2009 Awards Compendium

Cycle 15

CALIFORNIA
Breast Cancer
Research Program

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Introduction

"The mission of the CBCRP is to eliminate breast cancer by leading innovation in research, communication, and collaboration in the California scientific and lay communities."

The California Breast Cancer Research Program (CBCRP) is pleased to announce the funding of 58 new research grants that will advance our knowledge about the community impact, biology, detection, and treatment of breast cancer. With these new awards we are investing over $16 million for research projects being performed at 22 institutions across the state.

The CBCRP supports breast cancer research in California from funds obtained through:

- A portion of a 2¢ per pack State cigarette tax
- Contributions from individuals using the State's income tax check-off option
- Donations from concerned community members dedicated to defeating breast cancer

The CBCRP is administered by the University of California, Office of the President, in Oakland. Our overall objectives, strategies, and priorities are developed with the assistance of a volunteer advisory council, which sets program priorities and recommends the grants to be funded. The council consists of 16 members: five are representatives of breast cancer survivor/advocacy groups; five are scientists/clinicians; two are members from nonprofit health organizations, one is a practicing breast cancer medical specialist, two are members from private industry, and one is an ex officio member from the California Department of Health Services breast cancer early detection program, "Every Woman Counts."

The full abstracts of these newly funded grants, as well as those from previous CBCRP funding cycles, can be found on our website: www.CABreastCancer.org.

Special Research Initiatives

In 2005, the CBCRP launched its **Special Research Initiatives (SRI).** This multi-million dollar effort has identified and is pursuing research strategies that increase knowledge about and create solutions to both the environmental causes of breast cancer and the unequal burden of the disease. Through the SRI, we are leveraging California's unique and diverse geographic, population, and research resources to support critical studies that significantly move these fields forward.

From 2005-2008, an external Steering Committee guided the SRI's five-phase strategy development plan to identify and address critical environmental and disparities research topics. In 2007 the CBCRP hosted six stakeholder meetings across California to present results of our review of the science and receive public input on what research topics to pursue. Next, working closely with the SRI Steering Committee and California Breast Cancer Research Program staff, the Strategy Team provided the guidance and expertise to focus the topics and develop the research initiatives.

The CBCRP is funding nine ground-breaking research initiatives to directly address some of the most difficult questions in breast cancer research. This represents California's first state-wide, coordinated research effort to address the gaps in knowledge about disparities in breast cancer and the role of the environment in breast cancer. The following broad areas will be investigated:

- **Disparities:** Combine studies to explore racial and ethnic differences in breast cancer survival; identify demographic measures that will improve understanding of disparities in breast cancer; and study the characteristics of immigration that influence breast cancer risk and survival.
- **Environment:** Develop recommendations for chemical policies that consider breast cancer; create new protocols and methods for chemical testing; and investigate of the role of chemicals in breast cancer across generations.

- **Both Environment and Disparities:** Create statistical models that could provide a new approach to understanding the multiple, interacting factors that impact breast cancer and develop a new model for researching causes of breast cancer that could lead to prevention strategies.

The CBCRP has been reserving 30% of annual research funds for the SRI since 2005. The funding initiated in 2009 represents the initial investment in the planned multi-million dollar effort.

SRI Award Types & Review

In 2008-2009, we released the first calls for applications for this carefully planned, multi-million dollar effort. SRI uses three award mechanisms:

- **Request for Qualifications (RFQs)** to solicit applications to identify the most qualified researcher to conduct studies with specific pre-determined research questions and plans.
- **Program Directed Awards (PDAs)** to fund crucial projects identified during the SRI strategy development proposed by the Steering Committee and approved by the CBCRP advisory council.
- **Request for Proposals (RFPs)** investigator-initiated applications, similar to our Core Funding, responding to a specific initiative topic.

Calls for applications and requests for qualifications for these one-time research opportunities were sent out to researchers across the state and special effort were made to include potential applicants in these areas that have not traditionally been funded by the CBCRP. As shown in Table 1 (below), 24 applications resulted in 14 SRI awards.

Additional SRI initiatives will be funded in 2009-2010. Further details on the SRI program can be found on the CBCRP's website (www.CABreastCancer.org).

The submitted RFPs and RFQs were reviewed and scored for scientific merit by out-of-state external reviewers to minimize possible conflicts of interest, and the final funding recommendations were made by CBCRP's advisory council. In cases where a single application was submitted, careful attention was paid to ensure that the proposal met the goals of the initiative and truly merited funding. The Program Directed Awards were recommended to the CBCRP by the SRI Steering Committee and were programmatically reviewed by the advisory council.

SRI Funding Summary

In our first year of funding, SRI awarded 14 grants. Table 1 summarizes those awards, including the CBCRP research priority addressed by each. Most of the successful applications fall into the Community Impact (eight grants for $1,193,160) or Etiology and Prevention priority issues five grants for $5,989,355), although several investigate topics in both disparities and the environment and therefore could fit into either issue.

Table 1. 2009 SRI award types, priority issues, application submissions and grants by initiative

Amount awarded in 2009 = $7,341,849

Initiative	Award Type	Priority Issue	Applications	Grants Funded	Amount Funded
Chemicals Policy and Breast Cancer	RFQ	Community Impact (Health Policy)	1	1	$159,334
Demographic Questions for California Breast Cancer Research	RFQ	Community Impact (Disparities)	3	1	$430,988
Understanding Racial and Ethnic Differences in Stage-Specific Breast Cancer Survival	RFQ	Community Impact (Disparities)	6	6	$319,541
Biological/Ecological Models of Breast Cancer Causation and Prevention	RFQ	Etiology (& Prevention)	4	1	$229,732
Environmental Causes of Breast Cancer Across Generations	PDA	Etiology (& Prevention)	1	1	$5,000,000
Environmental Exposures and Breast Cancer Among a Large, Diverse Cohort of Women	PDA	Etiology (& Prevention)	1	1	$132,203
New Statistical Models to Address Disease Complexity	RFP	Etiology (& Prevention)	3	2	$627,420
		Community Impact (Disparities)	2	1	$442,631
		Detection, Prognosis & Treatment	3	0	0
Totals			24	14	$7,341,849

AVON Foundation for Women

Seven of the newly funded SRI grants were partially supported by a generous $500,000 gift from the Avon Foundation for Women.

Core Funding

The Core Funding program of the CBCRP offers a variety of awards in broad topic areas, within which researchers can propose their own best ideas for advancing breast cancer research. The development of the priority areas and mechanisms in the Core Funding is modified during the advisory council's priority-setting process.

The main focus areas of the CBCRP's Core Funding are to support:

- **Career development** to train new breast cancer researchers
- High-risk/high-reward **innovative research**
- **Translational research** for practical solutions applied in clinical or community settings
- **Collaborations between community groups and traditional researchers** that focus on breast cancer research questions relevant to communities in California.

Core Funding award types include:

- **Community Research Collaboration (CRC)** awards bring community organizations—such as breast cancer advocates, community clinics, or organizations serving under-represented women—together with experienced scientists to investigate breast cancer problems that are important to that community, using culturally-appropriate research methods. CRC Pilot (18-month) and CRC Full Research awards (three years) are available.
- **Innovative Developmental and Exploratory Awards (IDEAs)** are for promising high-risk/high-reward research. The CBCRP incorporates the "critical path" concept that requires applicants to place their project on a research continuum leading to practical applications. IDEAs are offered to both "junior" and established investigators.
- **IDEA-competitive renewals** allow recently-funded recipients of CBCRP IDEA grants to compete for additional funding if the project has met key milestones and is on a critical path for success.
- **Translational Research** awards support projects that overcome barriers and put prior research knowledge to practical use in the patient or community setting.
- **Postdoctoral Fellowships** are for career development-oriented training under a breast cancer research mentor.
- **Dissertations** fund the completion of dissertation research by either masters or doctoral degree candidates.
- **Joining Forces Conference** Awards support a conference, symposium, retreat, or other meeting to link breast cancer researchers, non-breast cancer investigators, and community members for the purpose of stimulating new ideas and collaborations.

Core Funding Submissions & Review

We received 168 submissions in response to our 2009 Call for Applications for new research grants on breast cancer. They were evaluated, discussed in review committee meetings, and rated for scientific merit by our out-of-state peer reviewers. Joining Forces Conference Award applications were reviewed by our advisory council.

The final tally of application submissions by CBCRP priority issues (i.e., invited research topics) and award types is shown below.

Table 2. 2009 Core Funding application submissions by award type and priority issue

Award Type	Priority Issue				Award Type Totals
	Etiology & Prevention	Community Impact	Detection, Prognosis & Treatment	Biology of the Breast Cell	
Postdoctoral Fellowship	1	1	19	19	**40**
Dissertation	2	1	6	7	**16**
Innovative, Developmental & Exploratory (IDEA)	9	6	48	33	**96**
IDEA-competitive renewal	0	0	2	2	**4**
Translational	1	2	3	0	**6**
Community Research Collaboration (CRC)	0	4	0	0	**4**
Joining Forces Conference	1	0	1	0	**2**
Priority Totals	**14**	**14**	**79**	**61**	**168**

Compared to the previous year (2008/Cycle 14), we received approximately 15 percent fewer applications. The main reasons for reduced application volume were: (1) stricter eligibility requirements for dissertation awards and postdoctoral fellowships, and (2) a severe drop in the volume of community research collaboration awards. However, IDEA applications increased by almost 20% in 2009. In terms of CBCRP priority issues (i.e., broad research topic), 83% of our submissions were in the topics of Detection, Prognosis & Treatment and Biology of the Breast Cell.

