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TITLE: Identifying the Molecular Mechanisms of Prostate Tumorigenesis Associated with Multigenic 3p13-14 Locus Loss Using a Novel CRISPR-Organoid Platform

PRINCIPAL INVESTIGATOR: Weiran Feng

CONTRACTING ORGANIZATION: Sloan Kettering Institute for Cancer Research

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14. ABSTRACT

Human prostate cancers can feature chromosome-scale alterations, but it remains challenging to determine the causal relationship between these alterations and cancer formation. We established a mouse primary prostate organoid platform to model the large 3p13-14 locus deletion, which typically spans six genes and occurs in 15~20% of prostate cancer patients.

We performed multi-omics analysis to study the role of Foxp1, a putative tumor suppressor from this region. To model the loss of the entire locus, we developed a CRISPR editing approach to efficiently generate the large deletions through a single step. We are continuing the analysis of the multi-omics data and the in vivo transplantation of the organoids carrying the desired deletions. Together, our study will provide both mechanistic insight and a comprehensive view about the putative tumor suppressor locus and serve as a paradigm for studying other frequent chromosomal alterations in prostate cancer.

15. SUBJECT TERMS

Prostate cancer genome, large chromosomal deletions, primary organoids, CRISPR editing, prostate cancer modeling, 3p13 locus, Foxp1

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1. **INTRODUCTION:**

Chromosomal alteration is a hallmark of the prostate cancer genome. One example is the large deletion of the hexagenic 3p13-14 locus, which occurs in 15~20% of prostate cancers. However, it remains unknown how this chromosomal deletion impacts cancer formation. While our preliminary data has revealed a tumor suppressor function of *Foxp1*, which resides in this region, further study of the entire locus is limited by the lack of effective tools to model this event. In this study, we developed a primary prostate organoid platform for efficient generation of the 3p13-14 deletion and rapid cancer modeling in vivo. We utilized this platform to 1) reveal the mechanisms of tumorigenesis upon *Foxp1* loss and 2) to identify additional tumor suppressive subregions from the locus that cooperates with *Foxp1* loss. Together, our study will provide both mechanistic insight and a comprehensive view about the putative tumor suppressor locus and serve as a paradigm for studying other frequent chromosomal alterations in prostate cancer.

2. **KEYWORDS:**

Prostate cancer genome, large chromosomal deletions, primary organoids, CRISPR editing, prostate cancer modeling, 3p13 locus

3. **ACCOMPLISHMENTS:**

What were the major goals of the project?

Specific Aim 1: Uncover the tumor suppressive mechanisms of Foxp1		
Major Task 1: Determine the oncogenic potential of a single copy loss of *Foxp1*	**Months**	**% completion**
Subtask 1: Prepare the *Foxp1*$^{+/-}$; *Pten*$^{-/-}$ organoid line for orthotopic transplantation # mouse: 1 Method: mouse prostate organoid culture; lentiviral transduction; adenovirus infection	1-3	100
Subtask 2: Compare the oncogenic potential of *Pten*$^{-/-}$, *Foxp1*$^{+/-}$; *Pten*$^{-/-}$ and *Foxp1*$^{-/-}$;*Pten*$^{-/-}$ mouse prostate organoid lines by orthotopic transplantation # mouse: 24 (total) Method: prostate orthotopic transplantation, bioluminance imaging, prostate histological analysis	3-12	20
Milestone(s) Achieved: Elucidation of the possible effects of Foxp1 haploinsufficiency in prostate tumorigenesis	12	50
Major Task 2: Determine the impact of Foxp1 loss on cell fitness		
Subtask 1: Examine whether an additional Foxp1 loss confers a growth advantage to Pten-null prostate organoids Mouse prostate organoid lines (already established): *WT*, *Pten*$^{-/-}$, *Foxp1*$^{-/-}$ and *Pten*$^{-/-}$;*Foxp1*$^{-/-}$ Method: CellTiter-Glo® proliferation assay	1-6	100
Subtask 2: Examine whether an additional Foxp1 loss alleviates cellular senescence triggered by Pten loss Method: Senescence-associated β-galactosidase assay	1-6	N/A (no growth advantage revealed)
Subtask 3: Pro/anti-proliferative signaling marker analysis	1-6	N/A

