**The Breast Cancer Puzzle: Using Interactive Media to Help Younger**

**African American Women Understand and Reduce Risks for Breast Cancer**

**RESEARCH STRATEGY**

Despite improvements in breast cancer detection, diagnosis and treatment, over 200,000 US women are diagnosed with the disease each year, and it remains the second leading cause of cancer death among US women. Furthermore, African American women are adversely affected by breast cancer with later stage diagnoses, higher mortality rates than Caucasian women, and more diagnoses before the age of 40 (ACS, 2008). While some of these inequities can be linked to socioeconomic factors, recent research has identified biological differences indicating that African American women younger than 50 are at increased risk for basal-like breast cancer, an aggressive subtype that occurs in 10-15 percent of diagnoses and is particularly aggressive in these women (Millikan, 2008; The Genome Cancer Atlas Network, 2012). For decades, researchers have sought to understand the complexities of breast cancer susceptibility among various populations as well as strategies for reducing risk. Despite these efforts, neither the results of these studies nor risk reduction strategies are widely known among health care providers; and even where providers have knowledge, they lack tools to effectively communicate with younger African American women in ways that meet the women’s needs.

In 2011-12, the UNC Breast Cancer and the Environment Research Program (BCERP) explored African American women’s knowledge about breast cancer to better understand their risk perceptions and found that age, race, and lack of family history of breast cancer contributed to women’s perceptions of low breast-cancer susceptibility(Allicock et al., 2013). Conflicting risk information from family, media, and health providers also lowered women’s sense of risk. Few women felt they had adequate information regarding breast cancer prevention, and a majority desired better access to risk information, particularly as it applied to them *as African American women*. A majority of participants identified electronic media as the most effective way to obtain information about breast cancer and other health issues. The women also emphasized that health communications should be personally relevant, culturally appropriate, and convenient. The goal of this project then is to more effectively reach younger African American women with emerging science on breast cancer risks and risk reduction, using methods identified by the women as most relevant to them. We will accomplish this goal through the following aims:

1. Develop and pilot test an interactive website that incorporates video components
2. Evaluate its effectiveness using built-in analytics
3. Market the site to health care providers and younger African American women

Through collaboration with experts in health informatics from UNC’s School of Information and Library Science (SILS), we expect to improve the translational aspects of the UNC BCERP while also furthering national BCERP communication and outreach goals. This project will rely on active collaboration among UNC BCERP and SILS scientists, our Community Partners and our Community Advisory Committee.

***Progress on Parent Award***

The UNC BCERP is researching the hypothesis that the period following pregnancy is a window of susceptibility and that obesity in this window alters the breast microenvironment, interacting with initiated cells and having a promoting effect on basal-like breast cancers. This research has three aims, which rely on mouse models (Aim 1), in vitro models with human breast cancer cells (Aim 2), and gene expression and histological evaluation of human breast tissue (Aim 3). In a fourth aim, investigators are working with our Community Partner to identify education needs related to tumor heterogeneity and obesity-related breast cancer risks, to implement targeted outreach that addresses these needs and to facilitate bidirectional communication between UNC BCERP researchers and the breast cancer community in North Carolina. We have completed work resulting in six published manuscripts, with three other submitted manuscripts under review. (See Troester biosketch for citations.) Two additional manuscripts are in preparation.

*Progress in Aim 1.* This aim addresses whether diet-induced obesity following pregnancy promotes carcinogenesis in a mouse model of basal-like breast cancer (BBC). C3(1)-Tag mice develop tumors that are phenotypically similar to human BBCs. We completed a study evaluating whether diet-induced obesity in the postpartum window of susceptibility leads to decreased tumor latency and increased tumor incidence in a C3(1)-Tag mouse. To induce obesity, mice were either fed a control, low fat diet (10% kcal from fat), a high fat diet (45% kcal from fat), or a very high fat diet (60% kcal from fat). Tumor latency (palpation of first tumor) was significantly decreased in mice fed high fat (45%) (17.5 weeks; P = 0.0285) and very-high fat (60%) (16.94 weeks; P = 0.0029) diets compared to the 10% low fat diet (18.99 weeks) in the NP group. However, there was no significant difference in latency between the 45% and 60% diets. These findings in animal models recapitulate findings in humans where BBC is associated with obesity. A manuscript reporting these findings is under review. We also established important methods that will be applied in U01 ES019472 (described below).

