2007 Awards Compendium

Cycle 13

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 35 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 $7.1 million for research projects being performed at 21 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 also 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 DHS breast cancer early detection program, "Every Woman Counts."

Below and in the sections to follow are:

- Application submission and new award data broken down by CBCRP research topics (priority issues) and award types
- Highlights of 2007 funding
- A portfolio summary and list of grants for our four main research priority issues

- Funded California institutions and amounts awarded
- Description of the application evaluation process and the review committee membership

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

Submissions & Review Process

We received 220 submissions in response to our 2007 *Call for Applications* for new research grants on breast cancer. They were evaluated, discussed in a study section format", and scored for scientific merit by our out-of-state peer reviewers. 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 1. Distribution of 2007 CBCRP application submissions by award type and priority issue

Award Types ↓	Priority Issues				Award Type Totals ↓
	Etiology & Prevention	Community Impact	Detection, Prognosis & Treatment	Biology of the Breast Cell	
Postdoctoral Fellowship	3	3	11	31	48
Dissertation	1	0	11	10	22
IDEA	14	3	51	35	103
IDEA-competitive renewal	0	0	4	4	8
Translational	1	0	9	0	10
Conference	1	1	0	0	2
CRC Pilot	2	19	0	0	21
CRC Full	1	5	0	0	6
Priority Totals	23	31	86	80	220

Compared to the previous year (2006/Cycle 12) we received almost 10% more applications. For our award types, we received 10 percent fewer IDEA applications; however, career development (Dissertation and Postdoctoral Fellowship) and CRCs increased in number. The Translational Research award was new for 2007. Although the majority of our applications are submitted under the "Detection, Prognosis & Treatment" priority issue, many of these are actually basic-science projects.

After the peer review, applications in the upper 2/3 of average scientific merit were rated by our advisory council for "responsiveness" to CBCRP programmatic criteria. There are seven criteria for each award type. To select grants for funding, the Council balanced the scientific merit scoring and programmatic ratings. Thus, the successful applicant responded both in terms of presenting a high quality research project *and* by meeting the interests of CBCRP stakeholders.

Overview of 2007 Funding

Applications submitted = **220**
Applications offered and accepting funding = **35**
Applications offered funding, but declined = **3**
Overall success rate (38/220) = **17%**
Amount awarded in 2007 = $7,101,642

The two tables below summarize the 2007 funding distribution by award type and priority issue.

Table 2. 2007 portfolio distribution by CBCRP award type

Award Type ↓	Number of Applications	Grants Funded (success rate)	Amount Awarded	Percentage of total funding
Dissertation	22	8 (36%)	$599,863	8.4%
Postdoctoral Fellowship	48	6 (12.5%)	$540,000	7.6%
IDEA	103	9 (9%)	$1,478,389	20.8%
IDEA-Competitive Renewal	8	3 (37.5%)	$1,004,677	14.1%
Translational	10	1 (10%)	$851,559	12.0%
CRC Pilot Award	21	3 (14%)	$566,641	7.8%
CRC Full Award	6	3 (50%)	$2,020,513	28.5%
Joining Forces Conference	2	2 (100%)	$40,000	0.6%

Table 3. 2007 portfolio distribution by CBCRP priority issue

Priority Issue ↓	Number of Applications	Grants Funded (success rate)	Amount Awarded	Percentage of total funding
Community Impact	31	6 (19%)	$1,935,241	27.3%
Etiology & Prevention	23	2 (9%)	$911,413	12.8%
Biology of the Breast Cell	80	13 (16%)	$1,488,841	21.0%
Detection, Prognosis & Treatment	86	14 (16%)	$2,766,147	39.0%

Comparing the 2007 vs. 2006 portfolios reveals a number of significant changes. Due to decreases in our revenue from the cigarette tax, we were able to award $2.7M *less* in 2007. As a result, the number of grants was reduced from 53 in 2006 to 35 this year. Three other reasons account for the reduced number of grants funded. First, the Translational Research award was introduced in 2007, and we awarded one in this cycle at a cost of $851,559. Second, we received a number of high quality IDEA-competitive renewals in 2007, so the funding for this award type increased by over $600,000. Third, funding for CRC-Full Research awards increased by over $500,000 this year. The net result of these factors substantially reduced our ability to fund IDEAs and postdoctoral fellowships in 2007 at levels comparable to the previous years. IDEA funding for 2007 was reduced by over 50% in terms of grant number and over 60% in terms of dollar amount when compared to 2005-2006 levels. Postdoctoral fellowships were also reduced modestly in award number and funding. In terms of research topics, we achieved a good portfolio balance between "treatment-oriented" and "basic science" projects, while "community impact" funding increased due to the excellent quality of CRC-Full Research award applications. Finally, In order to accommodate the 2007 portfolio into our available budget, our advisory council limited all postdoctoral fellowships to two-year grants; and the submitted budgets of the CRC-Full Research, IDEA-competitive renewal, and Translational Research grants were reduced by 10%.

