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 27 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 nearly $20 million for research projects being performed at 16 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 Breast Cancer Research Council (BCRC), which sets program priorities and recommends the grants to be funded. The BCRC 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.”

CBCRP research funding is organized through a number of sub-program units including:

- **Special Research Initiative (SRI)** grants target topics related to environmental causes of breast cancer, disparities in disease incidence and survival in various populations, and novel strategies for prevention based on environmental causes and related to disparities.

- **Community initiatives** supports research grants that incorporate both traditional researcher and community group co-investigators to study a problem specific to a community, but with wider dissemination potential.

- **Core funding** focuses on investigator-initiated traditional grants to support smaller, innovative projects, larger translational grants, and conferences.

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](http://www.CABreastCancer.org).
Overview of CBCRP award types

CBCRP offers a variety of award types:

- **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 12-18 month grants for targeted high-risk/high-reward projects. 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 new 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.

- **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.

- **SRI Program Directed Awards (PDA)** fund specific projects identified during the SRI strategy development process developed by an SRI Steering Committee and approved in 2008 by the CBCRP Council.

- **SRI Requests for Proposals (RFP)** competitively fund investigator-initiated research responding to a specific initiative topic.

- **SRI Requests for Qualifications (RFQ)** identify and support the most qualified researcher to conduct studies with specific pre-determined research questions and plans.

### LOI and application submissions & review

IDEA and Translational Research Awards projects must pass through a letter of intent (LOI) screening process conducted by our Council to select projects that best meet our award type and programmatic criteria. This also reduces the volume of full application to better match our available funds. We view this as a benefit to both the applicants and Program in terms of reducing the effort to prepare full applications and the CBCRP’s corresponding peer review costs.

<table>
<thead>
<tr>
<th>Award Type</th>
<th>LOIs submitted</th>
<th>LOIs approved</th>
<th>Percent approved</th>
<th>Grants funded (% approved LOIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDEA</td>
<td>97</td>
<td>57</td>
<td>59%</td>
<td>10 (18%)</td>
</tr>
<tr>
<td>Translational Research Award</td>
<td>22</td>
<td>7</td>
<td>32%</td>
<td>1 (14%)</td>
</tr>
</tbody>
</table>

After the LOI process the full application statistics are shown in the table below.
Overall, the number of applications was reduced by nearly 50% compared to the previous 2010 cycle. This was due to both the elimination of the career development (dissertation and postdoc) award types and an almost 40% reduction of IDEA applications due to the LOI screening process described above.

Both the application volume and final funding through CBCRP’s SRI efforts are shown in the following table.

### Table 3. 2011 SRI award types, topics & priority issues, number of applications and grants funded by initiative

<table>
<thead>
<tr>
<th>SRI Initiative</th>
<th>Award Type</th>
<th>Topic / Priority</th>
<th>Applications</th>
<th>Grants Funded</th>
<th>Amount Funded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Environmental Exposure &amp; Breast Cancer in a Diverse Cohort</td>
<td>PDA</td>
<td>Environment &amp; Disparities / Etiology</td>
<td>2</td>
<td>1</td>
<td>$4,850,028</td>
</tr>
<tr>
<td>Racial &amp; Ethnic Differences in Breast Cancer Survival</td>
<td>PDA</td>
<td>Disparities / Community Impact</td>
<td>1 collaborative / 4 issues / 4 institutions</td>
<td>5 awards</td>
<td>$2,734,669</td>
</tr>
<tr>
<td>Understanding Behavioral, Social and Physical Environmental Factors and Breast Cancer among Immigrants</td>
<td>RFP</td>
<td>Disparities / Etiology</td>
<td>7</td>
<td>1</td>
<td>$730,192</td>
</tr>
<tr>
<td>Making Chemicals Testing Relevant to Breast Cancer</td>
<td>RFP</td>
<td>Environment / Etiology</td>
<td>10</td>
<td>5</td>
<td>$4,909,249</td>
</tr>
<tr>
<td>California Breast Cancer Prevention Initiatives</td>
<td>RFQ</td>
<td>Environment, Disparities &amp; Prevention / Prevention</td>
<td>1</td>
<td>1</td>
<td>$1,103,827</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td></td>
<td></td>
<td>21 (25)</td>
<td>13</td>
<td>$14,327,965</td>
</tr>
</tbody>
</table>
Table 4. 2011 Core Funding and Community Initiatives grant distribution by award type

<table>
<thead>
<tr>
<th>Award Type</th>
<th>Number of Applications</th>
<th>Grants Funded (Success Rate)</th>
<th>Amount Awarded</th>
<th>Percentage of Total Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDEA</td>
<td>53</td>
<td>10 (18%)</td>
<td>$2,097,729</td>
<td>37.6%</td>
</tr>
<tr>
<td>IDEA-Competitive Renewal</td>
<td>13</td>
<td>2 (15%)</td>
<td>$943,519</td>
<td>16.9%</td>
</tr>
<tr>
<td>Translational</td>
<td>7</td>
<td>1 (14%)</td>
<td>$1,169,860</td>
<td>20.9%</td>
</tr>
<tr>
<td>Community Research Collaboration (CRC)</td>
<td>8</td>
<td>3 (38%)</td>
<td>$1,328,085</td>
<td>23.8%</td>
</tr>
<tr>
<td>Conference</td>
<td>2</td>
<td>2 (100%)</td>
<td>$45,000</td>
<td>0.8%</td>
</tr>
<tr>
<td>Total</td>
<td>86</td>
<td>18 (21%)</td>
<td>$5,584,193</td>
<td>100%</td>
</tr>
</tbody>
</table>

Funding highlights

Three awards are of special interest, and are supported by revenue received from the voluntary California State Income Tax Check-off. They are a Translational Research Award to David Feldman, Stanford University School of Medicine for “Vitamin D and Breast Cancer in Obesity: Therapeutic Trials”; an IDEA grant to Joy Melnikow, University of California, Davis to investigate “Cost-effectiveness Analysis to Inform Breast Cancer Screening Policy”, and IDEA renewal grant to Brunhilde Felding-Habermann, from the Scripps Research Institute for “Combating Breast Cancer with the Wellderly Immune Repertoire.”

