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The WRNMMC Clinical Breast Care Project/Winder Research Institute will continue to help lead the way in the 21st century in the crusade against breast disorders. The project will continue utilizing a multidisciplinary approach as the standard of care for treating breast diseases and breast cancer. This multidisciplinary model integrates prevention, screening, diagnosis, treatment and continuing care, but the project is further unique in the incorporation of advances in risk reduction, informatics, tissue banking and research. These efforts focus on decreasing the morbidity and mortality of breast cancer among American women.

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1. INTRODUCTION

The Breast Cancer Translational Research Center of Excellence (BCTR-CoE) provides a multidisciplinary approach as the standard of care for treating breast diseases and breast cancer. This approach integrates prevention, screening, diagnosis, treatment and continuing care, incorporation of advances in risk reduction, biomedicinformatics, tissue banking and translational research. The project is based on a discovery science paradigm, leveraging high-throughput molecular biology technology and our unique clinically well-characterized tissue repository with advances in biomedical informatics leading to hypothesis-generating discoveries that are then tested in hypothesis-driven experiments.

2. KEYWORDS: None

3. OVERALL PROJECT SUMMARY:

Objective/Hypothesis: Utilize and extend our unique DoD biorepository of well characterized biospecimens from a broad subset of patients with breast cancer and other breast diseases to broaden our knowledge of the etiology and pathology of breast disease specifically focused on breast cancers affecting the readiness of active duty women. Leverage the technological and information technology advances in genomic, proteomic, and total metabolomics research to further our understanding of breast cancer through discoveries in molecular biology, pathway analysis and systems biology that can be readily translated into the clinic.

Background: Breast cancer is the most common non skin-related malignancy among women in the western world. It accounts for one-third of all cancers diagnosed. Age is the single most important risk factor for the development of breast cancer, as incidence and mortality both increase with age. However, a significant number of breast cancers are diagnosed among young women and this shift towards younger women developing breast cancer has increased in the past five years. Each year, over 10,000 new breast cancer cases are detected in women under the age of 40. Over 90% of these occur among women aged 30-39 years and 8 women per 10,000 in this age group die from breast cancer every year. Breast cancer is the single leading cause of death in women aged 40-49 years. Despite the low absolute risk of breast cancer in women under 40 years of age, the incidence is increasing in this age group. The incidence in younger women is probably underestimated based on the current understanding of the biology of breast cancer. The focus of the Breast Cancer Translational Research Center of Excellence (BCTR-CoE) is to work towards decreasing the morbidity and mortality of breast cancer among American women with a specific focus on the problem as it pertains to the active duty military population, an increasing number and proportion of which are female and are in this under-40 age group of increasing breast cancer development, risk, and poorer outcomes. As all jobs and
positions in the military are now available to women including combat positions, the increasing incidence of breast cancer in younger (military-age) women and the increased lethality of that subtype of breast cancer, coupled with the military’s critical reliance on a Total Force of all personnel inclusive of a high and increasing percentage female, demands a continued effort of the DoD through the BCTR-CoE to focus on surveillance, screening, early detection, curative treatments, and post-treatment Return To Duty Survivorship programs. The BCTR-CoE has had a 15 year history of doing just that, and we are robustly moving into the future by targeting our valuable resources to the active duty military cancer problem, aligning ourselves with other DoD and federal agencies in order to increase efficiencies and allow best use of government funds, and ensuring we are in complete alignment with the DoD QUAD AIM with the central pillar of our efforts focused on READINESS of the Total Force.

Military Relevance: Breast cancer is the most common non-skin cancer in women. It is the single greatest cause of cancer deaths among women under 40, and is a significant cause of mortality for women in the United States Armed Forces. Breast cancer mortality among women <50 years accounts for >40% of years of life lost due to this disease. The economic, social and emotional costs to families are far greater when a young woman dies than when an older woman dies of breast cancer. The more aggressive nature of the disease in young patients along with the attendant costs underscores the importance of early detection of breast cancer in young women. Breast cancer is a curable disease if it is detected early; as such early detection is related to survivorship, cost of treatment and quality of life for the affected woman.

The majority (>90%) of women in active military service are <40 years of age. The Department of Defense (DOD) with its high percentage (and increasing percentage, as all roles in the military are now open to all genders, including combat roles) of young women and its commitment to health care is particularly concerned about breast cancer. When discovered at a later stage, treatment of breast cancer is expensive, aggressive and results in considerable disruption to the woman’s ability to contribute to the military and society. Cost and disruption to life are considerably less when the carcinoma is discovered at an earlier stage and therefore treatable with less invasive methods and curable in up to 90% of cases for Stage I disease. Furthermore, the DOD has a high percentage of African-American (~30%) and Hispanic (~10%) women. Death rates from breast cancer tend to be particularly high in these ethnic groups owing in part to later stage of detection and to the more aggressive nature of breast cancer in these groups.

The active duty military force is approximately 20% female. Most of these service members are in the age range (30-40 years) where routine screening for breast cancer consists only of clinical breast examination. Both mammography and clinical breast examination have a very poor accuracy in the young active duty force in determining which breast abnormalities require treatment, and which are benign and can be left alone. The immense scale and impact of this problem for the military can be assessed by the fact that there were over 2,000 cases of breast cancer diagnosed in active duty service members over the last ten years (source: ACTURS DoD Tumor Registry data).

Furthermore, there were over 8,000 unnecessary breast biopsies done on active duty women during this time because it takes 4 breast biopsies of normal non-cancerous lesions to find each individual breast cancer. Hence, women often need to take lengthy amounts of time off from duty in order to undergo multiple tests leading up to the biopsy as well as time off from duty because of the biopsy itself. This translates into approximately 10,000 weeks, or 30 person-years, of time lost in the
evaluation of normal, benign breast lesions in active duty service members. This would be unacceptable for any other healthcare issue, and should be so for this one. Unfortunately, at the present time there is no completely accurate screening tool currently available to diagnose breast cancer in the early, curable stages for women under the age of 40, who make up the vast majority of women in military uniform.

As indicated, approximately 20% of the active duty military force is female, most under the age of 50. Breast cancer strikes one in eight women in her lifetime, and there is a documented change in breast cancer incidence in recent years, such that breast cancer is being detected and diagnosed more often in younger women (under age 50), and the same is true in our military members. In the same way that diagnostic and therapeutic efforts through the military and US Army are carried out in infectious disease care and research, eg. Malaria, Typhoid, etc., so too must the military continue to address the effects of the scourge of breast cancer and breast diseases on the 20% of total active duty force who are women.

Moreover, CBCP/BCTR-COE, developed and to this day maintains the only specialty breast cancer evaluation and treatment center in the US Army, which is at the CBCP Comprehensive Breast Center at Walter Reed National Military Medical Center.

Additionally, our Breast Center is the only Army facility that financially supports direct genetic testing of active duty (all Services) women who are identified in our Center as being in a high risk category of carrying a BRCA genetic mutation, which when present can signify an up to 90% increased risk of breast cancer development, and for which we then deploy individualized cancer preventive therapies.

