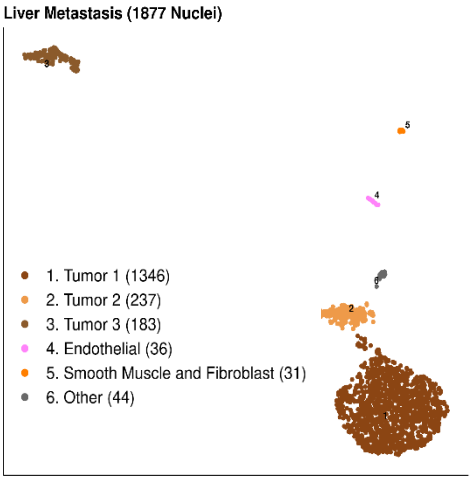

Figure 20. tSNE plot depicting cell types in metastatic prostate tumors (liver).

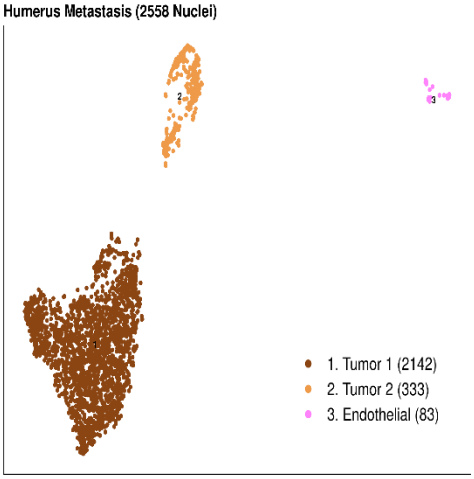

Figure 21. Figure 18. tSNE plot depicting cell types in metastatic prostate tumors (bone).

A significant minority of prostate cancer patients progress to a lethal, metastatic from the disease that is resistant to castration and is called metastatic castration resistant prostate cancer (mCRPC). Some of these patients also bear tumors that bear neuroendocrine or small-cell morphological features - typically found in rare cells of the NE or arise from de-differentiation of prostatic epithelia (luminal or basal cells) by environmental factors (eg – induced by treatment) - and constitute NEPC, which is pathologically distinct from classical PRAD. We sought to understand the preponderance of rare NE cell originated- vs treatment-induced-NEPC, and whether cell composition differences can also explain the distinction between PRAD and NEPC.

To this end, we performed scRNAseq of the intact prostate (Fig.22) and retroperitoneal lymph node metastatic tumors (Fig.23) from one patient who succumbed to NEPC and was heavily treated with anti-androgens. We found that the treatment may have induced the loss of AR signaling, which drives prostatic cell identity, in the intact prostate, but was maintained at the metastatic site (Fig.23). Considering that we did not find NE cells in the intact prostate, our observation suggests that the tumor cells of the metastatic sites potentially originated from AR positive luminal epithelial cells which gained NE signatures through treatment. We are currently expanding our cohort to clearly distinguish the cell composition of localized prostate cancer, PRAD and NEPC across patients. Put together, we have curated the cell atlas for the normal mouse prostate, benign human prostate, localized prostate cancer, metastatic PRAD and metastatic NEPC, which is unprecedented.

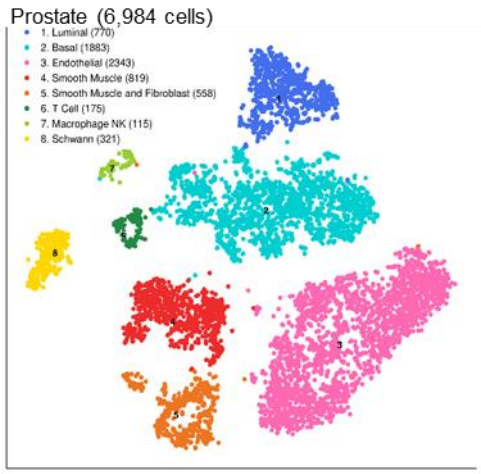

Figure 22. tSNE plot depicting cell types in the intact prostate (heavily treated patient).

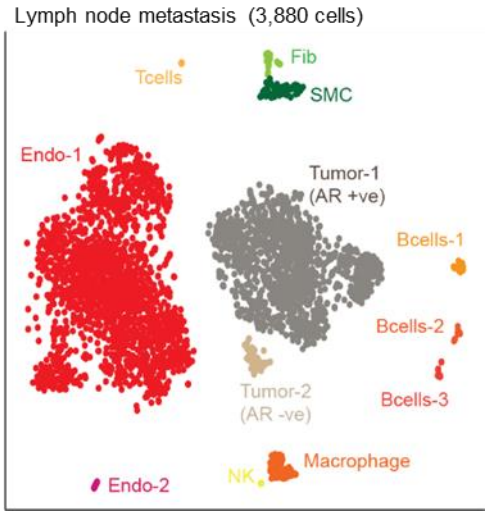

Figure 23. tSNE plot depicting cell types in metastatic prostate cancer (lymph node, heavily treated patient).

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

While the project and its associated resources do not directly provide training and professional development, the Michigan Center for Translational Pathology (MCTP) and the University of Michigan are committed in their educational and service-oriented missions. The MCTP engages in weekly group meetings that entail rigorous discussion of ongoing projects, with active participation from all students and faculty. On the other hand, the University of Michigan has plenty of opportunities for scientific training and career development for graduate students and postdoctoral fellows, via workshops. In addition, the MCTP has also uniquely provided me the opportunity to unofficially lead my own team, which focuses on single-cell and single-molecule analysis. Here, I provide mentorship to research scientists, and undergraduate, graduate and postdoctoral students, thereby paving the way for my career in the academia.

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?

With the resumption of partial lab activities (45% occupancy per unit time and in shifts) and access to the vivarium, we have resumed generation of GEMMs for Aims 1 and 2. If HRPO approval is

obtained within this period, we will start processing human samples for Aim 3, to potentially stay on track for completion of project by the end of year 3.

4. IMPACT

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

While the pandemic immensely hampered the execution of various aspects of this award, we were still able to seamlessly and quickly process a few pertinent samples, which in turn has provided preliminary insights on the cell-of-origin of various types of prostate cancer.

What was the impact on other disciplines?

With the general and pandemic-related difficulty in our ability to obtain fresh patient tissues for scRNAseq, we have developed the pipeline for single cell sequencing of nuclei from frozen tissues. Based on RNA quality of the sample, we either perform single-nucleus RNA sequencing (snRNAseq, high RNA quality), or single-nucleus ATAC sequencing (snATACseq, low RNA quality), wherein the latter sheds light on accessible chromatin that directly correlates with RNA levels in the nucleus. Thus, the technological advancement of sequencing individual nuclei and combining sequencing based information with spatial profiling will negate the need for fresh tissues for single-cell analysis and pave the way for the scientific community to probe abundantly available archived tissues with unprecedented single-cell resolution.

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

Not much of the approach has changed, but we have developed a new protocol for snATACseq, which will certainly help us access tissues with low RNA quality. In addition, this new tool will add mechanistic information by shedding light on chromatin (sequence) occupancy by transcription factors. For instance, understanding the accessibility of androgen receptor binding sites will

provide much needed information on androgen signaling status within tumor cells – a key to delineating PRADs from NEPCs.

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

The COVID19 pandemic has significantly impacted the entire research enterprise, leave alone our work. Resolution of this issue will be slow, but potentially steady, and as labs open up and resources become available our work will resume in full capacity.

Changes that had a significant impact on expenditures

Nothing to Report

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	Role	ORCID ID	CM	Contribution to project
Seema Chugh	Post-Doc	0000-0003-1486-0725	1.81	Animal model generation and sample acquisition.
Marcin Piotr Cieslik	Co-I	0000-0002-5467-1040	0.60	Bioinformatics.
Xia Jiang	Tech	N/A	7.83	Technical help with molecular biology, cell biology and biochemical assays. Sample collection and processing for single-cell and HITSFISH analysis.
Rohit Mehra	Co-I		0.30	Pathological evaluation of mouse and human tissues (IHC and ISH).
Sethuramasundaram Pitchiaya	PI	0000-0003-2529-5186	3.01	Single-cell analysis and HITSFISH. Mentoring Seema and Xia. Interface with the bioinformatician and infer data.
Arul Chinnaiyan	Collaborator	0000-0001-9282-3415	0.0	Advise on genomics of samples and provide access to samples and laboratory resources.
Ajjai Alva	Collaborator		0.0	Advise on choosing cohort from the VA and provide access to such samples.

Other funding support for key personnel are added as an appendix.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS

Nothing to Report

QUAD CHARTS

Nothing to Report

9. APPENDICES

Other funding support (OS) for key personnel are added.

Appendix1: OS for Pitchiaya

Appendix2: OS for Cieslik

Appendix3: OS for Mehra

Appendix4: OS for Chinnaiyan

Appendix5: OS for Alva

Appendix 1
PREVIOUS/CURRENT/PENDING

PITCHIAYA, SETHURAMASUNDARAM

ACTIVE

18YOUN20 (PI: Pitchiaya) 06/01/18 - 05/31/21 3.6 CM
Prostate Cancer Foundation
Unraveling molecular heterogeneities in advanced prostate cancer at single cell resolution
Goal(s): To identify vulnerabilities of anti-cancer therapeutic agents and unravel tumor cell evolution.
Specific Aim(s): 1) Investigate the role of heterogeneity in the development of therapeutic resistance against docetaxel, enzalutamide, BETi, CDK4/6i and CDK12i in advanced PCa using single-cell CRISPR interference technology; 2) Characterize the evolution of tumor cell heterogeneity during PCa progression and therapeutic intervention in syngeneic allograft models; 3) Develop a tumor cell atlas of advanced prostate cancer to enable robust clinical stratification of aggressive PCa subtypes in the general and veteran population.
Contact Information at funding agency: Audrey Gardner, PCF Applications (applications@pcf.org)
Role: PI

R35CA231996 (PI: Chinnaiyan) 09/01/18 – 08/31/25 0.6 CM
National Institutes of Health
Exploring Precision Oncology: From Gene Fusions to lncRNAs
Goal(s): Advance the field of precision oncology by providing new community resources, identifying novel biomarkers, exploring the therapeutic targeting of nominated molecular players, and adding to the knowledge-base of cancer development mechanisms, particularly those of lncRNAs.
Specific Aims: None.
Contact Information at funding agency: Tawnya McKee, mckeeta@mail.nih.gov, 240-276-5719
Role: Co-Investigator

W81XWH-18-PCRP-IDA (PI: Pitchiaya) 09/01/19 – 08/31/22 3.0 CM
Department of Defense W81XWH1910424
Unraveling tumor microenvironment heterogeneity in advanced prostate cancer
Goal(s): To understand the impact of tumor microenvironment heterogeneity, especially among immune infiltrates, cancer-associated fibroblasts and tumor vasculature, in the progression of advanced prostate cancer.
Specific Aim(s): (1) Investigate the evolution of tumor microenvironment during PCa progression in genetically engineered mouse models (GEMMs) of PCa. (2) Understand the impact of therapeutic intervention on tumor microenvironment and identify disease correlates of immunosuppressive vs immunocompetent microenvironment in GEMMs. (3) Integrative analysis and generation of a cell atlas of tumor cells and tumor microenvironment to stratify aggressive PCa subtypes in the general and veteran population, and identify the cell-of-origin for prostate cancers.
Contact Information at funding agency: Nicholas E. Simon, nicholas.e.simon2.ctr@mail.mil, 301-619-3146
Role: PI

19-PAF05746 (PI: Cieslik) 07/01/19 – 06/30/21 1.2 CM
Cancer Research Institute
TCR-FISH: a novel method for spatially and clonally resolved profiling of tumor-infiltrating lymphocytes
Goal(s): To develop a novel method for spatially and clonally resolved profiling of tumor-infiltrating lymphocytes
Contact Information at funding agency: Cancer Research Institute, grants@cancerreasearch.org, 212-688-7515
Role: PI

P50 186786 (PI: Chinnaiyan, Palapattu, Heath)) 09/11/14 - 08/31/24 0.3 CM
NIH/NCI

Michigan Prostate SPORE
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.
Contact Information at funding agency: Jennifer S. Meininger, 240-276-6330, jennifer.meininger@nih.gov
Role: Co-Investigator

PENDING:

3-P30-CA046592 (PI: Fearon) 05/01/20 – 10/31/20 0.6 CM
NIH/NCI
Targeting TMPRSS2 expression as a therapy for coronavirus infection and replication
Specific Aim(s): To provide a pre-clinical rationale to evaluate drugs that suppress lung epithelial TMPRSS2 expression to treat or prevent coronavirus.
Contact Information at funding agency: Ptak, Krzysztof: krzysztofptak@mail.nih.gov
Role: Co-Investigator

OVERLAP:
There is no scientific or budgetary overlap.

PREVIOUS:

16-40-44-PITC(PI Pitchiaya) 07/01/16 – 06/30/17
AACR – Bayer Prostate Cancer Research Fellowship
Androgen receptor regulation by lncRNA PRCAT47 in prostate cancer
Goal(s): To dissect the mechanism of PRCAT47 mediated AR regulation and cell proliferation.
Specific Aim(s): 1) To dissect the mechanism of PRCAT47 mediated AR regulation and cell proliferation; 2) To assess the therapeutic potential anti-PRCAT47 ASOs in CRPC treatment.
Contact Information at funding agency: Shannon M. Gallagher-Colombo, grants@aacr.org

P50 CA186786-05 (PI: Pitchiaya) 11/01/17 – 08/31/19 2.4 CM
NIH/NCI
Prostate SPORE, NIH SPORE Career Enhancement Award
Unraveling molecular heterogeneities in prostate cancer at single cell resolution
Goal(s): To investigate the role and quantify the extent of gene expression heterogeneity in prostate cancer.
Specific Aim(s): 1) Unravel the extent and basis of heterogeneity within a clonal population of PCa cells; 2) Investigate the role of heterogeneity in the development of resistance to BET inhibitors; 3) Identify cell types within normal mouse prostates, human prostates and human prostate tumors.
Contact Information at funding agency: Jennifer S. Meininger, 240-276-6330, jennifer.meininger@nih.gov

Appendix 2, PREVIOUS/CURRENT/PENDING

CIESLIK, MARCIN

CURRENT:

19-PAF05746 (PI: Cieslik) 07/01/19 – 06/30/21 2.4 CM
Cancer Research Institute
TCR-FISH: a novel method for spatially and clonally resolved profiling of tumor-infiltrating lymphocytes
Goal(s): To develop a novel method for spatially and clonally resolved profiling of tumor-infiltrating lymphocytes
Contact Information at funding agency: Cancer Research Institute, grants@cancerreasearch.org, 212-688-7515 Role: PI

R35CA231996 (PI: Chinnaiyan) 09/01/18 – 08/31/25 0.6 CM
National Institutes of Health
Exploring Precision Oncology: From Gene Fusions to lncRNAs
Goal(s): advance the field of precision oncology by providing new community resources, identifying novel biomarkers, exploring the therapeutic targeting of nominated molecular players, and adding to the knowledge-base of cancer development mechanisms, particularly those of lncRNAs.
Contact Information at funding agency: Tawnya McKee, mckeeta@mail.nih.gov, 240-276-5719
Role: Co-Investigator

1U01CA214170-01 (MPI: Chinnaiyan and Tomlins) 09/15/16 – 08/31/21 0.36 CM
NIH/NCI
The Early Detection Research Network: Biomarker Developmental Laboratories:
Discovery and qualification of transcriptomic biomarkers for the early detection of aggressive prostate cancer
Goal(s): 1) Identify and develop assays to study novel aggressive prostate cancer-associated transcriptomic alterations from our MiTranscriptome analysis. 2) Characterize transcripts from Aim 1 as tissue based aggressive prostate cancer biomarkers using individual in situ hybridization assays and a multiplexed next generation sequencing (NGS). 3) Characterize transcripts from Aim 1 as non-invasive, urine-based aggressive prostate cancer early detection biomarkers through collaboration with our industry partner and multiplexed NGS.
Contact Information at funding agency: Kagan, Jacob; jk308z@nih.gov
Role: Co-Investigator

1U24CA210967-01 (MPIs: Chinnaiyan and Nesvishkii) 09/15/16 – 08/31/21 2.28 CM
NIH
University of Michigan Proteogenomics Data Analysis Center
Goal(s): to perform integrative analysis of data generated using the Clinical Proteomic Tumor Analysis Consortium (CPTAC). The proposed Center at the University of Michigan will be one of the four Centers funded by CPTAC. It will work, in coordination with other Centers, to analyze and integrate proteomics, genomics, and transcriptomics data generated for 3-4 cancer patient cohorts, ~ 100 samples in each cohort. The Center will generate data analysis reports to be shared with other members of the Consortium.
Contact Information at funding agency: Rodriguez, Henry, rodriguezh@mail.nih.gov, 301 496-1550
Role: Co-investigator.