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 2011 Faith Fancher Research Award are Kimlin Ashing-Giwa (Beckman Research Institute of the City of Hope) and Carolyn Tapp (Women of Color Breast Cancer Survivors Support Project) for their community collaborative project, Sister Survivor: Improving Access to Survivorship Care Plan. The focus of the project is African-American breast cancer survivors and is based on a CBCRP-funded pilot study that found that many of these women had unmet health care needs. Thus, the investigators propose a peer navigator intervention to evaluate impact on access and adherence to survivorship care planning. They will train, through an evidence based curriculum, 25 peer navigators and then randomly assign 160 participants to two groups, one that provides patient navigation along with standard care and the other providing standard care only.
Special Research Initiatives: new grants

Overview: In 2005, the CBCRP launched its Special Research Initiatives (SRI) to identify and pursue 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, CBCRP is leveraging California’s unique and diverse geographic, population, and research resources to support critical studies that significantly move these fields forward. 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 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 reserved 30% of our annual research funds for the SRI from 2005 to 2009. In this final year of funding for the first phase of the SRI, the CBCRP awarded 13 grants for a total of $13,228,945. With the additional grants funded this year the total SRI projects represent an investment of $21,671,314.

In 2010, the CBCRP decided to expand beyond the environment and disparities, with a new $10 million, five year process that will expand the SRI to include funding for prevention research. An initial award of $1,103,827 supports a partnership to organize the California Breast Cancer Prevention Initiatives.

Special Research Initiatives Portfolio

The CBCRP funded eight SRI projects in the final phase of the first SRI addressing the role of the environment in breast cancer and the unequal burden of the disease.

One of the new awards, "California Breast Cancer Survivorship Consortium," is providing funding for a collaboration between four institutions representing five breast cancer studies. This follows-up on a pilot project, “Race & Ethnicity in Stage-specific Breast Cancer Survival”, in which the researchers successfully identified data that could be pooled and research questions that were both feasible and important. The investigators include: Leslie Bernstein of the Beckman Research Institute of the City of Hope; Scarlett Gomez of the Cancer Prevention Institute of California; Marilyn Kwan of the Kaiser Foundation Research Institute; and Kristine Monroe and Anna Wu of the University of Southern California. Together they are combining their data for 15,000 breast cancer cases to address racial and ethnic differences in survival in four areas: 1. contextual factors, including socioeconomic position, the built environment, and migration; 2. pre-diagnosis physical activity; 3. body size, and 4. co-morbidities, such as hypertension, diabetes and heart disease.

Another pilot project, the Environmental Exposures & Breast Cancer in a Large, Diverse Cohort of Women, will build upon existing breast cancer studies. Despite intriguing animal and other evidence, the potential for chemicals that persist in the environment and in human tissue to affect breast cancer risk is still uncertain. Peggy Reynolds of the Cancer Prevention Institute of California will look at the levels of previously-identified chemicals, such as PCBs and organochlorine pesticides, as well as newer flame retardants in diverse groups of California teachers (both geographically and racially.) This project, “Persistent Organic Pollutants & Breast Cancer Risk”, will analyze blood specimens of 1000 breast cancer cases and 1000 controls to identify disparities in body burdens of these chemicals and explore potentially important “windows” of susceptibility that may be associated with differences in breast cancer risk.

In order to address the need for assays that are relevant to the biological mechanisms of breast cancer, the CBCRP solicited applications to create new or more effective methods for testing chemicals. Five projects were funded, three of which focus on chemicals that interfere with the action and formation of
hormones in the body, disrupting the endocrine system. Although hormones are known to be critical in the development of the breast and important in breast cancer, the impact of endocrine disrupting chemicals in breast cancer has not been definitively established.

The first grant seeks to refine a high-throughput screening assay using a breast cancer cell line that is positive for estrogen receptors and aromatase. Shiuan Chen of the Beckman Research Institute of the City of Hope will test breast cancer-relevant genes as markers of the physiological importance the chemicals identified from the screening assay and identify additional novel markers. In the project, “Biologically Relevant Screening of Endocrine Disruptors”, he plans to confirm the utility of the screening cell line and gene expression signature in the prediction of the effects of endocrine disruptors in the human body.

Next, a team headed by Shanaz Dairkee of the California Pacific Medical Center Research Institute plans to build upon their work that found bisphenol A (BPA) significantly affected six sets of genes that are in human breast cells, including allowing damaged cells to survive and acquire additional defects, functional deficiencies also found within aggressive breast tumors. Their project, “Xenoestrogen-Specific Perturbations in the Human Breast”, will use established cell biology assays to define consistent changes caused by a panel of known xenoestrogens in non-malignant breast cells, thus establishing a basic battery of tests to screen unknown chemicals. They will apply novel technologies and computational approaches to enhance the understanding of xenoestrogen-induced functional changes and facilitate the development of additional tests. Finally, they will develop assays utilizing readily renewable and repeatedly available sources of non-malignant breast cells such as breast milk.