Method: Western blot		(no growth advantage revealed)
Milestone(s) Achieved: Determination of a tumor suppressive role for Foxp1 and on its functional interaction with Pten at the cellular level	6	100
Major Task 3: Evaluate Foxp1 transcriptional regulation of Ar signaling through transcriptomic, cistromic and chromatin accessibility profiling		
Subtask 1: Examine the functional interaction between Foxp1 and Pten on Ar transcription output Mouse prostate organoid lines (already established): *WT*, *Pten*$^{-/-}$, *Foxp1*$^{-/-}$ and *Pten*$^{-/-}$*;Foxp1*$^{-/-}$ Method: RNA-seq	1-6	100
Subtask 2: Examine how Foxp1 impacts the Ar cistrome and whether this explains its effects on Ar transcription output, in the presence of absence of Pten Method: ChIP-seq	1-9	80
Subtask 3: Measure the impacts of Foxp1 on the chromatin accessibility landscape and test whether this explains the Ar cistrome changes, in the presence of absence of Pten Method: ATAC-seq	1-9	80
Subtask 4: Unbiased identification of novel downstream target genes and pathways regulated by Foxp1, in the presence of absence of Pten Method: Pathway, motif and cross-reference analyses with data generated above	9-12	80
Milestone(s) Achieved: Publication of a peer-reviewed manuscript on the oncogenic molecular circuits triggered by Foxp1 loss in cooperation with Pten loss	12-18	80
Specific Aim 2: Identify tumor suppressors within *Foxp1-Shq1* that cooperate with Foxp1		
Major Task 1: Identify individual prostate tumor suppressor genes that cooperate with *Foxp1*		
Subtask 1: Individually perturb the five candidate genes (other than *Foxp1*) from the *Foxp1-Shq1* region in *Foxp1*$^{-/-}$*Pten*$^{-/-}$ mouse prostate organoids Method: Genome editing by CRISPR, western blot	1-6	0
Subtask 2: Tumor formation assay to identify individual prostate tumor suppressor genes that cooperate with *Foxp1* # mouse: 52 (total) Method: prostate orthotopic transplantation, bioluminescence imaging, prostate histological analysis	6-15	0
Milestone(s) Achieved: Identification of bi-genic cooperation within the Foxp1-Shq1 locus that stimulates prostate tumor formation and assessment of the relative effect of paired loss of Foxp1 and the candidate gene in comparison to the whole Foxp1-Shq1 locus	15	0

Major Task 2: Identify multigenic tumor suppressive subregions within *Foxp1-Shq1*		
Subtask 1: Generate a deletion series within the *Foxp1-Shq1* interval in *Pten*$^{-/-}$ organoids Method: Genome editing by CRISPR	1-3	50
Subtask 2: Tumor formation assay to identify multigenic tumor suppressive subregions within *Foxp1-Shq1* # mouse: 52 (at most) Method: prostate orthotopic transplantation, bioluminescence imaging, prostate histological analysis	6-18	30
Milestone(s) Achieved: Publication of a peer-reviewed manuscript on the cooperative events within the Foxp1-Shq1 locus that drive prostate cancer formation together with Foxp1 loss	18-24	30

What was accomplished under these goals?

The specific objectives for this period were to 1) elucidate the underlying mechanism of Foxp1-Pten functional interaction and 2) to establish genetic tools to identify the multigenic tumor suppressive subregions within *Foxp1-Shq1*.

To achieve the first objective, we set out to test whether *Foxp1* loss confers growth advantage to *Pten*-null cells. However, growth analysis did not reveal significant changes (data not shown), suggesting that additional Foxp1 loss may impact cell behaviors in a growth-independent manner. To test this possibility, we performed unbiased transcriptomic, cistromic and chromatin accessibility profiling assays using the organoids with different genetic backgrounds. Different organoids demonstrated distinct transcriptomic states (**Fig 1A**). Gene set enrichment analysis of differentially expressed genes revealed that Foxp1 loss activated inflammatory/interferon pathways in both *wt* and *Pten*$^{-/-}$ backgrounds (**Fig 1B,C**). Furthermore, cistromic analysis showed that Foxp1 is bound to either bodies or peripheries of various inflammation-related genes (**Fig 1D**). Given the putative role of Foxp1 as a transcriptional

