Spring 2022
Developmental Research Awards

Tier 1 — Basic Science

PI: Russell Broaddus, MD, PhD, Joe W. and Evelyn M. Grisham Distinguished Professor

Project Title: Identifying intra-tumoral spatial transcriptional changes in CTNNB1-mutant endometrial cancers: impact of nuclear localization of mutant b-catenin

Abstract
In contrast to most solid tumor malignancies, the mortality rate of endometrial cancer (EC) continues to rise. Current gaps in knowledge of the molecular features that drive poor EC outcomes continue to limit advances. Our group previously identified the importance of the Wnt/ β-catenin pathway in clinically aggressive endometrioid EC, demonstrating mutations in exon 3 of the CTNNB1 gene are associated with worse recurrence-free survival in early-stage patients. Activation of the Wnt/ β-catenin pathway via mutation in CTNNB1 is predicted to drive robust nuclear localization of mutant β-catenin protein, in turn activating transcription of signature genes that promote tumor progression. However, we have also found that nearly half of patients with CTNNB1 mutated EC have minimal to no nuclear localization of β-catenin protein. We hypothesize that patients with CTNNB1-mutated EC and robust nuclear localization of β-catenin protein will have higher levels of Wnt pathway activation and ultimately worse survival. The initial step in addressing this hypothesis is the proposed proof-of-principle study comprised of one specific aim. Specific Aim 1 is to identify local transcriptional differences in CTNNB1-mutant endometrioid EC, comparing regions with high nuclear localization of mutant β-catenin to regions with membrane and cytoplasmic mutant β-catenin. The NanoString GeoMx platform will be used to perform whole transcriptome analysis of 16 CTNNB1 mutant EC. For each EC areas of tumor with high nuclear localization of mutant β-catenin protein and foci with primarily membranous or cytoplasmic protein expression have been microscopically identified.

Tier 1 — Basic Science

PI: Michael East, PhD, Assistant Professor, Pharmacology

Project Title: Defining heterogeneity in kinase expression and dynamics in TNBC patient derived organoids using kinome targeted single cell RNAseq and ATACseq

Abstract
The human kinome consists of over 550 protein and lipid kinases and contributes to nearly every aspect of cellular signaling. Kinase dysfunction is implicated in a diverse array of human diseases, most notably cancer as important drivers of oncogenesis and proliferation. Bulk RNAseq in cell lines, xenografts, and window trials in patients has revealed sweeping changes in kinase expression in response to targeted therapies with striking heterogeneity across treatments and individuals. Transcriptional plasticity of the kinome is a key driver of adaptive and acquired resistance to targeted therapies in the clinic and in pre-clinical models. Kinome reprogramming in response to perturbation is driven largely by epigenetic remodeling of the promoter and enhancer landscapes and is regulated by the open chromatin state. Bulk RNAseq fails to determine changes in kinase expression in subpopulations of a specific cell type or within different cell types in the tumor microenvironment. Established single cell RNAseq (scRNAseq) workflows provide insufficient coverage of the kinome due to generally low kinase expression levels. We have developed a novel, targeted approach for enrichment of kinase cDNAs from 10X Genomics

scRNAseq libraries that significantly enhances coverage and depth of kinome sequencing. We propose to use kinome targeted scRNAseq to define heterogeneity in kinase expression and perturbation dynamics in TNBC patient derived organoids. Combined with 10X Genomics multiome gene expression and ATAC, we will define how kinase expression dynamics integrate with whole transcriptome gene expression changes and how these changes correlate with changes in open chromatin state in the same cells.