Estrogens are produced by the enzyme aromatase, which is overexpressed in mammary tissue containing a tumor, leading to localized overproduction of growth-stimulating estrogens. Elevated aromatase gene expression in breast cancer is caused by the increased activity of the specific aromatase promoters: pII, I.3, I.4 and I.7. Michael Denison of the University of California, Davis will construct breast cancer cells that contain these four promoters coupled to a luciferase (reporter) gene, causing them to produce light upon exposure to a chemical that stimulates one or more of them in “Cell Bioassays for Detection of Aromatase Gene Activators.” These gene-reporter constructs will be incorporated into the DNA of commercially available breast cancer cell lines, to be characterized and validated by measuring the response to compounds known to stimulate each of the aromatase promoters. Cell constructs that respond to these compounds as would endogenous aromatase will be selected for the screening of various chemicals known or suspected to cause endocrine disruption, including pesticides and flame retardants, and chemicals used in large quantities (e.g., phthalates, bisphenol A.)

In order to explore her hypothesis that environmental agents that increase the risk of breast cancer risk alter the sugar modifications of proteins made by mammary cells, Zena Werb of the University of California, San Francisco will use mouse and human breast tissues in three-dimensional culture systems that model the development of the normal mammary gland. In the project “Biomarkers for Environmental Exposures in Breast Cancer”, they will treat these tissues with environmental chemicals, look for abnormal development, and then for the production of proteins that have altered their sugar modification. Their use of the mouse mammary organoid model system, which undergoes branching like real breast, will test whether chemicals perturb breast cells division, branching, or production of milk proteins. These endpoints influence differentiation and may initiate cancer. Finally, Dr. Werb’s team will use mass spectrometry to look for exposure-related changes in sugars that modify breast proteins that could lead to novel biomarkers for assessing exposure in girls and women.

In a broader approach to chemical screening methods to fill current gaps, Chris Vulpe of the University of California, Berkeley has organized a team to build upon two federally-funded efforts: the US Environmental Protection Agency’s ToxCast program and the National Toxicology Program’s Tox21 program. Because data from these screening programs will be used to prioritize chemicals for further evaluation and regulation, it is important that they include breast cancer relevant tests. In “Building on National Initiatives for New Chemicals Screening”, Dr. Vulpe’s team will select the assays most
relevant to breast cancer from those already validated by ToxCast and transfer these tests into a variety of breast cell models. They will also develop two new assays that represent mechanisms likely to be important in breast cancer. The team will run these assays on about 60 chemicals, comparing the results of chemicals not associated with breast cancer to those of known carcinogens to prioritize assays that are most likely to predict whether a chemical will cause mammary gland tumors in animals.

Elevated and rapidly increasing incidence rates of breast cancer among California Asian Americans (AA) have been masked by rates reported for AAs as a single ethnic group. Scarlett Gomez of the Cancer Prevention Institute of California if being funded to increase our understanding the critical windows of exposure for risk factors like diet and weight gain, and for identifying new risk factors, including infectious exposures, family and community influences, and social stressors related to the process of immigration, being an immigrant, and due to discrimination. In a study “Immigrant Experience and Breast Cancer Risk in Asians”, Dr. Gomez will leverage ongoing recruitment of about 350 Asian American breast cancer cases residing in the Bay Area. She will incorporate existing data on community-level measures from our California Neighborhoods Data System, to relate community factors to individual-level risk factors and breast cancer risk. Other exposure data will be obtained through a telephone interviews. Approximately 700 controls will be recruited using one of four methods, to test the efficiency of each approach.

The CBCRP issued a Request for Qualifications to fund a team to collaborate in developing and implementing a planning process for the second phase of CBCRP’s SRI: the California Breast Cancer Prevention Initiatives. A team led by Tracey Woodruff of the University of California, San Francisco was chosen for the “Partnership to Advance Breast Cancer Research.” Together with the CBCRP, her team will build on the initial SRI strategy development process and work with a range of experts to develop sound and innovative recommendations to the CBCRP’s Breast Cancer Research Council. The result will be a new strategy for researching the priorities established by the Council: the role of the environment in breast cancer, disparities in the disease, and both population- and individual-level interventions.

**Special Research Initiatives Grant Listing**

**California Breast Cancer Survivorship Consortium (5 awards)**

<table>
<thead>
<tr>
<th>Award Type: SRI Program Directed Award</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Bernstein, Leslie, Ph.D. Beckman Research Institute of the City of Hope $435,775</td>
</tr>
<tr>
<td>2. Gomez, Scarlett, Ph.D. Cancer Prevention Institute of California $680,585</td>
</tr>
<tr>
<td>3. Kwan, Marilyn, Ph.D. Kaiser Foundation Research Institute $394,503</td>
</tr>
<tr>
<td>4. Monroe, Kristine, Ph.D. University of Southern California $216,689</td>
</tr>
<tr>
<td>5. Wu, Anna, Ph.D. University of Southern California $1,007,117</td>
</tr>
</tbody>
</table>

**Persistent Organic Pollutants & Breast Cancer Risk**

Award Type: SRI Program Directed Award

Reynolds, Peggy, Ph.D.

