AWARD NUMBER: W81XWH-14-2-0159

TITLE: Prostate Cancer Clinical Consortium Clinical Research Site: Targeted Therapies

PRINCIPAL INVESTIGATOR: David Nanus

CONTRACTING ORGANIZATION: Weill Medical College of Cornell University
New York, NY 10065-4805

REPORT DATE: DEC 2018

TYPE OF REPORT: Final Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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REPORT DOCUMENTATION PAGE			*Form Approved* *OMB No. 0704-0188*
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1. REPORT DATE DEC 2018	**2. REPORT TYPE** FINAL		**3. DATES COVERED** 30 Sep 2014 - 29 Sep 2018
4. TITLE AND SUBTITLE Prostate Cancer Clinical Consortium Clinical Research Site: Targeted Therapies			**5a. CONTRACT NUMBER** **5b. GRANT NUMBER** **W81XWH-14-2-0159** **5c. PROGRAM ELEMENT NUMBER**
6. AUTHOR(S) David Nanus, M.D. E-Mail: dnanus@med.cornell.edu			**5d. PROJECT NUMBER** **5e. TASK NUMBER** **5f. WORK UNIT NUMBER**
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Weill Medical College of Cornell University 1300 York Avenue, Box 89 New York, NY 10065-4805			**8. PERFORMING ORGANIZATION REPORT**
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			**10. SPONSOR/MONITOR'S ACRONYM(S)** **11. SPONSOR/MONITOR'S REPORT NUMBER(S)**
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited			
13. SUPPLEMENTARY NOTES			
14. ABSTRACT **The Weill Cornell Medical College Prostate Cancer Research Program (WCMC-PCRP) is a Clinical Research Site of the Prostate Cancer Clinical Trials Consortium (PCCTC). The purpose of the research is to lead and participle in Consortium therapeutic and correlative science research protocols. Specifically, our aims are to impact prostate cancer care and outcomes through the development and study of novel targeted therapeutics, discovery of mechanisms of therapy resistance/sensitivity, identification of new therapeutic targets through high quality genomic analyses, providing access to the highest quality PC tissue specimens, and development of molecular imaging techniques with direct relevance to targeted therapies. Our overarching goal is to more effectively bring novel agents and new biomarker driven trials directly to patients**			
15. SUBJECT TERMS NONE LISTED			
16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT** Unclassified	**18. NUMBER** 17	**19a. NAME OF RESPONSIBLE PERSON USAMRMC** **19b. TELEPHONE NUMBER** *(include area code)*
a. REPORT Unclassified	**b. ABSTRACT** Unclassified	**c. THIS PAGE** Unclassified			

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1. **INTRODUCTION:**

The Weill Cornell Medical College Prostate Cancer Research Program (WCMC-PCRP) is a Clinical Research Site of the Prostate Cancer Clinical Trials Consortium (PCCTC). The purpose of the research is to lead and participle in Consortium therapeutic and correlative science research protocols. Specifically, our aims are to impact prostate cancer care and outcomes through the development and study of novel targeted therapeutics, discovery of mechanisms of therapy resistance/sensitivity, identification of new therapeutic targets through high quality genomic analyses, providing access to the highest quality PC tissue specimens, and development of molecular imaging techniques with direct relevance to targeted therapies. Our overarching goal is to more effectively bring novel agents and new biomarker driven trials directly to patients

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

aurora kinase A, clinical trials, circulating tumor cells, monoclonal antibody, neuroendocrine prostate cancer, next-generation sequencing, prostate cancer, Prostate Cancer Clinical Trials Consortium, prostate specific membrane antigen, translational research program,

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the USAMRAA Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?

SOW Major Task 1: Adhere to performance metrics defined by Coordinating Center
SOW Major Task 2: Full participation in the consortium as a member of the Clinical Consortium Committee/Scientific Oversight Committee
SOW Major Task 3: Regulatory review, Clinical trial startup
SOW Major Task 4: Propose clinical trials to Consortium
SOW Major Task 5: Interim data analysis
SOW Major Task 6: Open other Consortium sponsored Clinical Trials at WCMC
SOW Major Task 7: Clinical trial performance
SOW Major Task 8: Investigator analysis, reporting of initial data
SOW Major Task 9: Analysis and reporting of final data

What was accomplished under these goals?