The CBCRP made several **changes to the review process in 2009** to reduce costs and increase efficiency. First, we initiated a triage process to reduce the number of applications receiving a full review committee discussion. This resulted in 96 (58%) applications being fully discussed in committee. Next, we eliminated the tertiary level of scientific review for most award types. Finally, we reduced the number of review committees from six in 2008 to four in 2009, and limited the meetings to one-day sessions. Taken together, these and other cost-cutting measures reduced the approximately $450,000 spent for peer review in 2008 to about $125,000 this year.

Finally, the 96 fully-reviewed applications were evaluated for programmatic responsiveness by the CBCRP's 16 member advisory council. There are seven programmatic criteria for each award type. To select applications to recommend for funding, the CBCRP advisory council balanced the scientific merit and programmatic ratings. **All funded applications represent projects of high scientific merit that also address the priorities of the Program.**

Core Funding Summary

Applications offered and accepting funding = **44**
Applications offered funding, but declined = **5**
Overall success rate (44/168) = **26%**

Amount awarded in 2009 = $8,604,239

The two tables below summarize the 2009 Core Funding grant distribution by award type and priority issue.

Table 3. 2009 Core Funding portfolio distribution by award type

Award Type	Number of Applications	Grants Funded (Success Rate)	Amount Awarded	Percentage of Total Funding
Dissertation	16	8 (50%)	$604,247	7.0%
Postdoctoral Fellowship	40	9 (22.5%)	$809,996	9.4%
IDEA	96	19 (20%)	$3,901,192	45.3%
IDEA-Competitive Renewal	4	2 (50%)	$608,000	7.1%
Translational	6	2 (33%)	$1,958,190	22.8%
Community Research Collaboration (CRC)	4	2 (50%)	$672,614	7.8%
Joining Forces Conference	2	2 (100%)	$50,000	0.6%

Table 4. 2009 Core Funding portfolio distribution by priority issue

Priority Issue	Number of Applications	Grants Funded (Success Rate)	Amount Awarded	Percentage of Total Funding
Community Impact	14	7 (50%)	$1,335,139	15.5%
Etiology & Prevention	14	3 (21%)	$1,983,190	23.0%
Biology of the Breast Cell	61	19 (31%)	$3,063,598	35.6%
Detection, Prognosis & Treatment	79	15 (19%)	$2,222,312	25.8%

Comparing the 2009 and 2008 portfolios reveals a number of changes. First, due primarily to cost reductions in the review process, we were able to award nearly $600,000 more in new funding this year. Thus, the number of grants increased from 42 in 2008 to 44 in 2009, and the success rate increased from 21% (2008) to 26% this year. Funding for IDEA grants increased the most (over 75%), addressing one of CBCRP's main programmatic goals to support research innovation. IDEAs and IDEA renewals represented over 50% of our total funding. Our support for translational research and career development topics remained about the same. However, community collaboration grant funding decreased dramatically (over 67%) due to the substantially lower number of CRC applications submitted.

In terms of research topics (priority issues), the basic science areas of Detection, Prognosis & Treatment and Biology of the Breast Cell received almost two-thirds of the 2009 Core Funding. The numbers of applications and funded grants in the Etiology & Prevention and Community Impact topics continue to decline, however this is offset by awards in these areas made under the SRI. The number of dollars spent is also balanced by the translational awards, both of which were funded in the Prevention topic.

Three awards of special interest are supported by revenue received from the voluntary **California State Income Tax Check-off.** They are a postdoctoral award to Yani Lu at the Beckman Research Institute of the City of Hope to investigate risk factors and breast cancer survival in African American and White women; a postdoctoral award to Karin Staflin of the Scripps Research Institute to investigate a new target for treating brain metastasis; and an IDEA award to Arash Naeim at the University of California, Los Angeles to investigate the effect of health literacy on breast cancer treatment in older patients.

Faith Fancher Research Award

Faith Fancher was a long-time television news anchor and personality with KTVU (Oakland) who waged a very public battle against breast cancer. She also was the founding member of the CBCRP Executive Team, which formed in 2001 to help raise the visibility and fundraising profile of our program. Faith passed away in October 2003 after a six-year struggle with breast cancer. In Faith's honor, and to commemorate all that she did for breast cancer education and research, we have created this annual award. The selected grant reflects the values that Faith held most closely and extends the work that Faith did for all women facing breast cancer.

The recipients of the **2009 Faith Fancher Research Award** are Anna Nápoles-Springer (University of California, San Francisco) and Carmen Ortiz (Círculo de Vida) for their community collaborative project, *Nuevo Amanecer: Promoting the Psychosocial Health of Latinas*. This project addresses the issue of culturally and linguistically appropriate support services for Latinas diagnosed with breast cancer. This collaboration will develop a community-based cognitive behavioral therapy intervention for newly diagnosed Spanish-speaking Latinas with breast cancer. The 12-week intervention (*Nuevo Amanecer—A New Dawn*) will be adapted from an evidence-based intervention for non-Latinas. The three-year program will be delivered by trained peers (Latina breast cancer survivors) in convenient community settings, through the Círculo de Vida group in San Francisco's Mission District.

2009 Portfolio Review

Community Impact of Breast Cancer: portfolio summary

Overview: California is comprised of diverse communities differing by multiple characteristics such as ethnicity, culture, language, sexual identity, immigration history, and socioeconomic status. This diversity offers the unique opportunity to investigate disparities and the unequal burden of breast cancer among underserved groups. Critical questions to be addressed include:

- How do poverty, race/ethnicity, and social factors impact incidence and mortality for breast cancer?
- What are the sociocultural, behavioral, and psychological issues faced by women at risk for or diagnosed with breast cancer?
- What services are needed to improve access to care in order to improve quality of life and reduce suffering?

The CBCRP has been supporting Community Research Collaborations (CRC) for 13 years. These partnerships are based on the established principles of community-based participatory research (CBPR), whereby academic and community investigators work together to identify the research question, develop the study design, carry out the research, analyze results, and disseminate information to scientific and lay communities.

In this award cycle, this priority issue will be studied through SRI awards, IDEAs, career development awards, and Joining Forces Conference Awards.

The CBCRP funded ten new projects in 2009 that address our Community Impact priority issue. Three CBCRP research topics are represented in this section:

- **Health Policy and Health Services: Better Serving Women's Needs**
- **Disparities: Eliminating the Unequal Burden of Breast Cancer**
- **Sociocultural, Behavioral, and Psychological Issues Relevant to Breast Cancer: The Human Side**

Community Impact Portfolio

The **health policies** established in Sacramento can have a significant effect on the community. Researchers can help by providing the science to guide evidence-based policies. California is in the process of developing a new approach to regulating chemicals, so it is an ideal time to ensure that any new rules protected Californians from chemicals that could cause breast cancer. **John Balmes** of the **University of California, Berkeley** is leading a project to show those developing **California's new chemicals policy** how to address breast and other hormonal cancers. They will develop an inventory of existing tests for chemicals that affect the biological mechanisms involved in breast cancer and define the tests that still need to be developed. Finally, they will offer recommendations for prioritizing the chemicals to be screened for their potential role in breast cancer.

Given the ethnic and cultural diversity in California, our state is well positioned to research issues related to **disparities in health care related to breast cancer.** Two studies will help us redefine how researchers will address the topic of disparities. **Scarlet Lin Gomez** of the **Northern California Cancer Center** is leading a project to determine how the burden of breast cancer differs between various groups. In collaboration with a panel of experts, she will create and test in multiple languages standard **questions for breast cancer research** on race, ethnic group, migration history, income and education level, disability, sexual orientation, and gender. This will promote a better understanding of who is affected by breast cancer and allow comparisons between and combinations with data from different studies. **Daniel Stram** of the **University of Southern California** will develop innovative statistical techniques to analyze complex genetic data from the ongoing African American Breast Cancer Study; evaluate which methods are most useful, particularly for people of mixed ancestry; and explore susceptibility.

The California Latino population is at increased risk for financial hardships, poor communication with clinicians, job disruptions, body image issues, rejection by partners, fear of recurrence, anxiety, depression, and poor health-related quality of life compared to white women diagnosed with breast cancer. Psychosocial interventions designed specifically for Spanish-speaking Latinas are sorely needed. **Anna Nápoles-Springer** from the **University of California, San Francisco** and **Carmen Ortiz** at **Círculo de Vida Cancer Support and Resource Center** are funded for a community collaborative project to address the issue of culturally and linguistically appropriate support services for Latinas diagnosed with breast cancer. Dr. Nápoles-Springer and Dr. Ortiz will develop a community-based cognitive behavioral therapy intervention for newly diagnosed, Spanish-speaking Latinas with breast cancer. The 12-week intervention (*Nuevo Amanecer*—A New Dawn) will be adapted from an evidence-based intervention previously designed for non-Latinas. The program will be delivered by trained peers (Latina breast cancer survivors) in convenient settings, through the Círculo de Vida community organization.

African Americans are diagnosed with more advanced cancer, experience lower survival and greater morbidity and mortality; and African American breast cancer survivors experience lower health perceptions with diminished physical and functional well-being. These negative outcomes indicate that the support needs of these women are extensive. **Kimlin Ashing-Giwa** and **Carolyn Tapp** from the **City of Hope National Medical Center** and the **Women of Color Breast Cancer Survivors Support Project** received a planning grant to conduct a health-related quality of life study of African American breast cancer survivors to determine the value of peer support groups. The team will compare peer group support vs. hospital/clinic-based support groups vs. non-support group women. During this project they will publish the "Culturally-Informed, Peer-based Breast Cancer Support Group Guidebook" developed from previous CBCRP grant support.