2007/Cycle 13 Funding Highlights

- Six awards are research projects to **community groups collaborating with traditional researchers** to address issues important to the community, such as rural access to support groups and risk factors impacting immigrant/underserved communities.
- Thirteen grants aim to further our understanding of **tumor biology**, such as the process of metastasis and the role of stem cells.
- Fourteen projects explore novel methods to **detect breast cancer and develop novel approaches for treatment**.
- Twelve projects are for **innovative, exploratory, and high-risk/high reward research** projects to push boundaries, challenge existing paradigms, and initiate new research programs. Nine of these grants are for new projects, and three grants are for renewal funding of past CBCRP IDEA grants showing excellent progress. Four recipients of IDEA grants are "junior investigators"—just starting independent research careers in breast cancer.
- Fourteen awards provide opportunities in **career development** at the levels of graduate student and postdoctoral training. These researchers bring fresh thinking to their respective disciplines.
-  **Seven awards are of special interest**, because they are funded in part by revenue from the **California State Income Tax Check-off**.
- **Faith Fancher Research Award**
  Faith Fancher was a long-time television news anchor and personality with KTVU (Oakland) who was taken from us in October 2003 after a six-year struggle with breast cancer. In her honor, and to commemorate all that she did for breast cancer education and research, we have created this award. The recipients of the 2007 Faith Fancher Research Award are **Kimlin Ashing-Giwa, Ph.D.** at the **City of Hope National Medical Center** (Duarte) and **Gloria Harmon** from the community group **Women of Essence** (Lynwood) for their project, *Sister Survivor: African American Breast Cancer Coalition*. Although African American breast cancer survivors (AABCS) bear some of the heaviest burden among all medically underserved breast cancer survivors, few investigations and interventions have focused on addressing their social and psychological support needs. The team will develop a preliminary "Culturally-Informed Breast Cancer Support Group

Guide" on how to organize and maintain support groups, based on the two sets of qualitative data. The team will also conduct needs assessment focus groups and key informant interviews in the Inland Empire to evaluate the psychosocial needs and resources of AABCS. Their goal is to document and disseminate the process and structure of peer-led support groups.

Description of CBCRP Award Types

- **Community Research Collaboration (CRC):** brings community organizations—such as breast cancer advocacy organizations, 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-Pilots (18-month), CRC-Full Research awards (three years), and CRC-Implementation and Dissemination (I&D) awards (18-month) are available.
- **Innovative Developmental and Exploratory Award (IDEA):** 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 renewal:** allows 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:** to support projects that overcome barriers and put prior research knowledge to practical use in the patient or community setting.
- **Postdoctoral Fellowship:** supports career development-oriented training under a breast cancer research mentor.
- **Dissertation:** supports the completion of dissertation research by masters or doctoral candidates.
- **Joining Forces Conference:** supports 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.

Community Impact of Breast Cancer:
The Social Context

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?

To address these issues the CBCRP solicits applications from community academic partnerships as well as individual investigators.

The CBCRP has been supporting Community-Research Collaborations (CRC) for over 10 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.

The CBCRP offers pre-application workshops and technical assistance to facilitate new partnerships and competitive grant applications. We are encouraged that many CRC grants focus on the underlying disparities of underserved populations through innovative and understudied research areas. For example, Cycle 13 grantees are proposing important research topics including participation in clinical trials, breast education for immigrant women, patient navigation, psychosocial support for rural and African American women, and end of life care. We feel that addressing these gaps in our knowledge will lead to promising solutions for underserved communities disproportionately affected by breast cancer.

In addition to the CRC awards, the CBCRP supports the ”Community Impact” priority issue with IDEA grants, career development awards, and the Joining Forces Conference Award.

The CBCRP funded six new grants in 2007 to advance our Community Impact priority issue. Three of the CBCRP’s 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 Summary

Few research studies focus on the enrollment of ethnic minority women into clinical trials, which provide the best in standard care and test promising new therapies. Minority groups have lower participation rates in clinical trials, partly due to lack of information about clinical trials and their potential benefits. **Natasha Riley** with **Vista Community Clinic** and **Georgia Sadler** of the **University of California, San Diego**, are conducting a pilot study to create an educational program, entitled *Scientific Literacy and Breast Cancer Clinical Trials Education Program*, to increase knowledge and awareness about clinical trials among African American and Hispanic

American women. The team plans a larger study where they will test whether women in the educational program arm are more likely to enroll in clinical trials and become a “Clinical Trials Ambassador” compared with those in the control group.

Breast cancer risk among immigrant women is another important research area given the cultural, linguistic, and socioeconomic barriers to treatment and care. **Joan Bloom** with the **University of California, Berkeley,** and **Aida Shirazi** with the **Afghan Coalition** are funded for a pilot study entitled, *Breast Health Behaviors of Immigrant Afghan Women*. While US-based data are not available, data collected elsewhere suggest that Afghan women are less likely to be screened than other groups and are more likely to have late diagnoses. This project aims to understand more about Afghan women’s concerns, knowledge, attitudes, behaviors and sources of information about breast care, and perceived barriers to care, as well as cultural modifications needed to adapt general education programs for this group. Information learned from the project has the potential to increase breast health awareness among Afghan women and also other groups of Muslim women in California and the US.