The BCTR-COE (CBCP) Breast Center is the Army-recognized and Military-recognized specialty referral center for tri-service active duty personnel from around the globe with medical disorders related to all breast diseases and breast cancer. CBCP Breast Center routinely cares for women on active duty Army from places such as the Middle East, Southwest Asia, OEF, Korea, Europe, and the Far East. CBCP at WRNMMC annually cares for over 7,500 patients.

**Public Purpose:** The BCTR-CoE is the continuation of the Clinical Breast Care Project (CBCP) that has been ongoing for 15 years. Its uniqueness and relevance has been attested to by numerous outside world-class cancer experts, from the innumerable public scientific and invited lecture presentations made by CBCP PI and investigators over the years, as well as by the extensive peer-reviewed publication record of CBCP researchers. The BCTR-COE has the world’s largest biorepository of highly-characterized and pristine-collected specimens from breast patients made up of human breast tissues, lymph nodes, sentinel nodes, sera, bone marrow aspirates, cancers, benign tumors, and pre-malignant disease, which amounts in-total presently to 67,076 as of 23 August 2016. This unique DoD resource, stored, maintained, tracked, and kept under strict QA in the CAP accredited CBCP-repository at the Windber Research Institute since 2001. As of 23 August 2016 the project has used 25,744 samples in support of both internal genomic and proteomic researchers, as well as targeted collaborations with extramural collaborators from academia, governmental organizations, and corporate entities.
This biorepository is also unique in that its specimens are tightly coupled to highly-accurate clinical, demographic, and pathologic data collected from its originating patients through robust IRB-approved and fully HIPAA (Health Insurance Portability and Accountability Act)-compliant protocols that exceed all existing regulatory requirements for patient consent, privacy, and oversight.

The BCTR-COE has one of the few fully integrated genomic and proteomic molecular biology research programs in the nation devoted exclusively to research in breast diseases. We have an established track record of publication and scientific communication in this field.

The BCTR-COE has deployed a unique biomedical informatics data warehouse system that integrates clinical, pathologic, and molecular data on breast research subjects, allowing for a novel in-silico biology discovery platform.

The BCTR-COE is a true translational research-clinical care environment, where there actually exists an organizationally-driven and structured collaborative effort between basic scientists, clinical scientists, clinicians, nurses, patients, and multiple other personnel.

**Pillar Specific Goals, Objectives for this annual period**

*I. Breast Cancer Risk Reduction:*

**Objectives:**

- To collect data on all female patients 18 and older who present to the CBCP Breast Center of Excellence at Murtha Cancer Center at Walter Reed National Military Medical Center - Bethesda and are found to be at an increased or elevated risk for developing breast cancer.
- To utilize this database to analyze the diagnosis, treatment, and treatment outcomes for patients found to be at an increased risk for developing breast cancer. Analysis includes but is not limited to: risk factors for developing breast cancer, effectiveness of various modalities of risk-reduction treatment (medical, surgical), and actual risk of developing cancer.

The Risk Reduction Clinic at WRNMMC is a multi-disciplinary program designed to identify, counsel and manage women at high risk for breast cancer. Patients receive an in-depth personal and family health history by a world renowned medical oncologist.

Current research shows there are risk factors that may influence the development of breast cancer. Identifying people with these risk factors and implementing closer surveillance and risk reduction techniques may detect cancer earlier. Earlier detection of breast cancer leads to better prognosis and outcomes. Calculations of risk are based on computer models extensively validated as accurate in identifying women at high risk.
II. Biorepository:

Objectives:

- Continue to collect and store a broad spectrum of biospecimens from every patient undergoing a breast biopsy and/or breast surgery at WRNMMC, Windber Medical Center (WMC), Anne Arundel Medical Center (AAMC), and our affiliated hospitals that consent to participate in BCTR-COE IRB-approved protocols.
- Continue to collect and store biospecimens (blood) from women who are free of breast disease who consent to participate in BCTR-COE IRB-approved protocols to act as controls.
- Utilize the power of this extensive biorepository as a major resource for breast disease research.
- Leverage the BCTR-COE biorepository to maximize the utilization of the repository, with BCTR-COE leadership approval, for the overall benefit of breast cancer patients and research, as able and appropriate.
- Participate in national/international projects that can benefit from resources of the BCTR-COE biorepository.

Although there have been remarkable improvements in breast cancer diagnosis and management, most of the complex molecular mechanisms associated with the onset, progression and/or severity of breast cancer are still not well understood. As part of the BCTR-COE we carry out molecular, biochemical and histological analysis of breast tissue and/or blood and blood components from breast cancer patients to provide insights into the molecular mechanisms that may be relevant in the development of breast cancer and breast diseases. To achieve this aim, a large supply and a wide variety of good quality tissue samples are needed. Unfortunately, good quality donor breast tissue is extremely scarce and when available is often not backed by a comprehensive medical history and/or is not a good representation of the target population or study area. The non-availability of a steady and consistent supply of good quality tissue limits the systematic analysis of tissues and negatively impacts the generation of biologically useful information in research laboratories and by extension negatively impacts new findings that benefit clinical practice. The objective of this project is therefore the acquisition and banking of breast tissue, lymph nodes, serum/plasma and other blood derivatives from informed and consenting donors.

III. Focused Research:

Objective:

The ultimate goal of all BCTR-CoE research projects is to generate new knowledge that will benefit breast cancer patient treatment. The large volume of molecular data from BCTR-COE patients, integrated with the clinicopathologic data including the highly valuable treatment and outcome information, provides a gold data mining opportunity for BCTR-CoE scientists to generate new hypotheses for study and validate new experimental findings. This opportunity is even more enriched by the availability of large-scale high-quality datasets such as those from TCGA across multiple cancer types. Such raw data, combined with public annotation databases on genes, proteins, pathways, and human diseases, will enable derivation of new knowledge for breast cancer patient treatment.
There are two themes for BCTR-CoE research. Theme 1 focuses on breast cancer mechanistic studies of clinically important questions, and Theme 2 focuses on therapy-relevant molecular studies of breast cancers. For Theme 1 studies, one important topic is integrative profiling of breast cancers. The current 4 major breast cancer subtypes—termed “intrinsic subtypes”—were based on gene expression profiling. IHC-based subtyping using ER, PR, Ki67 and HER2 are available and are of clinical significance, although such subtyping is sometimes referred to as surrogate for intrinsic subtyping. Information on a broader panel of proteins and their post-translational modifications as well as their subcellular location information is needed for a more comprehensive understanding of breast cancer stratification which is important for cancer treatment. Thus such studies are important not only for Theme 1 but also for Theme 2, for example, the identification of protein markers for endocrine resistance.