California researchers are uniquely positioned to explore **why some groups of women are more likely to die** even when diagnosed at the same stage, with the same kind of cancer. Principal investigators from eight ongoing studies are collaborating on a pilot project to combine their data and address new and important questions about this disparity. If they are successful, the CBCRP could fund a study of up to $3.9 million to identify these differences, which could lead to ways to reduce breast cancer deaths or prevent the disease. **Anna Wu** from the **University of Southern California** will coordinate the study and also represent the Breast Cancer in Asian American Women Study. The other collaborators are: **Leslie Bernstein** from the **Beckman Research Institute of the City of Hope,** representing Women's CARE Study and In Situ Breast Cancer Study; **Katherine Henderson** from the **Beckman Research Institute of the City of Hope,** representing the California Teachers Study; **Esther John** from the **Northern California Cancer Center,** representing the SF Bay Area Breast Cancer Study; **Marilyn Kwan** from the **Kaiser Foundation Research Institute,** representing the Kaiser Pathways and Life after Cancer Epidemiology (LACE) studies; and **Kristine Monroe** from the **University of Southern California,** representing the Multi-Ethnic Cohort. This project is supported in part by a grant from the Avon Foundation for Women.

The Women's Contraceptive and Reproductive Experiences, Women's CARE study, is a multi-center, population-based case-control study of 2953 white women and 1622 African American women newly diagnosed

with invasive breast cancer. These women have been followed since their breast cancer diagnosis between 1994–1998. **Yani Lu** from the **City of Hope National Medical Center,** working with her mentor, **Dr. Leslie Bernstein,** will investigate a variety of risk factors from the CARE study to see to what extent they explain the racial disparities in breast cancer survival between African American and white women. The specific aims of this project are to determine whether breast cancer survival is affected by a woman's family history of breast cancer, body size measures, exercise before diagnosis, reproductive factors (age at menarche, parity, age at first full-term pregnancy, time since recent birth, and breastfeeding), and exogenous hormone use.

Prior studies have shown that macrophage infiltration into breast tumors is associated with a poorer prognosis. In preliminary studies, **Rita Mukhtar** from the **University of California, San Francisco** has found that 95% of breast cancers from women in West Africa display high macrophage levels compared to only 42% of cases from women seen at UCSF. Furthermore, the levels of macrophages were associated with disease recurrence independently of estrogen receptor status, chemotherapy response, and other clinical features. They also found that patients with breast cancer also have elevated levels of circulating macrophages, suggesting that this may be an important biomarker. In this fellowship project, Dr. Mukhtar will collect breast cancer specimens from African American women, look for pathogenic macrophages and compare blood samples from women in the U.S. and Nigeria in order to identify serum markers that correlate with increased macrophage levels in breast tumors.

The ability of older patients to communicate with healthcare providers in the clinic is a key parameter influencing the success of their treatment. Patients with lower health literacy have trouble understanding and recalling complex medical information, and they are less likely to be active participants in their medical care and participate in decision-making. **Arash Naeim** at **University of California, Los Angeles** will utilize a conceptual model to study patient literacy issues among older women with breast cancer. Prior to a physician interaction, patients will complete a questionnaire assessing socioeconomic status, health status, emotional state, and health literacy. After the interaction with the physician in the actual clinical setting, the questionnaires will assess self-efficacy, risk perception, and comprehension of informed consent if clinical trial is participation is offered. Dr. Naeim will also assess the value of a patient companion as a positive factor in the physician interaction.

Two other grants will focus on other **behavioral and psychological issues** relevant to breast cancer.

Many women diagnosed with breast cancer live as long as cancer-free women of the same age due to advances in early detection and treatment. Thus, quality of life for survivors is becoming increasingly important. One potential complication during the survivorship period is breast cancer-related lymphedema—a chronic condition resulting from lymph node dissection and characterized by irregular swelling of the arm, hand, and/or chest. Thus far, survivors have voiced dissatisfaction regarding their education on lymphedema risk and becoming informed about lymphedema risk reduction strategies from their healthcare providers. **Marilyn Kwan** from the **Kaiser Foundation Research Institute** will investigate the knowledge base of clinicians and their patient referral practices on this subject in a large HMO setting (Kaiser Permanente of Northern California). Most related studies have only collected data on the patient perspective for quality of care and have largely ignored the clinician perspective. Dr. Kwan's information will be gathered from both viewpoints to fully evaluate the clinical management of BCRL. In the Kaiser population of 3.2 million members, there are about 2,100 women diagnosed each year with breast cancer with about 18% of patients subsequently experiencing lymphedema.

Finally, breast cancer patients often suffer from sleep disturbance and daytime sleepiness before, during, and after chemotherapy, and they often have a high incidence of anxiety and depression that increases with age. Insomnia has a host of debilitating consequences that include tiredness, negative mood, inability to enjoy family and social relationships, increased severity of pain, and poor overall health. **Michelle Rissling** at the **University of California, San Diego** is funded for her dissertation research to elucidate the risk factors for insomnia in breast cancer patients. With her mentor, **Dr. Sonia Ancoli-Israel,** the 40 participants in this study will complete questionnaires on sleep, health anxiety, cognitive arousal, compensatory sleep effort, depression, anxiety, and menopausal symptoms. Participants will wear an actigraph activity recorder for three days. The goal is to identify potential targets for intervention during the early course of breast cancer therapy and provide methods for identifying breast patients at risk for insomnia.

Community Impact Grants Listing

Sister Survivor: Evaluating Best Practices in Social Support
Ashing-Giwa, Kimlin, Ph.D. (co-PI)
City of Hope National Medical Center
Tapp, Carolyn (co-PI)
Women of Color Breast Cancer Survivors Support Project
Award Type: CRC-Pilot planning grant
$5,000 (COH) & $5,000 (WOC)

CA Chemicals Policy & Breast Cancer
Balmes, John, M.D.
University of California, Berkeley
Award Type: Request for Qualifications
$159,334

Demographic Questions for California BC Research
Gomez, Scarlet Lin, Ph.D.
Northern California Cancer Center
Award Type: Request for Qualifications
$430,988

Patient and Clinician Knowledge of Breast Cancer Lymphedema
Kwan, Marilyn Ph.D.
Kaiser Foundation Research Institute
Award Type: IDEA
$227,784

Risk factors and breast cancer survival in black/white women
Lu, Yani, M.D.
Beckman Research Institute of the City of Hope
Award Type: Postdoctoral fellowship
$89,996

Macrophages in Breast Cancer Patients of African Descent
Mukhtar, Rita, M.D.
University of California, San Francisco
Award Type: Postdoctoral fellowship
$90,000

Health Literacy in Older Patient's Breast Cancer Treatment
Naeim, Arash, M.D., Ph.D.
University of California, Los Angeles
Award Type: IDEA
$180,890

Nuevo Amanecer: Promoting the Psychosocial Health of Latinas
Napoles-Springer, Anna, Ph.D., MPH (co-PI)
University of California, San Francisco
Ortiz, Carmen, Ph.D. (co-PI)
Circulo de Vida Cancer Support and Resource Center
Award Type: CRC-Full
$349,547 (UCSF) & $313,067 (Circulo de Vida)

Health Anxiety as a Risk for Insomnia in Breast Cancer
Rissling, Michelle
University of California, San Diego
Award Type: Dissertation
$73,855

New Methods for Genomic Studies in African American Women
Stram, Daniel, Ph.D.
University of Southern California
Award Type: Request for Proposals
$442,631

Race & Ethnicity in Stage-specific Breast Cancer Survival
Bernstein, Leslie, Ph.D.
Beckman Research Institute of the City of Hope
Award Type: Request for Qualifications
$33,062

Henderson, Katherine, Ph.D.
Beckman Research Institute of the City of Hope
Award Type: Request for Qualifications
$32,956

John, Esther, Ph.D.
Northern California Cancer Center
Award Type: Request for Qualifications
$29,000

Kwan, Marilyn, Ph.D.
Kaiser Foundation Research Institute
Award Type: Request for Qualifications
$30,480

Monroe, Kristine, Ph.D.
University of Southern California
Award Type: Request for Qualifications
$31,043

Wu, Anna, Ph.D.
University of Southern California
Award Type: Request for Qualifications
$163,000

Etiology & Prevention: portfolio summary

Overview: Although our foundation of knowledge for the basic science aspects of breast cancer (tumor biology) has expanded greatly over the past decade, there still remains a gap in our strategies for large-scale prevention due to uncertainties over the underlying causes of the disease and their relative importance. There is an extensive list of factors associated with increased or decreased risk for breast cancer. However, some of these factors (such as diet) remain controversial; how others affect breast cancer (such as socioeconomic status) remains a mystery, and true causes are yet to be discovered. Etiology/Prevention topics are particularly difficult to address. In 2009 we are attacking the question through eight primarily large-scale funding efforts including our Special Research Initiatives and Core Funding's translational research award.

Etiology & Prevention Portfolio

If a woman was exposed to chemicals years ago, could that cause breast cancer today? **Barbara Cohn** at the **Public Health Institute** is undertaking a five-year, $5 million study to find out if women exposed to certain chemicals while they were developing in the womb are more likely to get breast cancer. Exposure to endocrine disrupting chemicals (EDCs) in the fetus is thought to increase breast cancer risk, yet the decades-long gap to actual breast cancer incidence makes this connection difficult to prove. With rare access to samples taken from pregnant women 40 years ago, Dr. Cohn and her team will look at levels of toxins and breast cancer in the daughters. The prospective nested case control study will measure differences between an estimated 112 cases and 336 controls in CHDS daughters. This project will also look to see if exposures to those EDCs differ between women by race/ethnicity, neighborhood and education.