Few investigations and interventions have focused on addressing the support needs of African American breast cancer survivors (AABCS) in spite of this group bearing the heaviest burden among all medically underserved breast cancer survivors. While the basic emotional and informational needs of AABCS may be similar to the needs of other breast cancer survivors regardless of their ethnic group, how these needs are met will likely differ depending on cultural and community context. In their pilot study, *Sister Survivor: African American Breast Cancer Coalition*, **Kimlin Ashing Giwa** of **City of Hope** and **Gloria Harmon** with **Women of Essence** will answer the following questions: (1) What are the benefits and unmet needs of participants from five AABCS support groups in Los Angeles? (2) What are the elements of structure and process, and the most culturally-appropriate paradigm for developing a peer-led AABCS support group? (3) What are the unmet needs and psychosocial resources of AABCS in the Inland Empire region? The team will develop a preliminary “Culturally-Informed Breast Cancer Support Group Guide” on how to organize and maintain support groups, based on the two sets of qualitative data. Finally, they will conduct needs assessment focus groups and key informant interviews in the Inland Empire to evaluate the psychosocial needs and resources of AABCS. Their goal is to document and disseminate the process and structure of peer led support groups.

Alternative methods to delivering psychosocial support for rural and isolated women are being explored by **Cheryl Koopman** from **Stanford University, Mary Anne Kreshka** and **Jim Perkins** from the **Northern Sierra Health Network**. This team is conducting a three-year trial to assess the acceptability and efficacy of a video conferencing intervention to provide support groups to women with breast cancer and breast cancer survivors. Their study, *Expanding Rural Access: Distance Delivery of Support Groups,* hypothesizes that women in the intervention condition will have increases in social support, self-efficacy, knowledge of community resources, emotional expression, and decreases in depression and PTSD symptoms. In the trial, 100 women will be randomized to a video-conference support group or wait-listed for a support group. The intervention consists of eight weekly mediated support groups and a workbook; the latter was previously found to be efficacious in addressing psycho-social variables related to breast cancer.

Patient navigation involves assisting those affected by a breast cancer diagnosis in navigating various systems needed for complete medical care. Patient navigators are in need of a mechanism to bring organizations providing navigation services together to reap the benefits of mutual experiences, explore potential resource sharing, and/or develop ways to measure the benefit and quality of services provided. **Lisa Bailey** with **Alta Bates Summit Medical Center** is utilizing a Joining Forces Conference Award for a project entitled, *Networking Breast Cancer Navigator Programs in Northern California*. A full-day conference is planned to: (1) bring

together providers of breast cancer navigation services to encourage networking and resource sharing; and (2) facilitate the documentation and measurement of breast cancer navigation services to serve as a resource for new programs as well as provide evidence-based literature of the value of navigation services. The conference has important implications for facilitating a dialogue between local programs about navigator programs, needs for navigator support, and barriers that navigators encounter as they work to access appropriate health care for patients.

Finally, end of life care is a critical point in the cancer continuum that receives little research attention, especially studies that include underserved women who are often diagnosed at later breast cancer stages and have lower rates of survival. Based on data from a CRC-funded pilot project, **Shelley Adler** from **University of California, San Francisco,** and **Beverly Burns** from the **Charlotte Maxwell Complementary Clinic** will conduct a three-year, mixed-method, longitudinal study to evaluate the effectiveness of a narrative intervention. This intervention study, *Underserved Women with Breast Cancer at End of Life,* focuses on the construction of an ethical will (expressing individual values, beliefs, life lessons, hopes, love and forgiveness in a written document to loved ones) among women with metastatic breast cancer. The secondary aim is to construct a conceptual model that reflects the experiences of breast cancer patients at the end of life. One hundred and twenty women with metastatic breast cancer will be enrolled in the study and interviewed four times with a trained interviewer. These four interviews will form the basis for the construction of an ethical will in collaboration with the patient. The goal of the intervention is to reinforce dying women's sense of meaning of their lives and ease concerns regarding death.

Community Impact Grants Funded in 2007

Underserved Women with Breast Cancer at End of Life
Shelley Adler, Ph.D. (co-PI)
University of California, San Francisco
Beverly Burns, M.S. (co-PI)
Charlotte Maxwell Complementary Clinic
Award Type: CRC-Full Research
$270,000 (UCSF) / $337,500 (CMCC)

Sister Survivor: African American Breast Cancer Coalition
Kimlin Ashing-Giwa, Ph.D. (co-PI)
Beckman Research Institute of the City of Hope
Gloria Harmon (co-PI)
Women of Essence
Award Type: CRC-Pilot
$169,000 (BRI) / $62,500 (WOE)

Networking Breast Cancer Navigator Programs in Northern California
Lisa Bailey, M.D., F.A.C.S
Alta Bates Summit Medical Foundation
Award Type: Joining Forces Conference
$15,000

Breast Health Behaviors of Immigrant Afghan Women
Joan Bloom, Ph.D. (co-PI)
University of California, Berkeley
Aida Shirazi (co-PI)
Afghan Coalition
Award Type: CRC-Pilot
$70,481 (UCB) / $99,255 (AC)

Expanding Rural Access: Distance Delivery of Support Groups
Cheryl Koopman, Ph.D. (co-PI)
Stanford University
Mary Anne Kreshka, M.A. and Jim Perkins, Dr.P.H. (co-PIs)
Northern Sierra Rural Health Network
Award Type: CRC-Full Research
$341,100 (SU) / $405,000 (NSRHN)

Science Literacy & Breast Cancer Clinical Trials Education
Georgia Sadler, Ph.D. M.B.A.
University of California, San Diego
Natasha Riley, M.A.
Vista Community Clinic
Award Type: CRC-Pilot
$44,003 (UCSD) / $121,402 (VCC)

Etiology & Prevention:
Finding the Underlying Causes

Overview: Although our foundation of knowledge for the basic science aspects of breast cancer 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 lifestyle factors associated with increased and decreased risk for breast cancer. However, the relative importance of diet, exercise, family history, pregnancy, alcohol, hormone replacement therapy, and other factors remains controversial. The CBCRP's Special Research Initiatives (SRI) seeks to increase knowledge of and create solutions to the environmental causes of breast cancer. This $18 million effort will identify and support research strategies that increase knowledge about and create solutions to both the environmental causes of breast cancer and the unequal burden of the disease. The SRI will support coordinated statewide efforts to explore innovative ideas and new theories; leverage California's unique and diverse geographic, population, and research resources; and undertake critical studies that significantly move these fields forward.