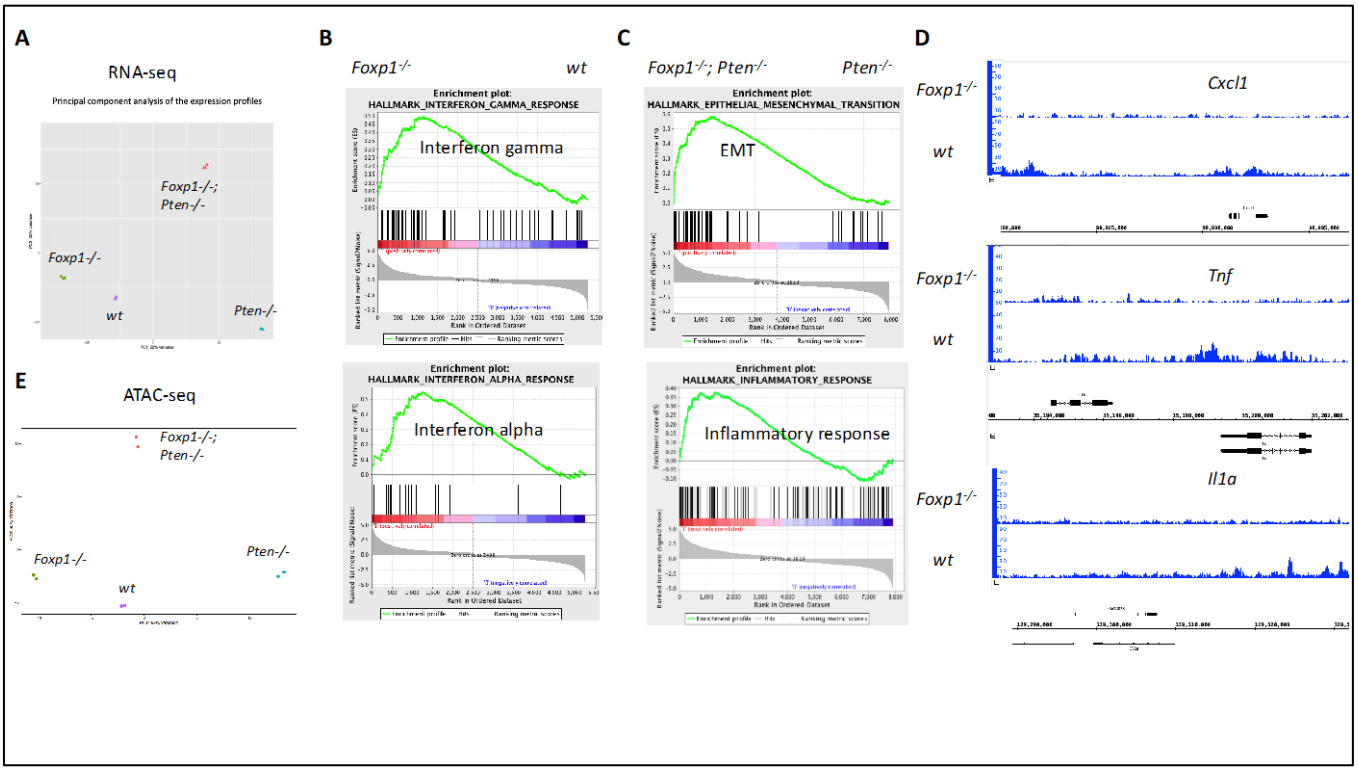

Figure 1. Multi-omic studies of mouse prostate organoids reveal an immune pathway activation by Foxp1 loss. (A) PCA analysis of RNA-seq data of indicated organoids. (B-C) Gene set enrichment assay. (D) Representative Foxp1 ChIP-seq binding. (E) PCA analysis of ATAC-seq data of indicated organoids.

repressor, these results converge on a model that Foxp1 loss activates inflammatory pathways in part by derepressing key players in the pathway. Initial chromatin accessibility analysis (ATAC-seq) also demonstrated highly separable chromatin opening profiles of different organoids, consistent with their distinct transcriptional status (**Fig 1E**). Further over-lapping analyses between the multi-omic approaches will help us identify key downstream effectors of Foxp1 that mediates the induction of immune-related pathways. We are also working to find in vivo evidence in GEMM tumors to support these findings.