*Progress in Aim 2*. This aim addresses interactions between cancer cells and obese microenvironments using in vitro models. We developed and employed a coculture system to examine the effects of BBC and luminal breast cancer cell lines on macrophage differentiation and polarization. Results demonstrated that BBCs drive THP-1 monocyte to macrophage differentiation significantly more than luminal breast cancer cells. THP-1 cells (monocytes) exposed to BBC cells in coculture had altered gene expression, with upregulation of both M1 and M2 macrophage markers by quantitative PCR arrays for more than 30 macrophage markers. Consistent with these BBC-induced changes in macrophage phenotype, a distinct pattern of cytokine secretion (measured by cytokine arrays) was evident specifically in macrophage-BBC cocultures, including upregulation of NAP-2, Osteoprotegerin, MIG, MCP-1, MCP-3 and IL-1β. Application of IL-1 receptor antagonist (IL-1RA) to cocultures attenuated BBC-induced macrophage migration. These data were published (Stewart et al., 2012), contributing to an understanding of the BBC-mediated activation of the stromal immune response.

*Progress in Aim 3.*This aim is focused on gene expression and histological changes induced by obesity. Our first analysis of gene expression data focused on obesity-associated patterns (Sun et al., 2011), but observed that age is an important confounder of obesity-gene expression associations. Because non-malignant tissue represents the microenvironment and/or field from which the tumor arises, an improved characterization of the age-related change in normal breast may identify important pathways in the etiology of distinct breast cancer subtypes. To identify age-related changes in normal breast tissue, 96 tissue specimens from reduction mammoplasty patients ranging in age from 14 to 70 were assayed by gene expression microarray. Significant associations between gene expression levels and age were identified and validated in an independent test set provided by BCERP collaborators, Michael Gould and Paul Yaswen. Finally, applying the age-associated signature to publicly available tumor datasets we identified two groups of tumors. The tumors that shared features of ‘younger’ breast tissue had poor survival, providing a biological link between aging of normal tissue and the qualitative patterns of tumor aggressiveness by age at incidence. This manuscript was published (Pirone et al., 2012). Also during year 2, we accessed existing data for metabolomics profiles of tumors, previously collected by Co-Investigator Charles Perou. We hypothesized that BBCs would have unique metabolic microenvironments. Our findings further suggest that metabolic signatures are strongly influenced by stroma. Observed patterns of glucose uptake and utilization are associated with wound response activation. A manuscript describing these findings is in press in *Clinical Cancer Research*.

*Progress in Aim 4.* In the past two years, the Community Partner (CP) conducted focus groups with 57 African American women to understand their knowledge, beliefs and attitudes about breast cancer and breast cancer risk and also interviewed 34 health care providers who serve these women. A manuscript of focus group findings has been accepted for publication, and we are currently analyzing data from the interviews. Based on focus group analysis, the CP has developed a conceptual framework for interactive educational materials targeted at younger African American women and designed for use by health care providers, and this proposal is an outgrowth of our prior work. The CP has also convened the UNC BCERP Community Advisory Committee (CAC), which includes representatives of health agencies, breast cancer advocates and survivors, and health care providers who critique existing and new educational tools and assist BCERP researchers in improving their communication with lay audiences.

In 2012, the UNC BCERP was awarded a $100,000 Opportunity Grant (U01 ES019472), *Premenopausal High Fat Diet, Obesity, and Breast Cancer Microenvironment,* to fund a mouse study that is examining pubertal versus post-partum high fat diet-exposure with and without obesity in two mouse models: one that gains weight and one that resists obesity. Investigators are examining the development of basal-like breast carcinoma and other subtypes and the role of the inflammatory microenvironment. This is a one-year collaborative project with the Michigan State University BCERP (Sandra Haslam, PhD and Rich Schwartz, PhD, Co-PIs). Investigators have started dosing the animals with the carcinogen, and results of this 9-month study are pending.

***Proposed Approach***

We propose to collaborate with SILS faculty and students to develop an interactive breast cancer education website, which will provide immediate, personalized access to emerging science and will educate women about the key risk factors that contribute to an individual woman’s breast cancer risk profile. We will use HTML 5, enabling the site to be accessed through any web-browser, regardless of computer or mobile platform.