Tier 1 — Basic Science

PI: Zibo Li, PhD, Professor, Radiology

Project Title: A Light Shield for Protecting Sensitive Organs Against Cytotoxic Therapeutics

Abstract
Widely overexpressed on prostate cancer tissues, Prostate Specific Membrane Antigen (PSMA) has become an attractive target for prostate cancer management. Despite exciting progress, PSMA targeted therapeutic agents could pose high radiation exposure towards normal organs that express the receptor. In fact, salivary glands (SGs) are often the dose-limiting organ that determines how much radioactivity can be administered, patient eligibility and the treatment outcome thereafter. This application addresses critical needs to reduce radiation exposure to normal organs while maintaining tumor uptake. Previously, PSMA-617 has been developed as a unique ligand to efficiently reduce kidney uptake of PSMA targeted radiopharmaceuticals. We therefore focus on using a “light-shield” approach to protect SGs by constructing a category of radiolabeled PSMA-B12-Cy5 agents. The Cy5 will serve as an antenna to capture long wavelength photons that trigger the cleavage of the B12-radiopharmaceutical from the PSMA-targeting ligand. The resulting agents will be evaluated for stability, PSMA binding affinity, cleavage efficiency and labeling yield. Initial evaluation in PSMA positive animal model will also be performed. Due to the similarity between 64Cu imaging agent and future therapy agents (same construct but labeled with therapeutic isotopes), we will select the most promising agents (high and persistent tumor uptake with low uptake in SGs) and define the optimal treatment course (when and how to administer the light) using positron emission tomography (PET). The success of the proposed approach would solve key issues in PSMA targeted radiotherapeutics (in this case exposure to SGs), which could greatly benefit prostate cancer management.

Tier 1 — Basic Science

PI: Cary Moody, PhD, Associate Professor, Microbiology and Immunology

Project Title: Virus:Host Interactions that Regulate HPV Replication

Abstract
Persistent HPV infections cause multiple human cancers, however there are no antivirals to treat these diseases. An increased understanding of the virus-host interactions that regulate the viral life cycle may reveal novel approaches for therapeutic development. We have shown that the ATM-dependent DNA damage response promotes the recruitment of homologous recombination (HR) repair factors (e.g., BRCA1, Rad51) to HPV genomes to facilitate productive viral replication, which is activated upon epithelial differentiation.

We recently identified a critical role for the ubiquitin ligase RNF168 in productive viral replication. RNF168 is recruited to DSBs by ATM signaling where it catalyzes ubiquitination of histones to recruit DNA repair proteins such as 53BP1. 53BP1 directs repair to error-prone non-homologous end joining (NHEJ) by establishing a barrier to HR. 53BP1 localizes to HPV replication foci, however 53BP1 is

redistributed to the periphery of viral replication foci upon differentiation. How HPV utilizes RNF168 activity to drive viral replication is unclear, although several recent studies have implicated RNF168 in HR repair. The HPV E7 protein interacts directly with RNF168, disrupting repair at cellular DSBs. The E7-RNF168 interaction may allow for preferential recruitment of DNA repair factors to viral genomes, promoting productive replication. The removal of 53BP1 from the core of viral replication foci may aid in this process. Understanding how HPV directs HR activity to viral DNA at the expense of cellular DNA repair will provide insight into mechanisms of viral persistence and genomic instability and may identify novel therapeutic targets to disrupt the viral life cycle.

Tier 1 — Basic Science

PI: Samantha Pattenden, PhD, Associate Professor, Chemical Biology and Medicinal Chemistry

Project Title: Development of a platform for therapeutic target discovery and diagnosis of alternative lengthening of telomeres (ALT) cancers

Abstract
Cancerous cells develop several mechanisms to evade the checks and balances that control growth and replication in normal cells. One of the mechanisms by which tumor cells become immortal is maintaining the length of DNA at the ends of chromosomes called telomeric DNA. Telomeric DNA is maintained by telomerase in ~85% of cancers and by the alternative lengthening of telomeres (ALT) pathway in the remaining ~15% of cancers. The ALT pathway is associated with poor prognosis, but the mechanisms by which ALT is induced are not well understood. ALT cells are frequently associated with the formation of extrachromosomal C-circles, which can be used as a readout for ALT activity. We are developing a high throughput assay to discover inhibitors of the ALT C-circle phenotype and to investigate the utility of monitoring C-circle levels as a blood biomarker for ALT cancers. Successful outcome of this proposal will inform the key protein players in ALT maintenance and reveal new therapeutic targets for ALT positive cancers.