To achieve the second objective, we proposed to perform a series of chromosomal interval deletions encompassing various combinations of genes at the *Foxp1-Shq1* locus. Our initial plan was to create these deletion series via lentiviral-based CRISPR deletions before orthotopic transplantations of the engineered organoids into immune-deficient mice. However, the inflammatory/interferon pathways prompted us to investigate tumor-immune interactions as a potential explanation of the tumor suppressive role of Foxp1. Given the immunogenic effects of Cas9, Cas9 stable expression via the proposed viral-based CRISPR approaches may induce unwanted artificial immune responses. In order to set up a system that is compatible with transplantation into immunocompetent hosts, we developed a CRISPR ribonucleoprotein (CRISPR-RNP)-based organoid editing approach. By electroporation, we achieved nearly saturating knockouts of either individual *Foxp1*, *Pten* genes or the combination of the two through a single step (**Fig 2A**). Dual RNPs also created the deletion of the entire 2 Mb *Foxp1-Shq1* locus at a remarkable efficiency of > 30% when assayed at the clonal level (**Fig 2B**). Interval deletions spanning either the entire *Foxp1* gene or the *Foxp1-Shq1* region sparing *Foxp1* (*Eif4e3-Shq1*) was also generated at comparable or even higher efficiencies (up to 50%). We conclude that the large interval deletions are sufficiently represented in the bulk organoid population. Importantly, RNP editing only involves transient presence of the editing machinery. In theory, the “hit-and-run” editing avoids artificial immune responses caused by chronic presence of the editing machineries and in turn allow for the downstream tumor-immune studies. We next sought to transplant the engineered bulk organoids into syngeneic immunocompetent hosts. Grafting signals from engineered *wt* organoids were lost by an early time point of 1 wk, indicating a grafting failure, whereas those from the *Pten*$^{-/-}$ correspondents persisted (**Fig 2C**). These early observations are consistent with a lack of tumor-prone phenotypes from