SOW Major Task 1: Adhere to performance metrics defined by Coordinating Center

Subtask 1. Accrue at least 25 patients per year to PCCTC trials: Fifty-six (56) patients have enrolled to the 9 currently active PCCTC protocols in this reporting period. Total enrollment number for the below PCCTC trials are updated below.

Study Title	Year 1	Year 2	Year 3	Year 4
A Phase II Trial of the Aurora Kinase A Inhibitor in Patients with mCRPC and NEPC [c12-105]	6	2		
Randomized Phase II 3-Arm Study of Abiraterone, Abiraterone Plus Degarelix, and Degarelix Alone for Patients with a Rising PSA Following Radical Prostectomy [c11-092]	3	3	0*	
Randomized Phase II Trial of Abiraterone With or Without Cabazitaxel in Treatment of mCRPC [c12-108]	1	2	1	3
Phase II trial assessing pain efficacy with Radium-223 in symptomatic mCRPC [c13-124]	5	6	5*	
Circulating Molecular Predictors of Chemotherapy and Novel Hormonal Therapy Benefit in mCRPC [c14-144]	1	18	1	
Phase Ib/II Randomised Study of BI 836845 + Enzalutamide versus Enzalutamide alone in mCRPC [c14-147]		0	2	0*
Phase I Trial to Evaluate Safety and Immunogenicity of INO-5150 Alone or in Combination with INO-9012 in Men with Biochemically Relapsed PC [c15-158]		2	0*	
Phase II Trial of Pembrolizumab (MK-3475) in Subjects with mCRPC Previously Treated with Chemotherapy [c16-184]			0	11
Phase I Trial of ARN-509 plus Abiraterone, Docetaxel, and Prednisone in Patients with mCRPC (c15-163)			6	3
A Phase I/II Study of Immu-132 (hRS7-SN38 Antibody Drug Conjugate) in Patients with Epithelial Cancer [c17-193]			3	0
Phase I dose-escalation study of fractionated dose 177Lu-PSMA-617 for progressive mCRPC [c17-199]			17	21
Phase 3 Study of 99mTc-MIP-1404 SPECT/CT Imaging to Detect Clinically Significant Prostate Cancer in Men with Biopsy Proven Low-Grade Prostate Cancer who are Candidates for Active Surveillance (proSPECT-AS) [c16-105]		3	21	1*
Phase I dose–escalation trial of 225Ac–J591 in patients with metastatic castration–resistant prostate cancer				7
ARN-509 + Abiraterone acetate + Leuprolide with Stereotactic, Ultra-Hypofractionated Radiation (AASUR) in Very High Risk Prostate Cancer: A Single Arm, Phase II Study [c15-163]				1
Total:	**16**	**36**	**56**	**47**

*Closed to enrollment during reporting period

Patient Sample Accrual

PCCTC LOI# c12-105: 60 pre-treatment tissue biopsies, and >100 serial plasmas samples were processed.
PCCTC 12-107 (which was closed to new patient accrual before 9/30/14 but circulating tumor cell (CTC) samples continued to be received by WCM), over 500 CTC samples were analyzed for drug target engagement.
PCCTC c14-144: 120 CTC samples have been analyzed by digital droplet polymerase chain reaction (ddPCR) for androgen receptor variants.

Subtask 2. Accrue at least 5% of patients from disproportionately affected populations per year

Eleven of forty-seven enrolled patients were from disproportionately affected populations (23.40%)

Demographic	African American	White NH	White H	Asian	Other	Total Subjects in Year
Year 4 9/16/17-9/30/18	2	36	3	1	5	47
	4.25%	76.6%	6.4%	2.12%	10.70%	

Subtask 3. Propose ≥ 2 clinical trials per year or 6 trials over 3 years for consideration by the consortium, which may include biomarker studies:

The table below displays all the clinical trials within the consortium that we are the PIs/lead investigators. In addition to the activated studies below, we have a number of protocols in various stages of start-up.