Cancer Prevention Institute of California

$4,850,028

**Biologically Relevant Screening of Endocrine Disruptors**

Award Type: SRI Request for Proposal

Chen, Shiuan, Ph.D.
Beckman Research Institute of the City of Hope  
$1,512,000

**Xenoestrogen-Specific Perturbations in the Human Breast**  
Award Type: SRI Request for Proposal  
Dairkee, Shanaz, Ph.D.  
California Pacific Medical Center Research Institute  
$900,000

**Cell Bioassays for Detection of Aromatase Gene Activators**  
Award Type: SRI Request for Proposal  
Denison, Michael, Ph.D.  
University of California, Davis  
$421,680

**Biomarkers for Environmental Exposures in Breast Cancer**  
Award Type: SRI Request for Proposal  
Werb, Zena, Ph.D.  
University of California, San Francisco  
$900,000

**Building on National Initiatives for New Chemicals Screening**  
Award Type: SRI Request for Proposal  
Vulpe, Chris, Ph.D.  
University of California, Berkeley  
$1,175,569

**Immigrant Experience and Breast Cancer Risk in Asians**  
Award Type: SRI Request for Proposal  
Gomez, Scarlett, Ph.D.  
Cancer Prevention Institute of California  
$730,192

**Partnership to Advance Breast Cancer Research**  
Award Type: SRI Request for Qualifications  
Woodruff, Tracey, Ph.D.  
University of California, San Francisco  
$1,103,827
Community Initiatives: new grants

Overview: California is comprised of diverse communities differing by 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 16 years. These partnerships are based on the established principles of community-based participatory research (CBPR). The CRC grants enable academic and community investigators working together to identify a research question, develop the study design, conduct the research, analyze results, and disseminate new information to the scientific and lay communities.

Community Initiatives Portfolio

The CBCRP funded three new community initiatives grants for a total of $1,328,085 that focus on underserved women in either specific ethnic groups or from rural areas of California.

African American breast cancer survivors (AABCS) have greater health care resources needs and poorer outcomes, compared to breast cancer survivors from other ethnic groups. Interventions that address these disparities are needed. The Sister Survivor Coalition with lead Co-PI Carolyn Tapp of Women of Color Breast Cancer Survivors Support Project along with Co-PI Dr. Kimlin Ashing-Giwa from City of Hope National Medical Center will implement and evaluate the impact of a multilevel, multi-session, peer navigator (PN) intervention on access and adherence to survivorship care plan. In this project, “Sister Survivor: Improving Access to Survivorship Care Plan”, 160 AABCS will be randomized to either the intervention group, receiving 4 individual sessions plus an optional booster session, or to the control group that will receive standard care. Within the intervention group, 25 trained PNs will employ an educational, supportive, role-model approach that focuses on providing information, support, access, and coordination.

Rural women often face the barrier of distance and the time involved when attempting to access cancer treatment centers and participating in local support groups following treatment. Recent technological advances offer exciting methods to address disparities in this area. Mary Ann Kreshka and Joanne Hild from Sierra Streams Institute, and Cheryl Koopman from Stanford University will conduct an 18-month CRC pilot study, “At-Home Group Video Calling to Support Rural Women”, utilizing a group-based, video calling intervention to examine its feasibility and acceptability among 32 breast cancer survivors. Women will be randomized to receive either the 8-week group video calling intervention based on the Supportive-Expressive group model, or to receive educational materials on exercise and nutrition.

The participation rates for ethnic minority individuals in clinical trials (CT) has remained low, despite federal regulations mandating their inclusion. Numerous patient, provider, and institutional barriers to participation exist. Maria Caprio of the Shanti Project, Inc and Galen Joseph of University of California, San Francisco have partnered to develop a CT education program for Shanti Care Navigators to deliver to their clients and a protocol for navigator-facilitated access to BCT.org. In this 18-month CRC pilot study, “Clinical Trials Education and Access for Underserved Women”, qualitative data such as key informant interviews (N = 8) and in-depth, in-person open-ended (e.g. ethnographic) interviews with SCN (N = 4) and Shanti clients (N = 24) will be collected to inform development of
educational materials and the CT access protocol. The trial will further include pilot testing of the materials and protocol among 24 Shanti clients.

Community Initiatives Grants Listing

Sister Survivor: Improving Access to Survivorship Care Plan
Award Type: CRC-Full
Ashing-Giwa, Kimlin, Ph.D. (co-PI)
City of Hope National Medical Center
$858,880
Tapp, Carolyn (co-PI)
Women of Color Breast Cancer Survivors Support Project
$93,750

Clinical Trials Education and Access for Underserved Women
Award Type: CRC-Pilot
Joseph, Galen, Ph.D. (co-PI)
University of California, San Francisco
$74,875
Caprio, Maria (co-PI)
Shanti Project, Inc.
$93,906

At-Home Group Video Calling to Support Rural Women
Award Type: CRC-Pilot
Koopman, Cheryl, Ph.D. (co-PI)
Stanford University
$94,174
Kreshka, Mary Anne & Hild, Joanne (co-PIs)
Sierra Streams Institute
$112,500
Overview: Since first awarding grants in 1995, the CBCRP has attracted new researchers to breast cancer and provided current breast cancer researchers with the resources to tackle the evolving landscape of the disease across a variety of award types and designated research disciplines. Currently, the core funding unit at CBCRP supports investigator-initiated research across a wide range of breast cancer topics. Funded projects must either correspond to the IDEA (innovative, developmental, exploratory award) level of research, or the research must be focused on translational, practical endpoints. Conference awards are also listed in this section. Research grants fall into four, broad topic and discipline categories:

1. The Community Impact of Breast Cancer including; health policy and health services; sociocultural, behavioral and psychological issues relevant to breast cancer; and disparities.
2. Etiology and Prevention including; environmental and biological factors interact to increase the risk of developing breast cancer; and xenoestrogens, exercise, studies of genetic variation, and methods to modify known breast cancer genes and risk factors.
3. Detection, Prognosis and Treatment including; imaging, early detection, biomarkers, emerging treatment strategies, and novel therapy targets and approaches.