The CBCRP funded two new grants in 2007 to advance our Etiology & Prevention priority issue.

Etiology & Prevention Portfolio Summary

A CRC-Full Research award entitled *Breast Cancer Risks in California Nail Salon Workers* focuses on immigrant women, specifically Vietnamese nail salon workers, who make up over 80% of nail salon workers in California. In their CBCRP funded pilot project, **Linda Okahara** with **Asian Health Services** and **Peggy Reynolds** of the **Northern California Cancer Center** found that many nail salon workers are concerned about the chemicals they are exposed to and are experiencing health problems associated with high levels of exposure to solvents. Using data from the California Cancer Registry, the team will explore: (1) whether nail salon workers have higher breast cancer rates than the general population; and (2) whether Vietnamese nail salon workers have a higher incidence of breast cancer than the general Vietnamese population. The second part of this study will document whether hydrocarbon solvents, especially benzene and toluene, found in nail salons exceed the health-based standards. Eighty nail salon workers will wear passive air monitors for two to three days to collect data on hydrocarbons. The study has important implications, because the nail salon industry is one of the fastest growing in the nation.

Lifestyle factors related to breast cancer risk, especially among high-risk overweight adolescents is another important area of research that has received little attention. In adults, obesity, physical inactivity, insulin resistance, and visceral fat have all been linked to increased breast cancer risk; however very little is known about this relationship during adolescence. Overweight Latina adolescents are often physically inactive, insulin resistant, and have high amounts of visceral fat (i.e., the fat around the abdominal organs). They may also start their menstrual cycles early in life and have an increased frequency of ovulatory cycles, which have been widely linked with increased breast cancer. **Jaimie Davis** at **University of Southern California** proposes a randomized controlled trial, entitled *Circuit Training and Breast Cancer Biomarkers in Adolescents* to determine whether a 16-week circuit training program can potentially impact breast cancer risk in adolescent girls through its effects on hormone profiles, menarche, ovulatory cycles, insulin sensitivity, adiposity, and therefore breast cancer risk. Forty Latina girls (ages 14 to 18, who are either overweight or at risk of being overweight) will be randomly assigned to either a 16-week circuit training program group, or to the control group (receiving 4 weeks of intensive circuit training at the end of the intervention). This study has

important implications for ethnic minority communities that are disproportionately overweight and susceptible to increased breast cancer risk.

Etiology & Prevention Grants Funded in 2007

Circuit Training to Lower Breast Cancer Risk in Latina Teens
Jaimie Davis, Ph.D.
University of Southern California
Award type: IDEA
$244,500

Breast Cancer Risks in California Nail Salon Workers

Peggy Reynolds, Ph.D.
Northern California Cancer Center
Linda Okahara
Asian Health Services
Award Type: CRC–Full Research
$349,303 (NCCC) / $317,610 (AHS)

Detection, Prognosis & Treatment:
Delivering Clinical Solutions

Overview: The detection, prognosis, and treatment of breast cancer is a constantly evolving landscape where information filtering in from basic scientists is selectively advanced along the 5-to-10 year stepwise "critical path" for translational application. Cancer stem cells (CSCs), first established in 2003 for breast cancer, are already gaining attention as possible novel targets for therapy. The inability to provide a durable cure for breast cancer is thought to be due to the chemo- and radiotherapy resistance of CSCs to current treatments. And, stem cells might even emerge as a delivery vehicle for therapeutics. Better early detection of disease remains a critical need. Using combined imaging modalities aims to improve both sensitivity and selectivity to reduce unnecessary biopsies and facilitate informative disease staging and prognosis. Genetic profiling of patients continues to move in the direction of "individualized therapy." New targeted therapies that began with the introduction of Herceptin® require validation of novel targets in the clinical setting and technologies to select patients most likely to benefit from these expensive drugs. Advances in nanotechnology promise new methods for detection and tumor-specific delivery to reduce drug side-effects. However, some clinical scenarios, such as "triple-negative" (ER, PR, and Her-2 negative) breast cancers and the "basal-like" gene expression pattern still account for a significant number of new diagnoses that have fewer treatment options.