P**eggy Reynolds** and **Susan Hurley** of the **Northern California Cancer Center** will investigate how we can use California's unique resources to identify breast cancer risk factors across the State. They are undertaking a one-year pilot project to develop methodology that will allow them to augment the California Teachers Study with more diverse members, collect more biological samples, and develop the most feasible and useful study for this unique cohort and data resource. The resulting research questions and study design will be reviewed in 2010 for up to $6 million, multi-year research into the environment's role in breast cancer. This project is supported in part from a grant from the Avon Foundation for Women.

With so many risk factors acting together to cause breast cancer, how can we understand and prevent it? **Robert Hiatt** of the **University of California, San Francisco** will lead a two-year project to develop a model for conceptualizing breast cancer causation and prevention approaches that includes combinations of interacting causes, such as genes, breast tissue structure, hormones, chemicals from the environment, events during development in the womb, diet, immigration history, barriers to exercise due to neighborhood, income and education level, social support, and cultural attitudes about breastfeeding. The result will be an evidence-based tool to improve research design and policy decisions.

To take advantage of new, more powerful computers and software, the CBCRP is funding research teams to develop new statistical analysis strategies and apply them to existing data sets. **David Nelson** of the **Northern California Cancer Center** will examine which, if any, of the thousands of pesticides used in California agriculture pose a risk of breast cancer to our state's teachers. The resulting modeling tool will be made available to other environmental health and breast cancer researchers. **Eric Roberts** with the **Public Health Institute** will use advanced computer power to make breast cancer data more useful for researchers, the public and advocates. His lab will create tools for exploring smaller geographic differences in breast cancer in California, while protecting patient privacy and allowing for the addition of other area-specific characteristics to identify vulnerable communities and generate new research ideas.

Identifying chemicals that increase the risk of breast cancer can lead to public health measures to reduce exposure. To understand which chemicals pose a risk, the CBCRP funded a conference award to **Lawrence Kushi** from the **Kaiser Foundation Research Institute.** A scientific workshop on November 17, 2009, brought together biologists and regulatory toxicologists. The goal is to develop standards for describing changes in mammary gland structure and development, and to recommend chemical tests that regulatory agencies can use to more thoroughly assess their effect on mammary glands. The conference will be held in conjunction with the annual meeting of the National Institutes of Environmental Health Sciences Breast Cancer and Environment Research Centers (BCERC).

As we gain a greater understanding of the risk factors for developing breast cancer, that information must be used to develop strategies to reduce the risk. A soy

isoflavone compound, called genistein, preferentially binds to one type of estrogen receptor (ER-beta) more than to another (ER-alpha) and may inhibit the growth-stimulating effects of activating ER-alpha. Soy isoflavones may act as Selective Estrogen Receptor Modulating agents (SERMs). Epidemiologic studies in Asian populations have found that consuming more high soy-containing foods is associated with lower breast cancer risk.

Anna Wu from the **University of Southern California** will conduct a three-year study to determine whether soy isoflavones supplements can be used to protect women at high risk of developing invasive breast cancer. Dr. Wu's team will conduct a double-blinded randomized study of 100 women of varying ages and ethnicities with DCIS and of women at high risk of developing breast cancer based on BRCA mutations and Gail model scores. Mammographic breast density, MRI breast volume, blood samples, and a breast biopsy will be obtained before and after the study. Subjects will take 25 g of soy protein daily while controls take 25 g of milk protein. Changes in breast density, ER-alpha/ER-beta ratio, and cell proliferation/apoptosis markers will be measured to determine the effectiveness of soy treatment.

During the last decade, new knowledge and technologies have led to recommendations to include breast cancer risk assessment in primary care. Yet, many women still don't know their individual risk, and many physicians haven't integrated risk assessment and discussion into their routine practices largely due to time constraints. Health information technology tools could provide physicians and patients with novel ways to assess breast cancer risk and educate patients.

Celia Kaplan at the **University of California, San Francisco** will test the efficiency of a tablet, PC-based breast cancer risk education (BCRE) intervention in a primary care setting. Patients enter their health information to produce a personalized risk score, patient BCRE feedback report and a referring physician report. This should promote discussion between the patient and physician about breast cancer risk and provide recommendations based on solid data.

Dr. Kaplan's team will conduct a randomized controlled trial over 14 months with 800 patients and 97 physicians. The three participating clinics serve a diverse population of African American, Latina, Asian, and Caucasian women.

Etiology & Prevention Grants Listing

Environmental Causes of Breast Cancer Across Generations
Cohn, Barbara Ph.D.
Public Health Institute
Award Type: Program Directed Award
$5,000,000

New Paradigm of Breast Cancer Causation and Prevention
Hiatt, Robert, M.D., Ph.D., M.P.H.
University of California, San Francisco
Award Type: Request for Qualifications
$229,732

Exploring Disparities, Environmental Risk Factors in Teachers
Hurley, Susan, M.P.H. (co-PI)
Reynolds, Peggy, Ph.D. (co-PI)
Northern California Cancer Center
Award Type: Program Directed Award
$132,203

Breast Cancer Risk Reduction: A Patient-Doctor Intervention
Kaplan, Celia, Dr. P.H.
University of California, San Francisco
Award type: Translational research
$740,690

Mammary Gland Evaluation and Risk Assessment
Kushi, Lawrence, Sc.D.
Kaiser Foundation Research Institute
Award type: Joining Forces Conference
$25,000

Model-building with Complex, High-dimensional Exposures
Nelson, David, Ph.D.
Northern California Cancer Center
Award Type: Request for Proposals
$278,195

Cancer Mapping: Making Spatial Models Work for Communities
Roberts, Eric, M.D., Ph.D.
Public Health Institute
Award Type: Request for Proposals
$349,225

Soy Treatment for High-risk Women and DCIS Patients
Wu, Anna, Ph.D.
University of Southern California
Award type: Translational research
$1,217,500

Detection, Prognosis & Treatment: portfolio summary

Overview: The detection, prognosis, and treatment of breast cancer represent a slowly evolving landscape. Information filtering in from hypothesis-driven basic science is screened for clinical relevance and promising new strategies. Drugs are slowly advancing along the 10+ year "critical path" for translation into practical use. Better early detection and staging/prognosis for breast cancer remains a critical need. The use of combined imaging modalities is aimed at improving both sensitivity and selectivity to reduce unnecessary biopsies. Genetic profiling of tumors in patients continues to move in the direction of true individualized therapy. New information from stem cell biology, immunology, and the refined knowledge of cellular processes, such as DNA repair and hormone signaling, are continually being probed for new detection, prognosis, patient stratification, and novel treatment potential.

The CBCRP funded 15 new grants in 2009 to advance our Detection, Prognosis, & Treatment priority issue. Two of the CBCRP's research topics are represented in this section:

- **Imaging, Biomarkers, and Molecular Pathology:** Improving Detection and Diagnosis
- **Innovative Treatment Modalities:** Search for a Cure

Detection, Prognosis & Treatment Portfolio

Two newly funded projects focus on advancing early detection imaging technologies.

Much research effort is being made to improve two-dimensional X-ray mammography and MRI images, such that either 3-dimensional or tomography (imaging by sections) can improve changes of detecting a breast tumor in the breast. **Jacob Nebeker** at the **University of California, San Diego** is funded for a dissertation award to adapt a conventional ultrasound system to produce "speed of sound" ultrasonic images. This approach is especially amenable to improve detection in dense breast tissue (which is present in most pre-menopausal women). Thus, speed of sound tomographic images of the breast can resemble those of computed tomography (CT), but with somewhat lower resolution. The project complements a current CBCRP grant to Mr. Nebeker's mentor, **Dr. Thomas Nelson,** to develop a dedicated ultrasound breast imaging instrument.

Imaging technologies also have the potential to assess treatment response in patients both in terms of tumor shrinkage and any preceding cellular changes. **Lisa Singer** from the **University of California, San Francisco** will compare two magnetic resonance imaging (MRI) technologies for their ability to assess neoadjuvant (prior to surgery or radiotherapy) chemotherapy response. The hypothesis is that tumor cell death as a result of neoadjuvant chemotherapy will increase localized water movement, which they can detect with a specific type of MRI and develop into a future clinical application. An advantage of the novel MRI technology is to eliminate the need for injected contrast agents to produce an image. Thus, the ability to monitor tumor physiological changes prior to actual tumor shrinkage would give clinicians a much greater lead time in evaluating an effective therapy.

Once cancer is detected there are numerous staging, treatment choices/failures, and survival/recurrence issues that create uncertainties in the eventual outcome for the disease and impact quality-of-life issues for the patient. Four new CBCRP innovative projects hope to advance our understanding into critical issues associated with treatment.

The widespread use of sentinel node biopsy has greatly reduced the need for more extensive axillary lymph node dissection as a method for breast cancer staging. Women subjected to axillary lymph node dissection are at risk for lymphedema (arm swelling), which is both painful and increases the risk for serious infection. **Stephen Chen** at the **University of California, Davis** will conduct a clinical trial to evaluate the use of axillary reverse mapping (ARM) to identify and preserve lymphatic channels and nodes draining the arm. When ARM is used as an adjunct to axillary lymph node dissection, it may reduce lymphedema incidence and result in improved quality of life. Dr. Chen has estimated that about 31% of breast cancer patients currently have node-positive disease, so the potential of ARM to improve axillary lymph node dissection is substantial. In fact, it is estimated that about 400,000 women in the US are currently suffering lymphedema as a result of breast cancer therapy.

