AWARD NUMBER: W81XWH-14-1-0466

TITLE: Clonal evaluation of prostate cancer by ERG/SPINK1 status to improve prognosis prediction

PRINCIPAL INVESTIGATOR: Scott A. Tomlins, M.D., Ph.D.

CONTRACTING ORGANIZATION: University of Michigan, Ann Arbor, MI 48109

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Prostate cancer is usually multiclonal, meaning that most men with prostate cancer have multiple, genetically distinct cancers. Pathologists cannot assess clonality by routine microscopic evaluation, and hence multiclonality is not incorporated into routinely reported pathological parameters. Given the importance of routine pathological parameters in prostate cancer prognosis, the potential to refine these parameters through assessing multiclonality represents a major opportunity. Hence, in this proposal we utilized dual ERG/SPINK1 immunohistochemistry (IHC)—as a readout of clonal, mutually exclusive molecular subtypes—to assess the frequency of multiclonality in key clinical scenarios at biopsy and resection and its impact on prognostic parameters. Our published and unpublished findings confirm multiclonality in key diagnostic scenarios, including discontinuously involved cores, multiple involved cores at biopsy, and collision tumors at prostatectomy. Our results are thus highly impactful for the management of men with prostate cancer.

15. SUBJECT TERMS
Multiclonality, ERG, SPINK1, immunohistochemistry, active surveillance, prostate biopsy, prostatectomy

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INTRODUCTION:
Prostate cancer is commonly multiclonal (also referred to as multifocal), meaning that more than 80% of men with prostate cancer actually have multiple, genetically distinct cancers in their prostate. Pathologists cannot assess focus clonality by routine microscopic evaluation, and hence multiclonality is not incorporated into routinely reported pathological parameters, such as the number of biopsy cores with cancer. Given the importance of routine pathological parameters in predicting the extent and behavior of prostate cancer, the potential to refine these parameters through assessing multiclonality represents a major opportunity. Hence, the objectives of this proposal were to utilize dual ERG/SPINK1 immunohistochemistry (IHC)—which can identify clonal, mutually exclusive molecular subtypes—to assess the frequency of multiclonality in key clinical scenarios at biopsy and resection. Secondly, we aimed to determine the impact of multiclonality on the ability of pathological parameters at biopsy to predict pathology at resection or outcome after resection. We hypothesized that incorporating multiclonality by IHC evaluation will improve the predictive ability of pathological parameters. Our results demonstrate that multiclonal prostate cancer is relatively frequent in clinically relevant scenarios, and clinical implementation in selected scenarios can likely increase the number of men eligible for active surveillance and enhance the well-being of men with prostate cancer through minimizing over-treatment and treatment-related side effects.

KEYWORDS:
Multiclonality, ERG, SPINK1, immunohistochemistry, active surveillance, prostate biopsy, prostatectomy

ACCOMPLISHMENTS:
What were the major goals of the project?:

SPECIFIC AIMS
1) Assess the frequency of multiclonality in clinically important scenarios using dual ERG/SPINK1 IHC.
2) Determine whether multiclonality assessment at biopsy improves prediction of pathology at prostatectomy.
3) Assess whether multiclonality assessment of index foci at prostatectomy improves outcome prediction.

What was accomplished under these goals?
To accomplish these aims, we developed a tri-institutional collaboration between Drs. Tomlins (PI; University of Michigan [UM]), Larry True (University of Washington [UW]) and Juan Miguel Mosquera (Weill Cornell Medical College). Our proposed statement of work was essentially the same for each site, with the exception of 100 cases to be scanned at the University of Michigan and reviewed by Drs. True and Mosquera (original UM, UW and WCMC statements of work Specific Aim 1.4.c). Hence, accomplishments (*in italics*) are reported using the UM statement of work.

Specific Aim 1: Assess the frequency of multiclonality in clinically important scenarios using dual ERG/SPINK1 IHC.

1) Obtain study IRB and DoD HRPO approval (months 1-2).

   All work sites (UM, UW and WCMC) received local IRB and DOD HRPO approval (Task 1.1 was 100% completed).

2) Retrospectively identify and review eligible cases (months 3-18)
   a. Retrospectively identify and review biopsy cases (n=100) from pathology database with discontinuous involvement (months 3-18).
   b. Retrospectively identify and review biopsy cases (n=100) from pathology database with Gleason score 6 or 3+4=7 and 2-5 positive cores (months 3-18).
   c. Retrospectively identify and review cases (n=134) from pathology database with Gleason score 3+4=7 at prostatectomy (months 3-18).

3) Prospectively identify and review eligible biopsy cases
   a. Prospectively identify and review biopsy cases (n=34) with discontinuous involvement (months 3-32).
   b. Prospectively identify and review biopsy cases (n=34) from pathology database with Gleason score 6 or 3+4=7 and 2-5 positive cores (months 3-32).

   After local IRB and HRPO approval, all institutions performed retrospective and prospective identification of eligible cases. Given challenges in obtaining enough eligible cases in year 2 across our three sites, we were able to obtain additional cases for evaluation from Dr. Tarek Bismar (University of Calgary). In total, across our sites, we performed histopathological review of over 1000 biopsy cases and 400 total radical prostatectomy specimens in an effort to identify sufficient cases for our analyses.

   For cohort 1 (discontinuously involved cohort), despite reviewing over 1000 biopsy cases, we were only able to identify a total of 70 completely evaluable cases (all involved blocks available for IHC and interpretation) where we had prostatectomy outcome data, given the rarity of discontinuously involved cancer in our in house biopsy specimens (vs. referred cases) and patients with somewhat limiting cancer undergoing prostatectomy.

   For cohort 2 (multiple positive biopsy cores with Gleason score 6 or 3+4-7), we were able to identify a total of 412 completely evaluable cases (all involved blocks available for IHC and interpretation).

   For cohort 3 (prostatectomy Gleason 7 with followup), we were able to identify a cohort of 300 completely evaluable (all involved blocks available for IHC and interpretation with sufficient prostatectomy data and follow-up).

   Hence overall, tasks 1.2a-c and 1.3a were ~ 90% completed.