Tier 1 — Basic Science

PI: Philip Spanheimer, MD, Assistant Professor, Surgery

Project Title: Targeting the RET Receptor Tyrosine Kinase in Tamoxifen Resistant Breast Cancer

Abstract
Breast cancer is the most common cancer and the second most common cause of cancer death in women. The majority of breast cancers express the estrogen receptor (ER) and are sensitive to antiestrogen therapy, such as tamoxifen. However, up to one third of ER+ tumors will be unresponsive or develop resistance to antiestrogen, which is the primary cause of treatment failure and death in patients with ER+ breast cancer. Novel therapeutics are needed to improve outcomes for patients with resistant tumors. Several findings demonstrate that expression and activation of the RET receptor tyrosine kinase impacts response to antiestrogen treatment. RET expression in ER+ breast cancer is associated with worse outcome and recurrent tumors that are resistant to antiestrogen express RET at higher levels than primary tumors. We have shown that RET can drive proliferation and ERK/MAPK which is a known driver of resistance to antiestrogen. Further, we showed that inhibiting RET sensitized ER+ cell lines to tamoxifen and that in ER+ xenografts, inhibiting both RET and ER reduced tumor growth more than either agent alone. Study of RET in ER+ breast cancer has been limited by lack of representative, translationally relevant models of ER+ disease. To address this, we have established and validated ER+ breast cancer organoids and obtained ER+ patient derived xenografts which we will use in this proposal to dissect precise mechanisms of how RET impacts sensitivity to antiestrogen in ER+ breast

cancer, and how ER+ breast cancer cells respond to RET inhibition. We hypothesize that high expression of RET in a subset of antiestrogen resistant ER+ breast cancers drives tamoxifen resistance and is a therapeutic target to overcome resistance. In Aim1, we will determine the relationship between RET and response to tamoxifen and the efficacy of targeting RET to slow growth, using ER+ cell lines, organoids, and patient derived xenografts. In Aim2 we will determine mechanisms and biomarkers of response to RET inhibition using a kinase inhibitor bead capture coupled with mass spectroscopy and using supervised analysis of organoid and PDX RNA sequencing based upon sensitivity to RET inhibition. Cumulatively, these studies will determine the preclinical efficacy of inhibiting RET to overcome tamoxifen resistance in ER+ breast cancer and identify patients most likely to respond to anti-RET therapy for biomarker based clinical trials.

Tier 1 — Clinical/Translational

PI: Kathryn Gessner, MD, PhD, Urologic Oncology Fellow

Project Title: Geospatial transcriptomic characterization of urothelial carcinoma in situ (CIS) to decipher cancer biology and enhance therapy

Abstract
Urothelial carcinoma in situ (CIS) is a high-grade precursor lesion to the development of invasive bladder cancer, which is the 5th most common cancer in the US. When present concurrently with a bladder tumor, CIS portends a worse prognosis. Additionally, up to 30-50% of patients recur or progress following the standard therapy for CIS, Bacillus Calmette-Guerin (BCG). CIS grows as a lesion of malignant cells within the urothelium, which is normally only 2-7 cell layers thick, and CIS lesions are typically either not or only minimally thickened. Due to this limited tissue availability, molecular profiling of CIS has been extremely challenging and we lack predictive biomarkers for BCG response. Additionally, global profiling of the CIS tumor microenvironment (TME), which impacts the response to immunomodulatory therapies, has not been performed. Geospatial profiling technologies are the perfect solution to situations where limited amounts of tissue are available for molecular profiling. Therefore, we propose to utilize geospatial transcriptomic profiling to characterize molecular alterations present in both CIS and the TME to decipher cancer biology and enhance therapy. Using this innovative technology, we will characterize spatial differences in the transcriptome and TME between CIS and high-grade non-muscle invasive bladder cancer. We will also identify geospatial characteristics associated with BCG response. Success in these aims will identify molecular factors driving CIS and response to BCG. We will use knowledge gained to compete for extramural funding with the goal of identifying high-risk patients for aggressive up-front intervention and the development of more effective therapies for CIS.