Cancer patients still mainly receive broad-spectrum, non-specific chemotherapy, and even patients receiving newer targeted drugs often have decreased response or develop drug resistance. New approaches and technologies are needed to identify those tumors responsive or resistant to various drugs. **Trent Northen** at **Lawrence Berkeley National Laboratory** has developed methods for detection of sphingolipids in breast cancer cells and tissue slices using a state-of-the-art mass spectrometry approach, called Nanostructure-Ini-

tiator Mass Spectrometry (NIMS). Sphingolipids, often thought of only as cell structural components, have important roles in signal transmission and cell recognition; and, importantly, are associated with reduced sensitivity to programmed cell death and increased expression of drug-resistance p-glycoproteins. Working with a breast cancer cell line library developed by **Dr. Joe Gray,** they will create sphingolipid metabolite profiles. The data will be mapped to tumor tissues sections from patient samples to create "pathology-type" (microscopic) images showing the distribution. The ultimate goal is the able to use this technology to screen breast cancers prior to treatment to inform drug selection by predicting potential response and possible future resistance to specific drug therapy.

Little is known about the survival of newly diagnosed (de novo) patients with metastatic breast cancer vs. patients where metastatic disease recurs after a disease-free period. **Sumanta Pal** at the **Beckman Research Institute of the City of Hope** will investigate whether there is a difference in survival between two groups; and, secondly, if there is a difference in survival before and after the introduction of paclitaxel. Information from this study may be the first to indicate differences in survival trends with chemotherapy in these two disease processes and could ultimately lead to a change in the current therapeutic approach for both. Furthermore, this research could serve as the rationale for laboratory explorations of biological differences between de novo and recurrent metastatic breast cancer; perhaps yielding distinct, novel drug targets for both.

Finally, the CBCRP continues to support exploration into the intraductal approach to detect and treat breast cancer. **Dixie Mills** at the **Dr. Susan Love Research Foundation** received a conference award to support the 6th Symposium on the Intraductal Approach to Breast Cancer that was held on February 19-21, 2009, in Santa Monica. Topics ranged from inflammation, breast endoscopy, breast biology, and the potential for intraductal-based treatments. The diverse participants included more than 100 oncologists, epidemiologists, biostatisticians, surgeons, pathologists, radiologists, endocrinologists, and breast cancer advocates.

The stem cell theory for breast cancer continues to be intensively studied as the new approach to understanding such disease aspects as tumor cell heterogeneity, resistance to therapy, the "seeds" of metastasis, and disease recurrence after seemingly successful therapies that shrink tumors. Although amenable to study in model systems, such as mice, the ability to isolate breast cancer stem cells from patient samples had proven difficult and controversies exist in this field of research. Three new CBCRP-funded grants focus on exploiting stem cell biology in the therapeutic direction.

First, we need new research tools to isolate and target breast cancer stem cells. **Claudia Gottstein** from **University of California, Santa Barbara** is using her expertise in nanotechnology to explore a novel method of isolating tumor stem cells. Her technology-oriented approach is to create combinatorial libraries from circulating tumor cells isolated from the peripheral blood of patients who are in remission from breast cancer. Then, Dr. Gottstein and collaborators will test candidate antibodies using tumor samples having co-expression of CD44, a potentially useful stem cell biomarker. If successful, this project would simultaneously validate the stem cell hypothesis (at least in the context of circulating tumor cells), identify useful tumor antigens for future study, and develop new antibody reagents for additional projects.

Although it may be difficult to isolate breast cancer stem cells, new therapies could be developed to better sensitize the stem cell-like tumor population to make them more sensitive to other treatments. **Frank Pajonk** at the **University of California, Los Angeles** has been awarded two additional years of IDEA funding to explore a functional marker, namely low proteosome activity, characteristic of breast cancer stem cells. The function of the proteosome within cells is to degrade unneeded or damaged proteins by proteolysis. With further study of how tumor stem cells reduce their proteosome activity to lower their sensitivity to radiotherapy, Dr. Pajonk is in a position to identify new therapy targets, perhaps utilizing existing drugs or other compounds in development.

Finally, **Xiaohua Wu** at the **Scripps Research Institute** will analyze cancer stem cell populations for defects in DNA repair pathways, and also determine the efficacy of multiple clinical trial stage HDAC (histone deacetylase) inhibitors to sensitize breast cancer stem cells to chemotherapy drugs and/or radiation. HDAC enzymes remove acetyl groups from histones, which increases their DNA binding activity to condense chromatin and reduce transcription of various genes. The goal is to develop proof-of-principle that targeting DNA repair pathways combined with a screen of the many HDAC inhibitors currently in clinical trials will better target stem cells. Importantly, useful therapeutics may have been overlooked in prior studies, since they are traditionally evaluated for tumor shrinkage in short-term assays that could easily miss significant effects on the small, but critical, tumor stem cell population.

Two newly funded projects explore novel approaches for immunotherapy of breast cancer.

Brunhilde Felding-Habermann at the Scripps Research Institute speculates that the immune repertoire of healthy elderly (over 80 years old) individuals will contain antibodies that are protective against cancer devel-

opment and, if identified, these antibodies may provide a novel approach to inhibit breast cancer growth in patients. Dr. Felding-Habermann is funded to develop an antibody library from the genes of the "Wellderly", a group of 1,000 healthy octogenarians. The risky element is the assumption that Wellderly breast cancer antibodies exist. Nevertheless, they will test antibodies for their ability to inhibit the growth of a cell line panel of inflammatory breast cancer. To complement this analysis, they will conduct a functional profile of the changes that occur with disease progression, identify determinants that seem to confer an advantage to the tumor, and look for overlap with tumor targets identified by screening the Wellderly antibody library.

As new information emerges on the immune system, especially the discovery and role of chemokines (e.g., chemoattractants to guide the migration of cells), more testing is required to find potential new ways of attacking breast cancer without resorting to exogenous non-specific chemotherapy or radiotherapy. **Russell Pachynski** at the **Palo Alto Institute for Research & Education** will study chemerin, a recently described chemo-attractant initially isolated from human inflammatory fluids (malignant ascites and rheumatoid synovial fluid). Chemokine-like receptor 1 constitutes the main cellular receptor for chemerin, and is expressed by macrophages, natural killer cells, and immature dendritic cells. Dr. Pachynski's postdoctoral fellowship is aimed at evaluating chemerin as a novel immunotherapeutic agent using a mouse model of breast cancer.

Novel therapies or potential tumor drug targets are the focus of four newly funded grants.

Natural compounds and their derivatives still represent a tremendous untapped, potentially safer, resource for drug discovery and development. **Jennifer Smith** from **University of California, Santa Barbara** will study the mechanism of action of eribulin, a synthetic analog of the natural compound, halichondrin B from the marine sponges. Eribulin disrupts cellular microtubules by inhibiting their growth and affecting cell division. Ms. Smith in her dissertation research will determine how eribulin activity is influenced by stathmin, an important regulatory protein of microtubule dynamics. Working with her mentor, **Dr. Leslie Wilson,** she will alter the amounts of stathmin in cells and determine the effects on erubulin activity, microtubule dynamics, and breast tumor cell proliferation.

Cellular DNA repair mechanisms are an attractive target for developing new breast cancer therapies. Although a relatively few number of women have heritable defects in BRCA1 and BRCA2, many other patients with sporadic cancers show "BRCAness"—that is, traits shared with those occurring in either BRCA1- or BRCA2-mutation carriers. **Kyoko Yokomori** at the **University of California, Irvine** is funded to isolate and study small molecule inhibitors of condensin-1, a dual-mechanism target because it is involved both in chromosome organization during mitosis and in DNA repair. Condensin-1 interacts with PARP-1, which is being intensively studied due to the fact that BRCAness cancers rely on PARP-1 as a sole means of DNA repair. Dr. Yokomori hopes to develop condensing-1 inhibitors that could enhance the activity of PARP inhibitors currently in clinical development.

Cindy Benod from the **University of California, San Francisco** is funded for a postdoctoral fellowship to develop inhibitors of LRH-1 (liver receptor homolog-1), a novel protein commonly found at high levels in breast tumor cells and surrounding adipose tissue. New information indicates that LRH-1 both enhances aromatase production (the only enzyme that converts androgen to estrogen) and controls the genes for two cyclins (which control the progression of cells through the cell cycle)—both of which are thought to be important in tumor growth. Thus, the discovery of LRH-1 specific inhibitors would provide a new route to block aromatase, and Dr. Benod's research on cyclins would provide additional mechanistic information for future studies.

Finally, estrogens are hormones that bind to estrogen receptors that were once thought to occur only in the cell nucleus, and the detection of estrogen receptors in the nucleus is a basis for treatment decisions. However, other studies show that alternate, membrane-associated estrogen receptors (mER) play important roles in activating signaling cascades critical to other aspects of tumor growth. **Richard Pietras** at **University of California, Los Angeles** is funded for an IDEA project to study patient samples for the presence of mER and develop useful clinical test to quantify mER and compare its expression to nuclear ER. These studies could proved to be paradigm-shifting, since only about half of advanced breast cancers with expression of ER (and/or PR) respond to endocrine therapy, indicating a need for improved ER assays designed to correlate not only nuclear ER, but also mER with patient outcome.