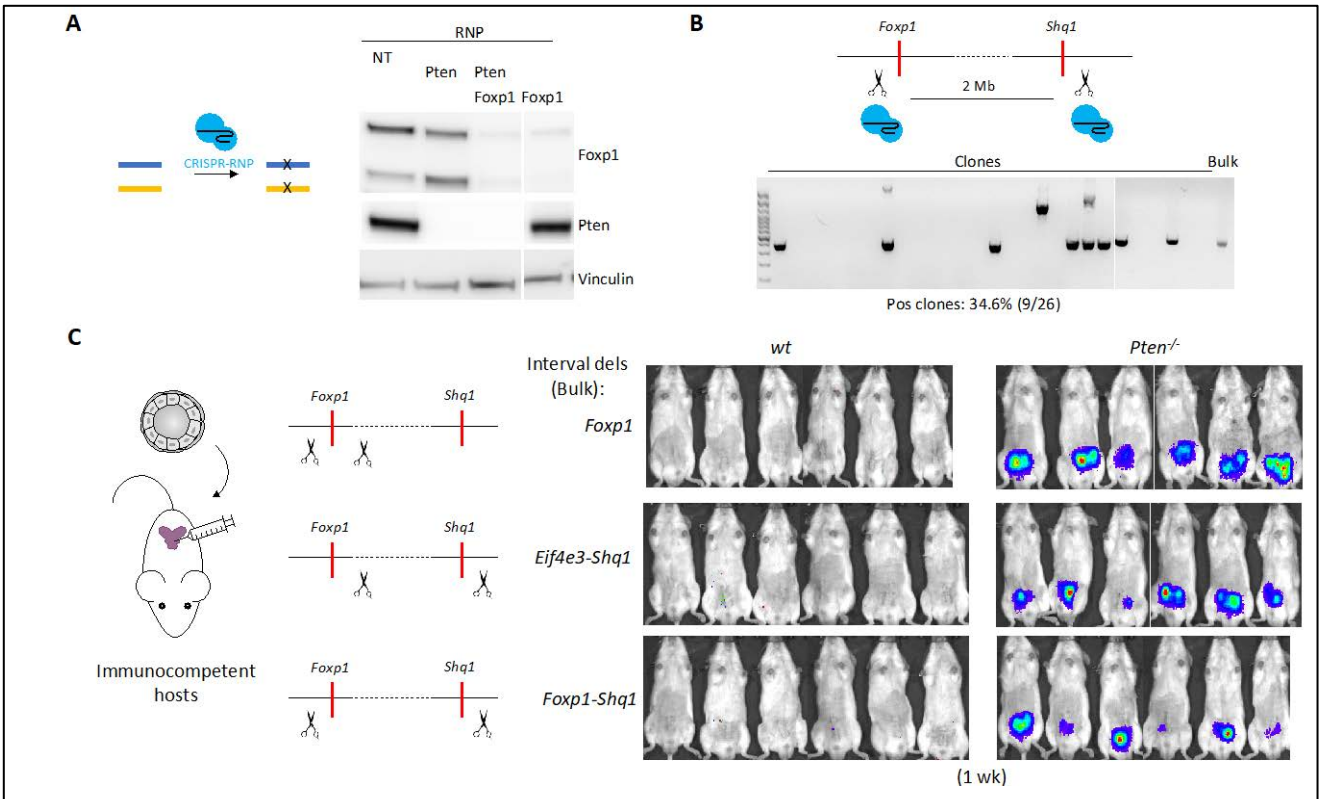

Figure 2. Efficient CRISPR-RNP-mediated organoid editing for immunocompetent transplantations. (A) WB after treatment with indicated RNP(s). (B) Fusion-specific PCR to detect dual-RNP-mediated *Foxp1-Shq1* deletions. (C) Bulk, luciferase-expressing *wt* prostate organoids treated with indicated RNP pairs were orthotopically transplanted to syngeneic immunocompetent hosts. Bioluminescence imaging at 1 wk post transplantation is shown on the right.

Foxp1-Shq1 loss alone in GEMMs. A follow-up comparison of these different interval deletions in *Pten*$^{-/-}$ transplants at a later time point will not only help us evaluate the tumor suppressive effects of these regions, but also provide additional in vivo models to interrogate potential tumor-immune responses as revealed by the above Foxp1 studies.

What opportunities for training and professional development has the project provided?
Training:
Mouse Genetics Workshop, MSKCC
Statistics for Basic Science, MSKCC

Professional development:
2019 Geoffrey Beene Retreat, Tarrytown (attended)
2020 13th Annual Prostate Cancer Program Retreat, Fort Lauderdale (attended)

How were the results disseminated to communities of interest?
1. Manuscripts describing the RNP technology in rapid organoid editing and cancer modeling is close to completion and will be submitted in the next one to two months.

2. Manuscripts describing the Foxp1 biology and *Foxp1-Shq1* locus manipulation is in preparation.

What do you plan to do during the next reporting period to accomplish the goals?
The data obtained in the past period have brought us to an advantageous standpoint to further tackle the research questions we initially asked. The preliminary multi-omics data already provide us a clear path to pursue in the next period. The powerful “hit-and-run” organoid editing platform that we established generates big deletions in the bulk organoid cells through one step, which in turn enables orthotropic modeling in hosts with intact immune systems.

Moving forward, first, we will first perform further data mining to identify key downstream factor(s) that are directly regulated by Foxp1. Second, we will seek for in vivo evidence for the activation of these pathways from GEMM-derived tumors. Third, we will leverage the edit-transplant pipeline to evaluate the tumor-suppressive roles of various deletion series of the *Foxp1-Shq1* locus to uncover novel tumor suppressors that cooperates with Foxp1 loss. Fourth, as a complementary approach, we will generate additional knockouts of individual genes from the locus in *Foxp1*$^{-/-}$*Pten*$^{-/-}$ organoids to test their tumor-suppressive potential in the context of Foxp1, Pten loss. Together, these efforts will provide us with a both comprehensive and in-depth understanding of the multigenic 3p13 locus that is frequently lost in human prostate cancer.

4. **IMPACT:**

What was the impact on the development of the principal discipline(s) of the project?
Prostate cancer genomes commonly feature chromosomal structural alterations. Modeling these alterations, especially starting from a normal background, is key to providing insights into disease biology but remains technically challenging. For example, loss of a large, multigenic chromosomal segment at the 3p-13 locus occurs in 15~20% of human prostate cancer but how this promotes tumor formation remains unclear. During the past funding period, we have made significant progress in 1) providing insight into the possible mechanism of how loss of the *Foxp1* gene from the locus causes tumors and 2) establishing the tools to model the deletions of the entire locus in primary mouse prostate cultures. Follow-up studies in the next period will provide both a deeper understanding of cancer-forming mechanisms and a broader comprehension of the tumor-causing subregions from the whole locus. Together, this project will provide a paradigm in studying chromosome-scale alterations that frequently occur in human prostate cancer.