Core Funding Portfolio
The CBCRP funded 15 new “core funding” grants for a total of $4,256,108 that are organized into the four research areas described below.

Community impact (1 grant):
One newly funded project focuses on the health policy needs in California, especially the issue of access to care. With the recent economic downturn, there has been a growing demand for services provided by public programs. An example is the California Cancer Detection Program’s Every Woman Counts (EWC) program, which provides breast cancer screening and diagnostic services to uninsured and underinsured women. However, with public program funding constraints, it is necessary to utilize validated and relevant methods, such as cost effectiveness analysis to optimize the best allocation of resources for the uninsured and underinsured. Joy Melnikow from the University of California Davis will adapt a recently created model, “Cost-effectiveness Analysis to Inform Breast Cancer Screening Policy”, to create a prototype user-friendly interface that will allow policy makers, breast cancer advocates, and interested members of the community to designate model inputs and obtain direct feedback on the projected costs and outcomes of breast cancer screening policy alternatives they are considering. As part of this 18-month IDEA award, qualitative methods (structured interviews; cognitive interviews) with breast cancer screening policy stakeholders will be utilized to (1) define high priority screening policy questions; (2) refine an existing BC screening model that is based on EWC data; and (3) gather feedback on the usability of the model.

Etiology and prevention (5 grants):
The intraductal approach to the breast refers to ability to gain access to the milk ducts via the nipple and study not only the ductal cells, but also precancerous cells for mutations to determine the conditions that will promote disease progression. Susan Love was funded through a conference award supporting the “7th International Symposium on the Intraductal Approach” held in Santa Monica on February 23-26, 2011. This year’s Symposium facilitated discussion and collaboration amongst a diverse group of researchers in order to identify the critical barriers to taking intraductal research to the patient level. More than 100 clinicians, epidemiologists, pathologists, basic scientists, translational investigators, and breast cancer advocates from 11 countries attended. Participants also had the opportunity to observe live demonstrations of nipple
aspirate fluid collection, ductal lavage, and ductoscopy. A public panel allowed community members to understand the highlights of the Symposium.

BRCA1 and BRCA2 mutation carriers have a 40% to 80% cumulative lifetime risk for developing breast cancer and a 60% to 90% cumulative risk for either breast or ovarian cancer. **Susan Neuhausen** from the City of Hope National Medical Center received an IDEA grant to investigate “Epigenetic Changes as Modifiers of BRCA1/ BRCA2 Cancer Risk.” They will develop novel, blood-based biomarkers to distinguish between those BRCA1 and BRCA2 mutation carriers that are more likely to develop breast cancer. This type of biomarker would be defined by a distinct DNA methylation (epigenetic) pattern in blood lymphocytes. Epigenetic mechanisms include DNA methylation at CpG (di-nucleotide) sites, genomic imprinting, chromatin modifications, and non-coding RNA. Specifically, Dr. Neuhausen’s group will study BRCA1 and BRCA2 mutation carriers in 13 families to identify genome-wide differences in DNA methylation among carriers who either developed or did not develop cancer.

In a similar topic, **Anna Wu** at the University of Southern California will study “Soy, DNA Methylation and Breast Cancer.” They will determine whether soy intake during adolescence and/or adulthood can influence the methylation status of specific genes involved in hormone- and receptor-mediated cell signaling DNA repair (including BRCA1), and cell-cell adhesion (CDH1). The study will be conducted within a subset (n=326) of women participating in an existing population-based, case-control study of Asian-American women with breast cancer, which has previously collected information on lifetime soy intake as well as tumor biopsy samples. Soy intake has been linked to reduced breast cancer development and recurrence in Asian populations but not in populations from North America or Europe. In previous studies a high daily intake of soy (at least 20 mg of isoflavones per day) leads to a moderate decreased risk of breast cancer by 30%, whereas a moderate intake can reduce risk by about 10% (10 mg of isoflavones/day). Dr. Wu’s study may provide a mechanistic association of soy intake with specific gene epigenetic changes influencing breast cancer development.

Exposure to environmental cadmium, a carcinogenic metal with estrogenic properties, may cause early pubertal development and increase breast cancer risk. **Rudolph Rull** at the Cancer Prevention Institute of California received an IDEA grant to study “Cadmium, Age at Menarche, and Early Puberty in Girls.” The hypothesis of the study is that urinary cadmium concentration, as a marker of lifetime body burden, is associated with earlier age at menarche and early onset of pubertal development. Dr. Rull’s group will use existing data and overnight urine specimens from 214 Caucasian and Chinese girls, aged 10-14, participating in the Growth and LifeStyle Study, which was designed to examine the effects of isoflavones on the timing and attainment of menarche. This is an important issue given that young children can be exposed to cadmium from a variety of sources, including toys and jewelry, cigarette smoke, diet, and polluted air. By including a population of Chinese girls, this study will also be able to assess the impact of ethnicity/immigration on cadmium exposure.