4) Perform ERG/SPINK1 dual IHC
   a. Perform dual ERG/SPINK1 IHC on retrospectively and prospectively identified cases (n=402) identified and reviewed above (months 6-32).
   b. Evaluate dual ERG/SPINK1 IHC (months 7-32).
   c. Scan 100 cases for evaluation by Drs. True and Mosquera (months 12-14).

Although we anticipated being able to combine all positive cores from a given case onto a single section for staining, this was not feasible at two of the three institutions. Hence, to stay within budget, all immunostaining was performed at UM. To date, we have performed dual ERG/SPINK1 IHC on 819 cases, which comprised over 1,000 individual prostate biopsy cores and 500 prostatectomy sections. Our final batch of prostatectomy and biopsy slides have just completed staining, but formal evaluation is ongoing. Hence, task 1.4a was ~75% completed (as we were unable to identify the pre-specified number of cases for cohort 1) and task 1.4b was ~90% completed.

Across our three cohorts, we were able to determine the frequency of multifocality in these potentially important scenarios, as shown in ***Table 1****.*

Table 1: Rate of multifocality by ERG/SPINK1 IHC in clinically important diagnostic scenarios

Cohort	% Multifocal
1: Discontinuously involved cores	17%
2: Multiple cores involved with Gleason score 6 or 3+4=7	16%
3: Gleason score 7 index tumor foci	8%

To assess intra-observer reproducibility and assess the need for scanning and inter-institutional review, we first had Drs. Tomlins and Udager (both trained genitourinary pathologists at UM) independently evaluate ERG/SPINK1 status in a cohort of 50 prostate cancer foci. We observed 100% concordance (Kappa = 1), and hence we determined there was no need for scanning and review of additional cases. Hence, task 1.4c was 100% completed.

Specific Aim 2: Determine whether multiclonality assessment at biopsy improves prediction of pathology at prostatectomy.

1) Input clinicopathological data into common database for cases stained and evaluated above (months 4-32).
2) Input ERG/SPINK1 dual IHC data into common database for cases stained and evaluated above (months 4-32).

3) Assess associations between extent tumor involvement and number of positive cores with and without multiclonality incorporation and parameters associated with significant pathology at prostatectomy (months 32-34)
4) Prepare manuscript on study (months 34-36)

Clinicopathologic data and ERG/SPINK1 IHC for all evaluated cases have been compiled into a single database at UM (Tasks 2.1 and 2.2 was 100% completed).

In cohort 1 (discontinuously involved cores), a final total of 70 cores had both foci evaluable for SPINK1/ERG IHC. In total, we found that 43 of 70 (61%) cores had at least one ERG+ focus, and 12 of 70 (17%) cores showed multifocality based on discordant ERG status between the two foci. Although we were unable to identify a large number of cases where the discontinuously involved core drove the decision towards prostatectomy, we identified 6 cases where only Gleason score 6 cancer was present on biopsy, the discontinuously involved core had the highest volume (when including the intervening benign tissue), and multifocality was present by ERG/SPINK1 staining. Critically, in all 6 cases, only Gleason score 6, organ confined cancer was present on prostatectomy and hence by incorporating multifocality assessment at the time of biopsy evaluation, the patient would have remained eligible for active surveillance. As described below under "IMPACT: What was the impact on the development of the principal discipline(s) of the project", although underpowered for formal statistical analysis, this finding has already changed our routine pathology practice in such cases (where discontinuous volume could drive active surveillance decision making).

*In cohort 2 (multiple involved cores), a total of 188 cases (with 528 individually involved cores) were completely evaluable for SPINK1/ERG IHC with follow-up prostatectomy data. In total, we found that 27 of 188 (14%) cases were multifocal (based on discordant ERG status between at least two involved cores). Importantly, as shown in **Table 1**, we found that multifocal vs. non-multifocal cases had similar biopsy parameters, with multifocal cases actually showing a statistically significant increase in the number of cores involved, suggesting they should have similar or worse pathology at prostatectomy). In contrast, as shown in **Table 2**, multifocal cases had an increased rate of all parameters associated with adverse pathology at prostatectomy (Gleason score >=4+3 or stage > pT2), however these results did not reach statistical significance.*

Table 2: Pathological parameters in cases with multiple invovled biopsy cores evaluated for multifocality by ERG/SPINK1 IHC

Parameter^	Multifocal Yes	Multifocal No	P value*
Biopsy score 3+4=7 (vs. 3+3=6)	70%	62%	0.63
# Involved Cores	3.5	2.7	*0.0005*
Max % Involvement	57%	50%	0.27
RRP >=4+3=7	7%	16%	0.38
>pT2	11%	17%	0.57
Either >=4+3=7 or >pT2	18%	27%	0.47

^% or mean. *Two-sided t-test or Fisher's exact test

For cohort 2, an additional 55 cases have just completed ERG/SPINK1 IHC and results from these samples will be combined with those in Table 2 for final analysis. Hence, task 2.3 was approximately 95% completed.

We have published the results of our discontinuous biopsy cohort (see results dissemination below). Formal drafting of a manuscript describing the complete biopsy cohort will begin once all data and analyses are finalized. Hence task 2.4 was 50% completed.

Specific Aim 3: Assess whether multiclonality assessment of index foci at prostatectomy improves outcome prediction.

1) Input clinicopathological data into common database for cases stained and evaluated above (months 4-32).
2) Input ERG/SPINK1 dual IHC data into common database for cases stained and evaluated above (months 4-32).
3) Assess associations between Gleason score and tumor volume with and without multiclonality incorporation and PSA recurrence (months 32-34)
4) Prepare manuscript on study (months 34-36)

Clinicopathologic data and ERG/SPINK1 IHC for evaluated and stained cases have been compiled into a single database at UM (Tasks 3.1 and 3.2 were 100% completed).

In this cohort, we have only observed 8% multifocality in Gleason score 7 prostatectomy cohort samples, significantly less than the 22% observed in our preliminary data (we now hypothesize this is now due to the preliminary data cohort

consisting of patients with germline HOXB13 G84E mutations, which may increase their rate of multiclonal disease in addition to general increased prostate cancer incidence). In our completed cases, no significant impact on prediction of recurrence was observed incorporating multifocality in the first 50 completed cases in this cohort. Staining of an additional 200 cases has just been completed and these will be incorporated into our final analysis, however the low rate of multifocality in these unselected cases likely diminishes our power to observe any effect (although it would likely be too rare to impact clinical practice. Hence, tasks 3.3 and 3.4 were ~40% completed.