Study Title
Phase II Trial of Pembrolizumab (MK-3475) in Subjects with Metastatic Castration-Resistant Prostate Cancer (mCRPC) Previously Treated with Chemotherapy (KEYNOTE-199)
Phase I Trial of ARN-509 plus Abiraterone acetate, Docetaxel, and Prednisone in Patients with Metastatic Castrate Resistant Prostate Cancer (mCRPC) [c15-163]
A Phase I/II Study of Immu-132 (hRS7-SN38 Antibody Drug Conjugate) in Patients with Epithelial Cancer.
Phase I dose-escalation study of fractionated dose 177Lu-PSMA-617 for progressive metastatic castration resistant prostate cancer
Phase I dose−escalation trial of 225Ac−J591 in patients with metastatic castration−resistant prostate cancer
A Phase II Trial of the Aurora Kinase A Inhibitor in Patients with mCRPC and NEPC [c12-105]
Phase Ib/II Randomised Study of BI 836845 + Enzalutamide versus Enzalutamide alone in mCRPC [c14-147]

Circulating Molecular Predictors of Chemotherapy and Novel Hormonal Therapy Benefit in mCRPC [c14-144]

Subtask 4. Participate as a Clinical Research Site in >6 trials initiated by other sites: We have opened 6 trials to date initiated by other sites, including one in which we are co-investigators on a PCF Challenge Award.

Study Title
An Exploratory Randomized Phase II Multicenter Trial of Abiraterone Acetate With or Without Cabazitaxel in Treatment of Metastatic Castration Resistant Prostate Cancer [c12-108]
Phase II open-non-randomized trial assessing pain efficacy with Radium-223 in symptomatic metastatic castration-resistant prostate cancer [c13-124]
Phase I, Open-Label Trial to Evaluate the Safety and Immunogenicity of INO-5150 Alone or in Combination with INO-9012 in Men with Biochemically Relapsed (PSA) Prostate Cancer [c15-158]
Phase 3 Study of 99mTc-MIP-1404 SPECT/CT Imaging to Detect Clinically Significant Prostate Cancer in Men with Biopsy Proven Low-Grade Prostate Cancer who are Candidates for Active Surveillance (proSPECT-AS) [c16-105]
ARN-509 + Abiraterone acetate + Leuprolide with Stereotactic, Ultra-Hypofractionated Radiation (AASUR) in Very High Risk Prostate Cancer: A Single Arm, Phase II Study
Prostate Cancer Outcomes: An International Registry to Improve Outcomes in Men with Advanced Prostate Cancer (IRONMAN)

SOW Major Task 2: Full participation in the consortium as a member of the Clinical Consortium Committee/Scientific Oversight Committee

Subtask 1. Participate in ≥1 PCCTC committee: Dr. Nanus is a member of the Scientific Oversight Committee and Dr. Tagawa serves as an Alternate.

Subtask 2. Attend all face-to-face meetings of the PCCTC: Dr. Nanus, Dr. Tagawa and/or Dr. Beltran attended all face-to-face meetings of the PCCTC.

Subtask 3. Participate in scheduled consortium conference calls: Dr. Nanus and/or Dr. Tagawa have participated in all PCCTC scheduled consortium conference calls. WCM investigators presented on the conference call in December 2015, March 2017 and June 2018.

Subtask 4. Participate in review meetings/evaluation by the External Advisory Board (EAB): No EAB meetings have yet occurred.

Subtask 5. Compliance with the operations manual of the Consortium: We have been compliant.

SOW Major Task 3: Regulatory review, Clinical trial startup.
Subtasks 1 thru 4 have each been completed (Submission of protocols for scientific (WCMC Protocol Review Committee) and WCMC Institutional Review Board (WCMC Clinical and Translational Science Center review if indicated); Completion of contractual agreements between Coordinating Center and WCMC; Clinical trial approval at WCMC; and Site initiation visits).

SOW Major Task 4: Propose clinical trials to Consortium

Subtask 1. Propose new therapeutic trial to Coordinating Center and other Consortium sites: See above (Major Task 1, Subtask 3).

