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TITLE: Prostate Cancer Biorepository Network (PCBN)

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5f. WORK UNIT NUMBER

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

NYU School of Medicine
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New York, NY 10016

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

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 fulfils 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. A main focus of the PCBN is to accrue biospecimens that are in "limited supply" and documented to be most needed by the prostate cancer community (e.g. castration-resistant disease, metastatic disease, primary untreated "de novo" metastatic disease, high-risk disease, tumors of the aggressive variant phenotype, disproportionately affected populations). The PCBN is funded as a consortium of participating network sites that include: New York University, University of Washington, Washington University, Institute of Cancer Research (United Kingdom) and overall guidance of the coordinating center at Johns Hopkins University. 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.

15. SUBJECT TERMS
Prostate Cancer, Biorepository, tissue microarrays, tissue bank, advanced cancer, ethnicity

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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 fulfils 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. A main focus of the PCBN is to accrue biospecimens that are in "limited supply" and documented to be most needed by the prostate cancer community (e.g. castration-resistant disease, metastatic disease, primary untreated "de novo" metastatic disease, high-risk disease, tumors of the aggressive variant phenotype, disproportionately affected populations). The PCBN is funded as a consortium of participating network sites that include: New York University, University of Washington, Washington University, Institute of Cancer Research (United Kingdom) and overall guidance of the coordinating center at Johns Hopkins University. 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.

2. KEYWORDS:

Prostate cancer, biorepository, biomarkers, tissue microarrays, tissue bank, rapid autopsy, advanced cancer, ethnicity, Covid-19

3. ACCOMPLISHMENTS:

a. What were the major goals of the project?

Major Goals	Timeline	% Complete
Specific Aim 1: Collect, process, and store biospecimens annotated with clinical and pathology data from well-characterized populations of patients.		
Task 1: Obtain HRPO and IRB approvals (will apply primarily to ICR Network Site, other sites have these in place for ongoing Network activities).	1-36	100%
Task 2: Each pathology resource site contributes prospectively collected biospecimens from a minimum of 50 patients per year with the expectation that biospecimen contribution will exceed the minimum requirement. A minimum of 50% of the samples collected across the entire Network will be those in limited supply and documented to be the most needed by the prostate cancer research community, as determined by the required annual survey	1-36	66.6%
Task 3: Annotate, perform quality control for processing, storage and clinical data collection for prospective specimen accrual	1-36	66.6%
Task 4: Report on performance metrics	Semi-annually	66.6%
Specific Aim 2: Maintain an informatics infrastructure for secure data storage and transfer, and a web-accessible portal for users to learn about and access specimens from the PCBN.		
Task 1: Data elements used to annotate demographic, clinical, pathology, and biospecimen life cycle provided to the Coordinating Center, and the Network Site participates in the process of defining and harmonizing a set of common data elements (CDEs).	1-6	100%
Specific Aim 3: Develop harmonized SOPs for biospecimen acquisition, processing, storage and quality control to increase the fidelity of biospecimens provided to investigators.		
Task 1: This encompasses the initial work required to develop standard operating procedures (SOPs) incorporated into the PCBN infrastructure. These SOPs govern how the prospective collection during this award at each Network Site is annotated, undergoes quality control, storage and is made available for distribution to investigators. The harmonization of SOPs is an ongoing PCBN effort.	1-6	100%
Task 2: Finalize SOPs for all 5 Network operations in Task 1	6-9	100%
Task 3: Review (annual) of Network operation, use of SOPs, composition of repository	12,24,36	66.6%
Specific Aim 4: Distribute biospecimens according to a prioritization plan to ensure maximal use by the prostate cancer community.		
Task 1: Continue offering biospecimens from all Network Sites to the research community using prioritization plan outlined in Tissue and Data Access Policy that is already developed and available to all investigators/detailed and posted online on our website	1-36	66.6%
Task 2: Review specimen requests, distribute specimens to approved scientists.	1-36	66.6%
Task 3: Review of sources of patients and biospecimens at each site that can be made available to the repository. Discussion every six months on what derivatives might be useful to the group. New TMAs, RNA, DNA, new methods to collect cfDNA etc.	Annual Review. discuss 6 monthly	66.6%

b. What was accomplished under these goals?

Regulatory Approval: NYU site is subject to regulatory approval by NYU IRB, VA IRB, Bellevue IRB, BRANY IRB for NYC Health & Hospitals facilities (H&H), and New York State Dept. of Health. These are all active and up to date.