The CBCRP funded 14 new grants in 2007 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 Summary

Two grants in 2007 focus on the breast ductal system, an underutilized access point for the detection, diagnosis, and treatment of breast cancer. A human breast has many lobes, which are highly variable in size and shape, each with one central duct, its peripheral branches and their associated glandular tissues. Nipple aspirate fluid and ductal lavage can be obtained to analyze the cellular and fluid by histological, proteomic, and genetic techniques. Improvements in mammary ductoscopy using a microendoscope allow for the direct visualization the ductal lining of the breast and the retrieval of epithelial cells. A leader in this field is **Susan Love** at the **Dr. Susan Love Research Foundation**. The CBCRP funded a Joining Forces Conference Award to Dr. Love to support the *5th International Symposium on the Intraductal Approach to Breast Cancer* in Santa Monica, California, March 1-4, 2007. In attendance were more than 120 oncologists, epidemiologists, biostatisticians, surgeons, biochemists, pathologists, radiologists, endocrinologists, and breast cancer advocates. Next, the CBCRP launched a new Translational Research Award in 2007, and the first recipient is Dr. Love for her three year clinical project, *Intraductal Therapy of DCIS: a Presurgery Study*. DCIS, an early stage, non-invasive breast cancer, is often over-treated with the same methods of surgery, radiation, and hormone medications as more advanced disease. Historical studies show that most DCIS remains dormant and only 30-40% of cases will ever progress to invasive cancer. The aim of Dr. Love's translational project is to test the practicality and efficacy of a local treatment of the affected breast duct itself. A currently approved drug, called Pegylated Liposomal Doxorubicin, will be introduced directly into the ductal system of women bearing DCIS lesions. If successful, this novel treatment strategy may eventually save countless women from undergoing disfiguring surgery and debilitating systemic chemotherapy.

Four new grants address the topic of breast cancer imaging with the potential for better earlier detection of breast cancer as well as improved diagnosis and staging of existing disease. Magnetic Resonance Imaging (MRI) is a more sensitive method than x-ray mammography to detect smaller tumors and image the "denser" breasts of younger women, but "standard proton" MRI suffers from limited specificity that leads to unnecessary biopsies. **Brian Hargreaves** at **Stanford University** received IDEA funding to develop new hardware and pulse sequence software for "multinuclear" MRI to quantitatively detect differences in sodium concentrations between tumors (increased sodium) and normal tissue. Next, ultrasound is an important adjunct to mammography to identify, characterize and localize breast lesions, and it is also not compromised by dense breasts. Ultrasound requires no radiation or compression. However, ultrasound is operator-dependent and this lack of consistency limits more widespread acceptance. **Thomas Nelson** from the **University of California, San Diego,** received an IDEA-competitive renewal grant to complete construction of a breast ultrasound scanner to image the entire breast. This volume breast ultrasound (VBUS) machine should be an improvement over hand-held devices currently being used. Dr. Nelson will also add blood flow imaging capability to the scanner to facilitate the discrimination between more vascular tumor lesions vs. benign/normal tissues. Next, accurate staging of lymph nodes is a critical parameter in determining whether a primary breast tumor is likely to have metastasized. Nodal staging dictates the therapeutic options for many cancer patients. Although sentinel node biopsy has reduced the need for more extensive lymphadenectomy (multiple node excision), imaging methods such as CT, MRI, and optical have not yet been developed to the point of accurately distinguishing normal and tumor-infiltrated lymph nodes. **Ella Jones** from the **University of California, San Francisco,** aims to develop a non-invasive imaging probe based on a nanotechnology-based dendrimer probe (i.e., uniform populations of repeatedly branched, synthetic molecules, like tiny snowflakes) having fluorogenic (light emitting) properties when cleaved by the tumor-specific Cathepsin B protease. If successful, this approach is predicted to selectively "light-up" cancer cell-continuing lymph nodes for fluorescence detection. First, Dr. Jones and colleagues will conduct testing in mice to show "proof of principle" prior to human translational work. Finally, standard neoadjuvant chemotherapy is used for the management of locally-advanced, large (>3cm) breast cancers to reduce the primary tumor size prior to surgery. However, some cancers are resistant to chemotherapy and earlier identification of these "non-responders" would help patients avoid toxic and ineffective treatments, and expedite the initiation of alternative therapy. **Catherine Klifa** also at the **University of California, San Francisco,** will combine two imaging modalities, Diffuse Optical Spectroscopy (DOS) and MRI, using an instrument already developed by **Bruce Tromberg** at the **University of California, Irvine,** and **Nola Hylton** at UCSF. The aim of Dr. Klifa's clinical study of 30 patients is to predict the neoadjuvant response by detecting changes in tumor physiology by DOS after one round of chemotherapy, which would be too soon to measure reduced tumor size using MRI.

Two CBCRP-funded grants explore novel therapeutics. Tumors express antigens that should induce immune-mediated rejection, but rejection of established tumors is uncommon. One reason is that tumors actively defeat host immunity, so researchers are always testing new ways to harness host immunity to battle cancer. One approach to making tumor immunotherapy more broadly applicable is to administer recombinant cytokines to strengthen the immune response and overcome tumor suppressive mechanisms. However, issues such as toxicity, poor drug half-life in circulation, and stimulation of T-regulatory cells (immune suppression) are obstacles to the clinical development of therapeutic cytokines. **Ananda Goldrath** at the **University of California, San Diego,** has found that IL (interleukin)-15 may not only offer a more favorable dose-limiting toxicity compared with IL-2, but may differentially affect T-regulatory cells. She will combine IL-15 with its soluble receptor (sIL-15Rα) prior to injection in mouse models of breast cancer. It is hoped that the IL-15/receptor complexes will improve the priming and survival of lymphocytes. Next, the capacity of malignant cells for invasion and metastasis is triggered in part by the metabolic needs of the growing tumor. As the cancer grows, its demand for nutrients and oxygen overwhelms the local blood supply. A low oxygen

level, or hypoxia, causes the cell to increase the amount of a DNA-binding protein, called hypoxia inducible factor (HIF). In addition to activating genes involved in blood vessel formation (angiogenesis), recent studies in breast cancer cells have shown that HIF also induces the expression or tumor cell genes directly implicated in invasion and metastasis. **John Phillips** from the **California Institute of Technology** received a dissertation award to target HIF using polyamides, a class of synthetic, sequence-specific DNA-binding molecules that can block transcription factor-DNA interactions. Most DNA-interacting drugs damage DNA in a non-selective manner, killing cancerous cells and healthy cells alike. Polyamides, on the other hand, are designed to control cancer-causing genes without DNA damage.