P50 186786 (PI: Chinnaiyan) 09/11/14 - 08/31/2024 0.6 CM
NIH/NCI
SPORE in Prostate Cancer, Core1

Overview: 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 Aim(s): 1) Discovery and nomination of novel molecular sub-types of prostate cancer; 2) Characterize associations of molecular sub-types of prostate cancer with clinical outcome and/or aggressiveness of disease in a radical prostatectomy cohort; 3) Characterize associations of molecular sub-types of prostate cancer with clinical outcome
Contact Information at funding agency: Jennifer S. Meininger, 240-276-6330, jennifer.meininger@nih.gov
Role: Co-Investigator

W81XWH-18-PCRP-IDA (PI: Pitchiaya) 9/1/19 – 8/31/22 0.6 CM
Department of Defense
Unraveling tumor microenvironment heterogeneity in advanced prostate cancer
Goal(s): To understand the impact of tumor microenvironment heterogeneity, especially among immune infiltrates, cancer-associated fibroblasts and tumor vasculature, in the progression of advanced prostate cancer.
Contact Information at funding agency: Nicholas E. Simon, nicholas.e.simon2.ctr@mail.mil, 301-619-3146
Role: PI

R01CA240991-01(PI: Morgan) 09/01/19 – 08/31/24 0.60 CM
NIH
Determining the clinical impact of gene expression testing in localized prostate cancer
Goal(s): Develop an integrated clinical-genomic risk stratification system designed to systematize interpretation of GEC testing. We hypothesize that by developing integrated clinical-genomic risk groups we can identify patients most appropriate for AS while maintaining a standard, category-driven framework.
Contact Information at funding agency: Grants.gov Customer Service, grantsinfo@nih.gov, 301-945-7573
Role: Co-Investigator

1R01NS110572-01A1(PI:Venneti) 09/01/19 – 05/31/24 0.36 CM
NIH
Unraveling metabolic dependencies in H3K27M mutant Diffuse Intrinsic Pontine Gliomas
Goal(s): (1) Define glutamine metabolism and elucidate the epigenetic mechanisms by which H3K27M enhances glutamine metabolism. (2) Interrogate the molecular mechanisms by which glutamine metabolism regulates global H3K27me3 reduction. (3) Elucidate the therapeutic potential of targeting glutamine metabolism as proof-of-principle.
Contact Information at funding agency: Grants.gov Customer Service, grantsinfo@nih.gov, 301-945-7573
Role: Co-Investigator

19-PAF06614 (PI:Cieslik) 02/19/20 – 02/18/22 0.60 CM
BMS
Identification of novel therapeutic vulnerabilities across immunophenotypes of refractory and metastatic tumors
Goal(s): To look at differences in outcomes between metastatic patients are partially explained by their associations with distinct immunological subtypes, and that progression from primary to metastatic disease is associated with a shift towards immune evasive genetic subtypes.
Contact Information at funding agency: Karen Martell, Karen.Martell@bmx.com, 650-260-9624
Role: PI

T2019-006 (MPI:Cieslik/Alva) 11/01/19-11/01/22 1.20 CM
The V Foundation for Cancer 180,000/yr
Large-scale discovery and validation of predictive biomarkers for immunotherapy across cancers and treatments
Goal(s): We propose to discover such biomarkers by analyzing tumor tissue samples from a large group of patients treated with immunotherapy.

Contact Information at funding agency: Carole C. Wegner, info@v.org , 919-380-9505
Role: PI

R01CA2345059 (PI:Ryan) 07/01/20 – 06/30/25 0.60 CM
NIH 250,000/yr
Identifying Functional Drivers of MYC Activation via Developmental Enhancers in Diffuse Large B-cell Lymphoma
Goal(s): The overall objective of this proposal is to define novel mechanisms of MYC regulation by distal enhancers.
Contact Information at funding agency: Grants.gov Customer Service, grantsinfo@nih.gov, 301-945-7573
Role: Co-Investigator

ICI 398672 (PI:Cieslik) 9/01/20-9/01/22 1.20 CM
Innovation in Cancer Informatics(ICI) $100,000/yr
Translational tools and resources to advance MHC (HLA) cancer genetics
Goal(s): Through genomic profiling and bioinformatics analyses understand how the cancer genotype shapes immunophenotypic traits, which can be leveraged as prognostic mechanism-rooted biomarkers of survival and/or treatment response.
Contact Information at funding agency: David Brown, grants@the-ici-fund.org
Role: PI

OVERLAP:
No scientific overlap. If the pending applications are funded, effort will be reduced on U24CA210967

PENDING:

20-PAF04679 (PI: Swenson) 04/01/2021-03/31/2026 1.2 CM
NIH $381,193/yr
The First Mechanistic Study of the Perineal Complex and Genital Hiatus Failure in Pelvic Organ Prolapse: MRI Functional Anatomy, Surgical Effects, and Genetics
Goal(s): to reduce treatment failures by developing an evidence-based strategy to phenotype POP based on patient-specific factors including structural defects, genetic predisposition, and clinical risk-factors.
Contact Information at funding agency: Grants.gov Customer Service, grantsinfo@nih.gov, 301-945-7573
Role: Co-Investigator

20-PAF07516 (PI: Fearon) 09/01/2020-8/31/2021 1.2 CM
NIH $320,513/yr
Enhancement of Data Sharing in Pediatric, Adolescent and Young Adult Cancers
Goal(s): To determine the role of JAK family kinases and Bcl-2 family members in the expansion and survival of T-cell lymphoma associated macrophages.
Contact Information at funding agency: Grants.gov Customer Service, grantsinfo@nih.gov, 301-945-7573
Role: Co-Investigator

20-PAF07345 (PI: Wilcox) 04/01/2021-3/31/2026 0.6 CM
NIH $321,166/yr
Novel therapeutic targets in T-cell lymphoma-associated macrophages
Goal(s): (1) Harmonize and submit our "Pediatric and AYA Cancer Touchstone Dataset", which represents a wealth of real-world integrative genomic and clinical data for over 1,000 qualified patients. (2) Package and distribute the cloud-based computational infrastructure powering bioinformatics analyses of DNA and RNA sequencing data. (3) Document and codify our processes for interpreting n-of-1 genetic and molecular findings in the context of rare and pediatric cancers.

Contact Information at funding agency: Childhood Cancer Initiative, NCIChildhoodCancerDataInitiative@mail.nih.gov
Role: Co-Investigator

20-PAF08352 (PI: Chinnaiyan) 09/01/2020-8/31/2022 1.2 CM
PCF $500,000/yr
Targeting transcriptional addiction in prostate cancer by impeding neo-enhancer accessibility
Goal(s): (1) we will elucidate the mechanism of action of SMARCA2/4 degraders in mediating preferential activity in AR-positive CRPC cells using an integrative, multi-omics strategy. Cancer phenotypic assays will be performed in a spectrum of cell lines to comprehensively determine the impact of AU15330 treatment on AR-positive prostate cancer cells. RNA-seq, ATAC-seq, ChIP-seq, and HiChIP-seq will be carried out to define the transcriptome, promoter accessibility, cistrome (AR, FOXA1, ERG), and 3D chromatin structure upon SMARCA2/4 degradation. (2) we will conduct comprehensive efficacy studies of AU15330 using multiple pre-clinical models of CRPC. Experiments will be performed with AU15330 as a monotherapy and in combination with other anti-androgen therapies, and we will employ CRPC xenografts, genetically engineered mouse models, and patient-derived xenografts. (3) will determine predictive biomarkers of response and initiate the first-in-man study with a SMARCA2/4 degrader.
Contact Information at funding agency: Howard Soule, applications@pcf.org , 301-570-4596
Role: Co-Investigator

20-PAF08390 (PI: Salami) 09/01/2020-8/31/2022 0.6 CM
PCF $500,240/yr
Seeing the Unseen: Using Machine Learning and Molecular Profiling to Characterize Prostate Cancer Visibility on Multiparametric MRI
Goal(s): The goal of this project is to develop a machine learning algorithm for the detection of mpMRI visible and invisible GG ≥2 PCa and to characterize the molecular basis of high grade cancer visibility on mpMRI. In a pilot cohort using a targeted sequencing approach, we observed that the molecular profile of mpMRI visible and invisible cancer foci are indistinguishable, indicating that image-guided biopsy strategies and therapeutic interventions may miss biologically relevant cancer foci.
Contact Information at funding agency: Howard Soule, applications@pcf.org , 301-570-4596
Role: Co-Investigator

20-PAF08619 (PI: Green) 04/01/2021-3/31/2026 0.5 CM
PCF $373,452/yr
Targeting Immunogenic Cell Death with Radiotherapy to Enhance Immunotherapy Efficacy
Goal(s): is to define and harness the molecular determinants of inflammation which shape anti-tumoral immunity and influence cancer therapy efficacy. Our overall objective for this application is to determine the contribution of radiation-induced ferroptosis to innate and adaptive immune responses. Our central hypothesis is that radiation-induced ferroptosis generates oxidized lipids which act as DAMPs to stimulate innate immune cells and promote functional adaptive immune responses (Schema 1). We further hypothesize that enhancing immunostimulatory ferroptosis will augment immune checkpoint blockade efficacy. This hypothesis is supported by our preliminary unpublished data which suggests ferroptosis may be an immunogenic form of cell death. These results will be leveraged therapeutically to design rational combinatorial approaches with radiotherapy and immunotherapy to enhance combined therapy efficacy.
Contact Information at funding agency: Grants.gov Customer Service, grantsinfo@nih.gov, 301-945-7573
Role: Co-Investigator

20-PAF08943 (PI: Dlugosz) 04/01/2021-3/31/2026 1.2 CM
NIH $436,577/yr
Genetically-engineered mouse modeling of Merkel cell carcinoma: cross-species credentialing studies
Goal(s): (1) Perform a detailed cross-species comparison of an expanded cohort of K5/SLAP mouse MCCs and human MCCs. (2) Generate, characterize, and validate a single-locus, 2A-linked multi-transgene GEMM of MCC, carrying a fluorescent reporter and MCPyV TAgs, +/- Atoh1, on a pure background. (3)

Perform proof-of-principle translational studies using MCC-bearing mice as well MCC cell lines grown in syngeneic hosts.
Contact Information at funding agency: Grants.gov Customer Service, grantsinfo@nih.gov, 301-945-7573
Role: Co-Investigator

19-PAF05134 (PI: Robinson) 09/01/2020-8/31/2022 1.2 CM
BMS/PCF $500,000/yr
The Role of Precision Therapy in the Treatment of CDK12 Altered Metastatic Prostate Cancer
Goal(s): 1) Delineate the mechanisms by which CDK12 mutations generate an immune response 2) Investigate therapeutic strategies that confer synthetic lethality with CDK12 loss. 3) Identify molecular determinants of response in the first clinical trial of immune checkpoint blockade for CDK12-mutant mCRPC patients.
Contact Information at funding agency: Howard Soule, applications@PCF.org, 310-570-4596
Role: Co-Investigator

21-PAF00195 (PI:Narla) 07/01/2021-06/30/2024 0.2 CM
Dept. of Defense $129,269/yr
Investigation of Lynch Syndrome phenotypes through interactions between germline and somatic genetic Variation
Goal(s): Explain tumor susceptibility through germline-somatic variants.