Importantly, however, our cohort is by far the largest whole slide cohort assessed for ERG/SPINK1 status. This assessment revealed near complete heterogeneity in SPINK1 in a single cancer focus (not multifocality). ***Fig 1*** *shows a remarkable case with heterogeneity of SPINK1 expression and an apparent collision with an ERG+ tumor focus. Although heterogeneity of SPINK1 expression had been suggested by previous TMA based studies, it has not been comprehensively assessed in whole slide studies. Previous TMA based studies supported SPINK1 positivity in ~10% of all prostate cancer, however in our whole slide cohort, 27% of 99 foci were SPINK1 positive considering any staining in tumor cells (always strong staining), consistent with TMA sampling underestimating SPINK1 positivity. This observation is extremely important, as the molecular cause of SPINK1 over-expression and down-stream mediators have not been identified. Our findings suggest that SPINK1 positive and negative areas from the same tumor focus must be dissected prior to molecular profiling.*

What opportunities for training and professional development has the project provided?
Nothing to Report

How were the results disseminated to communities of interest?

We have published our first set of results from this award that reported on the frequency of multiclonality in discontinuous biopsy cases.

Fontugne J, Davis K, Palanisamy N, Udager A, Mehra R, McDaniel AS, Siddiqui J, Rubin MA, Mosquera JM, Tomlins SA. Clonal evaluation of prostate cancer foci in biopsies with discontinuous tumor involvement by dual ERG/SPINK1 immunohistochemistry. Mod Pathol. 2016 Feb;29(2):157-65. doi: 10.1038/modpathol.2015.148. Epub 2016 Jan 8. PMID: 26743468 PMCID: PMC4732921

Dr. Tomlins also presented this work at the 2016 DOD Impact meeting.

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

Although funding has ended, data is still being analyzed (all sites have continuing local IRB approval) and will be included in a publication reporting on the frequency of multifocality in these relevant clinical scenarios.

IMPACT:

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

Our identification of multifocality in discontinuously involved cores has already changed our clinical practice at UM, and our diagnostic genitourinary pathology team routinely performs ERG staining and reporting to guide management decisions.

In addition, our study is the only study to perform whole slide immunohistochemistry for SPINK1 on a significant number of prostatectomy cases. Importantly, this revealed near universal heterogeneity in SPINK1 staining in a given cancer focus (see Fig 1). Critically, we and others had previously failed to identify the molecular consequences of the SPINK1 over-expressing subtype, in part due to the lack of expression signatures correlating with SPINK1 expression. Our results in this proposal largely explain this finding, as the heterogeneity of SPINK1 expression suggests that profiling must specifically separate SPINK1 positive and negative regions of the tumor focus. Hence, we will now pursue this approach (through separate funding mechanisms) which we expect will have profound impact on the understanding of the molecular mediators of the SPINK1 positive subtype.

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to Report

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

Significant delays in obtaining local IRB and HRPO challenged review and evaluation and cases, which delayed final analyses. These are ongoing now that all experimental work is complete.

Changes that had a significant impact on expenditures

Distribution of funds from UM to WCMC and UW was delayed while waiting for HRPO approval. Likewise, centralization of IHC resulted in less expenditures than budgeted from the UW site.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Nothing to Report

PRODUCTS:
Publications, conference papers, and presentations
As described above, we have published our first set of results from this proposal that report on the frequency of multiclonality in discontinuous biopsy cases.

Fontugne J, Davis K, Palanisamy N, Udager A, Mehra R, McDaniel AS, Siddiqui J, Rubin MA, Mosquera JM, Tomlins SA. Clonal evaluation of prostate cancer foci in biopsies with discontinuous tumor involvement by dual ERG/SPINK1 immunohistochemistry. Mod Pathol. 2016 Feb;29(2):157-65. doi: 10.1038/modpathol.2015.148. Epub 2016 Jan 8. PMID: 26743468 PMCID: PMC4732921

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

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Scott Tomlins
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	N/A

Nearest person month worked:	1
Contribution to Project:	Dr. Tomlins has led all aspects of the study as the PI, including directing database queries at UM, reviewing cases and over-seeing dual ERG/SPINK1 immunohistochemistry. Dr. Tomlins has also assisted in the IRB/DOD HRPO submissions for WCMC and UW.
Funding Support:	

Name:	Juan Miguel Mosquera
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1
Contribution to Project:	Dr. Mosquera evaluated and reviewed UW cases.
Funding Support:	

Name:	Larry True
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1
Contribution to Project:	Dr. True has evaluated and reviewed UW cases.
Funding Support:	

Name:	Aaron Udager
Project Role:	Pathologist
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	3

Contribution to Project:	Participated in evaluation and review of UM cases as well as ERG/SPINK1 immunohistochemistry.
Funding Support:	

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

  Please see the Appendix for updated Other Support documents for Drs. Tomlins, Mosquera and True during the final funding period.

- **What other organizations were involved as partners?**

As in original submission

University of Washington
1959 NE Pacific St
Seattle, Washington 98036
Collaborator (Dr. Larry True, Co-I)

Joan & Sanford Weill Cornell Medical College
1300 York Ave
New York, New York 10065
Collaborator (Dr. Juan Miguel Mosquera, Co-I)

SPECIAL REPORTING REQUIREMENTS

Collaborative Awards:
N/A

Quad Charts:
N/A

APPENDICES (see next page):
Figure 1
Updated Other Support for Dr. Tomlins
Updated Other Support for Dr. Mosquera
Updated Other Support for Dr. True