For Theme 1 studies, the BCTR-COE provides a good research environment on young breast cancer patients and African American patients. Young age at breast cancer diagnosis and being African American are considered risk factors for poor outcomes of breast cancer patients. BCTR-COE has enrolled a high percentage of AA patients, and there is also a good size of young breast cancer patients enrolled due to the demographics of the active-duty military population. Using these resources BCTR-COE scientists have conducted molecular studies, and have proposed additional molecular, epidemiologic, and comparative survival analysis using both BCTR-COE data and the data in the public domain.

The topic of tumor heterogeneity is not only important to the understanding of breast cancer development (Theme 1), but also of therapeutic significance (Theme 2). Tumor heterogeneity refers to the cellular heterogeneity of tumor development environment, where there are cancer cells, stromal cells, lymphocytes, etc., and the MCC has chosen “Inflammation, Infection, Immunity, and Stroma (I3S) as one of the focuses for research. Tumor heterogeneity also refers to the fact that one physical tumor could contain multiple lineages of tumors that are not necessarily of the same molecular subtype. When only one subtype was diagnosed and treated, the other subtypes could be left untreated which could lead to detrimental outcome of the patient.

Additional topics are proposed to be studied on mechanistic understanding of breast cancer development. These include genetic dispositions, exposure to environmental risks, access to healthcare and treatment disparities, and impact of certain life style factors as well as comorbidities.

For Theme 2 studies, profiling of human biospecimens alone is important but insufficient; biospecimens are no longer alive after excision from the human body, and in order to study the impact of drugs or the response to drugs of a mutated gene, a live model system is needed. BC-COE scientists has developed tissue culture systems for both 2D and 3D model systems of breast cancer cell lines, with a focus on the triple-negative subtype that are currently difficult to treat. Findings from such studies are validated or sometimes guided by bioinformatics analysis of the data on human tissues. In addition, collaboration with university faculty members have been developed to use animal models to validate findings made from cell lines.
IV. Biomedical Informatics:

Objective:

As one of the five pillars of the CBCP, Biomedical Informatics (BMIX) has developed a comprehensive informatics system supporting the activities in all of the other 4 pillars. Biomedical Informatics also provides support to other research projects and leads its own research, by working with scientists both within and outside of the WRI. In the recent years, the BCTR-CoE has been conducting or participating in several large-scale molecular studies, including the TCGA-BC, Massive Parallel Molecular Processing in collaboration with the Pacific North Western National Lab, a Komen Promise Grant for therapy relevant molecular stratification of breast cancers in collaboration with Thomas Jefferson, etc. New initiatives are in development. The BCTR-CoE is now also addressing the collection of treatment and outcome data for invasive cancer patients enrolled in the study. These projects, combined with the research conducted by scientists at the WRI, has generated a large amount of molecular data as well as new types of clinical data. It is thus critical to expand our current informatics infrastructure to manage all these data, and more importantly, it is critical we expand our bioinformatics research capability to conduct integrative analysis to analyze these data, mine for new hypothesis for validation both computationally and experimentally, so as to make the best use of the data towards making important findings in understanding cancer development mechanisms, identifying cancer treatment drug targets, and develop physician decision support system to aid in cancer treatment.

Biomedical Informatics is now broadly defined as a multi-disciplinary subject for the management and utilization of biomedical information encompassing clinical informatics, public health informatics, and bioinformatics [2]. This definition is increasingly important as new concepts and technologies enter into medical practice and related basic research, and require new types of information management and data analysis that relies on sophisticated statistical and computational technologies. Figure DD.0 shows the major components in this definition of BMIX [3].
Clinically, patients receive treatment, subjects are enrolled in the study, and clinical data as well as specimens are collected. To protect the privacy of human subjects, de-identified subject IDs and specimen IDs are created and properly mapped before being transferred to the research side with the corresponding clinical data and the specimens. On the research side, clinical data are properly stored, tissues properly banked and genomic and proteomic studies conducted. All data are then warehoused, analyzed, and mined for biomarkers, risk factors, and disease models. Newly obtained knowledge is fed back to the clinic to aid in clinical decision-making.

From the data flow point of view, these BMIX components include 1) supporting data collection and generation across clinical, genomic, and proteomic platforms, 2) data tracking, 3) data centralization, 4) data analysis and mining, and 5) knowledge generation and presentation to research and clinical applications. We have been working towards developing a complete BMIX infrastructure for the BCTR-COE. The system we are developing was designed to be flexible to enable expansion to support translational research in other disease areas. In the following we will present the background, the current status, and the plan for each of these 5 components of BMIX.

V. Translational Clinical Care:

Objectives:

- Decrease the negative psychological impact on the patient of having an evaluation or treatment intervention for breast disease by utilizing objective measurement instruments to longitudinally assess the patient’s psychological response to evaluation and intervention, and base modifications of these procedures on those results.
• Create and maintain an environment (medical, physical, psychological) conducive to the multiple needs of the patient undergoing breast disease evaluation / treatment.

• Recruit patients into the various BCTR protocols to obtain the clinical data and biospecimens needed to meet the BCTR’s translational research goals.

This pillar of the BCTR is the foundation upon which all the success of and project rests. Without patients enrolled in our biospecimen repository protocols, there would be no translational research center of excellence. These patients come from the clinical care environment. Since its inception in 2001, the CBCP has had as a priority, the development and staffing of the core clinical centers at Walter Reed National Military Medical Center, the Joyce Murtha Breast Care Center in Windber, PA and at our newest site, the Pat and Lesly Sajack Breast Center at Anne Arundel Medical Center in Annapolis, Maryland. Under the direction of Lorraine Tafra, MD more than 500 newly diagnosed cases of breast cancer are seen at AAMC each year.

At each center the staff is dually trained as clinical/research providers, to seamlessly integrate the need for a strong research focus in the clinical center with the requirement to provide state-of-the-art clinical care to the patients. The reputation of CBCP is that of an exceptional translational research project with very possibly the world’s most pristine collection of breast tissue. This has resulted in a number of well-respected medical centers expressing interest in joining us as research partners. The care of our patients is provided by Physicians, Advance Practice Nurses (Nurse Practitioners) and certified Nurse Navigators with all personnel having as their prime job description, the research aspects of the BCTR.

Walter Reed National Military Medical Center in Bethesda, MD has a state of the art comprehensive breast care center with women’s imaging co-located with the breast care center. The Breast Center has a procedure room, recovery room enabling surgery within the center as well as a designated Aurora Breast MRI machine. We evaluate on average 7,500 patients per year and diagnose approximately 250 new breast cancers per year. Of note, the Breast Care and Translational Research Center of Excellence received a 3 year full accreditation by the NAPBC (National Accreditation Program for Breast Centers) and are accredited through September 2018.

4. KEY RESEARCH ACCOMPLISHMENTS:

 Breast Cancer Translational Research Center of Excellence (BCTR-COE)
 Statement of Work

Task 1: Identify and counsel 100 patients annually at high risk for development of breast cancer, and employ risk reduction strategies. Ongoing

CBCP evaluated a total of 336 patients; 283 patients were seen in the clinic and 53 telephone consults were conducted at Walter Reed National Military Medical Center in Bethesda, MD from 23 August 2015 – 24 August 2016.
Task 2: Accrue over 500 patients annually to the “core” BCTR-COE protocols through consenting patients in the main BCTR-COE clinical sites. Ongoing

Total Patients Consented from 24 August 2015 – 23 August 2016.