PREVIOUS:

Award No. 701640 01/20/14 - 01/20/17 1.2 CM
Prostate Cancer Foundation, Young Investigator Award $75,000/yr
Clinical Implications of Expressed Pseudogene Transcripts in Metastatic Castration-resistant Prostate Cancer
Goal(s):1) Systematic characterization of expressed pseudo-genes across a compendium of human normal tissues and cancers with special emphasis on primary and metastatic prostate cancer. 2) Nomination and experimental validation of pseudogene based biomarkers of prostate cancer development and progression from tissue samples and liquid biopsies. 3) Discovery of biological mechanism of pseudogene function in disease and homeostasis. Specifically, the study of transcriptional co-regulation of gene-pseudogene expression patterns.
Contact Information at funding agency: Audrey Gardner, PCF Applications (applications@pcf.org)
Role: PI

UM1HG006508 (PI: Chinnaiyan) 07/19/13 – 06/30/17 2.4 CM
National Institutes of Health $1,288,110/yr
Exploring Precision Cancer Medicine for Sarcoma and Rare Cancers
Goal(s): The overall goal of this project is to bring together expertise at the University of Michigan including clinical oncology, cancer genetics, genomic science/bioinformatics, clinical pathology, social and behavioral sciences, and bioethics in order to implement clinical cancer sequencing of patients with sarcomas and other rare cancers to enable the detection of clinically significant molecular lesions (point mutations, insertions/deletions, gene fusions and rearrangements, outlier expressed genes, and amplifications/deletions).
Contact Information at funding agency: Harvey, Zephaun, harveyz@mail.nih.gov, 301 435-7859
Role: Co-Investigator

W81XWH-17-1-0224 (PI: Cieslik) 06/01/17 - 05/31/20 3.0 CM
Department of Defense $129,597/yr
Regulatory networks of immune evasion in metastatic prostate cancer
Goal(s): To understand the molecular mechanisms involved in the immune escape of mCRPC we propose to focus on tumor-host immune interactions within cancer metastatic sites by leveraging pan-cancer genomic and

clinical data sets. Foundational to our approach is the computational dissection of the magnitude and diversity of immune infiltration in mCRPC using RNA sequencing.
Contact Information at funding agency: Juan A. Rodriquez/ 301-619-2367; juan.a.rodriguez236.civ@mail.mil

P50 CA186786 (PI: Pitchiaya) 11/1/17 – 08/31/19 0.6 CM
NIH/NCI $60,000/yr
SPORE Career Enhancement Award - *Unraveling molecular heterogeneities in prostate cancer at single-cell resolution*
Goal(s): To investigate the role and quantify the extent of gene expression heterogeneity in prostate cancer.
Specific Aim(s): 1)Assist Investigators in the design of clinical, laboratory, and high-throughput genomic sequencing experiments 2)Assist Investigators in the analysis and interpretation of data from clinical and laboratory experiments, the processing and examination of high-throughput genomic datasets, and in writing of manuscripts relaying Michigan Prostate SPORE results to the scientific community 3)Undertake translational biostatistics and bioinformatics research to develop methodology and software implementation relevant to prostate cancer including the development of algorithmic toolkits for emerging types of genomic assays and the adaptation/refinement of existing computational approaches to the needs of the Michigan Prostate SPORE 4)To provide expertise and support for immunogenomics in prostate cancer. The Core will provide state-of-art support for interdisciplinary research at the interface of cancer immunology and genomics and facilitate the rapid clinical translation of immunogenomic findings.Contact Information at funding agency: Jennifer S. Meininger, 240-276-6330, jennifer.meininger@nih.gov
Role: Co-Investigator

Appendix 3, OTHER SUPPORT

MEHRA, ROHIT

CURRENT:

1U01CA214170-01 (PI: Chinnaiyan) 09/15/16 – 08/31/21 0.48 Calendar MO
NIH/NCI $372,000/yr Source Country: USA
The Early Detection Research Network (EDRN): Biomarker Developmental Laboratories (U01)
Discovery and qualification of transcriptomic biomarkers for the early detection of aggressive prostate cancer
Goal(s): 1) Identify and develop assays to study novel aggressive prostate cancer-associated transcriptomic alterations from our MiTranscriptome analysis. 2) Characterize transcripts from Aim 1 as tissue based aggressive prostate cancer biomarkers using individual in situ hybridization assays and a multiplexed next generation sequencing (NGS). 3) Characterize transcripts from Aim 1 as non-invasive, urine-based aggressive prostate cancer early detection biomarkers through collaboration with our industry partner and multiplexed NGS.
Role: Co-Investigator
Program Official: Jacob Kagan, jk380z@nih.gov

2 P50 CA186786-06 09/03/2019 – 08/31/2024 0.30 Calendar MO
NCI/NIH (PI: Chinnaiyan) Source Country: USA
Annual Direct: $1,191,863 Total Award: $9,215,218
Michigan Prostate SPORE: Biospecimen/Pathology Core
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-I
Program Official: Julia Arnold, jarnold@mail.nih.gov

W81XWH1910424 09/01/2019 – 08/31/2022 0.30 Calendar MO
DOD (PI: Pitchiaya) Source Country: USA
Annual Direct: $184,452 Total Award: $936,000
Unraveling tumor microenvironment heterogeneity in advanced prostate cancer
Major Goals: 1) Investigate the evolution of tumor microenvironment during PCa progression. Temporally profile genetically engineered mouse (GEM) models of aggressive PCa (Pten-/-, and High-Myc), to characterize the evolution and diversity of cancer cells, immune infiltrates and cancer-associated fibroblasts. 2) Understand the impact of therapeutic intervention on tumor microenvironment. Investigate the impact of immunotherapeutic drugs on cell type composition of tumors in GEM and syngeneic mouse (MycCaP) xenograft models. 3) Create a human prostate tumor cell atlas to stratify aggressive PCa subtypes in the general and veteran population. Use SCA to profile normal human prostates, localized PCa and metastatic castration resistant PCa (mCRPC) to identify the spatial co-ordinates of distinct tumor cell types.
Role: Co-I
Grants Specialist: Thomas Winter, Sidney.t.winter.civ@mail.mil, 240-357-1590

W81XWH-19-10407 09/01/2019 – 08/31/2023 0.60 Calendar MO
DOD (PI: Udager) Source Country: USA
Annual Direct: $148,882 Total Award: $1,169,017
Intratumoral heterogeneity of aggressive molecular biomarkers in lethal primary prostate cancer
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.

Role: Co-I
Grants Specialist: Thomas Winter, Sidney.t.winter.civ@mail.mil, 240-357-1590

1 R01 CA240991-01 09/01/2019 – 08/31/2024 0.36 Calendar MO
NCI/NIH (PI: Morgan) Source Country: USA
Annual Direct: $402,521 Total Award: $3,018,336
Determining the clinical impact of gene expression testing in localized prostate cancer
To do this, we propose the following aims:
Specific Aim 1: Develop an integrated clinical-genomic risk stratification system designed to systematize interpretation of GEC testing. We hypothesize that by developing integrated clinical-genomic risk groups we can identify patients most appropriate for AS while maintaining a standard, category-driven framework.

Specific Aim 2: Prospectively define the utility and safety of GEC testing to reduce overtreatment of men with newly diagnosed PCa. Through the statewide MUSIC and MROQC initiatives, we will conduct a large randomized trial of men with newly diagnosed favorable risk PCa. We hypothesize that GEC testing will decrease the use of primary therapy and increase QOL at 3 years, while maintaining rates of grade reclassification and biochemical recurrence at the same time point.

Specific Aim 3: Determine the impact of GEC testing on treatment failure and patient-reported QOL in men at high risk of recurrence post-prostatectomy on the G-MINOR trial. The G-MINOR trial, randomizing 350 men at high risk of local failure after prostatectomy to clinicopathologic risk stratification +/- GEC testing, completed accrual in June 2018 to assess decision making based on use of a GEC. We hypothesize that use of a GEC in higher risk patients will provide more accurate risk stratification and targeted treatment decisions, leading to improved cancer control and QOL without increasing overall rates of adjuvant radiotherapy.
Role: Co-I
Program Official: Erica Breslau, breslaue@mail.nih.gov

5 P01 CA093900-15 7/2/2020-5/31/2025 1.00 Calendar MO
NCI/NIH (PI: Keller) Source Country: USA
Annual Direct: $1,072,376 Total Award: $7,440,901
The Biology of Prostate Cancer Skeletal Metastases: Core C (Bone Core)
Major Goals: The ultimate goal is to define the cellular and molecular mechanisms that surround PCa skeletal metastases to facilitate translation into clinical application. The Bone Core of the Program Project will provide shared facilities and services for processing and interpretation of tissues from the animal models utilized in all projects of the program. The overall goal of the core facility is to provide centralized histologic and image analysis support for investigators in the project. Such a standardized format with provide valuable information and consistency across the projects in the program.
Role: Pathologist
Program Official: Joanna Watson, watsonjo@mail.nih.gov, 240-276-6230

PENDING:

1 U01 CA 4/1/2021-3/31/2026 0.60 Calendar MO
NCI/NIH (PIs: Alumkal, Kumar-Sinha) Source Country: USA
Annual Direct: $400,000 Total Award: $3,041,600
Determinants of De Novo Resistance to Androgen Receptor Targeting and Lineage Plasticity in Lethal Prostate Cancer
Major Goals: Identify molecular and microenvironmental features that correlate with drug resistance and determine how that changes over time.
Role: Co-I

Program Official: not available at this time

PAST:

W81XWH-16-1-0314 (PI: Mehra) 07/01/16 – 6/30/19 1.2 CM
Department of Defense Idea Award: $81,189/yr
Discovery and characterization of PRCAT47: A novel prostate lineage and cancer specific long non-coding RNA (PC150246)
Goal(s): 1) To elucidate the molecular mechanism behind PRCAT47 function 2) To assess clinical utility of PRCAT47 as a prognostic or diagnostic biomarker 3) To interrogate the therapeutic potential of PRCAT47 using clinical grade antisense oligos (ASOs).

P01-CA093900 (PI: Keller) 06/17/15 – 05/31/20 0.9 CM
NIH $73,055/yr
The Biology of Prostate Cancer Skeletal Metastases
Goal(s): The ultimate goal is to define the cellular and molecular mechanisms that surround PCa skeletal metastases to facilitate translation into clinical application
Role: Pathologist of Core 3 (Bone Core)

W81XH1520018 (PI: Hussain) 06/15/15 – 06/14/18 0.12 CM
Department of Defense $95,585/yr
PCCTC Affiliate Clinical Research Sites - The University of Michigan Site
Goal(s): The objective of this RFA is to solicit applications for PCCTC Affiliate Clinical Research Site membership. Affiliate Clinical Research Site participation is intended to enrich the Consortium's research areas which include but are not limited to: Clinical development opportunities based on the strength of the underlying science, particularly the biologically-based translational science of its members.
Role: Co-Investigator
Overlap: None

Appendix 4, PREVIOUS/CURRENT/PENDING
CHINNAIYAN, A.M.

CURRENT

R35CA231996 (PI: Chinnaiyan) 09/01/18 – 08/31/25 6.0 CM
National Institutes of Health $582,000/yr
Exploring Precision Oncology: From Gene Fusions to lncRNAs
Goal(s): advance the field of precision oncology by providing new community resources, identifying novel biomarkers, exploring the therapeutic targeting of nominated molecular players, and adding to the knowledge-base of cancer development mechanisms, particularly those of lncRNAs.
Specific Aims: None.
Contact Information at funding agency: Tawnya McKee, mckeeta@mail.nih.gov, 240-276-5719

U24CA210967 (MPIs: Chinnaiyan, Nesvishkii, Dhanasekaran) 09/15/16 – 08/31/21 0.6 CM
NIH $487,901/yr
University of Michigan Proteogenomics Data Analysis Center
Goal(s): to perform integrative analysis of data generated using the Clinical Proteomic Tumor Analysis Consortium (CPTAC). The Center at the University of Michigan is one of the four Centers funded by CPTAC. It will work, in coordination with other Centers, to analyze and integrate proteomics, genomics, and transcriptomics data generated for 3-4 cancer patient cohorts, ~ 100 samples in each cohort. The Center will generate data analysis reports to be shared with other members of the Consortium.
Specific Aim(s): 1) Assemble a comprehensive proteogenomics data analysis pipeline enabling application of two complementary strategies: (a) using mass spectrometry-based (MS) proteomics data for protein-level "validation" (and thus prioritization) of novel and aberrant cancer-specific transcripts (including alternative splice forms, mutations, etc.) identified from genomics and transcriptomic data.
2) Apply our computational pipelines to CPTAC-wide data, with a focus on presenting the results to the cancer research community in an easily accessible, highly visual form.
3) UM-PGDAC will engage, in coordination with other CPTAC centers, in a second round of prioritization work to select candidate cancer-specific proteins and peptides for subsequent targeted validation using multiplex proteomic assays.
Contact Information at funding agency: Rodriguez, Henry, rodriguezh@mail.nih.gov, 301 496-1550

1U01CA214170-01 (MPI: Chinnaiyan) 09/15/16 – 08/31/21 1.8 CM
NIH/NCI $360,840/yr
The Early Detection Research Network: Biomarker Developmental Laboratories (U01) *Discovery and qualification of transcriptomic biomarkers for the early detection of aggressive prostate cancer*
Goal(s): 1) Identify and develop assays to study novel aggressive prostate cancer-associated transcriptomic alterations from our MiTranscriptome analysis. 2) Characterize transcripts from Aim 1 as tissue based aggressive prostate cancer biomarkers using individual in situ hybridization assays and a multiplexed next generation sequencing (NGS). 3) Characterize transcripts from Aim 1 as non-invasive, urine-based aggressive prostate cancer early detection biomarkers through collaboration with our industry partner and multiplexed NGS.
Specific Aim(s): 1) Identify novel aggressive prostate cancer-associated transcriptomic biomarkers nominated from our MiTranscriptome analysis; 2) Develop transcriptomic tissue biomarkers of aggressive prostate cancer; 3) Develop non-invasive urine transcriptomic biomarkers of aggressive prostate cancer
Contact Information at funding agency: Kagan, Jacob; jk308z@nih.gov

1 R01 CA200660-01A1 (PIs: Grembecka, Chinnaiyan) 08/01/16 - 07/31/21 0.48 CM
NIH/NCI $233,568/yr
Targeting the MLL complex in Castration Resistant Prostate Cancer
Specific Aim(s): 1) Develop highly potent small molecule inhibitors of the menin-MLL interaction with significantly improved potency in prostate cancer models and optimal in vivo properties. 2) we propose to study

the mechanism of pharmacologic inhibition of the MLL complex in prostate cancer cells 3) we will assess the in vivo efficacy of the menin-MLL inhibitors in mice models of prostate cancer and investigate the mechanism of resistance of response to these compounds in prostate cancer models. Upon successful completion of this project we expect to identify promising candidate compound(s) that could be further developed for clinical use to treat metastatic CRPC.
Goal(s): to develop new therapy for castration resistant prostate cancer patients by blocking the menin-MLL interaction.
Contact Information at funding agency: Elesinmogun, Funmi, elesinmf@mail.nih.gov, (240) 276-6313

P50 186786 (PI: Chinnaiyan, Palapattu, Heath)) 09/11/14 - 08/31/24 2.4 CM
NIH/NCI $1,191,863/yr
Michigan Prostate SPORE
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.

Overall: Michigan Prostate SPORE
Specific Aim(s): 1) Support multidisciplinary, collaborative projects that pair basic and clinical investigators and draw on expertise of scientists from within and from outside the prostate cancer field. 2) Provide support for pilot projects with high potential to advance prostate cancer research to obtain preliminary data that will form the basis for grant submissions to extramural sponsors.3) Recruit and train early-stage scientists to become the next generation of leaders in translational prostate cancer research through access to mentors that are renowned senior investigators and leaders in basic and clinical arenas, as well as networking opportunities among other project Co-Leaders. 4) Provide world-class infrastructure to carry out innovative, high-quality, high-impact translational prostate cancer research. 5) Support efforts to develop bench-to-bedside discoveries for clinical diagnostics and therapies. 6) Foster collaborations among investigators within the institution and with other institutional SPORES or extramural prostate cancer programs.