Four new grants focus on new approaches for existing breast cancer targets or to identify patient sub-populations that would receive the most potential benefit from existing therapies. ErbB receptors (e.g., EGFR and Her-2) are displayed on the exterior surface of many breast tumor cells and transmit molecular signals from the extracellular environment to the inside of the cell. In this way, they mediate normal cell processes and functions, but in breast tumors can trigger aberrant cell growth. **Jennifer Lahti** at **Stanford University** received a dissertation award to study whether “knottins”, which are mini-proteins with a high potential for drug design, when combined with fragments of natural epidermal growth factor (EGF) ligands can be selected and developed as novel inhibitors of tumor cell signaling and progression. Second, the taxane compounds, paclitaxel (Taxol) and docetaxel (Taxotere) have been important components of chemotherapy regimens to treat metastatic breast cancer. However, a patient’s intrinsic or acquired resistance to these drugs limits their widespread clinical utility. Taxanes specifically target the cellular microtubules, and **Tatana Spicakova** also from **Stanford University** will study whether altered levels and/or aberrant modification of microtubule associated proteins (MAP-Tau, MAP4 and MAP2) confer resistance to taxanes. Next, HSP90 (heat shock protein 90) is a molecular chaperone (involved in correct protein folding) and is one of the most abundant cellular proteins. In tumor cells HSP90 can act as a "buffer" for mutated proteins. **Cynthie Wong** at the **Beckman Research Institute of the City of Hope** will investigate specific antibiotics, called geldanamycin derivatives, which bind to HSP90. She will test the ability of geldanamycin derivatives to inhibit cell proliferation through known cell cycle and apoptosis pathways in Tamoxifen- and aromatase inhibitor (AI)-resistant breast cancer cell lines. Elucidating the mechanism of how geldanamycins can inhibit the proliferation of drug-resistant breast cancers will be beneficial for the development of the next generation of therapies to target endocrine-resistant breast cancers. Finally, DNA repair mechanisms are emerging as promising avenues to target breast cancer, especially since the role of BRCA genes in DNA repair processes have been elucidated. Although only a small percentage of women carry BRCA gene mutations, it is thought that defects in the BRCA1/2 pathways (i.e., “BRCAness”) are common in sporadic breast cancers. Poly (ADP-ribose) polymerase (PARP) repairs DNA single strand breaks through its activation and recruitment of other DNA repair enzymes. PARP inhibitors may overcome defense mechanisms of tumor resistance against standard chemotherapy. **Karlene Cimprich** from **Stanford University** received IDEA funding to “profile” genetic biomarkers of sporadic human breast cancers with the aim of detecting tumors that would be sensitive to PARP inhibitors.

Two newly funded grants have a focus on stem cells, an emerging topic of great importance in cancer research over the past few years. First, **Brunhilde Felding-Habermann** at the **Scripps Research Institute** received a renewal of previous CBCRP IDEA funding for a project to inhibit breast cancer brain metastases by harnessing neural stem cells (NSCs), the body’s own mechanism for healing and regeneration in the brain. As a shielded “sanctuary site”, the brain may harbor breast cancer cells that resist current treatments and can develop into metastases, long after chemo-, radiation- or immuno-therapies have been applied. In Dr. Felding-Habermann’s unique approach, NSCs are “armed” with cytosine deaminase, and then allowed to migrate to sites of tumor growth. At this point they have the potential to kill nearby proliferating breast cancer cells by converting non-toxic 5-fluorocytosine into highly toxic 5-FU.

Lastly, a major reason for failures in cancer therapy is the incomplete elimination of a special type of cell, termed cancer stem cells (CSCs). The CSC model argues that tumors arise from small population (1-2% of the tumor) of cells that retain the properties of adult stem cells, particularly for their ability to self-renew and differentiate into multiple cell types, commonly seen as the heterogeneity of tumor cell types in patient samples. **Frank Pajonk** from the **University of California, Los Angeles,** received IDEA funding to explore ways to increase the radiation therapy sensitivity of a type of CSC, called the breast cancer initiating cell population (BCIC). In fact, breast cancer stem cells exhibit increased radioresistance, such that ionizing radiation interferes with the stem cell "niche" (i.e., the local environment of cells that are important for their regulation) resulting in inhibition of asymmetric cell division, thereby increasing the number of cancer stem cells responsible for treatment failure. Dr. Pajonk hopes to elucidate the signaling pathways, especially radiation-induced "Notch" activation, of the BCIC stem cell population to point the way for potential novel therapies.