Figure 1

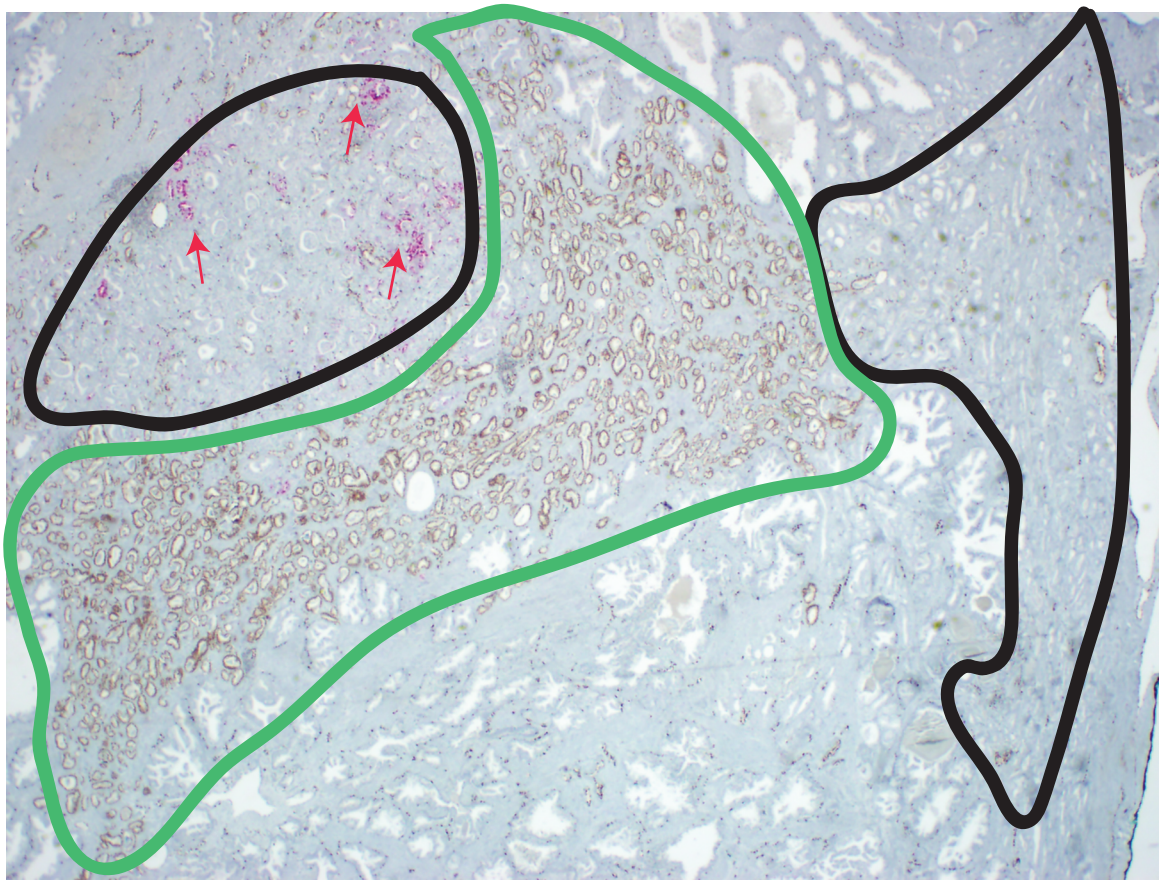

Figure 1. ERG/SPINK1 dual immunohistochemistry identifies collision of ERG+ and ERG-/SPINK1 positive tumor as well as heterogeneous SPINK1 expression. Dual ERG (brown chromogen) / SPINK1 (red chromogen) immunohistochemistry on a single morphologic prostate cancer focus (overall Gleason score 3+4=7) revealed an apparent collision tumor, with an ERG+/SPINK1- Gleason 3+3 tumor focus (brown staining, outlined in green) bisecting and colliding with a ERG-/SPINK1+ Gleason score 3+4=7 tumor focus (outlined in black, focal SPINK1 staining identified by red arrows). SPINK1 heterogeneity within a single focus has been observed in all SPINK1+ cancer foci. Original magnification 2x.

OTHER SUPPORT

TOMLINS, SCOTT

ACTIVE

5 P50 CA069568-15 (PI: Chinnaiyan) 09/01/14 - 08/31/19
12.5% NIH
SPORE in Prostate Cancer
Overview: 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.
Role: Co-Leader of Project 2
Contact Information at funding agency: Andrew Hruszkewycz, 301-496-8528, hruszkea@mail.nih.gov

R01CA183857 (PI: Tomlins) 04/3/14 - 02/28/19 21%
NIH
Exploiting drivers of androgen receptor signaling negative prostate cancer for precision medicine
Goal(s): Identify novel potential drivers of AR- prostate cancer through sequencing xenografts and tissue samples. Qualify novel drivers of AR- prostate cancer through in vitro models. Develop novel treatment strategies for AR- and AR+ prostate cancer through in vivo models.
Specific Aims: 1) Identify novel potential drivers of AR- prostate cancer. 2) Qualify novel drivers of AR- prostate cancer through *in vitro* models. 3) Develop novel treatment strategies for AR- and AR+ prostate cancer through *in vivo* models exploiting AR- drivers.
Contact information at Funding Agency: Morrow, Charles, 301-451-4467, morrowcs@csr.nih.gov

R01 CA181605 (PI: Nelson) 01/01/14 - 12/31/18 10%
NIH
Non Invasive Biomarkers for Diagnosing Clinically Significant Prostate Cancer
Goal(s): Test the hypothesis that biomarkers indicative of adverse prostate cancer behavior—Gleason grade, tumor volume and detrimental molecular alterations—can be reproducibly detected in the urine of men with prostate cancer; Determine whether initial sampling of a panel of urine biomarkers and the repeated assessment of a urine biomarker panel over time will associate with the presence of significant versus insignificant cancer in the prostate, and thus can be used in informing decisions for continuing surveillance or proceeding with definitive treatment.
Specific Aims: 1) Determine if PCA3 and TMPRSS2:ERG mRNA concentrations in urine associate with the presence or development of clinically-significant prostate cancer using longitudinal repeat assessments in men on Active Surveillance; 2) Evaluate a panel of long non-coding RNAs (lncRNAs) in tissue and urine for the detection of significant prostate cancer in men on Active Surveillance; 3) Define and evaluate a panel of Gleason Pattern-associated RNAs in tissue and urine for the detection of significant prostate cancer in men on Active Surveillance.
Role: Co-Investigator
Contact information at Funding Agency: Alexander Moreno, amoreno@fhcrc.org