Subtasks 2- thru 7. Subtasks 2 thru 7 are completed for each WCMC initiated protocol. (Submission of protocol for scientific review; start up at additional sites; clinical trial initiation at WCMC and other collaborating sites; Screen, enroll, and treat subjects; ongoing communication with study sites; Ongoing communication with IRB, DSMB, FDA).

SOW Major Task 5: Interim data analysis
Data from numerous studies underwent interim data analysis leading to final data analysis and presentation (see below). Ongoing data analyses continue on samples from numerous studies, including CTC data sample analysis from PCCTC c12-107 (TAXYNERGY, a phase II trial to evaluate benefit of early switch from first-line docetaxel/prednisone to cabazitaxel/prednisone and the opposite sequence, exploring molecular markers and mechanisms of taxane resistance in men with metastatic CRPC who have not received prior chemotherapy); CTC data analysis from Circulating Molecular Predictors of Chemotherapy and Novel Hormonal Therapy Benefit in mCRPC [c14-144]; molecular data analyses of tissue from A Phase II Trial of the Aurora Kinase A Inhibitor in Patients with mCRPC and NEPC [c12-105]

SOW Major Task 6: Open other Consortium sponsored Clinical Trials at WCMC

See above in Major Task 1 for details.

SOW Major Task 7: Clinical trial performance

See above in Major Task 1 for details.

SOW Major Task 8: Investigator analysis, reporting of initial data

Subtask 1. Verification of data

This milestone has been reached for c12-107 and c12-105 with data published (see below).

Subtask 2. Analysis of initial data

This milestone has been reached for c12-107 and c12-105 with data published. Correlative data

continues to be analyzed on c12-107.

Protocol c14-147 (Phase Ib/II Randomised Study of BI 836845 + Enzalutamide versus Enzalutamide alone in mCRPC) is closed to accrual and data analysis has been completed.

Subtask 3. Reporting of initial data

Over the past reporting period, Dr. Beltran presented data from c12-105 at the ESMO Annual Meeting, Munich Germany, October 2018 (Conteduca V, Oromendia C, Sigouros M, Sboner A, Nanus DM, Tagawa ST, Ballman K, Beltran H, Clinico-genomic profiling and outcome prediction of neuroendocrine prostate cancer).

SOW Major Task 9: Analysis and reporting of final data

c12-105: A manuscript describing this trial was published in *Clin Cancer Research.*
Beltran H, Oromendia C, Danila DC, Montgomery B, Hoimes C, Szmulewitz RZ, Vaishampayan U, Armstrong AJ, Stein M, Pinski J, Mosquera JM, Sailer V, Bareja R, Romanel A, Gumpeni N, Sboner A, Dardenne E, Puca L, Prandi D, Rubin MA, Scher HI, Rickman DS, Demichelis F, Nanus DM, Ballman KV, Tagawa ST. A phase II trial of the aurora kinase A inhibitor alisertib for patients with castration resistant and neuroendocrine prostate cancer: efficacy and biomarkers. Clin Cancer Res. 2018 Epub.

c12-107: A manuscript describing this study has been published in the *Journal of Clinical Oncology.*
Antonarakis ES, Tagawa ST, Galletti G, Worroll D, Ballman K, Vanhuyse M, Sonpavde G, North S, Albany C, Tsao C-K, Stewart J, Zaher A, Szatrowski T, Zhou W, Gjyrezi A, Tasaki S, Portella L, Bai Y, Lannin TB, Suri S, Gruber CN, Pratt ED, Kirby BJ, Eisenberger MA, Nanus DM, Saad F, Giannakakou P. A randomized non-comparative phase II trial of early switch from docetaxel to cabazitaxel or vice versa, with integrated biomarker analysis, in men with chemotherapy-naïve metastatic castration-resistant prostate cancer. J Clin Onc 2017;35:3181-3188.

A second manuscript describing a more detailed bio-marker analysis of samples from c12-107 was published in *Clinical Cancer Research*.
Tagawa ST, Antonarakis ES, Gjyrezi A, Galletti G, Kim S, Worroll D, Stewart J, Zaher A, Szatrowski TP, Ballman KV, Kita K, Tasaki S, Bai Y, Portella L, Kirby BJ, Saad F, Eisenberger MA, Nanus DM, Giannakakou P. Expression of AR-V7 and ARv567es in circulating tumor cells correlates with outcomes to taxane therapy in men with metastatic prostate cancer treated in TAXYNERGY. Clin Cancer Res. 2018, Epub.