Tier 1 — Clinical/Translational

PI: Joannie Ivory, MD, MSPH, Fellow, Medicine, Division of Oncology

Project Title: Impact of race and age on intrinsic subtype distribution and treatment decisions in hormone receptor-positive metastatic breast cancer

Abstract
Breast cancer is the second leading cause of cancer mortality in women worldwide. Advances in screening tools and treatment options have led to an improvement in breast cancer's 5-year survival rate. Despite an overall improvement in survival, non-Hispanic Black women have the highest death rate. The most significant disparity in outcomes is seen in hormone receptor-positive (HR+), human epidermal growth receptor 2 (HER2) negative disease. In early-stage breast cancer (ESBC), it has been

shown that HR+/HER2- tumors in Black women and younger women tend toward less endocrine-sensitive and poorer-prognosis intrinsic subtypes, a type of heterogeneity hidden by clinical phenotype, but identifiable by gene expression profiling (GEP). Although there are clear benefits of GEP in treatment of ESBC, there is a lack of clinical application in metastatic breast cancer (MBC). The ongoing HARMONY study (NCT03769415) is a single-center, prospective clinical trial that seeks to understand the potential uses of GEP in patients with newly diagnosed MBC. The trial has accrued 232 of 500 participants, and GEP is performed on all tumors using the PAM50 assay to determine the intrinsic subtype. In this proposed sub-study, we will perform a secondary analysis upon reaching approximately 60% of the target sample size (i.e., 300 participants) to address two specific aims: 1) To characterize differences in intrinsic subtype by race and age among newly diagnosed MBC in the HARMONY cohort and 2) To explore if intrinsic subtype differences by race and age are reflected in treatment patterns in newly diagnosed HR+/HER2- disease.

Tier 1 — Clinical/Translational

PI: Kelly Tan, PhD, Postdoctoral Research Fellow

Project Title: Development of a person reported outcomes monitoring and resource bridging intervention for caregivers of bone marrow transplant recipients.

Abstract

Caring for a person receiving a bone marrow transplant (BMT) is an often intensely stressful experience for caregivers (family/friends providing typically unpaid care to a person with a chronic illness). Caregivers provide essential physical, emotional, medical, and logistical support to BMT recipients for after transplant and are often solely responsible for their 24/7 care. Despite their important role in the care of BMT recipients, caregivers of BMT recipients often report declines in their own physical and mental health as a result of caregiving related burden. Patients are required to have a caregiver ready to support them following transplant, and prior to transplant, caregivers are assessed for readiness and capacity. Caregivers often experience high levels of caregiving related stress and accompanying stress related symptoms throughout the time after transplant. However, caregiver health is rarely assessed following transplant. Poor caregiver health can affect a caregiver's capacity to provide support and is associated with poorer long term health outcomes. The purpose of our study is to develop an intervention aimed at addressing caregiver access to care challenges, and the need for more robust caregiver health monitoring. Our multi-disciplinary team will develop a caregiver health focused person reported outcomes and resource bridging intervention (Care4Caregivers) utilizing stakeholder engagement with past caregivers, current caregivers, inpatient BMT clinicians, outpatient BMT clinicians, social work, nurses, and supportive care services.