WRNMMC: 225
Windber: 396
AAMC: 140

Task 3: Acquire through consented protocol acquisitions, over 5,000 specimens annually (neoplastic and non-neoplastic breast tissues and tumors, lymph nodes, metastatic deposits, blood and its components, bone marrow) on patients with all types of breast diseases and cancer.

Total Samples Collected from 24 August 2015 – 23 August 2016.

Total Blood: 5018
Total Breast: 479
Total LN: 57
Total Other: 53

Specimen types and processing formats are summarized below:

<table>
<thead>
<tr>
<th>CBCP Tissue Types</th>
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<tbody>
<tr>
<td>Breast Tumor</td>
<td>OCT, Flash Frozen</td>
</tr>
<tr>
<td>Benign Breast Tissue</td>
<td>OCT, Flash Frozen</td>
</tr>
<tr>
<td>Lymph Node</td>
<td>OCT, Flash Frozen</td>
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<table>
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<tr>
<th>Blood Collection Tubes</th>
<th>Components Stored</th>
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</thead>
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<tr>
<td>Green Top Tubes (Sodium</td>
<td>plasma, blood cells</td>
</tr>
<tr>
<td>Heparin)</td>
<td></td>
</tr>
<tr>
<td>Red Top Tubes</td>
<td>serum, clot</td>
</tr>
<tr>
<td>Paxgene Blood RNA Tubes</td>
<td>whole blood for RNA</td>
</tr>
</tbody>
</table>

Task 4/5: Bank these biospecimens in the BCTR-COE Biorepository as the substrate for all molecular analyses carried out in BCTR-COE labs, as outlined in the BCTR-COE Core Protocols. Utilize this repository as the basis for intramural and extramural collaborations for secondary usage research. Ongoing

Since the inceptions of the Clinical Breast Care Project the Biorepository Pillar has been critical to the success of the project. As we move forward into the establishment of the BCTR-COE it is important to look at the success of the biorepository and to understand the firm foundation that it has laid for building the Center of Excellence.

The charts below show the cumulative patient accrual into the CBCP protocols and total number of specimens stored in our biorepository since 2002. These patients, who have been recruited and
consented into the CBCP protocols at WRAMC, WRNMMC, AAMC, WMC and other participating CBCP clinical intake sites are the foundations of the translational research that has occurred within the CBCP and which will continue in the BC-TRCOE. From these patients we have collected and stored in our biorepository over **67,076 biospecimens (Figure BB-1)** donated by **7,808 fully consented subjects** to our IRB approved tissue and blood protocols. (Figure BB-2)

![CBCP Specimens - Cumulative Annual Total thru 8/23/16](image)

**Figure BB-1** Total biospecimens collected and banked by the biorepository.
Figure BB-2. Cumulative patient accruals into CBCP protocols since 2002.

Figure BB-3. The numbers and types of biospecimens collected by the CBCP.
These specimens represent a broad spectrum of tissues, blood and blood products (Figure BB-3) that are not only a unique and valuable resource for the CBCP but are also the substrates for our translational research program. Along with the biospecimens that have been collected from CBCP participants, each consented patient also provides demographic, medical, life and family history data as well as complete pathology data on donated tissues. Patients have been recruited from a number of partnering clinical intake sites over the history of the CBCP (Figure BB-4), conversely the primary partners are WRNMMC, the Windber Medical Center/Joyce Murtha Breast Care Center in Windber, PA, and the Anne Arundel Medical Center in Annapolis, MD.

**Task 6:** Perform whole genome DNA sequencing on DNA from 40 or more cases of breast cancer over the life of the project.

- Completed.

**Task 7:** Develop and support a robust laboratory information management system to ensure proper tracking of data acquisition and a clinically relevant and laboratory research-linked prospective, longitudinal computerized data warehouse to support translational research and ultimately support physician decision making. Ongoing.

- We finished Phase I and Phase II development of the CBCP Data Tracking System (CBCP-DTS) – replacement for CLWS. Phase I was released in April and Phase II was released at the beginning of July. The current DTS system includes 11 modules (Pathology, Security, Enrollment, Clinical and Outcome, Treatment, Prognostic Studies, Sample: Registration, Sample: Shipment, Sample: Verification, and Sample: Export to FreezerWorks modules).

- The process of extracting data from CBCP-DTS and importing to FreezerWorks has been completed.

- We completed framework for the reporting system that executes pre-defined reports and distributes results via e-mail. This system is working for the data from CBCP-DTS and from the Data Warehouse. We will continue implementing new reports throughout next year.
- The design and implementation of the QA/QC system is currently in progress and will be completed next year.
- A number of documents have been created including SOP documents, Phase I and Phase II releases, data dictionary, and Use Case documents. All changes to the system have been and currently are tracked.
- We performed multiple software demonstration and user training sessions tailored for different functional groups of CBCP-DTS users.
- We finished clinical data conversion from DW4TR to CBCP-DTS.
- We are in the process of completing Pathology conversion. We converted surgical procedures, grouping, and Masterlist. We will continue finishing conversion of pathology data.

**Task 8: Develop an analytical system for integrative data analysis and mining, and develop a breast knowledgebase to support clinical and research activities in BC-COE. Ongoing**

- With the deployment of the CBCP-DTS we retired the CLWS. All data in CLWS have been processed and loaded into the DW4TR.
- We continued loading data to the Data Warehouse and continue to develop and analyze data sets for internal and external users.
- We started the process of loading data from CBCP-DTS to Data Warehouse and implemented a process for import data from FreezerWorks to Data Warehouse.
- In collaboration with the tissue bank we continue to develop a list of the reports that need to be implemented; requirement collection has started.

**Task 9: Conduct quantitative analysis of therapy relevant proteins by immunohistochemistry within subclasses of breast cancer to provide better patient selection into clinical trials for targeted and combination therapies.**

- A proof of principle of the analysis for 27 markers have been performed for over 200 cases, connecting the information on ER, PR, and HER2 to other markers for increased understanding of molecular connectivity in breast cancer tumors.
- Analysis of markers CD163 and phospho-histoneH3 has been performed with has been shown to be associated with patient survival and patient or tumor characteristics. The findings were presented at the SABCS 2015 in two posters.

- Additional markers and sets of markers have been analyzed, with observations confirmed reported results. For some markers, such as the HER family receptors, more cases would be needed to derive a robust result. A program has been developed to enable semi-automatic analysis of any markers when more results (more cases, or more markers) are available.

- After the initial preliminary Bayesian analysis of the whole dataset, we were able to improve the quality of the data and conducted another round of Bayesian analysis. The results are more solid and more known results are observed. More cases will be needed in order to make robust new findings.