Specific Aim 1) Develop and pilot test an interactive website that incorporates video components

Based on research findings from Allicock (2013), we plan to accommodate the target audience’s preferences for online and video formats for learning about and personalizing breast cancer information. At the outset, the research team will outline the key content that should be conveyed to the target audience, and what types of interactions, in what contexts, are expected. Working with SILS, we will construct a website that will act as a portal to deliver information to the target population. This site will include an educational component, as well as material aimed at inducing behavioral change. The content will be captured separately from presentation, with specific presentations expected to be developed for mobile and possibly tablet platforms as well as the initial computer (desktop/laptop) platform. The website will be dynamic and interactive to best engage the young adult audience. The development plan is to design a mockup, which will be shared and critiqued by the full project team. This process will result in a revised design plan, which will be used to build an initial prototype. Using an iterative design process, we will continue to evolve the interface, receiving feedback from the project team, followed by testing with users from the target population, before finalizing a design for the study evaluation. The website will be open, and source code licensed under creative commons attribution-noncommerical-sharealike license, and made publicly available. The website will be developed by a graduate research assistant, under the direct supervision of Dr. Bradley Hemminger, as well as the BCERP team. The CP has previously developed environmental health videos for diverse audiences and plans to produce video clips of UNC BCERP researchers and young African American breast cancer survivors for use on the site ([www.nchealthyhomes.com/?page\_id=181](http://www.nchealthyhomes.com/?page_id=181); <http://www.sph.unc.edu/cehs/asthma_18447_12655.html>).

The UNC BCERP has also developed the conceptual framework that underpins the website: that of a puzzle, with puzzle pieces representing how obesity, family history, age, genetic mutations, exposure to environmental contaminants, pregnancy, breastfeeding and other as-yet-unknown factors assemble as component causes of breast cancer into a completed puzzle that represents a woman’s aggregate risk profile. (See initial graphics in Appendix A.) We envision that the puzzle will engage women, encouraging them to seek information about breast cancer risk factors and providing them with strategies for addressing the modifiable risk factors. As envisioned, a user may click on a specific puzzle piece (such as one marked *obesity*, or any of the featured risk factors) and a current research finding would be revealed (such as *studies show that obesity among women, especially those with large waists, may double a woman’s risk for postmenopausal breast cancer*). The user would then be directed to risk reduction strategies related to that research finding. We plan to explore the option of having women upload their own pictures at the outset, superimposing their image on the puzzle pieces to personalize the content to a greater degree.

This puzzle schematic has been successfully pilot tested with the BCERP CAC and several audiences of African American women to gauge its effectiveness. In all cases, test audiences better understood how individual risk factors came together into an aggregated profile, and they responded with enthusiasm to the idea of an interactive puzzle that would enable further exploration based on individual interests. Additionally, when this concept was presented to the national BCERP consortium in November 2011, other CPs requested copies of the images and expressed a strong desire to see the concept transitioned into electronic media.

Specific Aim 2) Evaluate site effectiveness using built-in analytics

As was done with the original puzzle concept, the UNC BCERP will pilot test the website with its CAC, the BCERP consortium community partners, and a select number of lay health advisors and health care providers.

At this stage, and continuing once the site is fully operational, the UNC BCERP will use quantitative and qualitative data to determine the effectiveness of this website and to further understand the information needs of our target population, focusing on the following parameters, among others: 1) the number of people who access the site in any of its forms and, to the extent possible, their demographic information (race/ethnicity, age, zip code/city); 2) the number of people who seek specific pages in the site (such as strategies for addressing specific risk factors); 3) tracking of risk reduction actions that women record in the site to reduce their risk for breast cancer; and 4) the number of people connecting to the UNC BCERP site or contacting UNC BCERP staff for additional information. To the extent possible, staff will use site-collected data to explore opportunities for additional, directed outreach with the target population.

