AWARD NUMBER: W81XWH-14-2-0185

TITLE: Prostate Cancer Biorepository Network

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REPORT DATE: DECEMBER 2019

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; distribution is unlimited.

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
DECEMBER 2019	Final	30SEP2014 - 29SEP2019

4. TITLE AND SUBTITLE

Prostate Cancer Biorepository Network

5a. CONTRACT NUMBER
W81XWH-14-2-0185

5b. GRANT NUMBER
PC131930P2

5c. PROGRAM ELEMENT NUMBER

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

New York University School
of Medicine
550 First Avenue
New York, NY 10016

8. PERFORMING ORGANIZATION REPORT NUMBER

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 goal of this proposal is to contribute as a network site to the continued development of infrastructure and operations of the Prostate Cancer Biorepository Network (PCBN). The aim of the PCBN is to provide prostate researchers with high-quality, well-annotated biospecimens obtained in a systematic, reproducible fashion using optimized and standardized protocols. The PCBN is funded as a consortium of participating network sites that includes New York University, under the overall guidance of the coordinating center at Johns Hopkins. The NYU network site works collaboratively to contribute to the PCBN goals, through infrastructure development, biospecimen accrual and biospecimen specialized processing and disbursement to investigators. The NYU network site procures specimens from more than 3 facilities, from primary localized as well as metastatic and disproportionately affected prostate cancer patients and stores them to provide for high quality biospecimens. Additionally, clinical data including pathology and outcome data are annotated with the biospecimens. Specialized processing consists of tissue microarray design and construction. Biospecimens (mainly tissue microarrays) are disbursed to investigators approved through the PCBN. The combined effort of the network site enables the PCBN consortium to successfully provide much sought after biospecimens for prostate cancer research.

15. SUBJECT TERMS
Prostate Cancer, Biorepository, tissue microarrays, tissue bank

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	11	19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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1. INTRODUCTION:

The goal of this proposal is to contribute to the continued development of infrastructure and operations of the Prostate Cancer Biorepository Network (PCBN). A prostate cancer biorepository fulfills an important need to enable prostate cancer research to be conducted by the wider research community through making readily available clinical biospecimens. Only few academic centers with high volume prostate cancer clinical services and an already developed banking infrastructure are well positioned to enable biospecimen collection. An external funding source as provided by the DOD enables support for the consortium of institutional biorepositories of the PCBN to provide to the wider research community. The major goal of the PCBN is to develop a biorepository with high-quality, well-annotated biospecimens obtained in a systematic, reproducible fashion using optimized and standardized protocols. The PCBN is funded as a consortium of participating network sites that include: New York University, Johns Hopkins, University of Washington and Memorial Sloan Kettering, under the overall guidance of the coordinating center at Johns Hopkins. The goal of the NYU network site is to collaboratively contribute toward the PCBN goals, through participation in infrastructure development, biospecimen accrual and derivative product development for the purpose of disbursement to investigators to enhance prostate cancer research. The several years' effort toward these goals are detailed herein.

2. KEYWORDS:

Prostate cancer, biorepository, biomarkers, tissue microarrays, tissue bank, rapid autopsy, advanced cancer, ethnicity

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Task 1. Review of sources of patients and biospecimens at site that can be made available to the repository (Month 1): Completed in 1st quarter (October 2014)
Task 2. Data elements used to annotate demographic, clinical, pathology, and biospecimen life cycle will be provided to the Coordinating Center, and Network Site will participate in in the process of defining and harmonizing common data elements (CDEs): Completed in 1st quarter (October 2014)
Task 3. Submit SOPs to Coordinating Center (Month 1): Completed in 1st quarter (October 2014)
Task 4. Participate in development of draft SOPs, common consent formats, and MTA (Months 1- 6): Completed in 1st quarter
Task 5. Report on performance metrics: Ongoing (accrual reports are provided on quarterly basis)
Task 6. Continue offering existing biospecimens to the research community (Months 6-36): Ongoing – we continue to offer biospecimens at increasing demand to the research community (with substantial increase in application volume).
Task 7. Participate in SOP training (Month 9): New staff were trained in SOPs in first and second quarter (100%)
Task 8. Annotate, perform quality control for processing, storage & clinical data collection, and distribute specimens (Months 10-36): Quality control steps for data collection are performed ongoing basis. Specimens continue to be distributed.
Task 9. Report on performance metrics (Months 12, 18, 24, 30, 36): Month 24- 36 including quarter 32-36 reported herein (prior quarterly reports until month 32 previously submitted)

What was accomplished under these goals?