R01 DK106618 (PI: Rainey and Tomlins) 03/01/16-02/28/20 10%
NIH

Adrenal Origins of Aldosterone Excess
Goals(s): This proposal will test the hypotheses that most adults have neoplastic cells bearing "first hit" somatic mutations that cause renin-independent aldosterone production. Primary aldosteronism and hypertension result from additional "multi-hit" mutations that increase cell proliferation, tumor development and pathologic levels of aldosterone. We will test the hypotheses that APCC are dysplastic cells bearing somatic gene mutations that activate aldosterone production and that APA have the same mutations seen in APCC, but exhibit additional mutations that cause cell proliferation and tumor development.
Specific Aims: 1) Define the somatic mutations found in normal adrenals that exhibit adrenal aldosterone-producing cell clusters (APCC). 2) Define the somatic gene mutations present in aldosterone-producing adenomas (APA).
Contact Information at Funding Agency: Saul N Malozowski Email: malozowskis@extra.niddk.nih.gov, Phone: (301) 451-4683

PC141474 (PI: Tomlins) 09/30/15-09/29/18 10%
DOD
Comprehensive Molecular Profiling of African-American Prostate Cancer to Inform on Prognosis and Disease Biology
Goal(s): Perform comprehensive expression profiling of prostate cancer (PCa) in AA men to assess the performance of PCa prognostic gene expression signatures and characterize known and novel gene fusions, mutations and copy number alterations.
Specific Aims: 1) Perform comprehensive expression profiling of PCa in AA men to assess the performance of PCa prognostic gene expression signatures. 2) Characterize known and novel PCa gene fusions in AA men. 3) Characterize known and novel PCa mutations and CNAs in AA men to develop an integrated prognostic signature.
Contact Information at funding agency: Tom Winter, thomas.s.winter2.civ@mail.mil, (240) 357-1590.

R01 CA196619 (PI: Cho) 05/01/16-04/30/19 2.5%
NIH
Credentialing Ovarian Cancer Models in the Context of the Dualistic Pathway Paradigm
Goal(s): Enhance the applicability of mouse models for translational research using novel genetically engineered mouse models (GEMMs). We have developed a new GEMM that employs the Ovgp1 promoter to direct expression of Tamoxifen (TAM)-inducible Cre recombinase in the fallopian tube epithelium (FTE). Ovgp1-iCreERT2 mice that also carry floxed alleles of tumor suppressor genes that are characteristically inactivated in ovarian endometrioid carcinoma (OEC, prototypical Type I tumor) and high grade serous ovarian carcinomas (HGSC, prototypical Type II tumor) can be induced to form tumors in the FTE following treatment with TAM, or tumors arising in the ovarian surface epithelium (OSE) following ovarian bursal injection of adenovirus expressing Cre.
Specific Aims: 1) To credential GEMMs of ovarian cancer (OvCa) arising from FTE- transformation as superior to those arising from OSE-transformation in terms of their morphological and molecular similarity to their human OvCa counterparts; and 2) To test a new tool strain for early detection of oviductal HGSCs based on cervical-vaginal lavage (murine Pap test).
Role: Co-Investigator
Contact Information at funding agency: Mariam Eljanne, Email: eljannem@mail.nih.gov, Phone: 301-443-3612

U01CA214170 (PI:Chinnaiyan and Tomlins) 10%
09/01/16-08/31/21 NIH
Discovery and qualification of transcriptomic biomarkers for the early detection of aggressive prostate cancer

Goal(s): Nominate and develop transcriptomic biomarkers as predictors of aggressive prostate cancer both at and prior to diagnosis.
Specific Aims: 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: Sudhir Srivastava, 240-276-7028, ss1a@nih.gov

PENDING

(PI Rubin) 04/01/17-03/31/22 5%
NIH
Towards Understanding the Genomic Heterogeneity of Metastatic Prostate Cancer (SPORE Project)
Goal(s): As part of the Weill Cornell Medical College S.P.O.R.E., this project aims to assess a large cohort of paired primary ADT-naïve and metastatic CRPC specimens to understand and exploit the molecular mediators of PCa progression to inform on optimal clinical pathologic practice, identify biomarkers, and inform on disease biology.
Specific Aims: 1). Collect and histologically characterize original primary ADT-naïve specimens from patients enrolled in the CRPC 500 trial. 2). Determine the molecular landscape of multiple tumor foci from the original ADT-naïve CRPC 500 specimens through DNA and RNA sequencing. 3). Identify molecular mediators of PCa progression and track the progressing clone through an integrative molecular profiling analysis of paired primary ADT-naïve and CRPC specimens
Role: Project Co-Leader (Co-Investigator)
Contact information at Funding Agency: Seran Lee-Johnson, sel2016@med.cornell.edu, (646) 962-6998

PC151032 (PI: Cooney) 09/30/18-09/29/19 3%
DOD
Characterizing the Genetic Landscape of Prostate Cancer in Young African American Men
Goals(s): The underlying hypothesis of this proposal is that African American men with early-onset prostate cancer are more likely to harbor germline variants that increase the risk of developing clinically significant prostate cancer, as well as novel driving somatic alterations. In this proposal, NGS approaches will be used to analyze germline DNA from 750 African American men with clinically significant prostate cancer diagnosed before age 60 years of age focusing on genes already known to be mutated in the germline or tumor of men with prostate cancer or other cancers as well as genes in functional pathways of interest (i.e. hormone biosynthesis and signaling and DNA damage repair).
Specific Aims: 1) Collect germline DNA from 750 young African-American men diagnosed with clinically significant prostate cancer. 2) Perform germline sequencing of candidate genes on the cohort to identify to identify deleterious variance. 3) Perform targeted next generation sequencing on tumor samples from the subset of the men with germline DNA mutations.
Role: Co-Investigator
Contact information at Funding Agency: Christine LaSalle, christine.lasalle@hsc.utah.edu, (801) 585-2734

RO1 (Wei) 8/1/2017-7/31/2019 5%
NIH
Clinical utility of multiplex biomarkers for high grade prostate cancer: A cost effective followup study expanding upon the existing EDRN prostate cancer reference set.