Administration Core
Specific Aim(s): 1)Provide scientific, programmatic, and administrative leadership to all aspects of the SPORE. Effective AC leadership is essential to the success of the Michigan Prostate SPORE. The Administration Core is the central decision-making group designed to encourage research productivity, promote interaction and collaboration, and set the vision, direction, and priorities for the Michigan Prostate SPORE. 2) Develop, facilitate, and monitor progress of translational aims with project Co-Leaders. The Clinical Applications Committee, the annual review with the External Advisory Board and Steering Committee, and the monthly meetings between Project Leaders and the PIs function to keep the Michigan Prostate SPORE robust and move the translational objectives forward. All of these interactions are facilitated by the Administration Core. 3) Identify, support, and facilitate scientific collaborations. The Administration Core is charged with creating a culture of collaboration through initiating and implementing successful interactions among those involved in the SPORE program. Formal horizontal and vertical collaborations are encouraged to accomplish research progress and move promising SPORE projects to the next step on the translational/clinical development pathway. 4) Facilitate communication. Effective and timely communication is crucial to the Michigan Prostate SPORE's success. The Administration Core is responsible for facilitating communication between investigators and groups within the Michigan Prostate SPORE as well as among the SPORE network, the NCI, and investigators across the spectrum of translational cancer research. 5) Perform fiscal and data management functions. The Core performs financial management for each SPORE project, core, and development project. The Core also oversees data management, an essential component of clinical research. 6) Provide functional and ethical oversight to projects and cores and coordinate patient advocacy. The Core provides support and oversight to ensure that all investigators have IRB and animal approvals in place to conduct research. The Core also coordinates quality assurance between the tissue banks and clinical databases. The Core will develop and maintain an advocacy portal to the prostate cancer patient community.

Project 1: Targeting Metastatic Prostate Cancer Patients with Biallelic Loss of CDK12
Specific Aim(s): 1) To assess the utility of MiPS-NGS as a prostate cancer early detection assay in men at high genetic risk. 2) To determine whether MiPS-NGS can predict grade progression in men on active surveillance.

Core 2: Biospecimen/Pathology Core

Specific Aim(s): 1) To protect patient welfare. The highest priority is given to assure that no research protocol compromises pathology diagnosis or tumor staging. Patient confidentiality is maintained through use of an IRB-approved database protocol. 2) The acquisition and processing of prostate tissues for research. The Core assures that the widest range of prostate tissues and derived biomolecules (i.e., protein, DNA and RNA) are available from several established and new sources. These include benign prostate tissue from patients without any known prostatic disease (cystoprostatectomy specimens and transplant donor prostates), clinically localized prostate cancer, and metastatic hormone refractory prostate cancer (Michigan Legacy Tissue Program). 3) To provide high quality pathologic review of prostate tissues. Expert GU pathologists assure uniform review of prostate tissue samples. 4) To provide expert pathology consultation for the purpose of designing translational research projects. This service focuses on determining the types of tissues and amount required for the successful completion of the projects. 5) To perform quality assessment of prostate tissues and clinical data. The Core staff regularly evaluates frozen and formalin fixed tissues for adequacy. 6) To develop technology appropriate for pathology-based translational research. In this renewal, FISHbased strategies are being developed to evaluate genomic biomarkers using tissue microarrays; clinical sequencing of genome and transcriptome from patient specimens to identify causative, driving mutations are being introduced and; organoid and patient-derived xenograft models. 7) Provide support to ongoing clinical studies. The Core will continue to provide tissue procurement services and/or high-quality pathology reviews of specimens from patients enrolled in various clinical trials and studies. 8) The maintenance of clinical and pathology data with links to molecular studies. The Core will continue to expand the detailed clinical and pathology database conforming to the National Cancer Institute's Common Data Elements (CDE) guidelines, permitting queries between molecular findings and clinically relevant outcomes.

Contact Information at funding agency: Jennifer S. Meininger, 240-276-6330, jennifer.meininger@nih.gov

Role: Overall Program Director, Core Leader of Administration Core, Basic Co-Leader of Project 1, Core Co-Leader of Core 2 (BioSpecimen Core).

15CHAS07 (PI: Chinnaiyan) 10/01/15 – 03/12/20 (NCE) 0.01 CM
Prostate Cancer Foundation $500,000/yr

Prostate Cancer Foundation Dream Team Continuation of the CRPC 500 Cohort Study

Specific Aim(s): 1) Continue to gather clinical follow-up on patients enrolled on the CRPC 500 cohort. This will fund the clinical coordination site to maintain data collection across the multi-institutional cohort. To help facilitate access of this data by the research community we will establish a "Data Sharing Core" to enable easy access and sharing of the sequence data along with valuable clinical parameters across the consortium. We will explore the use of commercial cloud based infrastructure to support this initiative. 2) Identify 150 patients out of 500 from the CRPC500 study who have progressed for re-biopsy and whole exome and transcriptome sequencing analysis. This will allow us to assess tumor evolution and decipher molecular mechanisms of resistance. Matched progression biopsies will markedly increase the statistical power to attribute causality to alterations identified. 3) Identify and sequence 150 CRPC patients that have progressed post-abiraterone and/or postenzalutamide. This will allow us to establish the molecular landscape of a post-Abi/post-Enza cohort of patients. Compare molecular and morphological alterations with the West Coast Dream Team.

Contact Information at funding agency: Dr. Howard Soule, applications@pcf.org, Prostate Cancer Foundation, 1250 4th Street, Santa Monica, CA 90401

ORSP 19-PAF05802 04/11/19 – 12/31/20 0.01 CM
(MPI: Chinnaiyan and Robinson) $595,500/yr
Multiple Myeloma Research Foundation

Multiple Myeloma Patients - MYDRUG

Specific Aim(s): To carry out the clinical sequencing of 300 patients with advanced multiple myeloma in our CLIA sequencing laboratory.

Contact Information at funding agency: Men Yesil, yesilil@themmrd.org, Multiple Myeloma Research Foundation, Inc., 383 Main Avenue, Norwalk, CT 06851.

ORSP 19-PAF05516 04/01/19 – 03/31/24 0.01 CM
(PI: Chinnaiyan) $226,800/yr
The West Side Institute for Science and Education / Prostate Cancer Foundation
VA/PCF Precision Center of Excellence Award - Jesse Brown VA Medical Center
Specific Aim(s): To carry out clinical sequencing of samples from veterans with metastatic prostate cancer in the form of germline, primary tumor, metastatic tissue (acquired under metastasis biopsy protocols) and ctDNA at time of treatment changes in an effort to ascertain DNA alterations which could provide treatment options through industry-sponsored and investigator-initiated studies.
Contact Information at funding agency: Kevin Hull, Kevin.Hull@va.gov, Jesse Brown VA Medical Center, 820 S. Damon Ave #151, Chicago, IL 60612.

18VALO03, Research Agreement Dated 10-8-19 04/01/19 – 03/31/24 0.01 CM
(PI: Chinnaiyan) $226,800/yr
Veterans Education & Research Assoc of MI / Prostate Cancer Foundation
VA/PCF Precision Center of Excellence Award - Ann Arbor
Specific Aim(s): To carry out clinical sequencing of samples from veterans with metastatic prostate cancer in the form of germline, primary tumor, metastatic tissue (acquired under metastasis biopsy protocols) and ctDNA at time of treatment changes in an effort to ascertain DNA alterations which could provide treatment options through industry-sponsored and investigator-initiated studies.
Contact Information at funding agency: Birgit Roller, birgit.roller@va.gov, VA Medical Center, Research Service #151, 2215 Fuller Road, Ann Arbor, MI 48105

18VALO10 - ORSP 20-PAF00091 11/18/19 – 11/08/24 0.01 CM
(PI: Chinnaiyan) $226,800/yr
Bay Pines Foundation, Inc / Prostate Cancer Foundation
VA/PCF Precision Center of Excellence Award - Bay Pines VA Healthcare System
Specific Aim(s): To carry out clinical sequencing of samples from veterans with metastatic prostate cancer in the form of germline, primary tumor, metastatic tissue (acquired under metastasis biopsy protocols) and ctDNA at time of treatment changes in an effort to ascertain DNA alterations which could provide treatment options through industry-sponsored and investigator-initiated studies.
Contact Information at funding agency: Eric Abercrombie, Eric. Ambercrombie@va.gov, Executive Director, 10000 Bay Pines Blvd, PO Box 416, Bay Pines, FL 33744

18VALO10 - ORSP 20-PAF03953 2/10/20 – 2/09/25 0.01 CM
(PI: Chinnaiyan) $226,800/yr
Tampa VA Research and Education Foundation / Prostate Cancer Foundation
VA/PCF Precision Center of Excellence - Tampa VA Research and Education Foundation
Specific Aim(s): To carry out clinical sequencing of samples from veterans with metastatic prostate cancer in the form of germline, primary tumor, metastatic tissue (acquired under metastasis biopsy protocols) and ctDNA at time of treatment changes in an effort to ascertain DNA alterations which could provide treatment options through industry-sponsored and investigator-initiated studies.
Contact Information at funding agency: Reeder, Douglas. dreeder@tampavaref.org, 813-780-2623 ext 103

PENDING:

PCF Challenge (MPIs: Chinnaiyan and Alva) 09/01/19 – 08/31/21 1.2 CM
Prostate Cancer Foundation $500,000/yr
The Role of Precision Therapy in the Treatment of CDK12 Altered Metastatic Prostate Cancer

Specific Aim(s): 1) Delineate the mechanisms by which CDK12 mutations generate an immune response 2) Investigate therapeutic strategies that confer synthetic lethality with CDK12 loss. 3) Identify molecular determinants of response in the first clinical trial of immune checkpoint blockade for CDK12-mutant mCRPC patients.
Contact Information at funding agency: Dr. Howard Soule, applications@pcf.org, Prostate Cancer Foundation, 1250 4th Street, Santa Monica, CA 90401

Award No: N/A (PI: Reddy) 07/01/20 – 06/30/27 0.12 CM
NIH $600,000/yr
Chromatin folding and nuclear architecture studies of donor T cells and host epithelial cell targets in GVHD
Specific Aiml(s): We will use our expertise in dissecting the immune-biology and IEC metabolism in GVHD and complement it with cutting edge technologies to assess chromatin organization to understand the fundamental nuclear architectural dynamics in regulation of T cells and IECs, which may lead to development of targeting of higher order chromatin structures as an entirely new strategy to mitigate GVHD.
Contact Information at funding agency: N/A

3-P30-CA046592 (PI: Fearon) 05/01/20 – 10/31/20 0.6 CM
NIH/NCI $250,000/yr
Targeting TMPRSS2 expression as a therapy for coronavirus infection and replication
Specific Aim(s): To provide a pre-clinical rationale to evaluate drugs that suppress lung epithelial TMPRSS2 expression to treat or prevent coronavirus.
Contact Information at funding agency: Ptak, Krzysztof: krzysztofptak@mail.nih.gov

20-PAF08352 (PI: Chinnaiyan) 09/01/20 – 8/31/22 0.6 CM
Prostate Cancer Foundation $500,000/yr
Targeting transcriptional addiction in prostate cancer by impeding neo-enhancer accessibility
Specific Aim(s): (1) Elucidate the mechanism of action of SMARCA 2/4 degraders in mediating preferential cytotoxicity in AR/FOXA1-driven CRPC using an integrative, multi-omics strategy (2) Conduct comprehensive efficacy studies of AU15330, a novel SMARCA2/4 degrader, using multiple pre-clinical models of CRPC. (3) Determine predictive biomarkers of response to SMARCA2/4 degraders and initiate a Phase I/II trial with AU15330 in mCRPC patients.
Contact Information at funding agency: Soule, Howard: applications@pcf.org, 310-570-4596

20-PAF07516 (PI: Fearon) 09/01/20 – 8/31/21 0.2 CM
NIH/NCI $320,513/yr
Enhancement of Data Sharing in Pediatric, Adolescent and Young Adult Cancers
Specific Aim(s): (1) Harmonize and submit our "Pediatric and AYA Cancer Touchstone Dataset", which represents a wealth of real-world integrative genomic and clinical data for over 1,000 qualified patients. (2) Package and distribute the cloud-based computational infrastructure powering bioinformatics analyses of DNA and RNA sequencing data. (3) Document and codify our processes for interpreting n-of-1 genetic and molecular findings in the context of rare and pediatric cancers.
Contact Information at funding agency: Guidry Auvil, Jaime, Jaime.guidryauvil@nih.gov

20-PAF08017 (PI: Fearon) 09/01/20 – 8/31/21 0.2 CM
NIH/NCI $192,308/yr
Development of National Childhood Cancer Registry
Specific Aim(s): (1) Identify and aggregate existing comprehensive clinical and genomic data from pediatric and adolescent and young adult (AYA) cancer patients using the Long-Term Pediatric Oncology Database. (2) Perform assessment of data quality and establish processes for correcting missing or inconsistent data. (3) Using well-established informatics tools and approaches, map our cancer data to established standards, and submit the data to the Cancer Research Data Commons or other NCI repositories.
Contact Information at funding agency: Lam, Clara, clara.lam@nih.gov

20-PAF08390 (PI: Salami) 09/01/20 – 8/31/22 0.6 CM
Prostate Cancer Foundation $500,000/yr
Seeing the Unseen: Using Machine Learning and Molecular Profiling to Characterize Prostate Cancer Visibility on Multiparametric MRI
Specific Aim(s): to develop a machine learning algorithm for the detection of mpMRI visible and invisible GG ≥2 PCa and to characterize the molecular basis of high grade cancer visibility on mpMRI. In a pilot cohort using a targeted sequencing approach, we observed that the molecular profile of mpMRI visible and invisible cancer foci are indistinguishable, indicating that image-guided biopsy strategies and therapeutic interventions may miss biologically relevant cancer foci.Contact Information at funding agency: Lam, Clara, clara.lam@nih.gov

OVERLAP
There is no scientific or budgetary overlap.

PREVIOUS:

Award No: N/A (PIs: Chinnaiyan and Heath) 12/31/16 – 12/31/19 (NCE) 0.12 CM
Prostate Cancer Foundation $500,000/yr
Development of an Autophagy Inducing Multi-Tyrosine Kinase Inhibitor ESK981 in the Treatment of Castration Resistant Prostate Cancer
Specific Aims: 1) To explore the mechanism of action of ESK981 in castration resistant prostate cancer; 2) To investigate the efficacy of ESK981 in pre-clinical models of castration resistant prostate cancer; and 3) To initiate a Pilot Phase II study of ESK981 in metastatic castration resistant prostate cancer. UM will be responsible for Aims 1 and 2 and also biomarker development for pre-clinical study in vivo in Aim 3.
Contact Information at funding agency: Dr. Howard Soule, applications@pcf.org, Prostate Cancer Foundation, 1250 4th Street, Santa Monica, CA 90401

W81XWH-12-1-0080 (PI: Chinnaiyan and Li) 09/15/12 – 09/14/19 (NCE) 0.12 CM
Department of Defense $589,661/yr
Collaborative Innovators Award: Advancing our understanding of the etiologies and mutational landscapes of basal-like, luminal A, and luminal B breast cancers
Goal(s): Sequencing of samples to find mutations; correlate with clinical pathologic and epidemiologic factors
Specific Aim(s): 1) Identify and quantify risk factors for each of the most common molecular subtypes of breast cancer, basal-like, luminal A, and luminal B tumors, in a large-scale population-based study.
2) Discover and validate the mutational landscape of basal-like, luminal A, and luminal B tumors.
3) Characterize the relationships between subtype specific risk factors and mutational signatures.
4) Develop and validate risk prediction models unique to each breast cancer subtype incorporating clinical, epidemiologic and mutation data. 5) Identify and quantify the relationships between various exposures and mutational changes on risk of breast cancer recurrence and survival among patients with basal-like, luminal A, and luminal B tumors.
Contact Information at funding agency: Cheryl A. Lowery, U.S. Army Medical Research Acquisition Activity, 820 Chandler Street (MCMR-AAA-R), Fort Detrick, MD 21702-5014, 301-619-7150, Cheryl.Lowery@us.army.mil

W81XWH-14-1-0555 (MPI: Chinnaiyan) 09/22/14 – 09/21/18 (NCE) 0.6 CM
Department of Defense $125,978/yr
Development of Personalized Cancer Therapy for Men with Advanced Prostate Cancer
Specific Aim(s): 1) Develop PDXs that reflect the lethal form of PCa; 2) Develop a responder ID profile hypothesis according to the treatment responsiveness of fully characterized PCa PDXs; 3) Validate the responder ID profile hypothesis in a clinical trial
Goal(s): to develop a strategy for identifying molecular therapeutic response markers of advanced prostate cancer to specific therapies by using patient-derived xenografts (PDXs) from patients with prostate cancer.