Detection, Prognosis & Treatment Grants Funded in 2007

Exploring the Role of PARP Inhibitors in Breast Cancer
Karlene Cimprich, Ph.D.
Stanford University
Award type: IDEA
$157,750

Neural Stem Cell Therapy for Breast Cancer Brain Metastases
Brunhilde Felding-Habermann, Ph.D.
Scripps Research Institute
Award type: IDEA-competitive renewal
$360,277

Novel Cytokine Immunotherapy for Breast Cancer
Ananda Goldrath, Ph.D.
University of California, San Diego
Award type: IDEA
$150,000

Multinuclear MRI of Breast Tumors

Brian Hargreaves, Ph.D
Stanford University
Award type: IDEA
$236,771

Molecular Imaging of Metastatic Lymph Nodes in Breast Cancer
Ella Jones, Ph.D.
University of California, San Francisco
Award type: IDEA
$150,000

Breast Cancer Treatment Monitoring Combining MRI and Optics
Catherine Klifa, Ph.D.
University of California, San Francisco
Award type: IDEA
$149,927

Engineering EGFR Antagonists for Breast Tumor Targeting
Jennifer Lahti
Stanford University
Award type: Dissertation
$75,992

Intraductal Therapy of DCIS: a Presurgery Study
Susan Love, M.D., M.B.A.
Dr. Susan Love Research Foundation
Award type: Translational Research
$851,559

Symposium on the Intraductal Approach to Breast Cancer
Susan Love, M.D., M.B.A.
Dr. Susan Love Research Foundation
Award type: Joining Forces Conference
$25,000

Early Breast Cancer Detection Using 3D Ultrasound Tomography
Thomas Nelson, Ph.D.
University of California, San Diego
Award type: IDEA-competitive renewal
$225,000

Modulation of Breast Cancer Stem Cell Response to Radiation
Frank Pajonk, M.D., Ph.D.
University of California, Los Angeles
Award type: IDEA
$150,000

Polyamide HIF Inhibitors to Block Breast Cancer Metastasis
John Phillips
California Institute of Technology
Award type: Dissertation
$76,000

Determinants of Response to Microtubule Stabilizing Drugs
Tatana Spicakova, Ph.D.
Stanford University
Award type: Postdoctoral Fellowship
$90,000

Mechanisms of HSP90 Inhibitor Action in Breast Cancer
Cynthie Wong
Beckman Research Institute of the City of Hope
Award type: Dissertation
$67,871

Biology of the Breast Cell:
The Basic Science of the Disease

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 co-ordinate migration, proliferation, and apoptosis (cell death) over space and time. In cancer progression these same processes become dysregulated, initially at the genetic level that leads to the physiological changes associated with malignancy. To better mimic breast and tumor architecture, 3-D cell culture models provide a means to explore potential underlying mechanisms and show how extracellular and breast/tumor stromal factors contribute to tumor progression. An emerging paradigm identifies 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 responses to hormones and pregnancy in the breast. If this theory proves correct, then only a small fraction (1-2%) of cells in a tumor mass retain stem cell properties, and these "cancer stem cells" must be selectively targeted to achieve an effective eradication of the disease.

The CBCRP funded 13 new grants in 2007 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 Summary

Three newly funded grants study the biology of the normal breast. Throughout a woman's life, the breast undergoes a series of hormonally-driven developmental changes that involve signaling pathways to prevent abnormal expansion of mammary cells. The retinoblastoma protein (pRb) is a tumor suppressor protein that becomes dysfunctional in many types of cancer. A major function of pRb is to prevent the cell from dividing or progressing through the cell cycle. Thus, when pRb is ineffective at this role, mutated cells can continue to divide and may become cancerous. **Deborah Burkhart** from **Stanford University** was funded through a dissertation award to study the function of the Rb-related proteins, p107 and p130, which need to be inactivated, in addition to pRb, before cancer can occur. She will focus on the regulation and function of p107 in the mammary gland of mice, with the specific goal of understanding how p107 can block cancer in pRb-deficient breast cells. Next, telomerase has been proposed as a key to cellular immortality, a so-called "fountain of youth." In both cancer and normal stem cells the presence of telomerase allows them to divide repeatedly. Telomerase is "turned on" in 90% of human breast cancers and DCIS, making its re-activation one of the most common changes in the disease. **Steven Artandi** also at **Stanford University** will examine an alternate function of telomerase (i.e., the Telomerase Reverse Transcriptase, or the TERT protein) to promote the proliferation and expansion of mammary stem/progenitor cells. In this IDEA renewal grant Dr. Artandi will further develop the hypothesis that conditional activation of TERT in adult mouse epithelium leads breast cancer by promoting an expansion of mammary stem/progenitor cell populations. Finally, many types of early breast cancer lesions are characterized by a loss of normal breast's acinar organization (i.e., the berry-shaped terminal regions of mammary ducts), including a loss of cell-cell adhesion and polarity, increased proliferation, and cellular invasion into the surrounding tissue. These changes are precursors to invasive, metastatic breast cancer. **Catherine Jacobson** from the **University of California, San Francisco,** will study the function of the microtubule-organizing center (MTOC) and the nuclear orientation of mammary epithelial cells along the direction of migration. She will test the function of proteins, such as

Rho GTPase and Cdc42, for their ability to shift the migration of normal mouse epithelial cells grown in three-dimensional culture from an acinar to a migratory phenotype.