Goals: The specific aims include: 1) To expand the existing EDRN's unique pre-diagnostic reference set with RNA sequencing of pre-biopsy urine; 2) To optimize the risk prediction for high grade prostate cancer within 5 years of initial prostate biopsy. This aim will focus only on those who were initially biopsied in the PCA3 cohort.
Role: Co-Investigator

RO1 (El Naqa, Piert) 2/1/2018-1/31/2023 5%
NIH
AN INTEGRATIVE HYBRID IMAGING RADIOMICS AND MOLECULAR BIOMARKERS FRAMEWORK FOR PREDICTING SIGNIFICANT PRIMARY PROSTATE CANCER
Goals: Our goal is to develop a personalized non-invasive diagnostic test to distinguish indolent from aggressive prostate cancer. The study will determine how a new promising PET tracers could be employed to improve prostate risk stratification by combining radiomics features from PET/MR with known laboratory biomarker tests.
Role: Co-Investigator

ENDED WITHIN THE LAST 5 YEARS

Award No. N/A (PI: Knudsen) 10/15/12 – 10/15/14 2%
Movember-Prostate Cancer Foundation
Challenge Award
Interrogating DNA Repair Defects to Improve Management of Advanced Prostate Cancer
Goal(s): The overall goal of this proposal is to identify therapeutic strategies to target DNA damage response pathway alterations in patients with advanced prostate cancer.
Specific Aims: 1) To identify and comprehensively determine the frequency of aberrations in DNA damage response pathways at different stages of prostate carcinogenesis; 2) To determine the clinical relevance of these DNA repair defects; 3) To evaluate the functional and biological consequences of these DNA repair defects and identify novel therapeutic strategies that will benefit patients suffering from such cancers.
Role: Co-Investigator
Contact Information at funding agency: Audrey Gardner, PCF Applications (applications@pcf.org)

Award No. N/A (PI: Knudsen/Feng/Tomlins) 12/01/13 - 11/30/15
2.5% Prostate Cancer Foundation
Targeting DNA Repair Alterations To Improve Treatment for Advanced Prostate Cancer
Goal(s): Comprehensively interrogate DNA repair alterations in both AR-positive and AR-negative CRPC to develop novel biomarkers and therapeutic strategies with the goal of improving outcomes for patients with these aggressive diseases
Specific Aims: 1) Determine the molecular and cellular consequence of tumor-associated DNAPK dysregulation; 2) Assess the impact of targeting DNAPK and the DDR on tumor progression & therapeutic response; 3) Targeting AR-mediated DNA repair through the requisite cofactor USP22; 4) Profiling DNA repair alterations in AR-negative, late stage disease.
Role: Co-PI
Contact Information at funding agency: Audrey Gardner, PCF Applications (applications@pcf.org)

Award No. N/A (Dream team leader: Chinnaiyan) 08/01/12 – 07/31/15 2.5%
AACR Stand up to Cancer and
Prostate Cancer Foundation Dream Team
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.
Role: Co-Investigator
Contact Information at funding agency: Frederic Biemar, (frederic.biemar@aacr.org), (215) 446-7261

PC120464 (PI: Cooney) 09/30/13 - 09/29/16
12% Department of Defense
High throughput sequencing of germline and tumor from men with early-onset, metastatic prostate cancer
Goal(s): To perform next generation sequencing on germline DNA, prostate cancer, and normal prostate tissue on samples from men with early-onset, clinically significant disease.
Specific Aims: 1. To identify and clinically characterize a set of 20 men who present with Stage 4 (Tx N1 and/or M1) prostate cancer at an early age defined as at or before age 60, and 2. To interrogate the germline exome and tumor exome/transcriptome from 20 men with early-onset Stage 4 prostate cancer to identify novel molecular alterations that may contribute to the early-onset, aggressive 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

PC121111 (PI: Scher, H.) 10/01/13 – 09/30/16 2%
Department of Defense
Toward the Practice of Precision Medicine: A Biomarker Validation Coordinating Center
Goals(s): Establish Multicenter Validation of Biomarker Assays for Clinical Management of Prostate Cancer 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 Aims: 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

UM1HG006508 (PI: Chinnaiyan) 07/19/13 – 06/30/17 2%
National Institutes of Health
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 Aims: 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.
Role: Co-Investigator
Contact Information at funding agency: Harvey, Zephaun, harveyz@mail.nih.gov, 301 435-7859

Award No. N/A (PI: Maher/Feng/Sharifi/Tomlins 01/01/15 - 12/31/16 1%
Prostate Cancer Foundation
Identifying Early Biomarkers of Anti-Androgen Treatment Resistance and Lethal Prostate Cancer
Goal(s): Radiation Therapy Oncology Group (RTOG) 96-01 represents a phase III trial of of salvage radiation therapy (RT) alone versus combined therapy (androgen deprivation therapy [ADT] and RT). This represents a highly unique population of 771 patients with aggressive localized prostate cancer following standard treatment options with long-term clinical outcomes (median follow-up of 9 years). The overarching goal of this proposal is to leverage this unique patient population to explore the molecular underpinnings predictive of treatment response and associated with lethal disease.
Role: Co-PI
Contact information at Funding Agency: Audrey Gardner, agardner@pcf.org

Award No. N/A (PI: Rubin/Tomlins) 07/01/15 - 06/30/17 1%
Prostate Cancer Foundation
Integrative Genomics of Prostate Cancer Progression
Goal(s): Retrospectively collect, review, and perform comprehensive molecular characterization on the original diagnostic biopsy or prostatectomy samples from men with castration resistant prostate cancer (CRPC) participating on the CRPC 500 trial to identify molecular determinants of prostate cancer progression.
Contact information at Funding Agency: Audrey Gardner, agardner@pcf.org

PC13065 (PI: Tomlins) 09/17/14 – 09/16/17 7%
Department of Defense
Clonal Evaluation of Prostate Cancer by ERG/SPINK1 Status to Improve Prognosis Prediction
Goal(s): Utilize ERG/SPINK1 status to assess the frequency of multiclonality in clinically relevant scenarios and to determine whether incorporating tumor clonality improves prognostic prediction.
Specific Aims: 1) Assess the frequency of multiclonality in clinically important scenarios using dual ERG/SPINK1 IHC; 2) Determine whether multiclonality assessment at biopsy improves prediction of pathology at prostatectomy; 3) Assess whether multiclonality assessment of index foci at prostatectomy improves outcome prediction
Contact information at funding agency: Theresa J. Miller, Ph.D , Phone: 301-619-6875; theresa.j.miller.ctr@mail.mil

OVERLAP

There is no scientific or budgetary overlap.