Contact Information at funding agency: Peggie Lesnow, 820 Chandler Street, Fort Detrick, MD, 21702, Phone: 301-619-2367, Email: margaret.a.lesnow.civ@mail.mil

U01-HL-126499 (PI: Tewari) 08/01/14 – 08/31/18 0.48 CM
NIH, NHLBI $112,197/yr
Reference Profiles of ExRNA in Biofluids from Well-Defined Human Cohorts
Specific Aim(s): 1) To sequence exRNAs present in biofluids of healthy individuals. 2) To identify and annotate both endogenously and exogenously-derived exRNA sequences. 3) To perform validation and absolute quantification of exRNAs using droplet digital PCR (ddPCR). 4) To perform cross-validation service and integrate scientifically with other Consortium teams.
Goal(s): To generate quality-controlled, comprehensive RNA sequencing-based profiles of human body fluids including plasma, serum and urine from healthy individuals.
Role: Co-investigator
Contact Information at funding agency: Tracee Foster Email: gilchrit@mail.nih.gov Phone: 301.402.3843

UM1HG006508 (PIs: Chinnaiyan, Pienta and Robert) 07/19/13 – 05/31/18 (NCE) 1.2 CM
National Institutes of Health $813,023/yr
Exploring Precision Cancer Medicine for Sarcoma and Rare Cancers
Goal(s): The overall goal of this project is to bring together expertise at the University of Michigan including clinical oncology, cancer genetics, genomic science/bioinformatics, clinical pathology, social and behavioral sciences, and bioethics in order to implement clinical cancer sequencing of patients with sarcomas and other rare cancers to enable the detection of clinically significant molecular lesions (point mutations, insertions/deletions, gene fusions and rearrangements, outlier expressed genes, and amplifications/deletions).
Specific Aim(s): Project 1) Clinical Genomic Study, 1) Accrue 500 patients with advanced or refractory rare cancer for participation in an integrated approach to Clinical Genomics; 2) Interpret results through a multi-disciplinary Sequencing Tumor Board and disclose results to patients and their physicians; 3) Measure the influence of sequence results provided to patients; 4) Determine the frequency of clinically significant germline mutations in patients undergoing comprehensive tumor sequence analysis.
Project 2) Sequencing, Analysis, and Interpretation of Sequencing Data; 1) Process and track specimens and ensure quality control; 2) Sequence tumor and germline biospecimens; 3) Analyze sequencing data to identify clinically significant variants; 4) Interpret and translate sequence variants into clinical oncology setting; 5) Assess and evaluate costs associated with clinical sequencing.
Contact Information at funding agency: Harvey, Zephaun, harveyz@mail.nih.gov, 301 435-7859

(MPIs: Chinnaiyan, Wang, Malik) 07/31/15 – 07/30/17 0.12 CM
Prostate Cancer Foundation – Movember Challenge Award $194,495/yr
Targeting the MLL complex for the development of new therapeutics for CRPC
Specific Aim(s): 1) To design and develop small molecular inhibitors of the menin-MLL interaction with improved potency in prostate cancer models and optimized drug-like properties for clinical development; 2) To study the mechanism of pharmacologic inhibition of the menin-MLL interaction in prostate cancer cells; 3) To establish in vivo efficacy of menin inhibitors in animal models of prostate cancer.
Goal(s): to discover and develop new small-molecule inhibitors for the treatment of advanced lethal prostate cancer by targeting MMSET.
Contact Information at funding agency: Dr. Howard Soule, applications@pcf.org, Prostate Cancer Foundation, 1250 4th Street, Santa Monica, CA 90401

U01CA183027 (PIs: Chinnaiyan, Linehan) 02/11/14 - 01/31/17 1.2 CM
NIH $257,334/yr
Integrative molecular imaging and sequencing of prostate cancer
Goal(s)/Aim(s)1) Enroll patients with known or suspicious for prostate cancer in the NIH MRI/metabolic imaging program, 2) Whole exome and transcriptome sequencing analysis of 60 patients identified with clinically localized prostate cancer from frozen biopsy material obtained in Aim 1. 3) Integrative analysis of

histopathology, molecular imaging, metabolism, mutational landscape and gene expression alterations of biopsy material from this clinical trial.
Contact Information at funding agency: Henderson, Lori A., hendersonlori@mail.nih.gov, 240.276.5930

PC121111 (PI: Scher, H.) 09/30/13 – 09/29/16 0.91 CM
Department of Defense $300,000/yr
Toward the Practice of Precision Medicine: Multicenter Validation of Biomarker Assays for Clinical Management of Prostate Cancer
Goal(s): Establish and validate TMPRSS2:ERG assays; Validate the utility of the TMPRSS2:ERG TMA assay for the non-invasive detection of clinically significant prostate cancer in urine; Validate the ERG rearrangement FISH assay on tissues and determine the prevalence of ERG rearrangements in isolated precursor and diagnostically challenging lesions
Specific Aim(s): 1) To cross-validate an initial set of assays for biomarkers corresponding to the AR and PI3K/PTEN axes ready for near-term filing with the FDA for use in prospective integral biomarker-driven trials in prostate cancer; 2) To use the centralized infrastructure of the Assay Validation Coordinating Center to cross-validate additional assays for biomarkers identified via established and emerging discovery platforms (i.e., NCI Prostate Cancer SPOREs, PCF, SU2C, and TCGA) for use in prospective integral biomarker-driven trials in prostate cancer.
Role: Co-Investigator; Contact Information At Funding Agency: Kathy E. Robinson, Grants Officer, Us Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick Md 21702-5014

AACR (Dream team leader: Chinnaiyan) 08/01/12 – 07/31/16 (NCTX) 0.6 CM
Stand up to Cancer & Prostate Cancer Foundation Dream Team $538,355/yr
Precision Therapy of Advanced Prostate Cancer
Goal(s): The overall goal of this proposal is to catalyze the interaction of a multi-disciplinary team of investigators, with a track record of accomplishments in prostate cancer research, to work together on the challenging problem of metastatic castration resistant prostate cancer (CRPC).
Specific Aim(s): 1) Establish a multi-institutional infrastructure incorporating 5 leading prostate cancer clinical sites, 2 sequencing and computational analysis sites, linked with appropriate sample and data coordination; 2) Establish a prospective cohort of 500 patients (the "CRPC 500") utilizing the multi-institutional infrastructure to support the clinical use of integrative prostate cancer sequencing, analysis, and clinical trial decision making; 3) Conduct parallel, preclinical *in vivo* functional studies of resistance biomarkers and of SU2C-PCF sponsored combination therapies; 4) Identify molecular determinants of abiraterone sensitivity and acquired resistance in patients; 5) Conduct clinical trials of novel combinations targeting AR and/or the PTEN pathway, based on existing preclinical data and an understanding of resistance mechanisms; 6) Identify molecular determinants of sensitivity and acquired resistance to PARP inhibitors in patients.
Contact Information at funding agency: Frederic Biemar, frederic.biemar@aacr.org, (215) 446-7261

R01 CA154365 (PIs: Beer and Chinnaiyan) 04/01/11 – 03/31/16 0.36 CM
National Institutes of Health $92,500/yr
Identification and Characterization of Gene Fusions in Lung Adenocarcinoma
Goal(s): This proposal will identify new gene-fusions in lung cancer utilizing a newly developed bioinformatics approach combined with next-generation sequencing data.
Specific Aim(s): 1) Functional characterization of the R3HDM2-NFE2 gene fusion in H1792 lung cancer cells, 2) Determine the frequency of occurrence in primary lung cancer and functionally characterize the novel HSPA1ANFKBIL1; 3) Functional characterization of novel gene fusions in lung cancer.
Contact Information at funding agency: Rebecca Brightful, **Email**: brightfr@mail.nih.gov **Phone**: 301-631-3011 **Fax**: 301-451-5391

R01 CA125612 (PI: Rubin) 04/01/13 - 03/31/16 0.24 CM
NIH $27,400/yr
Towards Understanding Prostate Cancer Heterogeneity

Goal(s): Determine protein-protein interactions and subsequent signaling cascades with mass spectrometry
Specific Aim(s): 1) To determine the substrate specificity of prostate cancer-derived SPOP mutants; 2) To determine the downstream pathways deregulated by SPOP mutations; 3) To establish the prevalence of SPOP mutation, its relation to other molecular changes, and its significance to patient outcomes in multiple populations of prostate cancer.
Contact Information at funding agency: Michelle Lewis, Joan & Sanford I Weill Medical College of Cornell University, 1300 York Avenue, New York, NY 10085
Role*:* Co-Investigator

No Award # (PIs: Chinnaiyan, Wang, Stuckey) 10/01/12 – 10/15/15 (NCTX) 0.12 CM
Prostate Cancer Foundation $252,002/yr
PCF Honorable A. David Mazzone Challenge Award*: Targeting ERG Fusion Protein for New Prostate Cancer Therapy*
Specific Aim(s): 1) Design of more potent and cell-permeable peptidomimetics targeting ERG; 2) Discovery and optimization of non-peptide small molecule inhibitors targeting ERG; 3) Characterization of candidate small molecules targeting ERG
Goal(s): discover and develop a new therapy for the treatment of prostate cancer by targeting ERG fusion protein in prostate cancer
Contact Information at funding agency: Dr. Howard Soule, applications@pcf.org, Prostate Cancer Foundation, 1250 4th Street, Santa Monica, CA 90401

U01CA111275 (PIs: Chinnaiyan and Rubin) 08/01/10 – 06/30/15 1.2 CM
NIH/NCI $486,120/yr
Early Detection Research Network: A Systems Biology Approach to the Development of Cancer Biomarkers
Goal(s): Develop "Omics based approaches to study solid tumor for the purpose of developing biomarkers.
Specific Aim(s): Platform technologies cover epigenetics, genomics, transcriptomics, proteomics and metabolomics.
Contact Information at funding agency: Jennifer Edwards, Jennifer.Edwards1@nih.hhs.gov

W81XWH-08-0110 (PI: Chinnaiyan) 09/01/08 – 08/31/13 2.28 CM
Department of Defense – Era of Hope $500,000/yr
A Search for Gene Fusions/Translocations in Breast Cancer
Specific Aims: 1) develop high-throughput adaptations of existing methodologies such as fluorescence in situ hybridization (FISH), 2) employ bioinformatics and associated analytical tools to elucidate recurrent gene fusions in breast cancers, 3) employ next generation whole transcriptome sequencing of breast tumors.
Contact Information at funding agency: Grants Officer: Cheryl A. Lowery, 301-619-7150, Cheryl.Lowery@us.army.mil, U.S. Army Medical Research Acquisition Activity, 820 Chandler Street (MCMR-AAA-R), Fort Detrick, MD 21702-5014 0284

W81XWH-11-1-0337 (PI: Chinnaiyan) 09/30/11 – 09/29/15 1.2 CM
Department of Defense $145,145/yr
Prostate Cancer Research Program Idea Development Award, Established Investigator
Discovery of Novel Gene Elements Associated with Prostate Cancer Progression
Goal(s): determine if prostate cancer harbors numerous uncharacterized ncRNAs and show that a subset of these is differentially-expressed transcripts
Specific Aims: 1) to employ next generation sequencing to comprehensively annotate expressed regions in the prostate cancer transcriptome; 2) to validate and characterize transcriptional units in poorly annotated regions; 3) to elucidate a functional and clinical role of poorly-annotated transcripts in prostate cancer.
Contact Information at funding agency: Janet Kuhns, 301-619-2827, janet.kuhns@us.army.mil, U.S. Army Medical Research Acquisition Activity, 820 Chandler Street (MCMR-AAA-R), Fort Detrick, MD 21702-5014

PI: Chinnaiyan 01/01/09 – 12/31/13 0.12 CM
Doris Duke Foundation $275,000/yr

Distinguished Clinical Scientist Award for Excellence in "Bench to Bedside" Research
Goal(s): to launch a new effort in the laboratory to comprehensively and systematically scour common human solid tumors for the presence of recurrent gene rearrangements. This effort primarily funds the training of new translational researchers under the mentorship of Dr. Chinnaiyan.
Specific Aims: 1) Develop and employ high-throughput fluorescence in situ hybridization (FISH) in order to interrogate solid tumors for recurrent chromosomal aberrations including gene fusions and translocations; 2) Employ bioinformatics and associated analytical tools to elucidate recurrent gene fusions in common solid tumors;. 3) Employ next generation whole transcriptome and paired-end sequencing of common solid tumors to identify recurrent gene fusions and integrated non-human sequences that may represent pathogens.
Contact Information at funding agency: Grants Officer: Betsy Myers, emyers@ddcf.org, Doris Duke Charitable Foundation, 650 5th Avenue, Fl 19, NY, NY; Phone: 212-974-7000

R01CA132874-01 (PI: Chinnaiyan) 03/01/09 – 12/31/13 0.96 CM
NIH/NCI $166,000/yr
Molecular Sub-typing of Prostate Cancer Based on Recurrent Gene Fusions
Goal(s): Identification of novel molecular subtypes of cancer, characterization of these subtypes, and correlation of these with disease outcome using prostate needle biopsy samples.
Specific Aims: 1) discovery and nomination of novel molecular sub-types of prostate cancer, 2) characterize associations of molecular sub-types of prostate cancer with clinical outcome and/or aggressiveness of disease in a radical prostatectomy cohort, 3) characterize associations of molecular sub-types of prostate cancer with clinical outcome and/or aggressiveness of disease using prostate needle biopsy samples.
Contact Information at funding agency: Grants Management Specialist: Rebecca Brightful, Email: brightfr@mail.nih.gov Phone: 301-631-3011

P50 CA69568 (PI: Chinnaiyan) 06/01/08 - 05/31/13 2.4 CM
NIH/NCI $177,509/yr
SPORE in Prostate Cancer
Project 1 Title: *Role of gene fusions in prostate cancer*
Goal(s): determine the role of ETS family gene fusions in prostate cancer cell lines; characterize the phenotype of androgen-regulated ETS transgenic mice.
Specific Aims: 1) Characterization of Oncogenic ETS Gene Fusions in Prostate Cancer; 2) Determine the role of ETS family gene fusions in prostate cancer cell lines; 3) characterize the phenotype of androgen-regulated ETS transgenic mice.
Role: Co-Investigator
Contact Information at funding agency: Andrew Hruszkewycz, 301-496-8528, hruszkea@mail.nih.gov

Appendix 5, PREVIOUS/CURRENT/PENDING SUPPORT

ALVA, AJJAI S.