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

Dr. Beltran led a multi-institutional clinical trial (PCCTC LOI# c12-105) as PI, communicating with other sites, and presented these trial results at the ESMO Annual Meeting. She also participates in PCCTC

group meetings and trials. She was recently appointed the GU correlative science committee chair for the Alliance cooperative group.

Dr. Beltran and Dr. Tagawa have presented during the PCCTC Investigator teleconferences for WCM.

Dr. Tagawa has presented at the annual ASCO meeting and attended the annual ESMO conference.

How were the results disseminated to communities of interest?

Press releases from WCMC have accompanied publications of our data.

The WCM GU Oncology Program informs professional and the public via digital and social media channels (Facebook page (facebook.com/WeillCornellGUCancer); Twitter handle (twitter.com/cornellGUcancer); and online website (weillcornell.org/gucancer) and blog (weillcornellgucancer.org).

On September 22, we held our inaugural New York City Prostate Cancer Summit at the New York Academy of Medicine together with colleagues from PCCTC member institutions MSKCC and CUMC. The Summit was designed specifically for prostate cancer patients and their families. With over 200 attendees, this educational and advocacy event was a great success, featuring panel discussions by local medical experts and national advocacy leaders, lectures on topics including nutrition and coping with prostate cancer, as well as resources and education sessions. Advocates and researchers from 5 other PCCTC sites outside of New York also attended. A short video summary of the Summit was shown at the PCCTC meeting help at the Prostate Cancer Foundation annual retreat in October 2018.

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

NA

4. IMPACT:

Nothing to Report

5. CHANGES/PROBLEMS:

Nothing to Report

6. PRODUCTS:

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Personnel	Role	Percent Effort
David Nanus	Principal Investigator	10%
Mark Rubin	Co-Investigator	3%
Scott Tagawa	Co-Investigator	3%
Himisha Beltran	Co-Investigator	3%
Jyothi Sreekumar	Clinical Research Coordinator	45%
Hoda Bashir	Research Nurse	45%
Aileen Lee	Data Coordinator	67%

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

David Nanus:

Dr. Nanus received the following new funding in the past year:

W81XWH-17-PCRP-CCA (Nanus)
Title: Prostate Cancer Clinical Consortium Clinical Research Site: Targeted Therapies
Effort: 1.44 calendar
Supporting Agency: Department of Defense
Grants Officer: Janet P. Kuhns, Contracting Officer, 301-619-2827, janet.p.kuhns.civ@mail.mil
Duration: 09/30/2018 – 09/29/2021
Direct Costs:
Project Goals/Aims: Our overall aim is to translate our PC expertise in targeted therapies, PC imaging, immunotherapy, and correlative science into novel therapeutic approaches that can be tested in multi-institutional studies performed within the PCCTC.

Dr. Nanus received the following projects end in the past year:

2014 Movember-PCF GTSC Award (Armstrong)
Title: Development of Circulating Molecular Predictors of Chemotherapy and Novel Hormonal Therapy Benefit in Men with Metastatic Castration Resistant Prostate Cancer (mCRPC)
Effort: 0.6 calendar
Supporting Agency: Prostate Cancer Foundation
Contact Person: Howard R. Soule, phone: 310-370-4598
Duration: 808/01/2014 – 07/31/2018 (NCE)
Direct Costs (current year):
Project Goals/Aims: This project aims 1. Assessment of a CRPC molecular taxonomy based on circulating tumor cell (CTC) molecular profiles in men prior to abiraterone acetate (AA) or enzalutamide therapy and, 2. To describe treatment-emergent CRPC genotypes during AA, enzalutamide, and taxane-based therapy using longitudinal CTC and circulating biomarkers.

Role: Co-Principal Investigator

Scott Tagawa:

Dr. Tagawa requested an additional no-cost extension on his DOD grant W81XWH-09-1-059, which is pending approval. The new end date for this project will be 8/16/19.