OTHER SUPPORT

MOSQUERA, JUAN M.

CURRENT
R01 CA184712 (Mosquera, JM / Lin, D.)
Precision Medicine Approach to Prostate Cancer Active Surveillance
1.8 calendar
National Institute of Health
Grants Officer: Sarah E. Scharf; email: sarah.scharf@nih.gov; phone: 240-276-5472
8/1/14-7/31/19

The goal of this project is to confirm a novel panel of tissue-based biomarkers to determine the presence of or progression to aggressive disease in early stage PCa and prove that these biomarkers will reliably predict PCa progression and/or under-staging and grading
Aim 1. Confirm a novel panel of tissue-based biomarkers to determine the presence of or progression to aggressive disease.
Aim 2. Evaluate emerging tissue-based biomarkers for aggressive PCa in men on AS.

P50 CA211024 (Rubin)
Weill Cornell Medicine (WCM) SPORE in Prostate Cancer
0.6 calendar
National Institutes of Health
07/01/2017-6/30/2022

The goal of this project is to take a novel precision medicine approach to PCA patient care, by aligning translational research goals with the care of men across the PCA spectrum. The WCM SPORE will be a major hub for paradigm-shifting translational research, which will establish new approaches to PCA, which will result in improved patient survival and quality of life.
Aim 1. Develop accurate biomarkers to assess the risk of PCa disease progression using genomic and liquid biopsy approaches (Projects 1 and 3).
Aim 2. Develop new therapeutic approaches for clinically localized and CRPC that are hypothesis-driven, based on newly acquired knowledge of PCa biology and genomic, and represent a paradigm shift in treatments (Projects 2, 3,and 4).
Aim 3. Leverage existing and expand new infrastructure for the successful translation of pre-clinical stidues into the clinic.
Aim 4. Train the next generation of PCa investigators

COMPLETED

W81XWH-14-1-0466 (Tomlins) -completed
Clonal Evaluation of Prostate Cancer by ERG/SPINK1 Status to Improve Prognosis Prediction
0.96 calendar
United States Dept. of Defense
Grants Officer: Emily Tran; email: tranc@mail.nih.gov; Phone: 240-276-6324
Goal(s): Utilize ERG/SPINK1 status to assess the frequency of multiclonality in clinically relevant scenarios and to determine whether incorporating tumor clonality improves prognostic prediction.
Specific Aims: To develop QIBC to assist radiologists in evaluation of bladder GTV on multimodality images (MM-bladder tumors); To develop decision support systems to assist clinicians in staging and monitoring of treatment response of bladder cancer by using image biomarkers, pathological information and diagnostic test

results, and immunohistochemical biomarkers; To evaluate the effects of QIBC and CDSS-T on clinicians' inter-observer variability, efficiency and accuracy in estimation of bladder GTV and tumor treatment response by observer studies; To evaluate the CDSS-S and CDSS-T as clinical decision support tools for estimation of tumor treatment response in pilot clinical studies.

AACR SU2C Dream Team (Chinnaiyan, A. / Sawyers, C.)
Precision Therapy of Advanced Prostate Cancer
1.2 calendar
American Association for Cancer Research
Grants Officer: Karen Giles; email: kargiles@umich.edu; phone: 734-763-3821
7/1/12-6/30/16

Project Goals: To examine the functional relevance of 5-10 candidate genes implicated by prostate cancer somatic mutations, develop companion functional approaches for the analysis of DNA and RNA sequencing and determine key targetable genes associated with prostate cancer.

Starr Foundation Grant, I7-A722 (Chen, Y. / Rubin / Carver, B. / Beltran, H.)
Co-clinical trials using organoids for patients with advanced prostate cancer
0.12 calendar
Starr Foundation Grant
Grants Officer: Sylvie LeBlanq; email: leblancs@mskcc.org; phone: 212-639-8489
1/1/14-12/31/15
This project will create organoid lines from advanced prostate cancer patients to generate mutational and copy number data of each organoid line, determine whether *in vitro* sensitivity can predict for patient response, and generate potential biomarkers.
Aim 1. Generate clinically well-annotated organoid lines that accurately recapitulate the clinical and molecular diversity of abiraterone-resistant CRPC and NEPC
Aim 2. Characterize the mutational profile and copy number profile of each organoid line
Aim 3. Determine the *in vitro* drug sensitivity profile of organoid lines and correlate with patient response

R01 CA179100 (Rickman)
Mechnistic Insights Underlying ERG-induced Taxane Resistance in Castration –Resistant Prostate Cancer
0.36 calendar
National Institute of Health
Grants officer: Sarah M. Lee; 240-276-6280; Sarah.Lee@nih.gov
04/11/14-02/28/19
Aim: To characterize the mechanism underlying ERG-induced taxane resistance in castrate resistant prostate cancer

U01 CA162148 (Garraway, L.)
Systemic Genetic Characterization of African American Prostate Cancer
0.6 calendar
National Institute of Health
Grants Officer: N/A
7/1/12-6/30/17
The over-arching goal of this proposal is to undertake a definitive somatic genetic and functional characterization of African-American prostate cancer.
Aim 1. Design and validation of hybrid capture-based genomic profiling protocol to genetically characterize African American prostate cancer tumor samples

Aim 2. Profiling of a cohort of African American prostate cancer samples
Aim 3. Functional and mechanistic studies of operant signaling pathways in African American cell lines in vitro

OTHER SUPPORT

TRUE, LARRY D.