What was the impact on other disciplines?
An ideal cancer modeling pipeline would 1) start from a normal cell, 2) generate the desired relevant genetic alterations and 3) create cancer within the relevant tissue microenvironment. This allows for a precise interrogation of the driving genetic events, as opposed to the myriad, non-relevant passenger events. One big challenge is then to effectively create the genetic alteration from an otherwise normal background. Additional complication is conferred by unwanted host-graft immune response upon

transplantation. We have addressed both challenges by creating the genetic alteration in primary cultures in an efficient and traceless manner. This in turn enables graftment into hosts with the same genetic background to minimize artificial immune responses. We anticipate that the pipeline we established can be broadly adapted for studying a spectrum of mutations across different cancer types.

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
To create the large deletion at the *Foxp1-Shq1* locus, we have decided to use CRISPR-RNP strategy as opposed to the viral-based strategy as we initially proposed. The primary reason is that our analysis on Foxp1-null organoids consistently revealed an upregulation of immune-related pathways (IFN, inflammation) regardless of *Pten* status, suggesting that an interaction with the immune system might play a role in tumor formation. Thus, a transient introduction of the editing machineries as the RNP strategy does provides the best fit for this purpose by minimizing unwanted immune responses from stable expression of potential immunogens (e.g. Cas9). Importantly, RNP editing proves to work at a much higher efficiency in both knocking out individual genes and creating large chromosomal deletions. Therefore, not only does RNP editing fit the purpose of this project alone, but serves as a superior tool for organoid genome editing in general.

Actual or anticipated problems or delays and actions or plans to resolve them
Nothing to report

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

Significant changes in use or care of human subjects
N/A

Significant changes in use or care of vertebrate animals.
Nothing to report

Significant changes in use of biohazards and/or select agents
Nothing to report

6. **PRODUCTS:**

Publications, conference papers, and presentations

Journal publications.
Nothing to report this period (manuscript in preparation to be submitted in next few months)

Books or other non-periodical, one-time publications.
Nothing to report

Other publications, conference papers, and presentations.
Nothing to report

Website(s) or other Internet site(s)
Nothing to report

Technologies or techniques
Development of an RNP-based approach primary organoid editing, which is highly efficient in creating large chromosomal deletions, and compatible with orthotopic transplantations in immunocompetent hosts.

Inventions, patent applications, and/or licenses
Nothing to report

Other Products
Data: manuscript in preparation
Research material: primary mouse prostate organoids carrying a variety of prostate-cancer-relevant alterations

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Weiran Feng
Project Role: Principal Investigator
Nearest person month worked: 12.00 calendar months
Contribution to Project: As the Principal Investigator of this project, Dr. Feng will oversee and coordinate all aspects of the project.
Funding Support: This award

Name: Zhen Cao
Project Role: Graduate Student
Contribution to Project: As a graduate student on this project, Mr. Cao assists Dr. Feng in the lab for work associated with this project.
Nearest person month worked: 6.00 calendar months
Funding Support: Dr. Cao is paid fully by Dr. Sawyers' (Mentor) department discretionary fund.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
There have been no changes to Dr. Feng's active other support since the last reporting. Dr. Sawyers' updated active other support is attached with the changes noted from the last reporting.

What other organizations were involved as partners?
Not Applicable

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:
Not applicable

QUAD CHARTS:
Not applicable

9. APPENDICES:
Nothing to report

Active Other Support Since Last Reporting

Sawyers, Charles L.

NEW ACTIVE

PC190310; W81XWH2010289 (PI: Sawyers) 9/30/2020 - 9/29/2023 0.60 calendar
Congressionally Directed Medical Research Programs $ 250,000
Defining Transcription Factor Networks Governing Androgen Receptor Null Prostate Cancer
Major Goals: Aim 1. Determine gene expression and chromatin landscape changes associated with potent AR inhibition Aim 2. Identify vulnerabilities responsible for maintenance of the AR low/null state Aim 3. Characterize the AR low/null state in CRPC patients using single cell and organoid technologies
Role: Principal Investigator
Agency Contact: Joshua Mckean, Grants Officer
Overlap: None