Dense breast tissue observed through mammography is one of the strongest predictors of breast cancer risk in women, although the underlying reasons are unclear. Currently there are no calibrated means to measure breast density in a clinical (radiological) setting. In addition, there are no validated risk models that include breast density. To address these issues CBCRP provided funding to **John Shepherd** from the University of California, San Francisco to support a conference, “5th International Workshop on Breast Cancer Risk Assessment.” The workshop was held on June 9-10 in San Francisco, CA, and included a variety of speakers and topics. The meeting topics included: (1) advances in quantifying breast density and non-density imaging features and how these relate to breast cancer risk and molecular subtypes, (2) the biology of breast density, and (3) methodologies of communicating breast cancer risk that incorporates breast density as a risk factor.
Detection, prognosis & treatments (6 grants):
Obesity is an established risk factor for the development of many cancers especially postmenopausal breast cancer. Obesity also negatively impacts prognosis and response to treatment. Today nearly one-third of Americans are obese exhibiting body mass index (BMI) of >30 and an additional one-third are moderately overweight (BMI >25). David Feldman from Stanford University received funding through a translational research award to study “Vitamin D and Breast Cancer in Obesity: Therapeutic Trials.” Obesity and the frequently associated insulin resistance cause changes in the fibroblastic stromal cells of the breast adipose tissue, resulting in inflammation and increased estrogen synthesis in the breast microenvironment. Dr. Feldman and collaborators will, (1) investigate whether the effects of calcitriol (man-made, bioactive vitamin D) or dietary vitamin D can counteract diet-induced obesity and tumor development using breast cancer stem cells in a novel mouse model to study key mechanistic modes of activity, and (2) conduct a clinical trial in obese and non-obese breast cancer patients to investigate the effects of neoadjuvant vitamin D administration. Since vitamin D is a low cost, easy to use product, positive results for its treatment benefits would be quite valuable.

Axillary Lymph Node Dissection (ALND) is commonly used for the staging and prognosis of breast cancer. Unfortunately, this procedure has the common side effect of lymphedema. Results from a recent clinical trial, called ACOSOG Z0011, showed that women with early-stage breast cancer who underwent sentinel lymph node biopsy (SLNB, the removal of one or two lymph nodes in the armpit to test for the presence of cancer cells) and whose sentinel nodes were positive for cancer, lived just as long as women who had SLNB followed by ALND. Although this trial may lead to a reduction in the use of ALND, surgeons still need improved ways of reducing lymphadema when ALND is performed. Steven Chen from the City of Hope National Medical Center is funded though an IDEA competitive renewal to study “Reducing Surgical Morbidity of Breast Cancer Staging.” Dr. Chen and collaborators at the University of California, Davis and the University of North Carolina will use an axillary reverse mapping (ARM) technique to identify lymphatic channels draining the arm so they can be avoided during ALND to prevent lymphedema. In the pilot phase of this study ARM identified an upper extremity (arm) lymphatic within the dissection area 90% of the time, so the CBCRP awarded a continuation of this research to further validate the ARM approach.

A major challenge in treating breast cancer occurs in those patients whose tumors lack the expression of estrogen and progesterone receptors and the HER2 oncogene, so-called “triple-negative breast cancers” (TNBC). In addition to there being a lack of targeted therapies for this group of patients (15-20%), TNBC is more prevalent in both younger and African American women. From the biological perspective, TNBC largely overlaps with the “basal” genetic subtype, such that disease progression is aggressive, especially in terms of metastasis potential. Andrei Goga from the University of California, San Francisco has been studying TNBC with a focus on the role of an oncogene, called Myc, along with other genes that regulate the cell cycle. In a newly funded IDEA project, “Identifying Novel Drugable Targets Against TNBC”, Dr. Goga will use the emerging concept of “synthetic lethality” to discover drug targets associated with high Myc expression in TNBC. This approach uses high cellular Myc levels as a prerequisite for the identification of collateral targets that could result in a “synthetic lethal” (i.e. finding the so-called ‘Achilles heel’) interaction, leading to the selective killing of tumor cells. It is becoming appreciated that combinations of therapies targeting interdependent biochemical pathways in cancer cells may offer synergistic benefits in terms of therapeutic potency and to reduce the capacity of tumor cell to mount drug resistance.
Another approach to treat TNBC focuses on the epigenetic process of histone acetylation. Control of chromosomal DNA “packaging” and global regulation of gene activity is thought to occur via the acetylation-deacetylation of histones by specific enzymes. In the context of cancer, tumor cells may escape growth and migration constraints by inactivating many endogenous tumor suppressor genes by histone acetylation. Ruth Gjerset from the Torrey Pines Institute for Molecular Studies is funded to study “Targeting Histone Acetyltransferase in Triple Negative BC.” Dr. Gjerset’s premise is that polyamine-CoA-based, histone acetyltransferase (HAT) inhibitors will be highly effective for the treatment of TNBC based on the potential for these agents to block DNA repair. This type of treatment strategy should synergize with intrinsic DNA repair defects characteristic of TNBC cells, leading to cell death via “synthetic lethality.” This project also aims to determine whether polyamine-based HAT inhibitors may be selectively internalized into cancer cells, thereby being more selective than conventional chemotherapeutic drugs.

Inflammatory breast cancer is an aggressive form of the disease with a poor prognosis. Brunhilde Felding-Habermann from the Scripps Research Institute has developed a model of triple-negative, inflammatory breast cancer using cell lines generated from the primary tumor, local recurrence, and pleural effusion of a patient with breast cancer. They will screen for molecules that affect epithelial-mesenchymal transformation (EMT) in these cell lines and also investigate gene expression differences during tumor progression. An interesting aspect of this project is “Combating Breast Cancer with the Wellderly Immune Repertoire.” The “wellderly” study at Scripps focuses on America’s “healthy elderly” (i.e., those 80 and older with no history of chronic disease) to help unlock the genetic secrets behind lifelong health. In this portion of the project, Dr. Felding-Habermann’s team will isolate antibodies derived from the “Wellderly” population and identify for those that inhibit tumor growth and/or reverse EMT.