Specific Aim 3) Market the site to health care providers and younger African American women

When completed, the website will be advertised broadly. We will rely on local channels—such as the CAC and other community contacts, on the UNC BCERP website ([www.sph.unc.edu/uncbcerp](http://www.sph.unc.edu/uncbcerp)), and by the Communications Department of the UNC Gillings School of Global Public Health—as well as national channels, such as the BCERP network and the breast cancer advocacy network. To ensure that African American women younger than 50 are informed of the website, UNC BCERP will use social media, sororities, faith-based organizations and other groups with whom African American women are associated, including outreach and advocacy groups such as the Pink Ribbon Girls, Save Our Sisters (SOS), Sisters Network, local Susan G. Komen for the Cure affiliates and the NC Comprehensive Cancer Advisory Council, among others. We will also work with associations of health care providers to share information about the site and also offer trainings in its use.

***Innovation***

Research shows a growing use of mobile Internet devices to aid in public understanding of health issues and ways to address them, with an estimated 500 million people projected to be using smartphone devices by 2015 to gather health-based information (Jahns et al, 2010). There are few, if any, educational videos and web-based tools that address breast cancer subtypes and depict African American women; and to date, when the search term “breast cancer risk” is entered into the iPhone App Finder application, only four apps are listed. Several of these apps include guidance for breast self-exam, which was discounted as a legitimate breast cancer prevention activity in 2009 by the US Preventive Services Task Force, suggesting that these apps have not kept pace with recent advances in the field. In addition, younger African American women have expressed a desire for electronically available health information, informed by current science and clearly addressing the complex risks that often confuse patients (Allicock et al., 2013). The proposed website is distinct from existing applications and websites in three important ways: 1) it enables personalization so that women can better understand their unique risk factor profiles; 2) it explains that risk factors are identified on a population level and may not play a role in an individual woman's health; and 3) it shows researchers and survivors discussing the science behind basal-like breast cancer and their experiences in surviving the disease. The scientific uncertainty and tension between population and individual level health messages are challenging concepts in risk communication. An interactive risk puzzle—such as the one we propose as a centerpiece of the website—that incorporates multiple risk factors and communicates scientific uncertainty in a tangible, easily comprehensible way has never been developed but would have broad appeal and potential for widespread dissemination. Additionally, UNC BCERP research has shown that although African American women were aware of susceptibility to an “aggressive” form of breast cancer, none of them could name the breast cancer subtype or its risk factors, meaning this approach has the potential to transform knowledge and understanding for a key audience.

***Timeline***

The proposed timeline for developing, piloting and disseminating the interactive website is as follows:

* July-August 2013: Define website content and outline video content needs
* September-November 2013: Draft website, develop and test interactive protocols, seek feedback from project team, make revisions as needed
* November 2013: Share initial outcomes at BCERP annual meeting
* December 2013: Produce videos (includes editing)
* January-March 2014: Pilot test web-based tool with UNC BCERP advisory committee and target audiences (women and health care providers)
* April 2014: Revise as needed, continue dissemination
* May 2014: Advertise broadly, continue dissemination including to BCERP partners across the country

***Benefits to Parent Award and BCERP as a Whole***

Engaging experts in health informatics from SILS will improve the translational aspects of the UNC BCERP while also furthering the national BCERP communication and outreach goals. SILS is currently ranked #1 in the nation in library and information studies and prides itself on educating innovative and responsible thinkers who will lead the information professions. SILS faculty and students create systems, techniques, and policies that advance information processes and services and promote information creation, access, use, management, and stewardship. SILS has a multi-faceted mission, including a focus on **design and development and engagement, in addition to research and teaching. The design and development mission** manifests in interacting systems that include computational components (hardware and software), organizational components (indexes, metadata, ontologies), access components (user interfaces), and policy components. SILS faculty and students develop and evaluate these interacting components in principled and systematic projects and investigations. In addition, its **engagement mission** is motivated by the recognition that information is socially embedded in culture and that real world problems are solved by people armed with knowledge of the past, contemporary information, and tools for exploration and decision making. To SILS, engagement means not only leveraging information and tools beyond the campus, but also that protocols, practices, rights, and responsibilities be defined and defended and that people learn about them in context. This philosophy dovetails with the BCERP engagement philosophy but also expands it significantly by engaging informatics and innovative communications technologies. Bringing this expertise into the BCERP fold should not only improve our ability to develop novel and engaging ways to reach our target audiences, but should also improve our overall understanding of the many ways that emerging environmental health science can inform personal and societal decision making.

***References***

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**Appendix A**

**Prototypes for Proposed Puzzle Educational Tool**