Tier 1 — Population Science

PI: Alice Ammerman, DrPH, Mildred Kaufman Distinguished Professor of Nutrition

Project Title: Formative study to inform cancer prevention (tobacco and diet) through an interactive digital intervention at Fort Bragg

Abstract

In the US Army, 17% of all service members are classified as obese, and 25% report current use of tobacco. Both health issues negatively impact individuals' cancer risk, pose a threat to US national security, and increase the cost of health care for the Departments of Defense and Veterans Affairs. Obesity may be responsible for almost 20% of cancer malignancies and 40% of all cancers diagnosed in the US are related to tobacco use. In a survey we conducted with Fort Bragg partners, more than 40% of

soldiers identified obesity as a top concern on base. One in 4 soldiers reported currently using tobacco, and nearly 25% of these soldiers started after being stationed at Fort Bragg. Soldiers living in Barracks report a higher prevalence (75%) of tobacco use, and the majority of soldiers report wanting to quit. Few studies have attempted to understand the influences impacting diet and tobacco use on a large military base. Building on a strong and growing collaboration with Fort Bragg leadership, and with a focus on the potential for digital behavioral interventions, we propose a formative study to better understand factors influencing poor diet and tobacco use among Fort Bragg soldiers and beneficiaries. This work will inform and test targeted behavioral nudge messages to be delivered through mobile devices, as well as policy level interventions addressing these behaviors on base. This work will provide background data needed to seek federal and foundation funding such as an R21 (PAR-19-309) or DoD grant (W81XWH18SBAA1).

Tier 1 — Population Science

PI: Chelsea Anderson, PhD, MPH, Biostatistician

Project Title: Care coordination and health after endometrial cancer

Abstract
By the year 2030, the number of U.S. women with an endometrial cancer history is expected to exceed 1 million. The care needs of older endometrial survivors include regular follow-up visits for detection of cancer recurrence, but also the prevention and management of other non-cancer chronic conditions, requiring the involvement of not only oncology care providers (e.g., gynecologic oncologists), but also obstetrician/gynecologists, primary care physicians and other specialists. The resulting complexity of healthcare needs for survivors may lead to fragmentation of care and, ultimately, poorer health outcomes. Care coordination refers to efforts to organize care activities between two or more providers involved in the patient's care to facilitate the appropriate delivery of health care services. Measures of care coordination, which model shared patient networks by connecting physicians with common patients, have been developed using administrative claims data, and have been validated as a means of accurately representing provider communication patterns, but have not been utilized within the endometrial cancer context. We propose to use the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked data resource to investigate claims-based measures of care coordination after endometrial cancer. Specifically, we will examine demographic and cancer-related predictors of greater care coordination and assess whether higher degrees of care coordination during years 1-3 after endometrial cancer diagnosis are predictive of greater adherence to guideline-recommended follow-up for detection of endometrial cancer recurrence. This research will inform the development of targeted interventions that seek to enhance the delivery of endometrial cancer survivorship care and improve patient outcomes.

Tier 1 — Population Science

PI: Matthew LeBlanc, PhD, RN, Assistant Professor, Nursing

Project Title: Patterns of multiple myeloma care and survival in North Carolina: An exploration of the influence of race, place, and time

Abstract
The past two decades have witnessed breathtaking innovations in the treatment of multiple myeloma along with impressive survival improvements, though these innovations have not benefited all patients equally. Significant survival improvement among White myeloma patients has been noted, though survival improvement in Black myeloma patients has been less substantial and largely non-significant.

Research suggests that survival disparities may result from disparities in myeloma treatment receipt. North Carolina is an important venue for studying disparities in myeloma survival and treatment receipt because it is one of the states with the highest myeloma mortality rates in the country, and boasts a robust racial, and geographic variability facilitating such explorations.
Our long-term goal is to reduce cancer care disparities and improve myeloma care for North Carolinians. To accomplish this, first we must better understand the influence of race, place, and time on patterns of myeloma survival and treatment receipt in North Carolina. To that end this project aims to describe survival and induction treatment in North Carolina myeloma patients across racial groups, regions, and time periods and to explore the individual and community level factors that influence these outcomes. Our findings will identify regions of North Carolina with poor myeloma outcomes and describe important contextual factors that influence them. This knowledge will lead to a K99/R00 submission centered on developing and implementing geographically targeted interventions in North Carolina, informed by the knowledge gained from the proposed work.