Detection, Prognosis & Treatment Grants Listing

Compounds Blocking Assembly of LRH-1 in Breast Cancer
Benod, Cindy, Ph.D.
University of California, San Francisco
Award Type: Postdoctoral fellowship
$90,000

Reducing Surgical Morbidity of Breast Cancer Staging
Chen, Steven, M.D.
University of California, Davis
Award Type: IDEA
$149,983

Combating Breast Cancer with the Wellderly Immune Repertoire
Felding-Habermann, Brunhilde, Ph.D.
Scripps Research Institute
Award Type: IDEA
$284,850

Antibody-based Targeting of Breast Cancer Stem Cells
Gottstein, Claudia, M.D.
University of California, Santa Barbara
Award Type: IDEA
$150,000

6th Symposium on the Intraductal Approach to Breast Cancer
Dixie Mills, M.D.
Dr. Susan Love Research Foundation
Award Type: Joining Forces Conference
$25,000

Sound Speed Tomography for Early Breast Cancer Detection
Nebeker, Jakob
University of California, San Diego
Award Type: Dissertation
$74,392

Metabolite Imaging to Identify Drug Resistant Breast Cancer
Northen, Trent, Ph.D.
Lawrence Berkeley National Laboratory
Award Type: IDEA
$172,237

Chemerin as an Immunotherapeutic Agent in Breast Cancer
Pachynski, Russell, M.D.
Palo Alto Institute for Research & Education
Award Type: Postdoctoral fellowship
$90,000

Modulation of Breast Cancer Stem Cell Response to Radiation
Pajonk, Frank, M.D., Ph.D.
University of California, Los Angeles
Award Type: IDEA renewal
$250,000

Survival in de novo and recurrent metastatic breast cancer
Pal, Sumanta, M.D.
Beckman Research Institute of the City of Hope
Award Type: IDEA
$249,000

Membrane-associated Estrogen Receptors in Breast Cancer
Pietras, Richard, M.D., Ph.D.
University of California, Los Angeles
Award type: IDEA
$150,000

Diffusion-Weighted MRI in Monitoring Breast Cancer Treatment
Singer, Lisa
University of California, San Francisco
Award Type: Dissertation
$76,000

A Predictive Factor for Eribulin Treatment of Breast Cancer
Smith, Jennifer
University of California, San Francisco
Award Type: Dissertation
$76,000

Targeting DNA Repair Function of Breast Cancer Stem Cells
Wu, Xiaohua, Ph.D.
Scripps Research Institute
Award Type: IDEA
$284,850

Inhibitors of Condensin I as Chemotherapy for Breast Cancer
Yokomori, Kyoko, Ph.D.
University of California, Irvine
Award Type: IDEA
$100,000

Biology of the Breast Cell: portfolio summary

Overview: To understand the origin of breast cancers, more research is needed on the pre-cancerous, causative events in the normal breast. In breast development, cell populations must coordinate migration, proliferation, and apoptosis (cell death) over space and time. In cancer progression these processes become deregulated, initially at the genetic level that leads to the physiological changes associated with malignancy. An inability to recognize and properly repair damage to DNA that occurs in normal cell physiology and enhanced by environmental factors is recognized as driving force of cancer progression. An emerging paradigm identifies progenitor stem cells as the key to the origin of tumors. Stem cell populations reside in body organs to provide the raw material for tissue regeneration, repair, and for the cyclic proliferation of breast cells in response to hormones and pregnancy. If this paradigm proves correct, then only a small fraction (1-2%) of cells in a tumor mass retain stem/progenitor cell properties, and these "cancer stem cells" must be selectively targeted to achieve an effective eradication of the disease.

The recent achievement of generating induced pluripotent stem cells (iPSCs) derived from differentiated adult cells by modulating four pivotal genes suggests that stem cell transformations related to cancer may involve a very limited number of key initiating events. Importantly, two recent publications supported by CBCRP funding have shed new light on the relationship of stem cells and breast cancer. First, **Dr. Steven Artandi** at **Stanford University** showed that telomerase affects a key Wnt/catenin signaling pathway in stem cell biology and differentiation that may explain a key process in tumor progression. Next, a major new research interest involves the discovery and study of microRNAs which regulate gene expression. CBCRP-funded postdoctoral researcher **Dr. Yohei Shimano** and his mentor, **Dr. Michael Clarke** and other colleagues, also from **Stanford University,** reported that certain microRNAs regulating a key self-renewal factor become decreased both in normal mammary epithelial stem cells and breast tumor-initiating cells. These findings suggest new ways of targeting cancer stem cells.

The CBCRP funded 19 new grants in 2009 to advance research knowledge in our Biology of the Breast Cell priority issue. Two of the CBCRP's research topics are presented in this section.

- **Biology of the Normal Breast:** The Starting Point
- **Pathogenesis:** Understanding the Disease

Biology of the Breast Cell Portfolio

Two newly funded grants explore aspects of normal breast biology relevant to breast cancer. Of course, knowing how cells function in their normal tissues and organs will prove crucial in explaining what goes wrong in cancer. In this respect, stem cells have gained increasing research attention. An entire functional mouse mammary gland can be regenerated using a single mammary stem cell. In fact, recently an entire mouse was generated from using iPSCs derived from the skin of adult animals. Despite these remarkable feats, it is still very difficult to isolate normal mammary or breast cancer stem cells for the mechanistic laboratory studies central to basic science. **Dannielle Engle** at the **Salk Institute for Biological Studies** is funded for a dissertation award to utilize special Wnt signaling reporter mice to define pathways during mammary gland development, which should provide a platform to characterize and isolate mammary stem cells. Under the direction of her mentor, **Dr. Jeffrey Wahl,** and working with other colleagues, Ms. Engle hopes to improve on the current level of mammary stem cell enrichment of only 1 in every 60 cells capable of re-populating a mouse mammary gland. Further, successful completion of this project will serve to identify the key pathways (i.e., definitive molecular markers) that regulate mammary stem cell self-renewal and reveal the actual location of the stem cells within the mammary gland.

Key biological mechanisms are often conserved in evolution, so there is great potential for extrapolating discoveries from lower organisms to humans. Thus, changes in the molecular switches that regulate stem cell proliferation versus differentiation may underlie the pre-neoplastic changes seen in cancer. **Margaret Fuller** from **Stanford University** is an accomplished Drosophila (fruit fly) researcher who will use RNA-interference strategies to test whether mammalian genetic counterparts of specific fruit fly tumor suppressors are required for the switch from proliferation to differentiation in mammary gland stem cell lineages.

Six newly funded grants focus on processes related to breast cancer metastasis.

Cancer cells are surrounded by a complex mixture of blood vessels, inflammatory cells, and different types of connective tissue cells. This supporting stroma is not cancerous, but has been shown to play a crucial role in cancer development and progression. For example, as a person ages, the stromal component of the breast deteriorates and becomes more permis-

sive for altered breast epithelial cells to progress into invasive cancers. In addition, it has been hypothesized that these stromal elements adjacent to tumors contain proteins and cellular genetic changes that could as biomarkers to predict cancer progression, classify tumors, and assess therapy outcome. **Robert West** at the **Palo Alto Institute for Research and Education** used previous CBCRP IDEA funding to develop a novel approach to discover unique types of "stromal reaction patterns" through gene expression profiling of soft tissue tumors (STT). In this approach, STTs are used as a discovery tool to classify various types of breast cancer stromal reaction patterns to the presence of tumors. Dr. West received two additional years of funding to screen 300 DCIS cases for validation that stromal reaction patterns predict disease progression. Thus, it may be possible to modulate stromal components to reduce the progression and invasion potential, especially for early stage cancers and DCIS.

During the metastatic spread of breast cancer, tumor cells must invade and grow in new organ sites that are receptive to metastatic spread. This concept was first put forth in Paget's 1889 proposal that metastasis depends on molecular cross-talk between selected cancer cells (the "seeds") and specific organ microenvironments (the "soil"), which still holds forth today (refined most recently by Dr. Isaiah Fidler). **Per Borgstrom** from the **Vaccine Research Institute of San Diego** will use a combination of intravital video-microscopy (IVM) and gene profiling to better identify the stromal requirements for selective tumor growth in various organ sites. In these studies, Dr. Borgstrom and collaborators will co-implant mouse mammary tumor cells with different stroma, including mammary fat pad, liver, lung, and skin to study primary and metastatic breast tumor growth. Using IVM will allow continuous monitoring of tumor growth and the removal of tumor/stromal tissues at various points of disease progression to analyze the underlying genetic changes in "seed and soil."

Brain metastases are the most feared complication in breast cancer, and occur in nearly 30% of patients. However, there are few animal models to allow researchers to study this process, so our basic science mechanistic knowledge for brain metastasis is minimal. **Karin Staflin** from the **Scripps Research Institute** will study the role of a unique protein, called p32, using unique human breast cancer cell lines that were established from patients with brain lesions. P32 is a multifunctional protein shown to localize to hypoxic/nutrient deprived areas within tumors. It is involved in the regulation of apoptosis (programmed cell death) and autophagy (degradation of a cell's own components), which are key stress responses in tumor cells. In this mouse model system, Dr. Staflin will be able to track brain metastasis by external bioluminescent imaging.

Frances Brodsky from the **University of California, San Francisco** is funded for an IDEA grant to study the role of a possible metastasis protein, called Hip-1 (Huntingtin Interacting Protein-1). Dr. Brodsy's lab will validate the relationship of Hip-1 in breast cancer with studies on a panel of cell lines, use animal models to study Hip-1's influence in forming tumors and metastasis, and screen a chemical library to isolate compounds interfering with the Hip-1/clathrin interaction that might prove useful for therapeutic investigation.

Serine proteases have been shown to be important regulators of breast cancer growth and metastasis and represent about 0.6% of the genes in the human genome. They catalyze one of the most pervasive post-translational regulatory processes in biology; cleavage of other proteins resulting in either activation or inactivation. Despite their fundamental importance, a complete endogenous substrate profile for most human proteases is lacking. An increase in the activity of certain proteases has been strongly linked to tumor spread. **Melissa Dix** from the **Scripps Research Institute** will focus her dissertation research on the urokinase-type

plasminogen activator (uPA), a protease which has proven to be a useful marker for the clinical diagnosis of breast cancer. Using a novel proteomics technology, called PROTOMAP (PROtein Topography and Migration Analysis Platform), developed in her mentor's (**Dr. Benjamin Cravatt**) lab, she will search for novel biomarkers which could then be integrated into a screening platform that would allow early detection of breast cancer in terms of disease progression and metastasis.