- More analyses are being planned.
Task 10: Study molecular differences between breast tumors from African American and Caucasian women as the identification of such differences will allow for the development of more effective therapies that will improve outcomes in African American women with breast cancer. Project complete. Tumors are not molecularly different and thus disparities are not attributable to molecular factors.

- Abstract reporting no molecular or survival differences in patients with luminal A tumors presented during Grand Rounds during SSO 2016 and corresponding manuscript accepted for publication in Ethn Dis.

NS Costantino, B Freeman, CD Shriver, RE Ellsworth. Outcome disparities in African American compared to European American women with ER+HER2- tumors treated within an equal-access health care system. Ethn Dis 26:407-416, 2016

Task 11: Using state-of-the-art 3D cell culture techniques and modern approaches to the study of cancer cell biology, study the mechanisms of cell invasion, migration and ultimately metastasis in breast cancer cell lines. Ongoing, several abstracts and publications have been presented on this topic.

Aim 1. CSPG4-NEDD9 interaction promotes triple-negative breast cancer progression and metastasis.

NEDD9 has been demonstrated to play a role in adhesion and migration of various cell types including lymphocytes and malignant cells. NEDD9 contains numbers of tyrosine residues phosphorylated by tyrosine kinases such as focal adhesion kinase, suggesting its role in promoting migration and invasion of cancer cells. Indeed in breast cancer progression models, previous studies provided evidence that NEDD9 is a key molecule to promote breast cancer progression by facilitating migration and invasion. However, the biochemical mechanism to characterize the role of NEDD9 in promoting progression and metastasis of breast cancer is not clear at present.

During the previous period, we performed yeast-two-hybrid (Y2H) assays for identifying partner proteins to NEDD9. We isolated several proteins that promote malignant phenotypes of breast cancer cells through this screening system. Among them, we are evaluating small GTPases (e.g. Arf4 and Rab11a), a kinase (e.g. DNA-PK), and mitochondria protein (e.g. HAX1) for promoting malignant phenotypes of breast cancer cells by characterizing mechanisms of interacting with NEDD9.

Presentation:
- (Poster) Tumor-associated glycans as key molecules to promote triple-negative breast cancer cells.

- (Poster) Tumor-associated glycans as key molecules to promote triple-negative breast cancer cells.
Aim 2. Development of DNA aptamers against CD44 that inhibit breast cancer invasion and metastasis.

During the previous period, we characterized CD44-EphA2 association for promoting malignant phenotypes of breast cancer cells using T47D and SKBr3 as model systems, since these cells express under detectable level of endogenous EphA2 and CD44. In this period, we further demonstrated that CD44 expression in T47D cells induces expression of EphA2 on a transcriptional level evaluated by quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR). Importantly, when the cytoplasmic domain of CD44 was deleted, induction of EphA2 was not observed, suggesting that signaling pathways through the cytoplasmic domain of CD44 plays a key role in stimulation of EphA2 transcription in T47D cells. In contrast, EphA2 expression in T47D cells failed to induce CD44 expression. Given that CD44 is a maker of breast cancer stem cells, our results provide a novel mechanisms of cancer cell growth involving cell adhesion receptor and growth factor receptor, which serves as promising therapeutic targets for breast cancer.

SOX10 is a transcription factor and plays a role in neural crest development. Recent studies demonstrated that SOX10 is a driver of melanoma progression as developing from melanocytes which is neural crest cell origin. In breast cancer tissues, SOX10 expression is a potential diagnosis marker especially in basal-like breast carcinoma. Thus, these results suggest that characterization of the mechanisms of SOX10-driven malignant phenotypes of cancer cells would provide significant insights for novel diagnostics and therapeutic tools.

During the previous period, we further characterized the mechanisms of SOX10-Zyxin interaction. We demonstrated that Sox10-Zyxin molecular complex was observed in adherent breast cancer cells. Interestingly, in non-adherent cells cultured on BSA-coated substrate, Zyxin was found in the precipitates of SOX10, suggesting that SOX10-Zyxin complex was pre-formed in cytoplasm and translocate into adhesion sites in breast cancer cells. Furthermore, our recent studies suggest that SOX10 was associated with cell adhesion receptors such as CSPG4 and CD44. These results suggest that SOX10 plays not only as a transcription factor but also cytoskeletal protein to regulate cell migration and invasion of breast cancer cells, which is a key step during the complex process of cancer metastasis. We are currently further characterizing SOX10-Zyxin complex as a transcription factor using CHIP-on-CHIP assays and microarray studies.

Aim 4. Development of novel Ruthenium (Ru)-compounds as anti-cancer reagents.

Previous studies suggest that transition metal complexes, such as cisplatin, are efficacious for treating various cancer types, including ovarian, lung, and breast. In order to further evaluate ruthenium (Ru) complexes as potential anti-cancer agents, we synthesized and evaluated ruthenium (Ru)–arene complexes. Two complexes with the general formula $[\text{Ru}(\eta^6-p\text{-cym})(N-N)\text{Cl}]^+$ were tested for their abilities to inhibit cancer cells. The complex with $p$-phenylenediamine ($o$-PDA) significantly inhibited
growth of breast (MDA-MB-231, MCF-7, SKBR-3, and SUM149), lymphoma (Raji), melanoma (Bowes), and osteosarcoma (HT1080); however, complex with o-benzoquinonediimine (o-BQDI) was ineffective. In contrast, o-PDA failed to inhibit growth of human breast epithelial cells, MCF-10A cells. Treatment of MDA-MBA-231 cells with o-PDA resulted in a significant reduction of productions of PDGF-AA, GM-CSF, and VEGF proteins at the transcriptional levels. Finally, we demonstrated that o-PDA synergistically inhibited MDA-MB-231 cell growth with cyclophosphamide but not doxorubicin and paclitaxel. These results suggest that Ru-arene complexes are promising anti-cancer drugs that inhibit progression and metastasis by blocking multiple processes for patients with various forms of cancer.

**Publication:** Inhibition of cancer cell growth by ruthenium complexes

**Task 12:** Use our unique collection of breast cancer biospecimens to characterize microRNA (miRNA) expression in breast cancer progression and metastasis.
- This project is on hold.

**Task 13:** Identify protein signatures associated with the development and progression of pre-malignant breast disease to improve our understanding of the biologic processes involved in early breast disease development and progression and to drive the development of personalized therapeutics for breast disease.
- This project is currently inactive.

**Task 14:** Identify genetic changes in low- and high-grade breast tumors to improve our understanding of the evolutionary process of breast cancer and to identify a protein signature that can discriminate low- from high-grade breast tumors, allowing for more accurate diagnosis and risk assessment.
- Data generation completed.

**Task 15:** Use our unique collection of breast cancer biospecimens to characterize molecular signatures that can differentiate primary breast tumors with and without metastatic potential, as well as between primary tumors and subsequent metastases.