MAJOR GOALS:

The major activities of the NYU network site are detailed under the following areas

A) Regulatory approval
B) Biospecimen accrual
C) Specimen characterization and data annotation
D) Specialized processing of biospecimens
E) Biospecimen disbursement

A. Regulatory Approval:

NYU Langone Health

Regulatory approval: The NYU site includes several hospital facilities, each of which requires its own approval for conduct of activities. NYU has access to three hospitals: NYU Langone Medical Center, Bellevue (an HHC hospital) and the New York Harbor VA hospital and actively case recruitment is performed at all site, each with its own regulatory oversight. The NYU PCBN maintains compliance with IRB issues at NYU Langone Medical center and Bellevue Hospital in accordance with the NYU IRB.

Manhattan & Brooklyn VA

The NYU PCBN maintains compliance with IRB issues at the Manhattan and Brooklyn VA Hospitals in accordance with the New York Harbor VA IRB.

NY State

NYU PCBN renewed its official tissue bank license with the NY State Department of Health through September 1, 2020.

Other collaborating sites

The NYU PCBN obtained IRB approval from the Biomedical Research Alliance of New York (BRANY) to add other sites as collaborating institutions (for access to archival material): NYC H+H Hospitals, (Coney Island Hospital, Elmhurst Hospital, Harlem Hospital, Jacobi Medical Center, Kings County Hospital, Lincoln Medical and Mental Health Center, Metropolitan Hospital Center

B. Biospecimen Accrual

The biospecimen procurement is a streamlined process at all three hospitals; with accrual volume reliant on several factors including clinical patient volume, treatment trends (specifically radical prostatectomy versus active surveillance) and subject recruitment. While the surgical specimen accrual is good and reaches expected metrics we continue to strive to enhance recruitment for different cohorts and facilities and reach out for greater efficiencies in the process.

These efforts include implementation of a) systems for regular communication and alerts from Urology and Oncology of potential patients for recruitment (daily monitoring of patient schedules at three hospitals; frequent email communications with providers) b) tiered consents which allow patients to determine their individual choice as to level of participation c) consents translated into Chinese and Spanish in recognition of diverse patient backgrounds and home language. All these steps enable greater recruitment of potential subjects and foster trust that improves willingness for participation. The NYU PCBN also conducts educational seminars with oncology and urology providers to promote awareness and encourage assistance with recruitment of subjects. An important influence on tissue accrual is of course of radical prostatectomy volume at each hospital. Even though there is a trend (nationwide) for decrease in radical prostatectomy

volume, the NYU Langone Urology Department continues to attract more patient interest and has managed to increase its volume of surgical cases over the last year. In conjunction with this, The NYU PCBN is able to accrue a high percentage of potential cases.

Over 2017 and 2018, NYU PCBN has increased our efforts to accrue active surveillance subjects, subjects treated by non-surgical means on clinical trials (HIFU treatment), as well as metastatic and rapid autopsy candidates. To enhance the rapid autopsy program, modifications were made to the consent form allowing the patient to provide permission for PCBN staff to contact their next of kin. In addition, the PCBN distributes an approved newsletter and links to its lab website to increase patient awareness.

Additionally in 2018, we were able to complete 2 rapid autopsy procurements. This involved follow up of the patients from date of consent and outreach to their families. Through our contact with the family, including in-person meetings, we were able to develop a rapport. We were in frequent contact with the patient's healthcare team from oncology to palliative care and eventually hospice.

In 2018, we increased our enrollment of patients from the Brooklyn site of the VA. Many VA patients often attend both the Manhattan and Brooklyn sites. However, now that the radiation oncology department of the Brooklyn VA has become the primary site of all radiation treatments, many high-risk and recurrent patients get all care at the Brooklyn VA. As a result, we now go onsite to the Brooklyn VA to consent patients. This has increased our enrollment of African-American patients, metastatic patients, and other patient with high-risk categorization.

Table 1.

NYU PCBN Accrual	2015	2016	2017	2018	Total Accrual
Patients Consented	218	264	259	215	956
Frozen Tissue	165	168	160	133	626
Serum	172	298	236	366	1072
Plasma	15	90	63	354	522
Buffy Coat	15	10	6	354	385
Urine	92	153	104	56	405
Prostatic Fluid	119	154	135	128	536
Seminal Vesicle Fluid	86	121	111	115	433
Rapid Autopsy Performed	0	0	0	2	2

C. Specimen Characterization and Data annotation

In 2016, due to the limitations of the NYU PCBN database system, alternative relational database systems were investigated. The NYU PCBN initial positive experience with REDCAP suggested that it would satisfy many of the site's data needs and still be useful as a collaborative tool beyond NYU through open REDCAP.

Some advantages of REDCAP are: a) Allows secure and HIPAA compliant sharing of data by seamlessly removing identifiers b) Provides more security and quality assurance checks than current system offers c) Allows multiple individuals of our team to work on the database at the same time

By June 2016, design of a NYU PCBN REDCAP database was completed. This consisted of implementation of data quality assurance steps, logic checks and algorithms and design of surveys that provide functionality to the database ahead of migration of the data into the new system.