It is well documented that breast cancer cells have altered metabolic programs, but the exact role of these metabolic shifts associated with tumor invasion and metastasis remains undefined. Recently it has been reported that the enzymes whose function is to oxidize and degrade proline (a cyclic structure, non-essential amino acid) are pro-apoptotic and can be activated by the tumor suppressor protein, p53. **Adam Richardson** from **The Burnham Institute for Medical Research** will create breast tumor lines with altered endogenous proline biosynthesis pathways to study this underlying proline connection. Dr. Richardson will confirm the alteration of key metabolic pathways, and then test the ability of increased proline biosynthesis to suppress apoptosis in both adherent and non-adherent cell settings. It is thought that metastatic cells are more resistant to the programmed cell death caused by increased cellular proline.

Three newly funded grants study various aspects of cell growth and growth factor signaling.

Most patients treated with selective endocrine receptor modulators (SERMs) (e.g., tamoxifen) or aromatase

inhibitors (AI) will eventually develop resistance, but the underlying mechanisms are unclear. For his dissertation project, **Hei Chan** at the **Beckman Research Institute of the City of Hope** will utilize special tamoxifen and AI-resistant cell lines cell lines developed in the lab of his mentor, **Dr. Shiuan Chen.** Mr. Chan will survey estrogen receptor binding to DNA in these cell lines to detect candidate transcription factors across the entire human genome. Together, they will correlate ER binding sites with bioinformatics analysis using the consensus sequences of other DNA binding proteins along with microarray (gene profiling) data. A comparison of the various resistant cell lines will reveal the differences in estrogen receptor signaling and potentially identify new pathways for therapeutic intervention for drug resistant breast cancers.

MYC is a transcription factor that regulates expression of nearly one-third of the genes in the human genome. Abnormal MYC amplification has been found in approximately 50% of human breast cancers, including those that are hormone receptor-negative. MYC amplification has also been linked to resistance to existing therapies and a decrease in breast cancer patients' survival. However, no targeted therapy currently exists to treat these difficult-to-treat breast cancers having high MYC levels. **Dai Horiuchi** from the **University of California, San Francisco** previously discovered that breast and other cell lines engineered to over-express MYC could be effectively killed by an inhibitor against a protein, called Cyclin-dependent kinase 1 (CDK1), a central regulator of cell division. Dr. Horiuchi, working in his mentor's lab (**Dr. Andrei Goga**), will test a large collection of breast cell lines established from primary human breast tumors, instead of using man-made engineered cells. In follow-up experiments they plan to study associated signaling mechanisms and apoptosis, in order to develop a strategy to target interactions between MYC and CDK1.

Breast cancer cells are highly adapted to resist stress that result from a lack of nutrients, a reduced blood supply (hypoxia), or are caused by radiation and chemotherapy (DNA damage). A molecular chaperone protein, called Grp78, has been identified as a key factor helping breast cancer cells resist stress by mediating a cell pathway, called the unfolded protein response (UPR). **Albert Wong** at **Stanford University** has discovered an epidermal growth factor receptor variant that retains only the C-terminus of the receptor, called mLEEK. Dr. Wong is funded to validate the relationship between mLEEK and Grp78 using breast cancer tumor samples, experimentally alter mLEEK amounts in cell lines, and evaluate a possible mechanistic link to cell growth and apoptosis. If successful, this project could set the stage for future work to generate a monoclonal antibody as a mLEEK inhibitor.

Five newly funded grants involve studies of novel genes and DNA repair processes associated with breast cancer.

Women that inherit a mutated BRCA1 gene have a lifetime risk of 36–85% for developing breast cancer. The large, multi-functional BRCA1 protein has been most studied for its role in DNA double-strand break repair. However, another of BRCA1's tasks is tagging proteins with a small protein called ubiquitin, which leads to protein turn-over inside cells. Interestingly, several inherited BRCA1 gene mutations prevent BRCA1 from ubiquitinating proteins, suggesting the importance of this task in protecting breast epithelial cells from becoming cancerous. To date, little is known regarding how loss of BRCA1's ubiquitin ligase function contributes to breast cancer development, and this has primarily been due to an inability of researchers to identify the proteins tagged by BRCA1. **Sonia del Rincon** from T**he Burnham Institute for Medical Research** will utilize a novel experimental method to identify proteins that become ubiquitinated by BRCA1. This involves probing protein microarrays consisting of glass slides that are spotted with more than 8,000 human protein samples. Any hits will be validated in cell systems, especially to determine whether cells having BRCA1 mutations exhibit shifts in key ubiquitination target proteins

In human cells, normal metabolic activities (oxidation) and environmental factors (UV light and radiation) result in DNA damage at an estimated level of 1 million individual events per cell per day. The BRCA2 tumor suppressor also functions in DNA repair, and the loss of its critical repair function leads to the genome instability that characterizes most cancers. **Damon Meyer** at the **University of California, Davis** will study the function of two BRCA2 accessory proteins, DSS1 and RAD54, using reconstituted test tube conditions. In this setting the purified proteins and portions of proteins are combined, and their ability to catalyze critical steps in DNA repair can be analyzed. This project is unique because so few researchers study BRCA biology using purified proteins.

A fusion gene is a hybrid formed from two previously separate genes. Fusion genes are found in hematological cancers, sarcomas and prostate cancer. These may result in the production of a novel fusion protein with cancer-causing activity. The prototypic example is the BCR-ABL gene fusion in chronic myelogenous leukemia. Importantly, this finding led to the development of the promising cancer drug, Gleevec. In 2005, a prostate cancer-specific TMPRSS2 and ETS fusion oncogene was discovered, which raised the possibility of comparable gene fusions in breast cancer. **Jonathan Pollack** from **Stanford University** is funded to apply a novel DNA microarray approach to discover fusion

genes in breast cancer. The goal is to focus on estrogen-regulated and oncogenic fusion partners by profiling 50 breast cancer cell lines and 150 primary breast tumors. New fusion gene discoveries in breast cancer offer the dual appeal that those producing a functional protein could prove to be a unique target for therapy, while silent fusion genes still offer the potential for developing a useful diagnostic test.

Emerging evidence suggests that disruption of circadian rhythms (the 24-hour cycle in the biochemical, physiological or behavioral processes) and circadian rhythm genes may play a significant role in cancer. Epidemiologic studies demonstrate that women with disrupted sleep cycles are more likely to develop breast cancer. In fact, Period 3 (PER3), a mammalian counterpart of the Drosophila circadian rhythm gene period, contains a DNA sequence change that is associated with an increased risk of breast cancer in younger women. **Kuang-Yu Jen** from the **University of California, San Francisco** will study multiple aspects of PER3 in breast cancer, including a role in the DNA damage response in mice, as a prognosis factor in patient samples and for the ability to alter cell sensitivity to hormones or anti-hormone therapies.

Helicases are motor proteins that move along a nucleic acid backbone, separating two annealed nucleic acid strands. They are involved in many aspects of DNA and RNA metabolism, such as replication, recombination, repair, and transcription. **Daojing Wang** at **Lawrence Berkeley National Laboratory** is taking a "systems biology" approach to examine an RNA helicase, called p68, in order to gain a mechanistic understanding of its role in breast cancer, with particular emphases on cell invasion and drug resistance. P68 expression in breast cancer cells could alter their drug and biological responsiveness by reprogramming a variety of signaling/transcription networks.

Three newly funded grants explore various aspects of tumor progression.

Breast cancers are heterogeneous in their clinical course and response to therapy. This is largely due to differences in the underlying biology, with at least five different types (gene-expression profiles) of breast cancers being recognized. Of these, "basal-like" is one of the most aggressive forms (akin to "triple negative" tumors) of breast cancer and is associated a high risk of metastases. **Graham Casey** from the **University of Southern California** will study podocalyxin (PODXL), a cell surface glycoprotein that is expressed on the surface of a wide range of cells. PODXL is best characterized in the kidney, where it functions to maintain open filtration pathways between neighboring podocyte foot processes. Dr. Casey will determine whether PODXL and PODXL signaling are associated with BRCA1 and the development of a basal-like breast cancer stem cell phenotype.

GATA3 is a protein expressed in normal breast epithelial cells to maintain their differentiated state. In human breast tumors, GATA3 expression is lost in malignant cells, which serves as a negative prognostic indicator. **Jonathan Chou** from the **University of California, San Francisco** received a dissertation award to search for microRNA targets of GATA3 that may promote or suppress tumor metastasis. Mr. Chou, working with his mentor (**Dr. Zena Werb**), will profile the microRNA landscape in mammary epithelial cells, then test those that are lost as breast tumor cells progress to the point of metastasis.

Chromatin is the complex association of DNA, RNA, and protein that makes up chromosomes. SATB1 (Special AT Sequence Binding Protein-1) is a genome organizer that works by tethering chromatin elements together. SATB1 expression is absent in normal breast epithelium, but, surprisingly, it is detected specifically in a subset of breast cancers that are aggressive and metastatic. **Laurie Friesenhahn** from **Lawrence Berkeley National Laboratory** will use genomics technologies to discover candidate genes that activate or maintain SATB1 expression in cancer cells. In addition, she will compare this information to other cancer stem cell markers and use mouse models to determine whether SATB 1 amounts affect the underlying metastatic potential.