**Task 16:** Improve our understanding of the molecular changes associated with HER2 amplification and over-expression to allow for more precise diagnosis of HER2+ patients and development of customized treatment options in patients with HER2+ breast cancer.

**Objective 1** Evaluate differences in the molecular profiles of patients with increased HER2 expression.
Ongoing.
- Preliminary data analysis of frozen OCT-embedded breast specimens showed a difference in gene expression profiles between patients with increased HER2 expression due to HER2 gene
amplification (n=18) vs. chromosome 17 polysomy (n=14). To increase sample size, additional cases with HER2 copy number alterations will be evaluated for gene and protein expression differences. Due to the limited number of HER2 amplified and polysomic cases available in OCT, we continue to develop and optimize protocols for utilizing RNA from FFPE specimens for gene expression analysis, specifically qRT-PCR. These protocols will be used to validate the gene expression differences identified from microarray analysis of the frozen breast tumor specimens as well as for pathway-focused gene expression analysis of FFPE specimens.

Task 17: Study the role of matrix metalloproteinases in breast cancer with the goal of developing diagnostic and prognostic marker of breast cancer based on expression of MMPs and polymorphisms in MMPs.
  - Complete with 4 publications.

Task 18: Identify molecular alterations in the breast tumor microenvironment that contribute to tumorigenesis and which may lead to improved methods of breast cancer prevention and treatment.
  - Adipose pilot study complete with publication in 2014. Complete.

Task 19: Use our unique collection of breast cancer biospecimens to study angiogenesis and lymphogenesis in different grades of DCIS and IDC.
  - This project is on hold.

Task 20: Incorporate the rapidly growing public genomic and proteomic datasets related to breast cancer into our data warehouse to be able to mine the combined data sets for the generation of new hypotheses regarding breast cancer development, progression and treatment. Ongoing, outgrowth of project with NCI/NHGRI TCGA project. Nothing new to report.
  - Subaim 2. Integrate gene expression microarray data for both Level 1 and Level 3 data. Complete for Level 3 and decided that Level 1 is not as important.
  - Subaim 3. Develop applications to use the integrated gene expression data. Complete at the query level and decided that more advanced applications will not be cost-efficient, as our resources are limited.
  - Subaim 4. Integrate Level 3 DNA Sequencing data, and make results available to scientists, using similar approaches. Complete, and same logic for applications study.
  - Subaim 5. Integrate SNP data and make the results available to scientists using similar approaches. This type of data is not immediately needed so this subaim is on hold.

Task 21: Compare biomarker expression in core biopsy and surgically resected tumors. This analysis is exploring whether the expression of biomarkers as measured by IHC are higher on core biopsies than surgically resected tumors, and whether such differences may impact the subtyping of the breast cancer from the patient.
  - Complete with a poster presented at SABCS 2013.

Task 22: Use the biomarkers of ER, PR, HER2, and Ki67 by IHC to classify luminal invasive breast cancers into LA, LB1 (HER2-), and LB2 (HER2+).
Task 23: Use bio-specimen research activities to evaluate the effect of a variety of pre-analytical variables on samples collected for tissue banking.

Maintaining efficient Quality Management Systems (QMS) to provide quality tissue for research. Performing Biospecimen Research activities so that data obtained will be utilized to design data driven protocols and procedures. These activities will help the biobank maintain the integrity of its biospecimen and thus provide a biorepository environment that meets the industry’s standards.

**College of American Pathology (CAP) Accreditation**

The biobank received CAP accreditation in May, 2015 after a successful inspection on April 7th, 2015. *CAP Self-Assessment*—In order to remain CAP accredited CAP Self-Assessment is required 60 days to the anniversary of the biobank’s accreditation. It is performed in place of a physical inspection by CAP. We successfully completed the required CAP Self-Assessment process on 6/17/2016 after CAP’s review of our Quality Management Annual Assessment and Deficiency Response documentations. This was followed by a closeout teleconference held with CAP officials. We were commended for the organized way we presented our reports for the year.

**Quality management Systems**

*Tissue Quality*-Maintaining tissue integrity is essential to obtaining quality nucleic acids from the tissue specimens. Nucleic acids are one of the main byproducts of the tissue that are utilized for downstream experiments and their quality is dependent on quality of the tissue. We have monitored nucleic acid quality over time to determine the effect of storage. Table 1 below shows quality of RNA over time in storage. RNA was assessed based on RNA integrity number (RIN).

Table 1: RNA integrity (RIN) over time in storage.

<table>
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<tr>
<th>Days in Freezer</th>
<th>N</th>
<th>RIN Mean</th>
<th>Std. Deviation</th>
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<tr>
<td>&lt;30 days</td>
<td>8</td>
<td>8.4</td>
<td>0.680</td>
</tr>
<tr>
<td>30-100 days</td>
<td>32</td>
<td>8.1</td>
<td>0.605</td>
</tr>
<tr>
<td>100-300 days</td>
<td>15</td>
<td>8.3</td>
<td>0.487</td>
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<tr>
<td>130-150 days</td>
<td>4</td>
<td>8.5</td>
<td>0.726</td>
</tr>
<tr>
<td>0.5-2 years</td>
<td>39</td>
<td>7.8</td>
<td>0.654</td>
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<tr>
<td>2-3 years</td>
<td>35</td>
<td>8.0</td>
<td>0.621</td>
</tr>
<tr>
<td>&gt;3.5 years</td>
<td>21</td>
<td>7.5</td>
<td>0.780</td>
</tr>
<tr>
<td><strong>Total</strong></td>
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</table>

Data indicates that nucleic acid that is stored for less than 30 days and up to 3 years and over continues
to maintain RIN numbers that are acceptable for research. To date therefore, we have data to show that
we are providing good quality tissue by-products for research and that the biospecimens collected
continue to provide nucleic acids of good quality for research. We will continue to monitor, collate and
analyze nucleic acid data to ensure that our quality systems are effective. We have also analyzed this
data to show that there is no significance difference in these RIN #s stored over different time frames
(Table 2).

Table 2: RIN # over different storage time points are not significantly different

<table>
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<tr>
<th>Days in Freezer</th>
<th>Mean RIN</th>
<th>p-value</th>
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<tr>
<td>≤30</td>
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<td>31-100</td>
<td>8.084</td>
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<td>&lt;30</td>
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<tr>
<td>101-300</td>
<td>8.274</td>
<td>0.541</td>
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<tr>
<td>&lt;30</td>
<td>8.438</td>
<td></td>
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<td>&gt;300</td>
<td>8.122</td>
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<td>31-100</td>
<td>8.084</td>
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<td>101-300</td>
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<td></td>
</tr>
<tr>
<td>&gt;300</td>
<td>8.122</td>
<td>0.267</td>
</tr>
</tbody>
</table>

Quality Assurance- In our continued efforts to improve quality, consistency and reliability in our
operations, we have performed the following additional audits;

- Director has completed the first CAP required Quality Management Appraisal Report.