NYU / Bellevue		
HRPO Log Number: E00073.1a		
NYU IRB Number: 8723		
Submission	**Submission**	**Approval**
NYU Continuing Review	2/6/20	2/7/20
HRPO Continuing Review	2/12/20	2/18/20
NYU/ BH Modification: Addition of Remote Consenting	5/28/20	6/11/20

NY Harbor VA Hospitals		
HRPO Log Number: E00073.1b		
VA IRB Number: 00036		
Submission	**Submission**	**Approval**
VA Continuing Review	6/20/20	7/17/20
HRPO Continuing Review	7/20/20	8/13/20
VA Project Modification: Addition of Remote Consenting	7/6/20	9/21/20

BRANY IRB: approved 7/17/2017 (retrospective study, exempt from continuing review)
New York State DOH: submitted 7/27/20

Regulatory work was performed to update IRB protocols and to submit modifications to enable remote consenting at NYU and the NY Harbor VA.

Accrual

Limited Supply Accrual

1) Concerted efforts have continued toward accrual of "limited supply" samples via outreach to additional facilities for recruitment of cases. The challenges posed by the COVID pandemic and disease mitigation restrictions (lockdowns and imposition of electronic only consent) however has decreased the volume of clinical activities, removed opportunity for direct access to patients for recruitment and therefore markedly decreased biospecimen accrual. After the easing of lockdown, there was some (albeit decreased) biorepository accrual. Now as vaccines are rolled out, we anticipate return to usual recruitment process and accrual when restrictions are eased. To compensate for the decreased prospective accrual, we have worked to identify cohorts from archival materials and at data annotation for the entire derivative products (Tissue Microarrays construction). These include castrate resistant and metastatic prostate cancer cases as well as African American cases.

Routine Biospecimen Accrual:

Biospecimen Accrual: Oct 1 2019 – Sept 30 2020	
Samples Collected	**Total Collected**
Tissue	
Radical Prostatectomy	55
Fluids	
Prostatic fluid	30
Seminal Vesicle fluid	22
Urine	31
Blood Samples	96 - *Serum (17), Plasma (40), Buffy Coat (39)*
TOTAL	**234**

Clinical Annotation Data

During this period (due to Covid19 restrictions and laboratory lockdown), the group has embarked on a comprehensive clinical data review and update of clinical outcome and annotation for more than 2000 cases in the biorepository database. In addition robust quality checks on the data have been performed and implemented to resolve inconsistencies, input missing information, and update clinical data.

Database & Clinical data	4/1/20 - 6/30/20		7/1/20 - 10/31/20		
REDCaP Database Enhancements	Consent forms added (scanned image) + tiered consent status	Quality assurance steps: Reports; Created Data dictionary for standardized data entry;	Added 3 data instruments: 1) MRI prostate results 2) Targeted biopsy fields (in Biopsy) 3) Prostate MAPs: diagrams of cancer distribution in RP 4) Molecular annotation (in progress)	Reports: PSA > 0.2 with follow-up status "nil relapse", Active surveillance cohort	Enzalumatide, Abiraterone cohort; High risk CAPRA; cryoablation --- New fields for outcome: low detectable PSA, Adjuvant exclusion, Salvage Therapy
Clinical Data	EPIC everywhere linkage CAPRA-S completed FFPE block inventory	Data retrieval and entry from previous database (excel)	Update of 1513 + 503 cases- length of follow-up, outcome status; 287 cases -new records added Post RP Therapy fields: Radiation (40%), hormonal (50%) chemo (7%)	Change in outcome status: 68 (of 2016) =2.3%;	PSAs added, including length of follow-up: Mean follow-up for 4321 cases = 6 years (max = 28 years)

Derivatives

The NYU PCBN laboratory performed an in-depth review of cases in the 125 Case Hormone Sensitivity TMA, (tumor samples from primary prostate cancer derived from transurethral resections of the prostate (TURP). to provide measures of treatment response and castration resistance.
Clinical outcome was updated for the 217 Case Biochemical Recurrence TMA, 114 Race Case TMA, 56 Hormone Sensitivity TMA. A new TMA for Biochemical Recurrence that includes 650 Cases set over 12 blocks (650 BCR TMA)

Products Created

NYU Hormone Sensitivity TMA composed of two blocks, consisting of 125 cases was released on the PCBN website for PCBN applications. New updated product datasheets were prepared for this and other NYU PCBN TMAs,

Products Requested and Fulfilled

Product	Amount	Investigator Site	Completed
125 Hormone Sensitivity TMA	2 sets	Henry Ford Health System	Sent 6/18/2020
217 Biochemical Recurrence TMA	1 set	Cold Spring Harbor Laboratories	Sent 6/18/2020
125 Hormone Sensitivity TMA	1 set	Washington State University	Sent 6/18/20
125 Hormone Sensitivity TMA	2 sets	University of Nebraska Medical Center	Sent 10/6/20
217 Biochemical Recurrence TMA	2 sets	University of California – Davis	Pending
125 Case Hormone Sensitivity TMA	2 sets	University of Newcastle	1/13/20
217 Biochemical Recurrence TMA	4 sets	Cold Spring Harbor Laboratories	10/1/19

c. What opportunities for training and professional development has the project provided?
Nothing to report

d. How were the results disseminated to communities of interest?
Nothing to report

e. What do you plan to do during the next reporting period to accomplish the goals?
(1) Construct block 2 of pN1 TMA (2) Release block 1 pN1 TMA (3) Construct HGPIN TMA to include AA cases for race comparison (4) After data QA is completed, release new 650 BCR TMA to replace 217 BCR TMA (5) Construct pre/post treatment TURP TMA (3) Expand access to NYU Long Island (Winthrop) via regulatory and facility approval