Another novel approach for treatment involves splice modulating oligomers, which are small molecules that can alter how the initial gene RNA product is spliced (i.e., processed into mRNA). Interference with pre-MRNA splicing would serve to create “dominant negative receptors” to block the action of growth-promoting receptors. If properly constructed, these inhibitory oligomers are stable in the blood and are readily taken up by cells. Ameae Walker at the University of California, Riverside will investigate “Targeting Prolactin as a Novel Treatment for Breast Cancer” via this approach. The prolactin receptors will be the proof-of-principle target, since they are expressed in 95% of primary tumors. Dominant negative varieties of the prolactin receptor have been identified and, if properly induced in tumor cells, would be expected to have a greater effect on tumor growth than trying to block them by other means.

Tumor biology and progression (3 grants):
Changes in the receptors at the surface of tumor cells that interact with the extracellular matrix (ECM) lead to altered growth and invasive potential. John Muschler at the California Pacific Medical Center Research Institute is funded to study “Novel Cell-matrix Markers and Drivers of Breast Cancer.” The focus of this project is BCAM (basal cell adhesion molecule, also called Luthern), a newly identified cell surface receptor that specifically interacts with α5 laminins (an ECM component), which are abundant in the breast tumor and bone metastatic microenvironment. Their preliminary data demonstrated elevated expression of BCAM in tumor cell lines and in clinical breast cancer biopsies. Thus, BCAM’s functions may represent a novel process involved in tumor progression and metastasis.

The mechanisms that guide tumor cells to a specific secondary metastatic organ are largely unknown. Recently, the concept of a “pre-metastatic niche” has emerged, in which either cancer or non-cancer cells promote future metastasis into specific target organs. This raises the possibility that blocking these metastasis-enabling molecules could have therapeutic value. Shizhen Emily Wang from the City of Hope National Medical Center received IDEA funding to explore “Breast Cancer-secreted MicroRNAs in the Pre-metastatic Niche.” MicroRNAs are post-transcriptional regulators for specific groups of mRNAs that cause selective gene
silencing. Dr. Wang will use “massively parallel sequencing” technology to identify microRNAs that are secreted by a panel of breast cancer cell lines with differential metastatic potential. The microRNA “candidates” will be further narrowed down to those associated with progression from stage II-III breast cancer to stage IV using existing microRNA sequencing data from the serum of patients. Finally, microRNAs will be studied to determine their potential cellular targets and functions in breast cancer metastasis.

“Expression profiling” of breast cancer has led our current stratification of 5-6 major disease genetic subclasses. However, because of RNA degradation in archival tissue blocks, other breast cancer genetic subtypes may have been overlooked. Additionally, fresh biopsy material is only obtainable from tumor samples past the earliest stages of disease progression, so this critical phase of the disease is understudied. Robert West from Stanford University is funded to develop new information for the “Molecular Classification of Early Breast Neoplasia.” Using a novel technology developed by Dr. West, this project aims to genetically analyze progression from early microscopically visible lesions using a RNA-sequencing protocol (termed 3SEQ) to profile polyA+RNA extracted from formalin-fixed, paraffin-embedded archival tissue. This research may provide a new genetic “window” into the earliest stages of the disease.

Core Funding Grants Listing

Reducing Surgical Morbidity of Breast Cancer Staging
Award Type: IDEA competitive renewal
Chen, Steven, M.D.
City of Hope National Medical Center
$469,769

Combating Breast Cancer with the Wellderly Immune Repertoire
Award Type: IDEA competitive renewal
Felding-Habermann, Brunhilde, Ph.D.
Scripps Research Institute
$473,750

Vitamin D and Breast Cancer in Obesity: Therapeutic Trials
Award Type: Translational Research
Feldman, David, M.D.
Stanford University
$1,169,860

Targeting Histone Acetyltransferase in Triple-negative Breast Cancer
Award Type: IDEA
Gjerset, Ruth, Ph.D.
Torrey Pines Institute for Molecular Studies
$273,000

Identifying Novel Drugable Targets Against Triple-negative Breast Cancer
Award Type: IDEA
Goga, Andrei, M.D., Ph.D.
University of California, San Francisco
$150,000

7th International Symposium on the Intraductal Approach
Award Type: Conference
Love, Susan, M.D., M.B.A.
Dr. Susan Love Research Foundation
$25,000

Cost-effectiveness Analysis to Inform Breast Cancer Screening Policy
Award Type: IDEA
Melnikow, Joy, M.D., M.P.H.
University of California, Davis
$149,996

**Novel Cell-matrix Markers and Drivers of Breast Cancer**
Award Type: IDEA
Muschler, John, Ph.D.
California Pacific Medical Center Research Institute
$262,500

**Epigenetic changes as modifiers of BRCA1/ BRCA2 cancer risk**
Award Type: IDEA
Neuhausen, Susan, Ph.D.
City of Hope National Medical Center
$251,128

**Cadmium, Age at Menarche, and Early Puberty in Girls**
Award Type: IDEA
Rull, Rudolph, Ph.D.
Cancer Prevention Institute of California
$206,312

**5th International Workshop on Breast Cancer Risk Assessment**
Award Type: Conference
Shepherd, John, Ph.D.
University of California, San Francisco
$20,000

**Targeting Prolactin as a Novel Treatment for Breast Cancer**
Award Type: IDEA
Walker, Ameae, Ph.D.
University of California, Riverside
$150,000

**Breast Cancer-secreted MicroRNAs in the Pre-metastatic Niche**
Award Type: IDEA
Wang, Shizhen Emily, Ph.D.
City of Hope National Medical Center
$252,000

**Molecular Classification of Early Breast Neoplasia**
Award Type: IDEA
West, Robert, M.D., Ph.D.
Stanford University
$158,000

**Soy, DNA Methylation and Breast Cancer**
Award Type: IDEA
Wu, Anna, Ph.D.
University of Southern California
$244,793
### 2011 CBCRP funding by institution

The following 16 California research institutions and community organizations were awarded new CBCRP funding in the 2010-2011 grant cycle. Community collaborative (CRC) grants are split between institutions.