Biology of the Breast Cell Grants Listing

Breast Cancer Tumor-Stroma Interactions in an In Vivo Model
Borgstrom, Per, Ph.D.
Vaccine Research Institute of San Diego
Award type: IDEA
$284,250

A Molecular Strategy to Inhibit Breast Cancer Metastasis
Brodsky, Frances, D.Phil.
University of California, San Francisco
Award type: IDEA
$150,000

Podocalyxin as a Basal-like Breast Cancer Stem Cell Marker
Casey, Graham, Ph.D.
University of Southern California
Award type: IDEA
$243,676

The Role of Estrogen Receptor in Endocrine Resistance
Chan, Hei
Beckman Research Institute of the City of Hope
Award type: Dissertation
$76,000

Understanding the Role of GATA3 in Breast Cancer
Chou, Jonathan
University of California, San Francisco
Award type: Dissertation
$76,000

Finding BRCA1 Ubiquitinated Substrates in Breast Cancer
del Rincon, Sonia, Ph.D.
The Burnham Institute for Medical Research
Award Type: IDEA
$191,000

Substrate Profiling of Breast Cancer Related Proteases
Dix, Melissa
Scripps Research Institute
Award type: Dissertation
$76,000

A Genetic System for Identification of Mammary Stem Cells
Engle, Dannielle
Salk Institute for Biological Studies
Award type: Award type: Dissertation
$76,000

The Regulation of SATB1 in Metastatic Breast Cancer
Friesenhahn, Laurie, Ph.D.
Lawrence Berkeley National Laboratory
Award type: Postdoctoral fellowship
$90,000

Novel Tumor Suppressors in Breast Development and Cancer
Fuller, Margaret, Ph.D.
Stanford University
Award type: IDEA
$231,058

Targeting MYC in Human Breast Cancer
Horiuchi, Dai, Ph.D.
University of California, San Francisco
Award type: Postdoctoral fellowship
$90,000

Role of Circadian Rhythm Gene Homolog PER3 in Breast Cancer
Jen, Kuang-Yu, M.D., Ph.D.
University of California, San Francisco
Award type: Postdoctoral fellowship
$90,000

Control of BRCA2-mediated Homologous Recombination
Meyer, Damon, Ph.D.
University of California, Davis
Award type: Postdoctoral fellowship
$90,000

Discovery of Fusion Genes in Breast Cancer
Pollack, Jonathan, M.D., Ph.D.
Stanford University
Award type: IDEA
$160,000

Proline Metabolism in Metastatic Breast Cancer
Richardson, Adam, Ph.D.
The Burnham Institute for Medical Research
Award type: IDEA
$284,895

P32: New Functional Target in Breast Cancer Brain Metastasis
Staflin, Karin, Ph.D.
Scripps Research Institute
Award type: Postdoctoral fellowship
$90,000

Role of p68 in Breast Cancer
Wang, Daojing, Ph.D.
Lawrence Berkeley National Laboratory
Award type: IDEA
$165,339

Stroma Expression Patterns in Breast Cancer
West, Robert, M.D., Ph.D.
Palo Alto Institute for Research & Education
Award type: IDEA renewal
$358,000

The Role of EGF Variant mLEEK and Grp78 in Breast Cancer
Wong, Albert, M.D.
Stanford University
Award type: IDEA
$241,380

2009 CBCRP Funding by Institution

The following 22 California research institutions and community organizations were awarded new CBCRP funding in 2008-2009. Community collaborative (CRC) grants are structured as separate awards that are split between institutions.

Institution (city)	# Awards	Amount
Beckman Research Institute of the City of Hope (Duarte)	6	$486,015
Burnham Institute for Medical Research (La Jolla)	2	$475,895
Circulo de Vida Cancer Support and Resource Center (San Francisco)	1	$313,067
Dr. Susan Love Research Foundation (Pacific Palisades)	1	$25,000
Kaiser Foundation Research Institute (Oakland)	3	$283,264
Lawrence Berkeley National Laboratory	3	$427,576
Northern California Cancer Center (Fremont)	4	$870,386
Palo Alto Institute for Research & Education	2	$448,000
Public Health Institute (Berkeley)	2	$5,349,225
Salk Institute for Biological Studies (La Jolla)	1	$76,000
Scripps Research Institute (La Jolla)	4	$735,700
Stanford University	3	$632,438
University of California, Berkeley	1	$159,334
University of California, Davis	2	$239,983
University of California, Irvine	1	$100,000
University of California, Los Angeles	3	$580,890
University of California, San Diego	2	$148,247
University of California, San Francisco	10	$1,981,969
University of California, Santa Barbara	2	$226,000
University of Southern California	5	$2,097,850
Vaccine Research Institute of San Diego	1	$284,250
Women of Color Breast Cancer Survivors Support Project (Inglewood)	1	$5,000

2009 CBCRP Application Evaluation Process & Review Committee Rosters

The CBCRP thanks the participants in our 2009 review committees for their service and dedication to our Program!

In the first phase of the funding process, grant applications were peer reviewed and scored for scientific merit by review committees using a model that follows established practice at the National Institutes of Health (NIH). Each committee is composed of scientists and advocates from outside California. The Committee Chair leads the review process and is a senior researcher. Scientific Reviewers have broad expertise in topics associated with individual applications. Breast cancer Advocate Reviewers are women and men active in breast cancer advocacy organizations, and many of them are also living with the disease. Advocates bring their personal knowledge and commitment to the review process. Each committee also includes a California Advocate Observer, who does not review or vote, but represents California's advocacy community. The observer gains insight into our process and provides feedback to the Program. When additional expertise is needed, an Ad Hoc Member is brought in to the review the particular application.

The CBCRP uses a scientific merit scoring system that separates scientific merit into individual components (e.g., approach, innovativeness, impact). This allows our expert reviewers to better differentiate applications that might otherwise appear identical. Depending on the award type, we use four or five scientific merit components in the peer review process.

In 2009 the CBCRP began triaging Core Funding applications that scored in the lower 50% of a committee's portfolio using the preliminary scores of the assigned reviewers. Applications in the upper 50% of a committee's portfolio all received full committee discussion, as did any applications requested by one of the reviewers. The remaining applications were not discussed by the full committee.

SRI applications and Core Funding applications that were not triaged were rated by the CBCRP's advisory council for programmatic responsiveness. The following criteria were used:

- Responsiveness to the CBCRP's priority issues and award type (or initiative)
- Strength of individual scientific merit component scores (e.g., innovation for IDEA applications)
- Underfunded topic (Core only)
- Quality of the lay abstract
- Inclusion of advocates and sensitivity to advocacy issues/concerns
- Addressing the needs of the underserved
- Critical path/translation (IDEA and Translational Research Award), career plan/mentoring (dissertation, postdoctoral fellowship), or dissemination and translation potential (CRC)

This two-tiered evaluation and funding process ensures both scientific excellence and relevance of the research to the CBCRP's mission and goals.

SRI Chemicals Policy Review Committee

Chair:

Suzanne Fenton, Ph.D.
Research Biologist. Developmental Biology Branch
United States Environmental Protection Agency
Reproductive Toxicology Division
Research Triangle Park, NC

Scientific Reviewers:

Daryl Ditz, Ph.D.
Senior Policy Advisor, Chemicals Program
Center for International Environmental Law
Washington, DC

Ronald Melnick, Ph.D.
Senior Toxicologist & Director of Special Programs
National Institute of Environmental Health Sciences
Research Triangle Park, NC

Ruthann A. Rudel, M.S.
Senior Scientist
Silent Spring Institute
Newton, MA

Advocate Reviewer:
Anna Cluxton, MBA
Vice President, Young Survival Coalition/
Ohio State Univ. Comprehensive Cancer Center
Columbus, OH

SRI Demographic Questions Review Committee

Chair:
Charmaine D.M. Royal, Ph.D.
Associate Research Professor
Center for Genome Ethics, Law & Policy
Duke University
Durham, NC

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Hector G. Balcazar, Ph.D.
Regional Dean, El Paso Regional Campus
UT School of Public Health at Houston
El Paso, TX

Judy Bradford, Ph.D.
Director, Community Health Research Initiative
Virginia Commonwealth University
Richmond, VA

Advocate Reviewer:
Vernal H. Branch
Member, Board of Directors
The Virginia Breast Cancer Foundation
Richmond, VA

SRI Survival Review Committee

Chair:
Blase Polite, MD, MPP
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University of Chicago
Department of Medicine
Chicago, IL

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Columbia University Medical Center
Medicine Hematology/Oncology
New York, NY

Stephanie Smith-Warner, Ph.D.
Assistant Professor
Harvard University
School of Public Health
Boston, MA

Advocate Reviewer:
Jacquelin Holland
Columbus Black Women's Health Project
Westerville, OH

SRI Biological/Ecological Model Review Committee

Chair:
Sarah Gehlert, Ph.D.
Director, Center for Interdisciplinary Health Disparities Research
Professor, School of Social Service Administration
University of Chicago
Chicago, IL

Scientific Reviewers:
Anthony C. Gatrell, Ph.D.
Dean-Designate of the School of Health and Medicine
Lancaster University
Institute for Health Research
Lancaster, UK

Neil Theise, M.D.
Professor, Deptartments of Pathology and Medicine
Beth Israel Medical Center
New York, NY

Advocate Reviewer:
Vernal Branch
Vice President, Board of Directors
Virginia Breast Cancer Foundation
Richmond, VA

SRI Statistical Models Review Committee

Chair:

Julia G. Brody, Ph.D.
Executive Director
Silent Spring Institute
Newton, MA

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University of Michigan, Cancer Center
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Edwin S. Iversen, Ph.D.
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Susan Pelletier
Vermont Breast Cancer Coalition
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CRC/Sociocultural/Health Policy Review Committee

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University of Maryland, Baltimore - School of Medicine
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Maryellen Delapine
Linda Creed Breast Cancer Foundation
Gilbertsville, PA

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Innovative Treatments/Earlier Detection Review Committee

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Professor of Medicine
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Pathogenesis Review Committee

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Etiology, Prevention & Progression Review Committee

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Susan G. Komen Breast Cancer Foundation
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