4. IMPACT:

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

b. What was the impact on other disciplines?
Nothing to report

c. What was the impact on technology transfer?
Nothing to report

d. What was the impact on society beyond science and technology?
Nothing to report

5. CHANGES/PROBLEMS:

a. Actual or anticipated problems or delays and actions or plans to resolve them
Due to Covid-19 impact on the USA and New York City in particular, there was a long duration (> 3 months) where elective surgery was stopped and no research activities permitted on site, which resulted in lower case accrual. Biorepository efforts were focused on activities that could be performed off-site including updating clinical data from EPIC and other HIS systems, expanding the biorepository database, regulatory assurance measures (adding scanned consent forms to database) and identification of additional cases from archival files. The process of clinical data annotation led to a significant change in extent of clinical follow-up. During this period we also implemented robust quality assurance interventions to identify and resolve missing data and correct data inconsistencies. Development measures were worked upon for expansion of extent of annotation of the database, specifically instituting sections and common data elements for molecular annotation, prostate MRI findings, and radical prostatectomy cancer distribution "maps"). Plans for additional TMA construction were pursued toward HGPIN and Nodal metastasis (pN1) TMA, with plans to begin construction once constraints for on-site work are lifted.
The NYU Biorepository worked according to institutional guidance toward a remote consenting process to recruit patients. In Mid June, regulatory approval was obtained for an electronic consent strategy for remote recruitment of patients. While this provided for some recruitment and prospective biospecimen accrual, the remote interaction has proven to be only occasionally successful in patient recruitment (called 197 patients [3 separate calls + emails], of these 53 agreed to receive email consents, 26 of whom opened the consent but did not progress further while 27 (13%) ultimately completed the consent and agreed to participate). Additionally, as presurgical testing of patient is not performed on site but rather through outside laboratories, accrual of presurgical biospecimens has also been impacted resulting in fewer biospecimens per patient. We have worked with Urology staff (Urologists and Nurse practitioners) to communicate to patients about the biorepository to enable greater success in recruitment, and continue to identify measures that may be used to improve communication and increase patient willingness to participate (different times of days were tried - found 12-1 pm and 4-5 pm as best times to reach patient and not voicemail). We expect accrual to continue to improve through different communication strategies, however ultimately will require the end of the pandemic to resume to usual procedures and prior accrual volume. Now with the rollout of mass vaccination, we are optimistic that

we are only months away from the end of the pandemic, when we can return to normalcy. We will make every effort to remedy the missed opportunities at recruitment over the covid period, and will request a waiver of consent from the IRBs for use of FFPE material from surgical and biopsy procedures during 2020 and possibly the first quarter of 2021.

b. Changes that had a significant impact on expenditures
Covid lockdown has decreased expenditure as laboratory and clinical activities have decreased

c. Significant changes in use or care of human subjects
Nothing to report

6. PRODUCTS:

a. Publications, conference papers, and presentations
Publications that acknowledge use of resource:
1) Bhagirath D, Dahiya R, Majid S, Tabatabai ZL, Saini S. Sequencing Small Non-coding RNA from Formalin-fixed Tissues and Serum-derived Exosomes from Castration-resistant Prostate Cancer Patients. Journal of Visualized Experiments: Jove. 2019 Nov 19(153).

2) Sater HA, Marté JL, Donahue RN, Walter-Rodriguez B, Heery CR, Steinberg SM, Cordes LM, Chun G, Karzai F, Bilusic M, Harmon SA. Neoadjuvant PROSTVAC prior to radical prostatectomy enhances T-cell infiltration into the tumor immune microenvironment in men with prostate cancer. Journal for Immunotherapy of Cancer. 2020;8(1).

b. Biospecimen Collections:

Biospecimen Accrual: Oct 1 2018 – Sept 30 2019	
Samples Collected	**Total Collected**
Tissue	
Radical Prostatectomy	104
Fluids	
Prostatic fluid	77
Seminal Vesicle fluid	73
Urine	51
Blood Samples	267
Serum (63)	
Plasma (102)	
Buffy Coat (102)	
TOTAL	**572**

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

a. What individuals have worked on the project?
Jonathan Melamed, MD: no change
Peng Lee, MD PhD: no change
Emily Dube, MS: no change
Raveena Vakil, BS: no change

b. 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

c. What other organizations were involved as partners?
Nothing to report