<table>
<thead>
<tr>
<th>Institution (city)</th>
<th># Awards</th>
<th>Amount</th>
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<tbody>
<tr>
<td>California Pacific Medical Center (San Francisco)</td>
<td>2</td>
<td>$1,162,500</td>
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<tr>
<td>Cancer Prevention Institute of California (Fremont)</td>
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<td>City of Hope National Medical Center (Duarte)</td>
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<td>The Scripps Research Institute (La Jolla)</td>
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<td>Torrey Pines Institute for Molecular Studies (San Diego)</td>
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<td>University of Southern California (Los Angeles)</td>
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<td>Women of Color Breast Cancer Survivors Support Project (Inglewood)</td>
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2011 CBCRP application evaluation process & review committee rosters

The CBCRP thanks the participants in our 2011 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 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 a particular application not covered by the other committee scientist reviewers.

The CBCRP uses a scientific merit scoring system that rates individual components (e.g., approach, innovativeness, impact). This allows our expert reviewers and Council 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.

We triage some applications that score in the lower range of a committee’s portfolio using the preliminary scores of the assigned reviewers. Applications in the upper range of a committee’s portfolio all receive full committee discussion, as do any of the lower scoring applications nominated to full review by one reviewer.

Applications that were not triaged were rated by the CBCRP’s 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
- 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), or dissemination and translational 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.
Community Impact Review Committee

► Chair:
Shiraz I. Mishra, M.B.B.S., Ph.D.
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Sherrie L. Flynt Wallington, Ph.D.
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Breast Cancer Option, Inc
Rhinebeck, NY

Susan Pelletier
Vermont Breast Cancer Coalition
Stockbridge, VT

► California Advocate Observers:
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Connie Engel, Ph.D.
Breast Cancer Fund
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► Ad-Hoc Reviewers:
Ellyn E. Matthews, PhD, RN
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Aurora, CO

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Durham, NC

Etiology and Prevention Review Committee
► Chair:
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The Annie Appleseed Project
Delray Beach, FL

Sara Williams
The Carolina Breast Cancer Study (UNC)
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USC Norris Cancer Survivorship Advisory Council
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SRI Chemicals Testing Review Committee
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Acting Director, Integrated Risk Information System
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Treatment, Detection & Prognosis Review Committee

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Scientist President & CSO
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Bethesda, MD

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Susan G. Komen Foundation
Camano Island, WA

Kimberly Newman-McCown
Susan G. Komen Foundation
Melrose Park, PA

Beverly Parker, Ph.D.
Y-ME National Breast Cancer Organization
Naperville, IL

California Advocate Observer
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Breast Cancer Action
San Francisco, CA

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University of Washington Medical Center
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Matthew Rowling, Ph.D.
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Iowa State University
Ames, IA

John H. Ward, M.D.
Professor and Chief
Huntsman Cancer Institute at the University of Utah
Oncology Division, Department of Internal Medicine
Salt Lake City, UT

Tumor Biology Review Committee

Chair:
Harikrishna Nakshatri, Ph.D.
Marian J. Morrison Professor in Breast Cancer Research
Walther Oncology Center
Indiana University School of Medicine
Indianapolis, IN

Scientific Reviewers:
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Associate Professor of Medicine
Beth Israel Deaconess Medical Center
Harvard Medical School
Boston, MA

**Qihong Huang, M.D., Ph.D.**
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Molecular and Cellular Oncogenesis Program
The Wistar Institute
Philadelphia, PA

**Julie E. Lang, M.D.**
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University of Arizona
Tucson, AZ

**Joan Lewis-Wambi, Ph.D.**
Assistant Professor
Fox Chase Cancer Center
Philadelphia, PA

**Cindy K. Miranti, Ph.D.**
Scientific Investigator
Van Andel Research Institute
Grand Rapids, MI

**Weston W. Porter, Ph.D.**
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Department of Veterinary Integrative Biosciences
College Station, TX

**Patricia Schoenlein, Ph.D.**
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Cellular Biology & Anatomy
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Augusta, GA

**Joyce A. Schroeder, Ph.D.**
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Department of Molecular & Cellular Biology
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► **Advocate Reviewers:**

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Michigan Breast Cancer Coalition
Huntington Woods, MI

**Theresa Martyka**
Breast Cancer Network of Strength
Chicago Ridge, IL

**Nancy Singleton**
SHARE
Hoboken, NJ
California Advocate Observer:

Chira Chen-Tanyolac
University of California, San Francisco
San Francisco, CA

Ad-Hoc Reviewers:

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Director, Division/ Personalized Nutrition and Medicine
FDA/NCTR
Jefferson, AR

Thomas Ludwig, Ph.D.
Associate Professor
Columbia University, Institute for Cancer Genetics
Department of Pathology
New York, NY