Tier 2 — Basic Science

PI: Shobhan Gaddameedhi, PhD, Associate Professor, Biological Sciences, NC State University

Project Title: The Role of Circadian Clock in Protection Against Radiation- and Doxorubicin-Induced Cardiotoxicity

Abstract
Despite improvements in the precision of targeted cancer therapy, there are still significant risks of off-target effects that impact patient health and overall quality of life. Cardiotoxicity, for example, is a major concern for treatments like ionizing radiation (IR) and anthracycline chemotherapeutics, with long-term damage leading to heart failure. Novel strategies like chronotherapy have been implemented to maximize treatment efficacy and limit side effects; however, the mechanisms driving favorable outcomes are poorly understood. The principle behind chronotherapy is to harness the 24-hour oscillatory program of gene expression controlled by the circadian rhythm. At certain times of the day, circadian-regulated elements of DNA repair are more efficient in resolving DNA damage. Utilizing this concept, this project seeks to investigate how key circadian clock protein BMAL1 impacts the response of human cardiomyocytes to IR and doxorubicin (DOX). Based on our recently published data and preliminary findings in this proposal, we hypothesize that BMAL1 plays a protective role in cardiomyocytes via pathways of DNA damage repair and cell death against IR and DOX. To test our hypothesis, we will assess BMAL1's role in DNA damage response through ChIP-Seq, RNA-Seq, and Western blotting following IR and DOX treatment. We will also evaluate this system without direct cytotoxic insult using an IR-treated plasmid reporter to assess rates of double-strand (ds) DNA break repair under modified BMAL1 expression. Overall, this proposal will provide a novel mechanism for improved chronotherapy outcome.

Tier 2 — Basic Science

PI: Jesse Raab, PhD, Assistant Professor, Genetics

Project Title: Defining the role of the BAF complex in primary liver cancers

Abstract
Incidence and mortality from primary liver cancer are increasing and few effective therapies exist for this deadly disease. Mutations in genes important for chromatin mediated gene regulation commonly occur in both hepatocellular carcinoma and cholangiocarcinoma, the two most common primary liver cancers. Chromatin regulators have been shown to be key modulators of both sensitivity and resistance

to therapy response, and therapeutic targeting of chromatin regulators is under development for a wide range of cancers.

To uncover chromatin genes that modulate therapy response, we performed epigenome-focused CRISPR screening in the presence of a multikinase inhibitor, sorafenib. We found that disruption of a specific form of the SWI/SNF chromatin remodeling complex, called BAF, led to sorafenib resistance. The BAF complex is frequently mutated in both hepatocellular carcinoma and cholangiocarcinoma. Recent studies show that loss of ARID1A and ARID1B, members of the BAF complex, gives rise to liver tumors with morphologies of both hepatocellular carcinoma and cholangiocarcinoma. Critically, because sorafenib, and other multikinase inhibitors, are the most common treatments for advanced hepatocellular carcinoma, our findings suggest patients with BAF mutations would not respond well to these drugs.

Thus, in the proposed work we focus on understanding this mechanism of resistance, modeling BAF mutant primary liver cancers, and developing new therapeutic targets. In the following two aims we will uncover the mechanisms used by the BAF complex to modulate sorafenib response and identify novel targets of BAF mutant tumors.

Tier 2 — Population Science

PI: Katherine Reeder-Hayes, MD, MBA, MSCR, Associate Professor, Medicine

Project Title: Using Patient-Reported Data to Address Racial Disparities in Cancer Treatment Delay