1 P01 CA228696 01A1 (PI: Kantoff/ Sawyers) 9/1/2019 - 8/31/2024 0.60 calendar
NCI $ 380,663 ($323,663 to DFCI; $57,000 to MSK)
The Impact of DNA Damage Repair Abnormalities in Prostate Cancer (RP3: Functional Evaluation and Interpretation of DNA Damage Response Variants in Prostate Cancer)
Alterations in genes that help repair damaged DNA are seen in 25% of men with metastatic castration resistant prostate cancer, the lethal form of prostate cancer.
Role: co-Project Leader (with Alan d'Andrea, DFCI)
Agency Contact: Kelly Filipski, Kelly
Overlap: None

INACTIVE SUPPORT

3 P30 CA008748 52 S2 (PI: Thompson) 1/1/2014 - 12/31/2019 0.00 calendar
NCI $ 36,683
Cancer Center Support Grant
We propose to establish a two-year Science Enrichment Program (SEP) at Memorial Sloan Kettering Cancer Center (MSK) for high school students who don't have easy access to resources that would help to develop their scientific curiosity.
Role: Program Director

1 U54 CA224079-02 S1 (PI: Sawyers) 9/30/2017 – 8/31/2019 0.00 calendar
National Cancer Institute $19,948
The MSKCC-UW/Fred Hutch Prostate Cancer Drug Resistance and Sensitivity
The research in this grant aims to use a collection of patient-derived prostate cancer models to test resistance and sensitivity to novel drugs and therapeutic combinations quickly and efficiently. This supplement will support a collaboration to use related approaches in mouse models of prostate cancer to corroborate our findings and gain insight into mechanisms of drug response.

CURRENT SUPPORT

Howard Hughes Medical Institute (PI: Sawyers) 3/1/2008- 8/31/2025
Major Goals of this project: Patient oriented research into molecularly targeted therapy of cancer
Agency Contact: Edit Biro, MAS, Howard Hughes Medical Institute, 1230 York Ave, Box 269, New York, NY 10065

Overlap: None

2 R01 CA155169-08 (PI: Sawyers) 5/1/2012-12/31/2022 1.81 calendar
NCI/NIH $218,250
Understanding Resistance to Next Generation Antiandrogens
Major Goals: This project focuses on a novel mechanism of acquired resistance to hormone therapy in castration resistant prostate cancer (CRPC) called lineage plasticity. During the initial 5 year funding cycle, we focused primarily on two other mechanisms of resistance: mutation or amplification of the androgen receptor (AR) and bypass of AR signaling through upregulation of the closely related glucocorticoid receptor. **Agency Contact**: Grants Management Specialist: Rogers Gross **Overlap**: None

5 R01 CA193837-05 (PI: Sawyers) 4/1/2015 -3/31/2021* 1.20 calendar
NCI $ 280,382
Defining the Role of ERG in Modulating the AR Cistrome and Antiandrogen Sensitivity
Major Goals: This project will shed light on the molecular mechanism by which ERG causes prostate cancer and the impact of ERG on response to therapies directed against the androgen receptor, the common form of treatment for metastatic prostate cancer.
Specific Aims: Aim 1. Decipher the mechanism of ERG-mediated reprogramming of the AR cistrome
Aim 2. Understand the role of PTEN loss in modulating the ERG transcriptome.
Aim 3. Determine the role of ERG expression in sensitivity to AR and PI3K inhibition.
Agency Contact: Funmi Elesinmogun
Overlap: None
*1-Year No-Cost Extension until 3/31/2021

1 U54 CA224079-03 (PI: Sawyers) 9/1/2017-8/31/2022
NCI/NIH
The MSKCC-UW/Fred Hutch Prostate Cancer Drug Resistance and Sensitivity Center
- Admin Core (PI: Sawyers) $36,914 0.91 calendar
- Project 1 (PI: Sawyers) $191,000 0.91 calendar
- Project 2 (PI: Chen; Co-I: Sawyers) $199,492 ($0 to lab) 0.46 calendar

Major Goals: 26,000 men die each year in the US from metastatic prostate cancer because the disease develops resistance to the primary treatment, called hormone therapy. DNA sequencing studies of tumors from these patients has revealed new strategies to treat prostate cancer with novel drugs in combination with hormone therapy. This application assembles a team of experts on this topic to work together to test these new therapies in laboratory models of prostate cancer developed directly from patients and identify those that should be accelerated into clinical development.
Agency Contact: Funmi Elesinmogun
Overlap: None