In August 2018, REDCap released a new edition version (8.0). With this update, NYUPCBN improved and upgraded its current design. The format of data collection and organization was streamlined. By streamlining and allowing all informational tabs to be viewed concurrently, it has allowed for easier understanding of a patient's chart for follow-up data compilation and entry. A separation of patients into cohorts based on their clinical cancer category, has allowed logical segregation of early cancer (active surveillance) from advanced cancer/high-risk patient groups

The NYU PCBN staff perform regular updates of clinical data through data extraction and searches of electronic medical records (EPIC, Quadramed and CPRS), Pathology databases (Powerpath & CoPath), Urology research databases and tumor registry records. Clinical data update is performed on an ongoing basis, with quality control checks (relook at a subset of cases) to assure accuracy. Additionally, tissue microarray cohort data are also updated on a regular basis (6 monthly for biochemical recurrence TMA).

NYU PCBN has implemented a spatial characterization of prostate cancer in surgical specimen through annotation of prostate on "maps" which allow 2 dimensional representations and characterization of focality (advantage in preparation for multifocal or MRI occult TMA design/construction).

D. Specialized processing (Derivatives of biospecimens)

Tissue Microarrays (TMAs): The NYU site contributes several TMA sets to PCBN that are regularly requested by investigators. During the entire duration of the project, relevant clinical data associated with PCBN TMAs has been updated quarterly. Additionally, new TMA sets have been designed/constructed and are included in the PCBN menu of TMAs available to investigators.

135 Case Grade/Stage Radical Prostatectomy: For testing biomarkers expression in non-indolent prostate cancer. Includes Gleason 7 and higher, of varying stage. 135 cases and matched normal – 2 cores each, with key clinical variables across 3 blocks.

Biochemical Recurrence (BCR) \TMA: The current TMA that NYU provides to PCBN investigators is a 217 case BCR TMA that enables assessment of biomarkers strongly associated with known prognostic factors (e.g. stage, grade). It includes patients with versus without biochemical recurrence, to a total of 217 cases, 23 with adjacent normal (4-5 tumor cores, 4 normal cores) and 13 BPH cases (4 cores). Since this TMA is frequently requested, NYU PCBN focused effort on construction of an expanded cohort BCR TMA. This is complete – providing a 645 case biochemical recurrence TMA (over 12 TMA Blocks, 4 cores for each case). The associated clinical data for this cohort has recently been aggregated and updated: 9% with biochemical recurrence, mean age = 59 years, 75% > 5year PSA follow-up, mean follow-up duration = 135 months.

Hormone Sensitivity TMA: The NYU site provides a 56 case Hormone sensitivity TMA, which enables testing of biomarkers associated with androgen biology. It includes hormone naive versus hormone refractory cases totaling 56 cases; 18 hormone resistant, 18 hormone naïve, 10 radical prostatectomy (RP) cases with neo adjuvant treatment, 10 RP without neo adjuvant treatment. Due to the rarity of castration resistant prostate cancer tissue samples, this TMA required searching across the entire archive of 3 major hospital sites for candidate cases. NYU PCBN continues to seek more partners with archival resources to enable identify more cases and is working to expand this TMA. Additional cases have been identified and the TMA awaits construction.

HGPIN TMA: NYU PCBN has a current TMA however is preparing for expansion of this TMA cohort through an additional TMA. The challenges to this TMA are finding sufficiently large microscopic foci to allow accurate sampling into a TMA. The detailed work at identifying these tiny foci on slide sand then matching to blocks is underway

Autopsy/Metastatic TMA: Recently, all tissue from rapid autopsies has been reviewed and blocks selected. Map design is currently underway and the TMA construction. Update (2019): TMA constructed including 5 cases with representation from up to 7 metastatic sites, including prostate in some of the cases.

E. Disbursement of Biospecimens

Year 1 Disbursement:
217 case Biochemical recurrence TMA (1 set) to investigator at Georgetown University
217 case Biochemical recurrence TMA (1 set) to investigator at University of Illinois
114 Race Disparity TMA (3 sets) to investigator at Johns Hopkins University
Biochemical recurrence TMA (1 set) to an investigator at University of Pittsburgh
High grade PIN TMA (1 set) to an investigator at Johns Hopkins University

Year 2 Disbursement:
56 case Hormone Sensitivity TMA (3 sets) to investigator at Johns Hopkins University
56 case Hormone Sensitivity TMA (3 sets) to investigator at The Chinese University of Hong-Kong
Metastatic Frozen Tissue Samples (5 samples) to investigator at New York VA Medical Center
56 case Hormone Sensitivity TMA (3 sets) to investigator at University of Wisconsin
217 case Biochemical recurrence TMA (2 sets) to investigator at New York University
217 case Biochemical recurrence TMA (1 set) to investigator at New York University