Abstract
Black-White disparities in both colorectal and breast cancer deaths have widened since the 1980s despite overall improvements in mortality, and exist among patients with similar stages of disease, suggesting that advances in treatment are not equally benefitting Black Americans. Treatment delays are associated with decrements in both breast and colorectal cancer survival, and Black patients bear a disproportionate burden of cancer treatment delay. We have previously demonstrated that racial disparities in breast cancer treatment delay begin at diagnosis and are compounded across the cancer care continuum. The period between diagnosis and treatment initiation may be a window of opportunity to close racial gaps in breast and colorectal cancer mortality. Although automated electronic health record (EHR) systems have shown promise to identify patients with impending delays, the patient voice is missing from these warning systems, and specific barriers to timely treatment are not apparent from automated warning systems alone.
In this proposal, we plan to build on prior research regarding treatment delays to develop and test a brief electronic patient-reported outcome (ePRO) tool that allow patients to self-identify impending delays (Aims 1-2); to compare the performance of ePRO and EHR tools, separately and jointly, for real-time estimation of treatment delay (Aim 3); and to gather preliminary data regarding social risk factors associated with treatment delay (Aim 4) that can be used in conjunction with ePRO and EHR tools to flag patients at risk of delay and cue timely intervention for modifiable treatment barriers in a future, externally funded, randomized interventional study.

Tier 2 — Population Science

PI: Ebonee Butler, PhD, Assistant Professor, Epidemiology

Project Title: An interdisciplinary approach to improve instruments of pre-diagnostic health care in a racially diverse North Carolina population

Abstract
Black women with breast cancer have been known to suffer a higher rate of breast cancer-specific mortality for more than thirty years, with disappointing progress to eliminate these gaps. The Carolina Breast Cancer Study has been studying Black-White breast cancer outcomes disparities for nearly three decades, beginning with etiologic studies (CBCS Phases 1-2) and more recently (CBCS Phase 3, 2008-2013), emphasizing interactions of molecular tumor features with underlying access to care. We suggest that a disease-focus research lens has inhibited our ability to identify correlates of health disparities, by framing women's cancer experiences as beginning at the time of diagnosis. By understanding the pre-diagnostic health care experiences of breast cancer patients, we may be able to better understand race-specific patterns of diagnosis, thereby allowing us to contextualize observed breast cancer outcomes. CBCS is uniquely positioned to disentangle contributions of biology and access to better understand disease outcomes trough interdisciplinary collaborations between public health and the humanities that will allow us to adequately characterize both tumor biology and the health care experiences of study participants. In this pilot study that aims to develop and implement improved measures of individual-level health inequities by identifying pre-diagnostic barriers to care, we hypothesize that racism in health care manifests as decreased agency among Black women in their ability to obtain care, thereby resulting in delayed diagnosis. Distinguishing between tumor biology and healthcare access is critical to closing the breast cancer mortality gap between Black and White women diagnosed with breast cancer in North Carolina.

Tier 2 — Population Science

PI: Lorinda A. Coombs, PhD, FNP-BC, AOCNP, Assistant Professor, Nursing

Project Title: Values assessment tailored for women with metastatic breast cancer and their caregivers: Adaptation and Pilot Study of a Values Assessment Tool (VAST)

Abstract
More than 400,000 women are diagnosed with breast cancer in the U.S. each year; it is the second leading cause of cancer deaths for women in North Carolina. Metastatic breast cancer has numerous treatment options with an average survival of 2-3 years and can involve multiple treatment decisions over the care continuum. Patients and families often have different perspectives from their oncology clinician when making treatment decisions, suggesting the importance of a systematic elicitation of values of patients and their families to ensure value-aligned treatment decisions. There is no standardized approach to values assessment in mBC, a significant gap in patient-centered clinical practice. The goal of this proposed research is to develop, adapt and test a new tool developed from existing tools and stakeholder input—the Values Assessment Tool (VAST), designed to facilitate communication and shared decision-making for women with mBC and their caregivers.

Specific Research Aims are: 1) Using cognitive testing, develop and refine VAST domains and items to integrate patients' and caregivers' perspectives on values communication that inform shared decision making; 2) elicit breast oncology clinician perspectives in refinement and administration of VAST; 3) Conduct a mixed methods pilot with 20 women/caregiver dyads to gather preliminary data on the impact of VAST on decisional engagement, decisional conflict and communication perceptions at baseline and 3 months after administration. Ambulatory clinic encounters will be audio recorded and analyzed to identify the impact of the VAST on the communication of patient and caregiver values, and upon shared decision-making with oncology clinicians.