Standard Operating Procedures (SOP) - Standard Operating Procedures (SOP) continue to be
designed to allow efficient operations and processes at all levels of the biobank’s daily activities. We
continue to update our SOPs and have some edits to reflect any activity that has been revised, new
protocols to reflect new activities. To date we have over 100 active SOPs generated over 76 Logs or
Forms for documentation. These all help us achieve the required standards and Best Practices of the
industry.

Proficiency Testing-Samples from IBBL for the next proficiency testing activity are expected in the
next week.

Biospecimen Research
Experiments are ongoing in the area of biospecimen science research to support our SOPs. Below is a
summary of the activities for this reporting period.

- RNA Quality-Effect of room temperature storage on tissue integrity - write up stage
- DNA quality from tissue biopsies: Effect of different processing methods - write up stage.
• RNA quality from laser microdissected tissue - Effect of different slide treatments - Data analysis stage
• Nondestructive methods for assessing biospecimen quality - Assessing proteome markers for tissue quality - experiments ongoing.
• RNA from tissue imprints - potential as a routine collection/source of tissue RNA - initial experiments completed, data compilation and interpretation ongoing
• RNA from blood imprints - potential as a routine collection/source of blood RNA - project on hold as we were focusing on the tissue imprint for RNA.

Education and Training: We continue to explore avenues for improving our knowledge and keeping abreast with new developments in the industry. This is achieved through online webinars/seminars.

• Objective 1: Complete.
• Objective 2: Outcome data is required from WRNMMC which has not yet been provided.
• Objective 3: Complete with negative results.

• Objective 1: Demographic and path analysis was completed and presented at AACR. Treatment data not yet provided by WRNMMC.
• Objective 2: Completed. Manuscript ready to submit pending WR approval
• Objective 3: Completed.

Task 26: Identify blood-based signatures of breast disease that help in the generation of gene expression data from breast cancer patients with and without metastasis from blood, generation of gene expression data from control patients without breast disease and generation of protein expression data from serum from patients with and without metastatic disease using Discovery Map arrays. Complete.
• Objective 1: Completed. Produced negative results.
• Objective 2: Completed. Negative results were yielded.
• Objective 3: generation of protein expression data from serum from patients with and without metastatic disease using DiscoveryMap arrays.
  This project has not begun. Currently, no agreement exists between WRNMMC and Myriad. We do hope to carry out this project however it will have to be paid for with CBCP supply funds rather than Myriad offering to run the samples for free.

Task 27: Analyze effect of a diagnosis of invasive breast cancer on lifestyle choices.
• Objective 1. Data from lifestyle factors including fat intake, alcohol and tobacco use, exercise, BSE, HRT use and BMI will be collected from patients diagnosed with invasive breast cancer or benign breast disease who have filled out core questionnaires from baseline and follow-up visits. The data collation is complete.
Objective 2. Statistical analysis will be performed to determine whether these factors improve in the invasive group and if they improve more significantly compared to the benign group. Data analysis completed. Corresponding abstract and manuscript to be completed by year's end.

Abstract submitted to SABCS and corresponding manuscript under revision.

Task 28: Assess the abundance and distribution of polychlorinated biphenyls (PCBs) in breast tissue.

Abundance and distribution of polychlorinated biphenyls (PCBs) in breast tissue. The objective of this project is to assess the abundance and distribution of PCB congeners in human breast tissue through a comprehensive survey of mastectomy specimens from the Clinical Breast Care Project. Breast tissues have been collected from 302 quadrants from 62 patients with pathological diagnoses ranging from disease free prophylactic mastectomy samples to metastatic breast cancer. Analysis of 98 PCB congeners in these tissues has been conducted by pressurized liquid extraction followed by high resolution capillary gas chromatography. In collaboration with Paul J. Kostyniak, Toxicology Research Center, State University of New York at Buffalo.


Task 29: Examine genomic heterogeneity in primary breast carcinomas and among sentinel lymph node metastases: implications for clinical management of breast cancer patients.


5. CONCLUSIONS:

The goal of identifying and counseling 100 patients annually at high risk for development of breast cancer while employing risk reduction strategies was achieved – 336 patients counseled.

BCTR-CoE successfully accrued and consented patients to our protocols, which continued to increase the specimen total in our biorepository. As of 23 August 2016 BCTR-CoE had banked more than 67K biospecimens in the BCTR-COE Biorepository, which are then used as the basis for intramural and extramural collaborations for secondary usage research.
During the year BCTR performed focused research on the biospecimens and clinical data collected under the BCTR-COE Core protocols, which resulted in multiple publications, abstracts and presentations by CBCP staff at peer-reviewed national meetings. National meetings included the San Antonio Breast Cancer Symposium, Society of Surgical Oncology Annual Cancer Symposium and the American Association for Cancer Research, Annual Meeting. See publications, abstracts and presentations on page 27.

The Breast Care Center/BCTR-Coe underwent a thorough National Accreditation Programs of Breast Centers (NAPBC) inspection on 9/10/2015 and received an outstanding summary from the Surveyor where she described our Center as being excellent, we are exceeding all standards and there are “no discrepancies” with our program. Our breast center received a full 3 year accreditation and is now accredited through September 2018.

The BCTR-Coe held its combined annual retreat with the Murtha Cancer Center on 29 July 2016 at the Uniformed Services University of the Health Sciences. There were multiple presentations at the offsite meeting covering the 5 pillars of the CBCP, as well as a wide range of other cancers (GYN and Prostate related) - see attached Agenda (Attachment 3).

The Murtha Cancer Center hosted its Fourth Annual Cancer Research Seminar on Monday 20 June 2016 from 8am-4pm at WRNMMC. There were presentations given by Scientist of the CBCP covering the topics of: “Biobanking for CBCP: An update and a look into the future” and “Functional Characterization of Therapeutic Targets for Promoting Malignant Phenotypes of Triple-Negative Breast Cancer”.

**6. PUBLICATIONS, ABSTRACTS AND PRESENTATIONS:**

**CBCP Publications 24 AUG 2015 – 23 AUG 2016 (newest to oldest)**

Constantino N, Freeman B, Shriver CD, Ellsworth RE. Outcome disparities in African American compared to European American women with ER+HER2- tumors treated within an equal-access health care system. Ethnicity and Disease, 2016 Jul 21; 26(3):407-16.

Rummel SK, Shriver CD, and Ellsworth RE. Contribution of germline mutations in cancer predisposition genes to tumor etiology in women diagnosed with invasive breast cancer before 40 years. WRNMMC publication clearance approved, 24 Jun 2016.


independent automated immunofluorescence image analysis platforms. Mod Pathol. 2016 Jun 17.


Lovejoy L, Constantino N, Shriver CD, Ellsworth RE. Relationship between obesity and breast tumor pathology in a contemporary set of patients. WRNMMC publication clearance approval, 8 Jun 2016.


Toro AL, Costantino NS, Shriver CD, Ellsworth DE, Ellsworth R. Effect of obesity on molecular characteristics of invasive breast tumors; gene expression analysis of 405 tumors by BMI. San Antonio Breast Cancer Symposium, San Antonio, TX, 8-15 Dec 2015.