Year 3 Disbursement:
56 case Hormone Sensitivity TMA (2 sets) to investigator at New York VA Medical Center
56 case Hormone Sensitivity TMA (2 sets) to investigator at University of Pittsburgh
High grade PIN TMA (2 sets) to investigator at New York VA Medical Center
56 case Hormone Sensitivity TMA (3 sets) to investigator at University of Iowa
High grade PIN TMA (2 sets) to investigator at New York University
56 case Hormone Sensitivity TMA (1 set) to investigator at University of Iowa

Year 4 Disbursement:
56 case Hormone Sensitivity TMA to an investigator to Northwestern University
135 Case Grade/Stage Radical Prostatectomy TMA to an investigator at University of Rochester
217 Biochemical Recurrence TMA to an investigator at University of Rochester
114 Race TMA to an investigator at University of Minnesota
217 Biochemical Recurrence TMA to an investigator at University of Minnesota
56 case Hormone Sensitivity TMA (2 sets) to an investigator at University of Minnesota

Disbursement of biospecimens is primarily of tissue microarray sets. In order to make these more useful to investigators NYU PCBN has prepared "product datasheets", which in addition to outlining the design, layout, construction, quality assurance steps and control tissues of the tissue microarrays, also provides a smart score sheet to enable easier pairing of cells in score sheet to data . These datasheets are available for the biochemical recurrence and hormone sensitivity TMAs.

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

- Several of the staff trained in database design and implementation skills for REDCAP
- Emily Dube, research coordinator is studying part-time to complete a Master's degree in Biomedical Informatics through the NYU School of Medicine. Update: graduated September 2019.

How were the results disseminated to communities of interest?
Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?
Nothing to Report

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?
Nothing to Report

What was the impact on other disciplines?
Nothing to Report

What was the impact on technology transfer?
Nothing to Report

What was the impact on society beyond science and technology?
Nothing to Report

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Due to the initial low activity in the rapid autopsy program, our group sought to identify expanded recruitment opportunities to identify and recruit patients with metastatic prostate cancer and their next of kin to allow end of life consent for autopsy. This entailed more frequent contact and communication with next of kin to maintain interest and sense of contribution to the program. This paid dividends in that we completed 2 cases within a 3-month period (albeit with a 2-3 year "gestation" period from recruitment to autopsy). We have sought to advance our data capture methods and data system (migration to REDCAP) in concert with expansion of institutional bioinformatics resources.

Actual or anticipated problems or delays and actions

At the Manhattan VA campus influx of new patient cases dropped over the course of the year. On average, new case volume dropped to 3-4 new adenocarcinoma cases per month, with many being referred for radiation treatment at the Brooklyn VA campus. To combat this problem, NYU PCBN provided personnel at the Brooklyn VA oncology clinic to enable recruitment.

Changes that had a significant impact on expenditures
Nothing to Report

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

6. PRODUCTS:

Publications, conference papers, and presentations

Fang-Ming Deng, Nicholas M. Donin, Ruth Pe Benito, Jonathan Melamed, Julien Le Nobin, Ming Zhou, Sisi Ma, Jinhua Wang, Herbert Lepor, Size-adjusted Quantitative Gleason Score as a Predictor of Biochemical Recurrence after Radical Prostatectomy, European Urology, Volume 70, Issue 2, August 2016, Pages 248-253

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Guedes, L. B., Morais, C. L., Fedor, H., Hicks, J., Gurel, B., Melamed, J., . . . Lotan, T. L. (2018). Effect of Preanalytic Variables on an Automated PTEN Immunohistochemistry Assay for Prostate Cancer. Archives of Pathology & Laboratory Medicine. doi:10.5858/arpa.2018-0068-oa

Lee, J. K., Bangayan, N. J., Chai, T., Smith, B. A., Pariva, T. E., Yun, S., . . . Witte, O. N. (2018). Systemic surfaceome profiling identifies target antigens for immune-based therapy in subtypes of advanced prostate cancer. Proceedings of the National Academy of Sciences, 115(19). doi:10.1073/pnas.1802354115

Williams, K. A., Lee, M., Winter, J. M., Gildea, D. E., Calagua, C., Curry, N. L., . . . Crawford, N. P. (2018). Prostate cancer susceptibility gene HIST1H1A is a modulator of androgen receptor signaling and epithelial to mesenchymal transition. Oncotarget, 9(47). doi:10.18632/oncotarget.25536

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

Other publications, conference papers, and presentation
Nothing to Report

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

Technologies or techniques
Nothing to Report

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

Other products
Research material: Biospecimen accrual – see table 1

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
No change

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
Nothing to Report

What other organizations were involved as partners?
Nothing to Report