Current

Title: A Phase 1 Study to Evaluate the Safety and Tolerability of Immunotherapy Combinations in Participants with Advanced Malignancies
Time Commitments: 1.4 Calendar Months
Supporting Agency: Arcus Biosciences, Inc.
Address: 3928 Point Eden Way, Hayward, CA 94545
Contracting/Grants Officer: Dayna Roberson, droberson@c3-research.com
Performance Period: 07/29/2019-05/31/2024
Level of Funding: $757,727
Project Goal: To assess the safety and tolerability of AB928 combination therapy in participants with advanced malignancies.
Specific Aims: N/A
Overlap: None

Title: A Randomized, Open-Label, Phase 3 Study of BMS-936558 vs. Everolimus in Subjects with Advanced or Metastatic Clear-Cell Renal Cell Carcinoma Who Have Received Prior Anti-Angiogenic Therapy
Time Commitments: 0.1 calendar months
Supporting Agency: Bristol-Myers Squibb Company
Address: 5 Research Parkway, Wallingford, CT 06492
Contracting/Grants Officer: Keleni Tukia, keleni.tukia@bms.com
Performance Period: 01/15/2013-01/13/2022
Level of Funding: $362,029
Project Goal: The primary endpoint of this study is OS. The final analysis of OS will occur after approximately 569 events (ie, deaths) have occurred. An interim analysis of OS will occur when at least 398 OS events (70% of total OS events needed for final analysis) have occurred. Progression-free survival (PFS) and objective response rate (ORR), each based on investigator assessments using RECIST 1.1 criteria, are key secondary endpoints that will be subject to hierarchical testing, with testing for PFS followed by testing for ORR if appropriate. Other secondary endpoints include duration of objective response, OS in PD-L1 positive vs PD-L1 negative subgroups, incidence of adverse events, serious adverse events, and specific laboratory abnormalities, and time to disease-related symptom progression rate.
Specific Aims: N/A
Overlap: None

Title: Biomarker-Based Tools for Treatment Response Decision Support of Bladder Cancer
Time Commitments: 1.4 calendar months
Supporting Agency: NIH
Address: 9609 Medical Center Drive, Bethesda, MD 20892-9760
Contracting/Grants Officer: Jennifer S Meininger, Jennifer.meininger@nih.gov
Performance Period: 05/06/2019-04/30/2024
Level of Funding: $3,154,182
Project Goal: The goal of this project is to conduct a multi-site pilot clinical trials to validate the effectiveness of our previously developed computer decision support tool for bladder cancer treatment response assessment as an assistant to clinicians in evaluation of bladder cancer change as a result of neoadjuvant therapy.
Specific Aims: To perform a preparatory clinical trial with the clinicians at UM, which will simulate the real prospective clinical trial, To deploy the QIBC and CDSS-T tools at the three collaborating clinical sites, To use the QIBC and CDSS-T tools at the three clinical sites in the pilot clinical trial, To compare the clinicians' performance results with and without the QIBC and CDSST tools in the pilot clinical trial
Overlap: None

Title: Translational tools and resources to advance MHC (HLA) cancer genetics
Time Commitments: 0.3 calendar months
Supporting Agency: Innovation in Cancer Informatics (ICI)
Address:
Contracting/Grants Officer: David Brown, grants@the-ici-fund.org
Performance Period: 09/01/2020-09/01/2022
Level of Funding: $224,000
Project Goal: Through genomic profiling and bioinformatics analyses understand how the cancer genotype shapes immunophenotypic traits, which can be leveraged as prognostic mechanism-rooted biomarkers of survival and/or treatment response.
Specific Aims: In the first Aim, we propose to systematically interrogate how genetic aberrations, and mutational processes shape the immunogenicity of tumors. We will carefully examine the distinct mechanisms contributing to HLA loss (mutation, LOH, silencing) and their impact on tumor immune-phenotypes (Aim 2). Finally, we propose to significantly expand the proposed prognostic biomarker discovery to almost 1,000 mCRPC and novel data-elements including whole-genome sequencing, which will enable more careful interrogation of the prognostic role of structural variants and CNVs in PCa progression.
Overlap: None

Title: An Open-label, Multicenter, Phase 1b Study of JNJ-63723283, a PD-1 Inhibitor, Administered in Combination with Apalutamide in Subjects with Metastatic Castration- Resistant Prostate Cancer
Time Commitments: 0.96 calendar months
Supporting Agency: Janssen Research and Development
Address:
Contracting/Grants Officer: Kim Bernard, kbernar4@its.jnj.com
Performance Period: 12/12/2018-11/30/2028
Level of Funding: $786,369
Project Goal: This is a Phase 1b study of metastatic prostate cancer subjects with castration resistance, i.e., who have progressed after therapy with a next generation AR-targeted therapy for metastatic disease. The primary hypothesis of this study is that treatment with JNJ-63723283 and apalutamide is safe and leads to improvement in the 12-week PSA response rate.
Specific Aims: The primary study objectives are:
• To evaluate the safety of the combination of JNJ-63723283 with apalutamide.
• To define a population of subjects with mCRPC who respond to treatment with the combination of JNJ-63723283 and apalutamide.
Overlap: None

Title: Phase II study of TAK228 in patients with previously treated metastatic Renal Cell Carcinoma
Time Commitments: 0.6 calendar months
Supporting Agency: Millennium Pharmaceuticals, Inc./Dana-Farber Cancer Institute
Address: Dana-Farber Cancer Institute, 450 Brookline Avenue, Boston, MA 02215
Contracting/Grants Officer: Taylor Lynn, Taylor_Lynn@dfci.harvard.edu
Performance Period: 09/27/2017-08/31/2022
Level of Funding: $152,000
Project Goal: This is a Phase II clinical trial to assess the overall response rate (ORR) of TAK-228 in previously treated Renal Cell Carcinoma (RCC) patients.
Specific Aims: N/A
Overlap: None

Title: An Open-label Phase 1/2A Study to Evaluate the Safety, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of TRC253, an Androgen Receptor Antagonist, in Patients With Metastatic Castration-resistant Prostate Cancer

Time Commitments: 0.7 calendar months
Supporting Agency: Tracon Pharmaceuticals, Inc.
Address: 8910 University Center lane, Suite 700, San Diego, CA 92122
Contracting/Grants Officer: Lillian Liu, lliu@traconpharma.com
Performance Period: 05/24/2017-06/30/2022
Level of Funding: $319,641
Project Goal: This is a multi-center, first-in–human, open-label, Phase 1/2A dose-escalation study in which eligible patients with metastatic castration-resistant prostate carcinoma (mCRPC) will receive oral doses of TRC253. The study will be conducted in 2 parts.
Specific Aims: N/A
Overlap: None

Title: Large-scale discovery and validation of predictive biomarkers for immunotherapy across cancers and treatments
Time Commitments: 0.9 calendar months
Supporting Agency: The V Foundation for Cancer Research
Address: 14600 Weston Parkway, Cary, NC 27513
Contracting/Grants Officer: Carole Wegner, Grants@jimmyv.org
Performance Period: 11/01/2019-11/01/2022
Level of Funding: $600,000
Project Goal: Discover predictive biomarkers for immunotherapy. Genomically characterize the MIRIE cohort. Large scale genomic association analysis
Specific Aims:
Overlap: None

Title: Michigan Prostate SPORE
Time Commitments: 1.2 calendar months
Supporting Agency: NIH/NCI, 2 P50 CA 186786 06
Address:
9609 Medical Center Drive
Bethesda, MD 20892-9760
Contracting/Grants Officer: Shane Woodward
Performance Period: 09/01/2019-08/31/2024
Level of Funding: $1,648,998
Project Goal: The goal of UM Prostate SPORE Tissue/Informatics Core is to collect biological material with associated clinical information to facilitate translational prostate cancer research.
Specific Aims: 1) Support multidisciplinary, collaborative projects that pair basic and clinical investigators and draw on expertise of scientists from within and from outside the prostate cancer field. 2) Provide support for pilot projects with high potential to advance prostate cancer research to obtain preliminary data that will form the basis for grant submissions to extramural sponsors. 3) Recruit and train early-stage scientists to become the next generation of leaders in translational prostate cancer research through access to mentors that are renowned senior investigators and leaders in basic and clinical arenas, as well as networking opportunities among other project Co-Leaders. 4) Provide world-class infrastructure to carry out innovative, high-quality, high-impact translational prostate cancer research. 5) Support efforts to develop bench-to-bedside discoveries for clinical diagnostics and therapies. 6) Foster collaborations among investigators within the institution and with other institutional SPORES or extramural prostate cancer programs.
Overlap: None

Title: Cancer Center Support Grant 2018-2023
Time Commitments: 1.98 calendar months
Supporting Agency: NIH/NCI, P30 CA046592
Address:

9609 Medical Center Drive
Bethesda, MD 20892-9760
Contracting/Grants Officer: Dr. Jeffrey Moscow
Performance period: 07/13/2018-05/31/2023
Level of funding: $4,860,671
Project Goals: The mission of the University of Michigan Comprehensive Cancer Center (UMCCC) is to reduce cancer burden and improve cancer outcomes through research, innovation, transdisciplinary collaboration, education, and outreach.
Specific Aims: Aim 1 – Define novel factors and mechanisms underlying cancer pathogenesis and phenotypes. Aim 2 – Harness knowledge to develop approaches to reduce cancer risk through improved cancer prevention and early detection. Aim 3 - Advance and deliver innovative treatments and predictive biomarkers to patients. Aim 4 – Evaluate and implement strategies to improve access to high quality care for cancer patients and survivors and to reduce cancer disparities in our catchment and beyond.
Overlap: None

Title: Phase Ib and Phase II Studies of anti-PD-1 Antibody Pembrolizumab (MK-3475) in Combination with Bevacizumab for the Treatment of Metastatic Renal Cell Carcinoma: Big Ten Cancer Research Consortium BTCRC-GU14-003
Time Commitments: 0.39 calendar months
Supporting Agency: Hoosier Cancer Research Network/Merck and Company, Inc.
Address:
351 W. 10th Street, Suite 330
Indianapolis, IN 46202
Contracting/Grants Officer: Karen Dutcher
Performance period: 11/13/2015-10/31/20 (NCTX)
Level of funding: $15,187
Project Goals: The primary objective of the Phase Ib portion is to determine the maximum safe dose of pembrolizumab when given in combination with bevacizumab in subjects with metastatic clear cell renal carcinoma after failure of at least one systemic therapy for metastatic disease. The maximum safe dose of pembrolizumab in combination with bevacizumab will be determined using a standard "3+3" design.The primary objective of the Phase II trial is to determine the activity of the combination of pembrolizumab and bevacizumab in first line therapy for subjects with metastatic clear cell RCC as assessed by response rates (complete or partial response) (RR) based on RECIST 1.1.
Specific Aims: 1) Correlate PD-L1 expression in archived diagnostic tumor tissue with clinical response. 2) Correlate tumor vascular density in archived diagnostic tumor tissue with tumor response during treatment. 3) Correlate CD4(+) and CD8(+) T-cell tumor infiltration in archived diagnostic tumor tissue with tumor response during treatment. 4) Correlate change in number of circulating tumor cells during therapy, relative to baseline expression, with clinical response. 5) Correlate change in soluble PD-L1 level in serum during therapy, relative to baseline level, with clinical response. 6) Correlate change in plasma VEGFc level during therapy, relative to baseline level, with clinical response**.**
Overlap: None

Title: The Targeted Agent and Profiling Utilization Registry (TAPUR) Study
Time Commitments: 0.12 calendar months
Supporting Agency: American Society of Clinical Oncology (ASCO)
Address:
2318 Mill Road, Suite 800
Alexandria, VA 22314
Contracting/Grants Officer: Kaitlyn Antonelli
Performance period: 03/01/2016-02/28/2021
Level of funding: $3,101
Project Goals: To describe the anti-tumor activity and toxicity of commercially available, targeted anti-cancer

drugs used for treatment of patients that harbors advanced solid tumors, multiple myeloma or B cell non-Hodgkin lymphoma with a genomic variant known to be a drug target or to predict sensitivity to a drug.
Specific Aims: N/A
Overlap: None

Title: A Phase III, Randomized, Open-label, Controlled, Multi-Center, Global Study of First-Line MEDI4736 Monotherapy and MEDI4736 in Combination with Tremelimumab Versus Standard of Care Chemotherapy in Patients with Unresectable Stage IV Urothelial Bladder Cancer
Time Commitments: 0.46 calendar months
Supporting Agency: Covance Inc./AstraZeneca PLC
Address:
AstraZeneca AB
151 85 Södertälje, Sweden
Contracting/Grants Officer: Connie Sawyer
Performance period: 03/14/2016-03/30/2020 (NCTX)
Level of funding: $19,543
Project Goals: The primary goals of this study is to assess the efficacy of MEDI4736 + tremelimumab combination therapy versus SoC in terms of PFS in patients with UBC.
Specific Aims: N/A
Overlap: None

Title: A Phase III Randomized, Controlled Clinical Trial of Pembrolizumab with or without Platinum-Based Combination Chemotherapy versus Chemotherapy in Subjects with Advanced or Metastatic Urothelial Carcinoma.
Time Commitments: 1.2 calendar months
Supporting Agency: Merck Inc.
Address:
One Merck Drive
P.O. Box 100
Whitehouse Station, New Jersey, 08889-0100
Contracting/Grants Officer: Cathleen Hrubos
Performance period: 11/17/2016-10/31/2021
Level of funding: $335,078
Project Goals: The primary goal of this Phase Ib study is to determine the efficacy and safety of pembrolizumab with or without chemotherapy versus chemotherapy alone in subjects with advanced or metastatic urothelial carcinoma (bladder cancer).
Specific Aims: N/A
Overlap: None

Title: Prostate Cancer Outcomes: An International Registry to Improve Outcomes in Men with Advanced Prostate Cancer (IRONMAN Registry)
Time Commitments: 0.32 calendar months
Supporting Agency: Prostate Cancer Clinical Trials Consortium (PCCTC)/ Movember Foundation
Address:
Movember Foundation
P.O. Box 1595
Culver City, CA 90232
Contracting/Grants Officer: Casey Sisco
Performance period: 10/11/2017-11/16/2022
Level of funding: $30,853
Project Goals: The IRONMAN Registry investigators intend to create an international, population-based, prospective registry of minimum 5,000 men with advanced prostate cancer.