2 P50 CA092629-19 (PI: Scher) 9/1/2016 – 8/31/2021
National Institutes of Health
MSKCC Spore in Prostate Cancer
- RP-3 (PI: Sawyers) $145,938 0.60 calendar
  Heterogeneity in metastatic CRPC and the role of TP53 mutation as a molecular determinant
- RP-4 (PI: Sawyers) $108,896 0.60 calendar
  Investigating and targeting the glucocorticoid receptor (GR) in enzalutamide- and abiraterone
- Core F (PI: Sawyers) $78,566 ($0 to lab) 0.60 calendar
  Administrative Core
- DRP (PI: Sawyers) $100,000 ($0 to lab) 0.30 calendar
  Development Research Program

Major Goals of this Project: As a public health concern, prostate cancer is the second deadliest cancer in men. The translational research projects in this program aim to use knowledge of animal and human prostate cancer biology to develop and test interventions related to the prevention, early detection, diagnosis, prognosis, and treatment of prostate cancer in men.
This allocation is split between the following: Development Research Program; Core F, Administrative Core; Project 3, Heterogeneity in metastatic CRPC and the role of TP53 mutation as a molecular determinant; and Project 4, Investigating and targeting the glucocorticoid receptor (GR) in enzalutamide- and abiraterone.
Role: Core Co-Director of Core F, Co-Director of Development Research Program, Principal Investigator of Project 3 and Project 4.
Specific Aims of the Overall Grant:
1. To interrogate the genomics and molecular pathways relevant to prostate cancer progression
2. To improve prognostic models for early detection of potentially lethal cancers
3. To identify and validate clinically relevant biomarkers
4. To develop novel agents and therapeutic strategies
Agency Contact: Renee Carruthers
5. **Overlap**: None

5 P30 CA008748-53 (PI: Thompson) 1/1/2014-12/31/2023 1.80 calendar
NCI $0 to lab
Cancer Center Support Grant (Cancer Biology and Experimental Pathology Program)
The CCSG funds support MSK's research infrastructure. These shared resources facilitate the research activities of the clinical, translational and laboratory programs at the Cancer Center.
Agency Contact: Funmi Elesinmogun
Overlap: None

2 T32 CA160001-09 (PI: Sawyers) 8/1/2016 - 7/31/2021 0.00 calendar
NCI $239,384 ($0 to lab)
Translational Research in Oncology Training Program
Major Goals: The training program for translational cancer research will provide opportunities to postdoctoral PhD trainees to learn about human oncology and pathogenesis, and work collaboratively with clinicians to advance the treatment of cancer patients. The goals are: to help basic scientists to develop a strong clinical background so that they may effectively bring discoveries from bench to bedside; and to foster interdisciplinary research and collaboration.
Specific Aims: 1) To provide broad and intensive translational research training for PhDs by offering enhanced opportunities to orient their research to biomedically relevant problems. 2) To prepare Trainees to successfully collaborate during their career with researchers with different backgrounds. 3) To prepare and assist Trainees to successfully transition to research independence.
Agency Contact: Renee Carruthers
Overlap: None

5 R25 CA057732-27 (PI: Sawyers) 07/11/2016 - 05/31/2021 0.50 calendar NIH/
NCI $ 249,978 ($0 to lab)
Molecular Biology in Clinical Oncology Workshop
Major Goals: The workshop is primarily designed for oncologists in training at the fellow level. Space is also made available to a limited number of senior oncologists. The development and application of a range of cellular and molecular biological approaches to the study of gene structure and expression, cellular growth control, and malignant transformation have resulted in remarkable advances in the diagnosis, treatment, and prevention of cancer.
Agency Contact: Jeannette F Korczak
Overlap: None

I12 0007 (PI: Sawyers) 1/1/2019 - 12/31/2020 0.36 calendar
Starr Cancer Consortium $ 350,000
Defining prostate cancer cells of origin through single cell profiling
This proposal fits the RFA category of “Disease Applications” because it applies the relatively new molecular technology of single cell RNA sequencing (scRNA seq) to the study of prostate cancer.
Agency Contact: Sylvie Le Blancq,\
Role: Principal Investigator
Overlap: None