Toro AL, Hueman MT, Shriver CD, Ellsworth RE. Epidemiological factors associated with breast cancer in young women. WRNMMC publication approval 2 Dec 2015.


Barrow TM, Barault L, Ellsworth RE, Harris HR, Binder AM, Valente AL, Shriver CD, Michels KB.
Aberrant methylation of imprinted genes is associated with negative hormone receptor status in invasive breast cancer. Int J Cancer. 2015 Aug 137(3):537-47.

7. INVENTIONS, PATENTS AND LICENSES: None

8. REPORTABLE OUTCOMES

Annual Report Numbers

Total Samples Collected from 24 August 2015 – 23 August 2016.

Total Blood: 5018
Total Breast: 479
Total LN: 57
Total Other: 53

Total Patients Consented from 24 August 2015 – 23 August 2016.
WRNMMC: 225
Windber: 396
AAMC: 140

9. OTHER ACHIEVEMENTS: NONE

10. REFERENCES: NONE

11. APPENDICES: Please see next page
• ATTACHMENT 1: List of personnel receiving pay from the research effort from 24 August 2015 – 23 August 2016.

Current Staff, role and percent of effort on project:

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<thead>
<tr>
<th>Full Name</th>
<th>Title</th>
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<tbody>
<tr>
<td>Shriver, Craig D.</td>
<td>Principal Investigator</td>
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<tr>
<td>Basham, Janice B</td>
<td>Licensed Practical Nurse</td>
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<tr>
<td>Bates, Mechelle Ariana</td>
<td>Administrative Coordinator</td>
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<tr>
<td>Boone, Jaime J.</td>
<td>Executive Director</td>
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<tr>
<td>Brockett, Stella Marie</td>
<td>Certified Cancer Registrar</td>
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<tr>
<td>Campbell, Jamie Leigh</td>
<td>Pathologist Assist./Site Coord</td>
<td>90%</td>
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<tr>
<td>Ellsworth, Rachel E.</td>
<td>Cancer Geneticist</td>
<td>100%</td>
</tr>
<tr>
<td>Fasaye, Grace-Ann O</td>
<td>Senior Genetic Counselor</td>
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<tr>
<td>Freeman, Benjamin Thomas</td>
<td>Research Assistant</td>
<td>82%</td>
</tr>
<tr>
<td>Hilton, Karrie R.</td>
<td>Research Nurse Manager</td>
<td>92%</td>
</tr>
<tr>
<td>Holden, Allan</td>
<td>Sr. Data Management Specialist</td>
<td>94%</td>
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<tr>
<td>Hooke, Jeffrey A</td>
<td>Head of Pathology</td>
<td>86%</td>
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<tr>
<td>Joseph, Julie</td>
<td>Research Assistant II</td>
<td>97%</td>
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<tr>
<td>Kovatch, Albert</td>
<td>Scientist</td>
<td>89%</td>
</tr>
<tr>
<td>Leeto, Jamie Lynn</td>
<td>Histology Tech</td>
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<tr>
<td>Medley, Vilisha</td>
<td>Certified Cancer Registrar</td>
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<tr>
<td>Miskovsky, Vicki Jones</td>
<td>Admin Reviewer CCC Protocols</td>
<td>33%</td>
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<tr>
<td>Mullican, Lynn Marie</td>
<td>Clinical Data Abstractor</td>
<td>87%</td>
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<tr>
<td>Patterson, Carol M</td>
<td>Medical Assistant</td>
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<tr>
<td>Pereira, Dianne</td>
<td>Office Manager/Admin. Assist.</td>
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<tr>
<td>Sakura, Sara Denman</td>
<td>Research Protocol Coordinator</td>
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<tr>
<td>Trupp, Rebecca Saron</td>
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<td>Wareham, Janet Andrea Yoder</td>
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<td>Zhu, Kangmin</td>
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<td>Zingmark, Rebecca N.</td>
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<td>Weiss, Raymond B</td>
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<tr>
<td>Bronsfan, Eileen T</td>
<td>Advisor</td>
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**Total Cumulative Expenditure**

for award W81XWH-12-2-0050

24 August 2015 – 23 August 2016

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Murtha Cancer Center (MCC) Retreat  
USUHS, Sanford Auditorium  
Friday, July 29, 2016

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:30 – 8:00 AM</td>
<td>Registration and Continental Breakfast</td>
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<tr>
<td>8:00 – 8:05 AM</td>
<td>Welcome and Opening Remarks</td>
<td>Craig D. Shriver, MD</td>
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<tr>
<td>8:05 – 8:15 AM</td>
<td>Greetings from Leadership</td>
<td>Dean Kellermann/CAPT Elster</td>
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<tr>
<td>8:15 – 8:40 AM</td>
<td>MCC Overview</td>
<td>Craig D. Shriver, MD</td>
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<tr>
<td>8:40 – 9:10 AM</td>
<td>GYN CoE Overview</td>
<td>George Maxwell, MD</td>
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<tr>
<td>9:10 – 9:40 AM</td>
<td>CPDR CoE Overview</td>
<td>Inger Rosner, MD</td>
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<tr>
<td>9:40 – 9:55 AM</td>
<td>NCI Collaboration Update</td>
<td>Dr. Stanley Lipkowitz</td>
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<tr>
<td>9:55 – 10:15 AM</td>
<td>CBCP CoE Overview</td>
<td>Craig D. Shriver, MD</td>
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<tr>
<td>10:15 – 10:30 AM</td>
<td>Break</td>
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<tr>
<td>10:30 – 11:15 AM</td>
<td>Visioning for Future – Research</td>
<td>Craig D. Shriver, MD / Group</td>
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<tr>
<td>11:15 – 12:00 PM</td>
<td>Visioning for Future – Admin/Regulatory</td>
<td>Craig D. Shriver, MD / Group</td>
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<tr>
<td>12:00 – 12:15 PM</td>
<td>Group Photo</td>
<td>Outdoor Quad Area</td>
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<tr>
<td>12:15 – 1:00 PM</td>
<td>Lunch on Your Own</td>
<td>USUHS Cafeteria</td>
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<tr>
<td>1:00 – 1:15 PM</td>
<td>MCC Recognition</td>
<td>Craig D. Shriver, MD</td>
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<tr>
<td>1:15 – 2:15 PM</td>
<td>Visioning for Future – Informatics</td>
<td>Craig D. Shriver, MD / Group</td>
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<tr>
<td>2:15 – 3:15 PM</td>
<td>Visioning for Future – Biobank</td>
<td>Craig D. Shriver, MD / Group</td>
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<tr>
<td>3:15 – 3:45 PM</td>
<td>Discussion / Wrap Up</td>
<td>Craig D. Shriver, MD / Group</td>
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<tr>
<td>3:45 – 4:00 PM</td>
<td>Concluding Remarks</td>
<td>Craig D. Shriver, MD / Group</td>
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