ACTIVE

W81XWH-16-1-0584 (Petros) 9/30/16-9/29/19 .56% effort
DOD
A Single Missense Mutation in 77% of Prostate Cancer Bone Metastases: Novel Opportunity for Genetic Biomarker and Novel Therapeutic Mitochondrial Target
Dr. True will be responsible for the histological assessment of the materials – characterizing tumor cell purity etc., and addressing any issues of tissue processing that might impair quality of the tissue and, thus, the findings.
Role: Co-Investigator
Sponsor Contact: CDMRP, (301)682-5507, help@cdmrp.org

2 P50 CA97186 (Nelson) 9/1/13-8/31/18
NIH 0.84 calendar *Pacific*
Northwest Cancer SPORE
Core B: Biospecimen Core
The Specimen Core provides part of the infrastructure support for Projects 1-4, as well as future pilot and developmental projects. It has been designed to meet the needs of these projects, plus serve as a stand-alone system of specimen collection, storage, distribution and related clinical/research information dissemination that is based on over two decades of experience.
Role: Dr. True will serve as the Pathologist and Co-Director of Core B.
Sponsor Contact: Peter Nelson, M.D., Fred Hutchinson Cancer Research Center (FHCRC), 1100 Fairview Avenue N., MS: J6-500, PO Box 19024, Seattle, WA 98109-1024, pnelson@fhcrc.org

R01 CA176844-01 (Vasioukhin) 05/01/13 - 03/31/18 0.72 calendar
NIH
The Hippo Pathway in Prostate Gland Homeostasis and Prostate Cancer
This project hypothesizes that biomarkers of disease aggressiveness and prognosis can be measured in early stage prostate cancer and that these biomarkers will aid not only in choosing the initial course of therapy but also in decision-making during AS (Active Surveillance). The project proposes to interrogate a large multi-institutional cohort of men undergoing AS to confirm a platform of tissue and urine-based biomarkers that will reliably predict prostate cancer progression and or under-staging and –grading, thus determining patients who may avoid radical treatment, concurrently identifying men who may benefit from early treatment rather than active surveillance.
Role: Co-I
Sponsor Contact: James Pendleton, Fred Hutchinson Cancer Research Center (FHCRC), 1100 Fairview Avenue N., PO Box 19024, Seattle, WA 98109-1024, jpendlet@fhcrc.org

P01 CA163227 (Balk) 5/1/13-4/30/18 0.696 calendar
NIH
Androgen Receptor Action In Castration Resistant Prostate Cancer
Core C: Biospecimen Core
The major goal of the Biospecimen Core is to provide a well-organized and standardized system of specimen collection, storage, distribution and related clinical/research information dissemination that is based on over two decades of experience. The Core will ensure consistency and quality assurance in the pathological analysis of tissue specimens. It will maintain a large series of prostate cancer xenograft lines developed by Core investigators, which will be used for proposed studies by the P01 investigators.

Role: Co-I
Sponsor Contact: Julienne Carty, Harvard University, 330 Brookline Ave. E/CLS 650, Boston, MA 02215, 617-735-2002, jcarty@bidmc.harvard.edu

W81XWH-15-1-0430 (Nelson) 7/1/15-6/30/18 2% effort
DOD
Minimally-Invasive Assessments of Prostate Cancer Molecular Heterogentity to Direct Precision Therapy
Dr. True will assist in the acquisition and assessment of tumors acquired from men with advanced prostate cancer, evaluate tumor purity, and assist with evaluations of tumor heterogeneity by histology and immunohistochemical methods.
Role: Co-Investigator
Sponsor Contact: CDMRP, (301)682-5507, help@cdmrp.org
Parent Institution: Fred Hutchinson Cancer Research Center

ENDED SINCE LAST SUBMISSION:

PC 130652 (Tomlins) 9/30/14-9/29/17 0.936 calendar DOD
Clonal evaluation of prostate cancer by ERG/SPINK1 status to improve prognosis prediction
The objectives will be to retrospectively and prospectively identify cases for cohorts 1-3. Dr. True will be responsible for performing and evaluating ERG/SPINK1 dual IHC stains on 300 cases. He will also be responsible for transferring the remaining cases/sections to Dr. Tomlins at UMHS and evaluating ERG/SPINK1 dual IHC stains on 100 cases stained at UMHS. He will also work with co-investigators at UMHS and Cornell in study design, data analysis and interpretation, and in manuscript preparation.
Role: Co-Investigator
Sponsor Contact: CDMRP, (301)682-5507, help@cdmrp.org
Parent Institution: University of Michigan

W81XWH1410595 (Lin) 9/30/14-9/29/17 1.2 calendar
DOD
Biomarkers for Early Detection of Clinically Relevant Prostate Cancer: a Multi-Institutional Validation Trial
Dr. True will be responsible for reviewing slides of prostate needle biopsies and characterizing the prognostic pathologic parameters in biopsies of participants in the PASS study. He will also identify areas of cancer for tissue samples used in Aim 1 of the project.
Role: Co-Investigator
Sponsor Contact: CDMRP, (301)682-5507, help@cdmrp.org
Parent Institution: Fred Hutchinson Cancer Research Center

W81XWH-14-2-0183 (Morrissey) 9/30/14-9/29/17 9.6 calendar
DOD
Prostate Cancer Biorepository Network
Dr. True participates in The Prostate Cancer Biorepository Network (PCBN). The goal of PCBN is to maintain and expand the current biorepository with high quality, well-annotated specimens that meet the critical needs of the prostate cancer research community, and which are obtained using optimized and standardized protocls.
Role: Co-Investigator
Sponsor Contact: CDMRP, (301)682-5507, help@cdmrp.org

W81XWH13-2-0070 (Scher) 9/30/13-9/26/16
DOD

Toward the Practice of Precision Medicine: Multicenter validation of Biomarker Assays for Clinical Management of Prostate Cancer
UW Subaward: *$103,827* 1.8 calendar
The goal of this proposal is to revolutionize the clinical management of prostate cancer by cross-validating assays of integral biomarkers for prostate cancer that can be used in prospective, biomarker-driven clinical trials. This will be accomplished by facilitating critical collaboration between multidisciplinary teams of investigators at multiple institutions in order to 1) develop a pipeline of biomarkers prioritized for assay development, 2) determine the appropriate platform(s) for analysis, and 3) systematically address the preanalytical, analytical, and post-analytical variables including data redaction to validate and conduct tissue based assays in a CLIA environment.
Role: Co-I
Sponsor Contact: CDMRP, PCRP, (301) 619-7079, cdmpr.pa@amedd.army.mil
Parent Institution: Memorial Sloan-Kettering Cancer Center; Award Administrator: Michael McGregor, mcgregom@mskcc.org