Specific Aims: 1. To describe the practice patterns of therapeutic agents for treatment of advanced prostate cancer internationally; 2. To assess whether specific treatment patterns are associated with clinically significant adverse events, and evaluate potential interactions with concomitant medications or demographic factors; 3. To identify associations between treatment sequences or combinations and overall survival; 4. To define the patient experience of men with advanced prostate cancer and identify unmet needs in their treatment; 5. To identify clinical and molecular disease subtypes that predict response to individual treatments, combinations, or sequences.
Overlap: None

Title: ABLE: Phase 2, Single Arm, Two-Stage Study of Abraxane with Anti-PD1/PDL1 in Cisplatin-Ineligible Patients with Advanced Urothelial Cancer
Time Commitments: 0.91 calendar months
Supporting Agency: Celgene Corporation
Address:
86 Morris Avenue
Summit, NJ 07901
Contracting/Grants Officer: Peter Lyn
Performance period: 11/14/2017-06/01/2019
Level of funding: $132,345
Project Goals: The goal is to determine the efficacy of abraxane and pembrolizumab antibody in cisplatin-ineligible patients with advanced urothelial cancer.
Specific Aims: N/A
Overlap: None

Title: Single Arm Phase Ib/II Study of Durvalumab and Guadecitabine in Advanced Kidney Cancer: Big Ten Cancer Research Consortium BTCRC-GU16-043
Time Commitments: 0.59 calendar months
Supporting Agency: Hoosier Cancer Research Network/AstraZeneca US
Address:
Hoosier Cancer Research Network
500 N. Meridian Street, Suite 100
Indianapolis, IN 46204
Contracting/Grants Officer: Karen A. Dutcher
Performance period: 12/18/2017-01/01/2023
Level of funding: $58,073
Project Goals: To estimate the safety and toxicities of durvalumab in combination with guadecitabine in metastatic clear cell renal cell carcinoma
Specific Aims: N/A
Overlap: None

Title: A phase 1b dose-escalation and dose-expansion study of enfortumab vedotin (ASG-22CE) in combination with immune checkpoint inhibitor (CPI) therapy for treatment of patients with locally advanced or metastatic urothelial cancer
Time Commitments: 0.05 calendar months
Supporting Agency: Seattle Genetics Inc.
Address:
Seattle Genetics, Inc.
21823 30th Drive SE
Bothell, WA 98021
Contracting/Grants Officer: Anne-Sophie Carret
Performance period: 01/26/2018-02/28/2023
Level of funding: $207,301

Project Goals: To assess the safety and tolerability of enfortumab vedotin in combination with CPI therapy.
Specific Aims: N/A
Overlap: None

Title: A Phase III, Randomized, Double-Blind, Placebo-Controlled Clinical Trial of Pembrolizumab (MK-3475) as Monotherapy in the Adjuvant Treatment of Renal Cell Carcinoma Post Nephrectomy
Time Commitments: 0.11 calendar months
Supporting Agency: Merck Inc.
Address:
One Merck Drive
P.O. Box 100
Whitehouse Station, New Jersey, 08889-0100
Contracting/Grants Officer: Tanesha Rowland
Performance period: 03/15/2018-03/31/2022
Level of funding: $662,195
Project Goals: The goal is to compare disease-free survival (DFS) as assessed by the investigator for participants treated with pembrolizumab versus those receiving placebo.
Specific Aims: N/A
Overlap: None

Title: A Phase 3 Study of Erdafitinib Compared to Vinflunine or Docetaxel or Pembrolizumab in Subjects with Advanced Urothelial Cancer and Selected FGFR Gene Aberrations
Time Commitments: 0.06 calendar months
Supporting Agency: Janssen Research and Development LLC
Address:
920 Route 202
Raritan, NJ 08869
Contracting/Grants Officer: William Dudley Jr.
Performance period: 05/09/2018-05/30/2023
Level of funding: $140,180
Project Goals: The primary objective of this study is to evaluate efficacy of erdafitinib versus chemotherapy or pembrolizumab in subjects with advanced urothelial cancer harboring selected FGFR aberrations who have progressed after one prior treatment.
Specific Aims: N/A
Overlap: None

Title: IMPACT: Immunotherapy in Patients with Metastatic Cancers and CDK12 Mutations
Time Commitments: 0.26 calendar months
Supporting Agency: Bristol-Myers Squibb Company
Address:
Bristol-Myers Squibb Corporate Headquarters
430 E. 29th Street, 14th Floor,
New York, NY 10016
Contracting/Grants Officer: Hua Qu
Performance Period: 06/21/2018-07/31/2023
Level of Funding: $139,804
Project Goal: To determine the efficacy of checkpoint inhibitor immunotherapy with nivolumab and ipilimumab combination therapy followed by nivolumab monotherapy in patients with metastatic prostate cancer harboring loss of CDK12 function.
Specific Aims: N/A
Overlap: None

Title: A Randomized, Double-Blind, Placebo-Controlled Phase 2 Study Comparing CB-839 in Combination with Cabozantinib (CB-Cabo) vs. Placebo with Cabozantinib (Pbo-Cabo) in Patients with Advanced or Metastatic Renal Cell Carcinoma (RCC)
Time Commitments: 0.05 calendar months
Supporting Agency: Calithera Biosciences Inc.
Address:
Calithera Biosciences, Inc.
343 Oyster Point Blvd, Suite 200
South San Francisco, CA 94080
Contracting/Grants Officer: Xuan Tran
Performance Period: 07/05/18-07/31/2025
Level of Funding: $71,800
Project Goal: To compare blinded Independent Radiology Committee (IRC)-adjudicated progression free survival (PFS) of patients treated with CB-839 + cabozantinib (CB-Cabo) versus placebo + cabozantinib (Pbo-Cabo) for advanced or metastatic clear-cell RCC (ccRCC).
Specific Aims: N/A
Overlap: None

Title: ATLAS: A Phase 2, Open-label Study of Rucaparib in Patients with Locally Advanced or Metastatic Urothelial Carcinoma
Time Commitments: 0.25 calendar months
Supporting Agency: Clovis Oncology Inc.
Address:
Clovis Oncology, Inc.
5500 Flatiron Parkway, Suite 100
Boulder, Colorado 80301
Contracting/Grants Officer: Jenn Hill
Performance Period: 07/02/2018-06/14/2023
Level of Funding: $42,586
Project Goal: To evaluate objective response rate (ORR) in molecularly-defined homologous recombination deficiency (HRD)-positive and intent-to-treat (ITT) populations using a prospectively defined molecular signature.
Specific Aims: N/A
Overlap: None

Title: ERICA: Phase 2 Multi-center Trial of ESK981 in Combination with Nivolumab in Patients with Metastatic Renal Cell Carcinoma
Time Commitments: 0.02 calendar months
Supporting Agency: Esanik Therapeutics Incorporating Services, Ltd.
Address:
Esanik Therapeutics
2 W. Liberty Blvd., Suite 110
Malvern, PA 19355
Contracting/Grants Officer: Brian Wood
Performance Period: 06/15/2018-07/31/2023
Level of Funding: $60,407
Project Goal: To determine the clinical efficacy of ESK981 in combination with nivolumab therapy in patients with metastatic renal cell carcinoma.
Specific Aims: N/A
Overlap: None

Pending

Processing Award
Title: VELOCITY: A Sequential Evaluation of Circulating Tumor DNA Burden in Urothelial Carcinoma
Time Commitments: 0.06 calendar months
Supporting Agency: Guardant Health, Inc.
Address:
Guardant Health, Inc.
505 Penobscott Drive
Redwood City, CA 94063
Contracting/Grants Officer: Becky Nagy
Performance Period: 07/12/2018-07/12/2019
Level of funding: $2,923
Project Goals: The overall goal of this prospective, multi-site, correlative-only study is to monitor the ctDNA levels in an advanced urothelial carcinoma cohort treated with any anti-PD1 or anti-PDL1 checkpoint inhibitor immunotherapy. A future long-term goal is potential development of a randomized clinical trial evaluating the use of changes in ctDNA VAF to alter treatment.
Specific Aims: N/A
Overlap: None

Title: The Role of Precision Therapy in the Treatment of CDK12 Altered Metastatic Prostate Cancer
Time Commitments: 1.0 calendar months
Supporting Agency: Bristol-Myers Squibb/Prostate Cancer Foundation
Address: 19-PAF05134
Contracting/Grants Officer:
Performance Period: 09/01/2019-08/31/2021
Level of funding: $1,000,000
Project Goals:
Specific Aims: N/A
Overlap: None

Title: A Registry-Based Study of Patterns of Use of Targeted Therapies for Metastatic Cancers in Diverse Populations
Time Commitments: 0.06 calendar months
Supporting Agency: NIH
Address: 20-PAF00675
Contracting/Grants Officer:
Performance Period: 07/01/2020-06/30/2024
Level of funding: $2,876,610
Project Goals:
Specific Aims: 1) To identify groups of patients with metastatic cancers who are vulnerable to non-receipt of targeted therapies; 2) To identify medical oncologists who are less likely to prescribe targeted therapies; 3) To quantify and explain the influence of attending medical oncologist on variation in use of targeted therapies.
Overlap: None

Title: A Phase 1 Open-label, Multicenter, Dose Escalation and Dose Expansion Study of the Safety, Tolerability, and Pharmacokinetics of HPN424 in Patients with Advanced Prostate Cancer Refractory to Androgen Therapy
Time Commitments: 1.2 calendar months
Supporting Agency: Harpoon Therapeutics, Inc.
Address: 20-PAF06903
Contracting/Grants Officer:
Performance Period: 07/01/2020-06/30/2026

Level of funding: $1,967,605
Project Goals:
Specific Aims: Part 1 Dose Escalation: Assess safety and tolerability at increasing dose levels of HPN424 in successive cohorts of patients with metastatic castrate resistant prostate cancer (mCRPC) to estimate the maximum tolerated dose (MTD) or maximum administered dose (MAD) and select the recommended Phase 2 dose (RP2D) or doses.
Part 2 Expansion: Evaluate preliminary clinical efficacy at RP2D(s).
Overlap: None

Title: A Registry-Based Study of Patterns of Use of Targeted Therapies for Metastatic Cancers in Diverse Populations
Time Commitments: 0.04 calendar months
Supporting Agency: NIH
Address: 20-PAF07490
Contracting/Grants Officer:
Performance Period: 04/01/2021-09/30/2025
Level of funding: $3,557,828
Specific Aims: 1) To identify groups of patients with metastatic cancers who are vulnerable to non-receipt of targeted therapies; 2) To identify medical oncologists who are less likely to prescribe targeted therapies; 3) To quantify and explain the influence of attending medical oncologist on variation in use of targeted therapies.
Overlap: None

<u>Previous</u> (Past 5 years)
Title: RESPECT Retrospective Study of Proscar and Casodex Therapy in Prostate Cancer
Time Commitments: 0.12 calendar months
Supporting Agency: Johns Hopkins University
Address:
The Brady Urological Institute
600 N. Wolfe Street
Baltimore, MD 21287
Contracting/Grants Officer: David Brandy Yeater
Performance Period: 03/15/2018-03/14/2020
Level of Funding: $8,209
Project Goal: To perform data collection from retrospective chart reviews of existing UM Patient data. It is estimated that approximately 200 patients will be included in this data set. This collected data will satisfy data fields to be used in a separately funded descriptive retrospective study of patients treated with finasteride (proscar) and bicalutamide (casodex) for prostate cancer at Michigan Medicine/University of Michigan Hospitals from 1/1/1990-12/31/2014.
Specific Aims: N/A
Overlap: None

Title: SPORE in Prostate Cancer
Time Commitments: 0.94 calendar months
Supporting Agency: NIH/NCI, P50 CA186786
Address:
9609 Medical Center Drive
Bethesda, MD 20892-9760
Contracting/Grants Officer: Andrew Hruszkewycz
Performance Period: 09/11/2014-08/31/2019
Level of funding: $1,490,829
Project Goals: The goal of UM Prostate SPORE Tissue/Informatics Core is to collect biological material with

associated clinical information to facilitate translational prostate cancer research.
Specific Aims: This application consists of four multidisciplinary projects: Project 1: A Precision Medicine Approach to Elucidate Mechanisms of Progression and Resistance to Therapy in Advanced PCa; Project 2: Mechanisms of Sensitivity and Resistance to Cabozantinib in CRPC; Project 3: Development of Novel BET Bromodomain Inhibitors for the Treatment of Advanced PCa; Project 4: Development of IncRNAs as PCa Biomarkers in Urine. 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 Tissue/Informatics.
Overlap: None

Title: The Prostate Cancer Clinical Trials Consortium: Affiliate Clinical Research Site
Time Commitments: 0.18 calendar months
Supporting Agency: Memorial Sloan-Kettering Cancer Center (MSKCC)/ Department of Defense, W81XWH-15-2-0018
Address:
Sloan Kettering Institute for Cancer Research
1275 York Avenue,
New York, NY 10065-6007
Contracting/Grants Officer: Jay Shahani
Performance Period: 06/15/2015-06/14/2018
Level of Funding: $100,000
Project Goal: Affiliate Clinical Research Site participation is intended to enrich the Consortium's research areas which include but are not limited to: • Clinical development opportunities based on the strength of the underlying science, particularly the biologically-based translational science of its members. • Informative, sequential trial development with individual trials incorporating A) outcome measures corresponding to the unmet needs associated with the specific clinical state of the disease for which the drug is being tested and B) biomarkers tailored to the compound's mechanism of action.• Investigator-initiated trials that optimize dose, explore novel combinations, and lead to the discovery and validation of predictive biomarkers of sensitivity that can guide the use of an investigational product.
Specific Aims: N/A
Overlap: None

Title: Exploring Precision Cancer Medicine for Sarcoma and Rare Cancers
Time Commitments: 0.30 calendar months
Supporting Agency: NIH/NHGRI, 4-UM1-HG-006508-04
Address:
31 Center Drive, MSC 2152
9000 Rockville Pike
Bethesda, MD 20892-2152
Contracting/Grants Officer: Bradley A. Ozenberger
Performance Period: 07/19/2013 – 05/31/2017
Level of Funding: $1,319,266
Project Goal: Three integrated Projects have the following themes: Project 1) "Clinical Genomic Study" will identify patients with a rare cancer (i.e., 15 out of 100,000 individuals per year) who are eligible for clinical trials, consent them to the study, obtain biospecimens (tumor tissue, germline tissue), store clinical data, and assemble a multi-disciplinary Sequencing Tumor Board to deliberate on return of actionable or incidental genomic results; Project 2) "Sequencing & Analysis" will process biospecimens and perform comprehensive sequencing and analysis of tumors to identify point mutations, copy number changes, rearrangements/gene fusions, and aberrant gene expression; Project 3) "Ethics & Psychosocial Analysis" will observe the expert review process for evaluating sequence results and will examine the clinician and patient response to the informed consent process, delivery of genomic sequence results, and use of genomic results.
Specific Aims: N/A