Dr. Tagawa received the following new funding in the past year:

W81XWH-17-PCRP-IA (Tagawa/ Beltran/ Bander)*
Title: *Molecular and clinical correlates with prostate-specific membrane antigen (PSMA)-targeted radionuclide therapy*
Supporting Agency: Department of Defense
Effort: 1.20 calendar
Grants Officer: Janet P. Kuhns, Phone: 301-619-2827, janet.p.kuhns.civ@mail.mil
Performance Period: 07/01/2018-06/30/2021
Level of Funding:
Project Goals/Aims: The goal of this project is to determine the best genomic, clinical, and imaging characteristics for successful PSMA-TRT and described immune response from PSMA-TRT. Specific Aims: 1. Prospectively and retrospectively assess genomic biomarkers and gene expression changes associated with outcome from anti-PSMA targeted radionuclide therapy. 2. Prospectively and retrospectively assess clinical parameters associated with outcome from anti-PSMA- TRT. 3. Prospectively and retrospectively assess PSMA expression as determined by PSMA molecular imaging associated with response to anti-PSMA -TRT. 4. Evaluate generation of an immune response following anti-PSMA-TRT in association with clinical outcome.
Role: Principal Investigator

PCF Challenge Award (Tagawa)
Title: Optimization of prostate-specific membrane antigen-targeted radiation
Time Commitment: 1.2 calendar
Supporting Agency: Prostate Cancer Foundation
Grants Officer: Howard R. Soule, Prostate Cancer Foundation; email: hsoule@pcf.org
Performance Period: 08/31/2017– 08/31/2019
Level of Funding:
Goals: To optimize the early-stage development of PSMA-targeted 177Lu, set the stage for continued development of PSMA-targeted alpha emitters, and initiate important correlative research into the potential immune effects of this approach (setting the stage for possible future combinations with immune checkpoint inhibitors). Aims: 1. To optimize dose and schedule of PSMA-targeted 177Lu, we will prospectively study the most commonly used PSMA small molecule and optimize therapy with dose-fractionation. 2. To prospectively and retrospectively assess the optimal patient population to receive 177Lu-radiolabeled PSMA agents. 3. To complete a phase I dose-escalation study of 225Ac-J591 with the primary endpoint of dose-limiting toxicity and MTD determination followed by expansion at the recommended phase 2 dose cohort to gain additional safety experience as well as preliminary efficacy data.
Role: Principal Investigator

R21 CA216800 (Giannakakou)
Title: Biomarkers of taxane chemotherapy response/resistance in prostate cancer
Effort: 0.24 calendar
Supporting Agency: National Cancer Institute
Grants Officer: Jaime L. Montes, National Cancer Institute, (240) 276-6288, montesj@mail.nih.gov
Duration: 4/1/2018 – 3/31/2020
Direct Costs:
Project Goals/Aims: The goal of this project is to determine the impact of AR-V and ERG expression on response/resistance to taxane chemotherapy and to identify additional clinically meaningful mechanism of taxane resistance by performing untargeted RNA sequencing of both pre-treatment and relapse CTC samples and correlate with clinical response and progression-free survival.
Aims: 1. Determine the impact of AR-V and ERG expression on response/resistance to taxane chemotherapy. 2. Identify additional clinically meaningful mechanisms of taxane resistance by performing untargeted RNA sequencing of both pre-treatment and relapse CTC samples and correlate with clinical response and progression-free survival.
Role: Co-Investigator

5R01CA207645 (Osborne)
Title: *A new technique to make 68GA-labeled pharmaceuticals widely available for clinical use.*
Supporting Agency: NIH/NCI
Effort: 0.30 calendar
Grant Officer:
Performance Period: 08/16/2018-06/30/2019
Level of Funding:
Project Goals/Aims: This proposal aims to establish a new technology for the production and distribution of a prostate cancer imaging agent based on the short-lived radioisotope Gallium-68. The new technology allows for the production of about 100 times larger quantities of Gallium-68 than existing techniques.
Role: Co-Investigator

W81XWH-17-PCRP-CCA (Nanus)
Title: Prostate Cancer Clinical Consortium Clinical Research Site: Targeted Therapies
Effort: 1.44 calendar
Supporting Agency: Department of Defense
Grants Officer: Janet P. Kuhns, Contracting Officer, 301-619-2827, janet.p.kuhns.civ@mail.mil
Performance Period: 09/30/2018 – 09/29/2021
Level of Funding:
Project Goals/Aims: Our overall aim is to translate our PC expertise in targeted therapies, PC imaging, immunotherapy, and correlative science into novel therapeutic approaches that can be tested in multi-institutional studies performed within the PCCTC.
Role: Co-Investigator

Dr. Tagawa had the following projects end in the past year:

WCMC SPORE Initiative (Tagawa/Bander/Vallabhajosula)

Title: PSMA-targeted alpha-radioimmunotherapy with 225Ac-J591
Time Commitment: 0 calendar
Supporting Agency: Weill Cornell Medicine Meyer Cancer Center
Contracting Officer: Kate Carbonell, Research Program Manager, WCM, 646-962-6165, kac2051@med.cornell.edu
Performance Period: 04/1/2017 – 03/31/2018
Level of Funding:
Project Goals/Aims: Aims: 1) to complete preclinical studies and obtain IND for 225Ac-J591 and 2) to initiate a phase I dose-escalation study of single-dose 225Ac-J591 in men with metastatic castration-resistant prostate cancer
Role: Co-Principal Investigator

2014 Movember-PCF GTSC Award (Armstrong)
Title: Development of Circulating Molecular Predictors of Chemotherapy and Novel Hormonal Therapy Benefit in Men with Metastatic Castration Resistant Prostate Cancer (mCRPC)
Time Commitment: 0.12 calendar
Supporting Agency: Prostate Cancer Foundation
Grants Officer: Howard R. Soule, Prostate Cancer Foundation; email: hsoule@pcf.org]
Performance Period: 08/01/2014 – 7/31/2018 (NCE)
Level of Funding:
Project Goals/Aims: This project aims 1. Assessment of a CRPC molecular taxonomy based on circulating tumor cell (CTC) molecular profiles in men prior to abiraterone acetate (AA) or enzalutamide therapy and, 2. To describe treatment-emergent CRPC genotypes during AA, enzalutamide, and taxane-based therapy using longitudinal CTC and circulating biomarkers.
Role: Co-Investigator

Mark Rubin:

Dr. Rubin did not receive new funding in the past year.

Dr. Rubin did not have projects that ended in the past year:

Himisha Beltran:

Dr. Beltran has moved to a full time faculty position at Dana Farber Cancer Institute (DFCI) as of 10/1/18. All funding will be transferred to DFCI and she will maintain adjunct status at Weill Cornell Medicine in New York.

Dr. Beltran requested and received approval for a no-cost extension on 2016 PCF Challenge Award with title, "Development and qualification of the PCF SELECT (Specific Evaluation in Liquid biopsies of Established prostate Cancer Targets) plasma DNA assay. New end date for funding will be 8/22/19. She also requested and was approved for NCE request on 2014 PCF Challenge award with title, "Early Detection of Neuroendocrine Prostate Cancer Transformation Using Circulating Genomic Signatures." New end date for this project will be 12/24/19.

Dr. Beltran received the following new funding in the past year:

W81XWH-17-PCRP-IA (Tagawa/ Beltran/ Bander)
Molecular and clinical correlates with prostate-specific membrane antigen (PSMA)-targeted radionuclide therapy
Supporting Agency: U.S. Department of Defense
Time Commitment: 0.36 calendar
Grants Officer: Janet P. Kuhns, Phone: 301-619-2827, janet.p.kuhns.civ@mail.mil
Performance Period: 07/01/2018-06/30/2021
Level of Funding:
The goal of this project is to determine the best genomic, clinical, and imaging characteristics for successful PSMA-TRT and described immune response from PSMA-TRT. Specific Aims: 1. Prospectively and retrospectively assess genomic biomarkers and gene expression changes associated with outcome from anti-PSMA targeted radionuclide therapy. 2. Prospectively and retrospectively assess clinical parameters associated with outcome from anti-PSMA- TRT. 3. Prospectively and retrospectively assess PSMA expression as determined by PSMA molecular imaging associated with response to anti-PSMA -TRT. 4. Evaluate generation of an immune response following anti-PSMA-TRT in association with clinical outcome.
Role: Principal Investigator