Overlap: None

Title: Phase II study of ponatinib for advanced cancers with genomic alterations in fibroblastic growth factor receptor (FGFR) and other genomic targets (KIT, PDGFRa, RET FLT3, ABL1)
Time Commitments: 0.02 calendar months
Supporting Agency: Ohio State University/Ariad Pharmaceuticals
Address:
Research Foundation Building
1960 Kenny Rd.
Columbus, OH 43210-1016
Contracting/Grants Officer: Vicky Tepley
Performance Period: 12/16/2015-10/31/2018
Level of Funding: $61,172
Project Goal: The goal of this project is to evaluate the response of ponatinib in solid tumor patients with FGFR alterations.
Specific Aims: N/A
Overlap: None

Title: Androgen Deprivation Therapy with or without Radium-223 dichloride in Subjects with Newly Diagnosed
Time Commitments: no current effort, previously 0.12 calendar months
Supporting Agency: Hoosier Cancer Research/Bayer Corporation
Address:
Hoosier Cancer Research Network
500 N. Meridian Street, Suite 100
Indianapolis, IN 46204
Contracting/Grants Officer: Karen Dutcher
Performance Period: 07/19/2016-03/31/2020
Level of Funding: $15,854
Project Goal: To determine whether the combination of ADT plus radium-223 dichloride is more effective than ADT alone based upon radiologic progression free survival (rPFS) in subjects with newly diagnosed metastatic prostate cancer with bone metastases.
Specific Aims: N/A
Overlap: None

Title: A Phase 1B, Open-Label Study of the Safety and Tolerability of Atezolizumab in Combination with Radium-223 Dichloride in Patients with Castrate-Resistant Prostate Cancer Who Have Progressed Following Treatment with an Androgen Pathway Inhibitor
Time Commitments: no current effort, previously 0.17 calendar months
Supporting Agency: Covance Inc./Genentech Inc.
Address:
Covance Inc.
180 Rustcraft Road
Dedham, MA 02026
Contracting/Grants Officer: Haley Dinh
Performance Period: 07/26/2016-08/31/2019
Level of Funding: $159,177
Project Goal: The primary goals of this Phase Ib study are to assess the safety and tolerability of atezolizumab when given in combination with radium-223 dichloride in patients with metastatic castrate-resistant prostate cancer (CRPC) and to identify a recommended treatment schedule.
Specific Aims: N/A
Overlap: None

Title: Biomarkers for Staging and Treatment Response Monitoring of Bladder Cancer
Time Commitments: 0.6 calendar months
Supporting Agency: NIH/NCI, U01 CA179106
Address:
9609 Medical Center Drive
Bethesda, MD 20892-9760
Contracting/Grants Officer: Jennifer A Edwards
Performance Period: 05/15/2014-04/30/2018
Level of Funding: $358,289
Project Goal: 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: To test our hypothesis, we will perform the following specific tasks: (1) to collect a database of multi-modality MR, CT exams of bladder cancers for development, training and testing of the QIBC and CDSS algorithms; (2) to develop advanced computer vision techniques to quantitatively estimate bladder GTV and image characteristics; (3) to develop predictive models using machine learning techniques to combine MM image-based, pathological and immunohistochemical biomarkers for cancer staging and determination of non-responders; (4) to compare the inter-clinician variability and efficiency in clinicians? estimation of GTV and treatment response with and without the proposed QIBC and CDSS-T by observer studies; and (5) to evaluate the CDSS-S and CDSS-T as decision support tools in pilot clinical studies.
Overlap: None

Title: A Phase III, Randomized, Open-label, Controlled, Multi-Center, Global Study of First-Line MEDI4736 Monotherapy and MEDI4736 in Combination with Tremelimumab Versus Standard of Care Chemotherapy in Patients with Unresectable Stage IV Urothelial Bladder Cancer
Time Commitments: 0.36 calendar months
Supporting Agency: Covance Inc./ Astra Zeneca AB
Address:
Covance Inc.
180 Rustcraft Road
Dedham, MA 02026
Contracting/Grants Officer: Connie Sawyer
Performance Period: 03/14/2016-03/30/2017
Level of Funding: $402,144
Project Goal: The goal of this study is to assess the efficacy of MEDI4736 + tremelimumab combination therapy versus SoC in terms of PFS in patients with UBC.
Specific Aims: N/A
Overlap: None

Title: Retrospective Analysis of Clinical Benefit from Radium 223 in Castrate Resistant Prostate Cancer
Time Commitments: 0.12 calendar months
Supporting Agency: Bayer Healthcare, LLC
Address:
100 Bayer Boulevard, P.O. Box 915
Whippany, NJ 07981-0915
Contracting/Grants Officer: Elisa Halbert
Performance period: 05/18/2015-05/17/2017
Level of funding: $43,400
Project Goals: The goal of this multi-institutional, retrospective chart review study is to perform a descriptive study to analyze the early clinical experience with radium-223 in the management of metastatic castration resistant prostate cancer (mCRPC) patients at four high volume sites.

Specific Aims: N/A
Overlap: No scientific or budgetary overlap with the proposed proposal

Title: Randomized Phase 2 Trial of ACP-196 and Pembrolizumab Immunotherapy Dual CHECKpoint Inhibition in Platinum Resistant Metastatic Urothelial Carcinoma (RAPID CHECK study)
Time Commitments: no current effort, previously 1.20 calendar months
Supporting Agency: Acerta Pharma LLC
Address:
Acerta Pharma BV
Kloosterstraat 9
5349 AB Oss
The Netherlands
Contracting/Grants Officer: Sophia Ng
Performance period: 07/10/2015-05/31/2020 (NCTX)
Level of funding: $8,341
Project Goals: To characterize the safety profile of ACP-196 and pembrolizumab in subjects with metastatic, platinum-refractory bladder cancer. -To determine the best overall response rate (BOR) and overall response rate (ORR) of pembrolizumab monotherapy and the combination of ACP-196 and pembrolizumab in subjects with metastatic, platinum-refractory bladder cancer.
Specific Aims: N/A
Overlap: None

Title: Phase II Trial of Pembrolizumab (MK-3475) in Subjects with Metastatic Castration-Resistant Prostate Cancer (mCRPC) Previously Treated with Chemotherapy (KEYNOTE-199)
Time Commitments: no current effort, previously 0.24 calendar months
Supporting Agency: Merck Inc.
Address:
One Merck Drive
P.O. Box 100
Whitehouse Station, New Jersey, 08889-0100
Contracting/Grants Officer: Jesse Bregman
Performance period: 09/01/2016-07/25/2019 (NCTX)
Level of funding: $403
Project Goals: The primary goal of this Phase Ib study is to estimate the objective response rate (ORR) by RECIST 1.1 and duration of response (DOR) by PCWG3-modified RECIST 1.1 in subjects with measurable disease (Cohorts 1 and 2), assessed by central imaging vendor for Cohorts 1 and 2 combined and by each cohort.
Specific Aims: N/A
Overlap: None

Title: Modular phase II study to link targeted therapy to patients with pathway activated tumors
Time Commitments: 0.05 calendar months
Supporting Agency: United BioSource Corporation/Novartis
Address:
920 Harvest Drive
Blue Bell, PA 19422
Contracting/Grants Officer: Rebecca Allhiser
Performance period: 03/04/2014-12/31/2017
Level of funding: $137,789
Project Goals: The goal of this study is to determine whether treatment with the study drug improves clinical benefit rate (CBR) in patients with select solid tumor and/or hematologic malignancies that demonstrate activation of select molecular pathway.
Specific Aims: N/A

Overlap: None

Title: Phase II Trial of Interleukin -2 and PD-1 Inhibitor in metastatic renal cell carcinoma
Time Commitments: no current effort, previously 0.02 calendar months
Supporting Agency: Prometheus Laboratories, Inc.
Address:
Prometheus Laboratories Inc.
9410 Carroll Park Drive
San Diego, CA 92121
Contracting/Grants Officer: Nancy Gregory
Performance period: 01/06/2017-01/05/2020
Level of funding: $81,124
Project Goals: The primary goal of this Phase Ib study is to estimate the safety and toxicities of High Dose Interleukin-2 in combination with the immune checkpoint inhibitor Nivolumab in metastatic clear cell renal cell carcinoma.
Specific Aims: N/A
Overlap: None

Title: A Phase 2/3 Multi-Center, Open-Label Study of 18F-DCFPyL PET/CT Imaging in Patients with PRostate Cancer: Examination of Diagnostic AccuracY (OSPREY)
Time Commitments: 0.51 calendar months
Supporting Agency: Progenics Pharmaceuticals
Address:
Progenics Pharmaceuticals, Inc.
One World Trade Center
47th Floor Suite J
New York, NY 10007
Contracting/Grants Officer: Jessie Ann Flaim-Spetsas
Performance period: 01/10/2017-12/08/2019 terminated
Level of funding: $290,259
Project Goals: The primary objective of the study is to assess the diagnostic performance of 18F-DCFPyL PET/CT imaging to detect prostate cancer in the prostate gland (i.e., sensitivity and specificity) and sites of metastasis or local recurrence (i.e., sensitivity).
Specific Aims: N/A
Overlap: None

Title: A Phase 1/1b Study of MGCD516 in Patients with Advanced Solid Tumor Malignancies
Time Commitments: 1.0 calendar months
Supporting Agency: Mirati Therapeutics
Address:
Mirati Headquarters
9393 Towne Centre Drive
Suite 200
San Diego, CA 92121
Contracting/Grants Officer: Saskia Neuteboom
Performance period: 04/15/2015-04/30/2018
Level of funding: $265,433
Project Goals: This is a multi-center, Phase 1/1b clinical trial evaluating the safety, PK, metabolism, PD and clinical activity of MGCD516 in patients with advanced solid tumor malignancies. The study will begin with an exploration of dose and regimen. As viable Phase 1b regimens are identified, expansion cohorts of patients having tumors with selected histological diagnoses and/or molecular markers will be opened to enrollment for the purpose of evaluating clinical activity.

Specific Aims: N/A
Overlap: None

Title: An Open-Label, Multicenter, Randomized Phase Ib/II Study of Eribulin Mesylate Administered in Combination with Gemcitabine Plus Cisplatin Versus Gemcitabine Plus Cisplatin Alone as First-Line for Locally Advanced or Metastatic Bladder Cancer
Time Commitments: 0.38 calendar months
Supporting Agency: Quintiles/Eisai
Address:
4820 Emperor Boulevard
Durham, North Carolina 27703
Contracting/Grants Officer: Jessica Gant
Performance period: 03/01/2013-02/28/2018
Level of funding: $344,783
Project Goals: The goal of this project is to evaluate the safety and tolerability of eribulin administered in combination with gemcitabine plus cisplatin, compared with gemcitabine plus cisplatin alone, in patients with locally advanced or metastatic bladder cancer.
Specific Aims: N/A
Overlap: None

Title: Access to Experimental Therapeutics Clinical Trials Network (ETCTN) Agents
Time Commitments: 0.24 calendar months
Supporting Agency: NIH/NCI, 3-P30-CA-046592-28-S4
Address:
9609 Medical Center Drive
Bethesda, MD 20892-9760
Contracting/Grants Officer: Dr. Jeffrey Moscow
Performance period: 06/01/2016-05/31/2018
Level of funding: $38,631
Project Goals: The University of Michigan (UM) Comprehensive Cancer Centers Genitourinary Oncology (GU) group has been a productive and successful member of the University of Chicago Phase ll affiliate network, since 2006, specifically as related to contract solicitation N01-CM-01018-83 "Early Therapeutics Development with Phase ll Emphasis. As a member of the Phase ll network, we are very familiar with the procedural, regulatory, and financial requirements of the NCI, NIH and ETCTN. The 3rd year of our current N01 contract began on 9/23/13, and since that date, our group has enrolled 45 patients to early phase UC Phase II consortium trials. Given our accrual history, our site will be able to meet or exceed the goal 5 patients per year to ETCTN studies selected to be included in this program. In our effort to fully realize the protocol accrual target, first priority will be given to the registration of patients eligible for the ETCTN protocol contract studies.
Specific Aims: N/A
Overlap: None

Title: Phase II Trial of Palbociclib (PD-0332991) in Patients with Metastatic Urothelial Cancer (UC) after Failure of First-Line Chemotherapy
Time Commitments: 0.02 calendar months
Supporting Agency: University of North Carolina/Pfizer
Address:
University of North Carolina at Chapel Hill
Chapel Hill, NC 27599-7295
Contracting/Grants Officer: Chris McIver
Performance period: 05/21/2015-05/31/2024 terminated
Level of funding: $42,420
Project Goals: The primary objective of this trial is to estimate progression free survival at 4 months in patients

with metastatic UC who have progressed after first-line chemotherapy.
Specific Aims: N/A
Overlap: None

Title: A Phase II, Multicenter, Single-Arm Study of MPDL3280A in Patients with Locally Advanced or Metastatic Urothelial Bladder Cancer
Time Commitments: 0.03 calendar months
Supporting Agency: INC Research/Genentech, Inc.
Address:
Corporate Headquarters
1030 Sync Street
Morrisville, NC 27560
Contracting/Grants Officer: Kevin Buell
Performance period: 09/15/2014-09/14/2019 terminated
Level of funding: $4,371,948
Project Goals: The goal of this study is to evaluate the efficacy of MPDL3280A in patients with locally advanced or metastatic urothelial bladder cancer.
Specific Aims: N/A
Overlap: None

Title: A Randomized, Double-Blind, Placebo-Controlled Phase 2 Study Comparing CB-839 in Combination with Everolimus (CBE) vs. Placebo with Everolimus (PboE) in Patients with Advanced or Metastatic Renal Cell Carcinoma (RCC)
Time Commitments: 0.03 calendar months
Supporting Agency: Calithera Biosciences, Inc.
Address:
Calithera Biosciences, Inc.
343 Oyster Point Blvd, Suite 200
South San Francisco, CA 94080
Contracting/Grants Officer: Andrew Rogers
Performance period: 10/25/2017-09/05/2022 terminated
Level of funding: $60,772
Project Goals: The primary endpoint of this Phase 2 study is progression free survival (PFS). The key secondary endpoint is overall survival (OS).
Specific Aims: N/A
Overlap: None

Title: Pilot Trial of Radium-223 and Atezolizumab in Patients with Urothelial Carcinoma with Bone Metastases Who Have Had Disease Progression after Platinum-Based Chemotherapy
Time Commitments: 0.24 calendar months
Supporting Agency: Bayer Corporation
Address:
100 Bayer Boulevard, P.O. Box 915
Whippany, NJ 07981-0915
Contracting/Grants Officer: Elisa Halbert
Performance period: 10/16/2017-09/14/2022 terminated
Level of funding: $47,835
Project Goals: The goal is to determine the preliminary efficacy of radium-223 in combination with atezolizumab in patients with metastatic urothelial carcinoma with bone metastases who have progressed after platinum-based therapy.
Specific Aims: N/A
Overlap: None