2017 PCF Challenge Award (PIs: Zoubeidi / Beltran)
Targeting BRN2 in Neuroendocrine Prostate Cancer
Time Commitment: 0.48 calendar
Supporting Agency: Prostate Cancer Foundation
Grants Officer: Howard Soule; phone: 310-570-4596
Performance Period: 12/31/2017– 12/31/2019
Level of Funding:
Goals/Aims: To assess if BRN2 inhibitors should be deployed alone or in combination with current standard-of-care to block the emergence and/or progression of NEPC.
Role: Principal Investigator

W81XWH-17-PCRP-CCA (PI: Nanus)*
Prostate Cancer Clinical Consortium Clinical Research Site: Targeted Therapies
Time Commitment: 0.60 calendar
Department of Defense: Prostate Cancer Research Program
Contracting Officer: Janet P. Kuhns, Contracting Officer, 301-619-2827, janet.p.kuhns.civ@mail.mil
Performance Period: 09/30/2018-09/29/2021
Level of Funding:
Project Goals/Aims: Our overall aim is to translate our PC expertise in targeted therapies, PC imaging, immunotherapy, and correlative science into novel therapeutic approaches that can be tested in multi-institutional studies performed within the PCCTC.
Role: Co-Investigator

Dr. Beltran had the following projects end in the past year:

DOD Physician Research Training Award (W81XWH-13-1-0275) (PI: Beltran)
A Changing Landscape of Advanced Prostate Cancer: Understanding Mechanisms of Resistance to Potent Hormonal Therapies
1.20 calendar
Department of Defense
Grant Officer: Janet P. Kuhns, Contracting Officer, 301-619-2827, e-mail: janet.p.kuhns.civ@mail.mil
Performance Period: 09/30/2013-09/29/2018 (NCE)
Level of Funding:
The goal of this study is to evaluate mechanisms of prostate cancer resistance to abiraterone by sequencing the genes of resistant tumors from patients and evaluating for biologic pathways that are altered.
Role: Principal Investigator

CTSC Precision Medicine Award (PI: Margolis)
Correlation of Molecular Expression with MRI Features
0.36 calendar
Weill Cornell Medicine CTSC, funded by NIH UL1 TR002384 (National Center for Advancing Translational Sciences)
Grant Officer: Juan Cordero, Weill Cornell Medicine, 646-962-8308, ctsc_pilot@med.cornell.edu
Performance Period: 07/01/2017-05/31/2018
Level of Funding:
Goals/Aims: Identify cases of prostate cancer visible and invisible on MRI and correlate with markers of molecular expression ("precision medicine") compared with the "ground truth" of surgical specimen histopathology. Investigate which molecular factors correlate with lesions being visible on mpMRI, whether these are also known markers of poor prognosis, and which correlate with adverse pathology on the surgical specimen.
Role: Co-Investigator

Alliance Scholar Award (PI: Beltran)
Impact of therapy on modulation of neuroendocrine-associated gene expression in patients with high risk, localized prostate cancer treated with neoadjuvant docetaxel and androgen deprivation therapy
0.36 calendar
Alliance for Clinical Trials in Oncology Foundation
Grants Officer: Denise Collins Brennan, Brigham and Women's Hospital, Boston, MA
Performance Period: 01/01/2015-12/31/2017
Level of Funding:
Project Goals/Aims: To assess the impact of neoadjuvant docetaxel and androgen deprivation therapy on modulation of gene expression of a panel of neuroendocrine prostate cancer (NEPC) pathway signature genes in high risk clinically localized prostate cancer patients treated on the Phase 3 CALGB 90203 PUNCH clinical trial.
Role: Principal Investigator

What other organizations were involved as partners?

This grant is for the PCCTC consortium, which is a collaboration between all consortium sites.

8. SPECIAL REPORTING REQUIREMENTS:

None

9. APPENDICES:

Copies of manuscripts (see Major Task 9).