Three newly funded projects focus on processes central to breast tumor cell invasion and metastasis. Transforming growth factor-beta (TGFβ) is a secreted protein that is generated in abundance from tumors cells, and there is a strong correlation between high levels of tumor-derived TGFβ and poor clinical prognosis. In cell culture and animal models, TGFβ has been shown to promote processes that stimulate metastasis. Various anti-TGFβ therapeutics are currently entering clinical trials for oncology applications, but despite the potent anti-metastatic action of TGFβ inhibitors for certain tumors, it has been known for a decade that TGFβ can have opposite, tumor-promoting actions in others. **Kelly Harradine** from the **University of California, San Francisco** plans to profile the gene expression patterns of breast tumors to study gene signatures associated with TGFβ. The goal is to develop useful information for clinicians that will predict the breast tumor's response to novel small molecule inhibitors of TGFβ signaling, ultimately facilitating patient selection for treatment. Next, Src is a tyrosine kinase oncogene and is found to be "activated" in most breast cancers. Src sits at the center of a complex web of cellular communication, taking messages from a variety of cell-surface receptors and passing them on to proteins that control cell differentiation and proliferation. Trask is a new Src target protein that, when phosphorylated (phospho-Trask) in breast cancer cells, causes the cells to detach and separate, similar to metastasis. **Ching Hang Wong** also at the **University of California, San Francisco** plans to test the hypothesis that that phospho-Trask brings Src kinases in proximity to the E-cadherin/β-catenin complex, where Src can phosphorylate β-catenin more readily. This would provide a novel mechanism of breast tumor cell metastasis. Finally, tissue factor (TF) is the primary initiator of the blood coagulation cascade, which is physiologically important to prevent excessive bleeding and initiate wound healing. In addition to its crucial role in blood clotting, TF is expressed by tumor cells and this correlates with a poor prognosis. **Florence Schaffner** from the **Scripps Research Institute** will study how blocking the function of TF in both coagulation and in cell signaling may influence breast cancer growth and metastasis. She will treat established tumors in mice with TF-specific antibodies to establish the differential effects of inhibiting either TF signaling or coagulation.

Three grants study processes central to breast cancer cell growth control. Elevated amounts of the ErbB2 (Her-2) oncogene growth receptor are clinically important in 25-30% of breast cancers. Yet, despite the availability of drugs (such as Herceptin®) that specifically target ErbB2, the therapy may fail because we still do not fully understand the cellular components that control ErbB2 activity. **Ralf Landgraf** from the **University of California, Los Angeles,** received IDEA funding to study the role cell membrane lipid domains, called "lipid rafts", play in modulating ErbB2 signaling, dimerization with other ErbB family members, and cell resistance to Herceptin®. It is possible that saturated fatty acids and gangliosides mediate this interplay between lipids and ERBB2, and this ErbB2-lipid raft interplay may provide new insights into the regulation of cell growth, resistance to therapy, and how environmental/dietary factors may influence the course of the breast cancer. Next, the dietary indole, indole-3-carbinol (I3C) found in cruciferous vegetables, has been shown to decrease estrogen receptor-α (ERα) levels, but the mechanism underlying this effect has not been determined. **Crystal Marconett** at the **University of California, Berkeley,** will determine which portions of the ERα gene promoter are sensitive to I3C. This new information could potentially connect critical breast cancer cell pathways known to be affected by I3C, of find novel I3C-regulated ERα pathways. Finally, phopshoinositide (PI) 3-kinases have been linked to a diverse group of cellular functions, including growth, proliferation, differentiation, motility, survival and intracellular protein trafficking. **Jun Zhang** at the **University of California, San Francisco,** aims to generate the first mouse model for examining the role of "activating mutations" in PI 3-kinase α in breast cancer. Once the mouse is generated, Dr. Zhang will examine the interplay PI 3-kinase α mutations with other common breast tumor genetic defects, such as p53 and ARF (GTP-binding proteins of the Ras superfamily). Lastly, this project involves using the mice to test the

effectiveness of a new generation of PI 3-kinase family inhibitors for the treatment of breast cancer.

Two newly funded grants focus on gene regulatory and epigenetic events in breast cancer. Epigenetics includes processes that alter gene activity without changing the DNA sequence. DNA methylation, a chemical modification involving addition or removal of methyl groups from DNA, is a common type of epigenetic mechanism that can "silence" genes, especially tumor suppressors and apoptosis genes that would otherwise block disease progression. Global changes in DNA methylation are known to occur during progression of breast cancer. A loss of the normal cell turnover mechanisms (apoptosis) that keep cell numbers in check is a common feature of breast cancer. **Lorena Puto** from **The Burnham Institute of Medical Research** will study the Daxx adapter protein (death-associated protein 6) that suppresses RelB, a DNA-binding protein that controls the activity of several anti-apoptotic genes. She will focus on the role that DNA methylation plays in the process. Very few examples exist in literature that would explain how specific genes are silenced by DNA methylation in cancer, and none exists in breast cancer. Next, 25% of breast cancers have inactivating mutations in the p53 gene. In the remainder of breast cancers, the p53 gene and protein is normal. Thus, it is unclear how p53 functions in most cancer cells are regulated. **Min Yang** at **University of California, Irvine,** will examine how two histone acetyltransferase (HAT) "docking factors", called ADA2 and ADA3, become altered in breast cancer to reduce p53 gene transcription. Dr. Yang's hypothesis is that transcription factors overexpressed in breast cancers, such as the estrogen receptor and β-catenin, not only turn on genes that promote growth, but also indirectly inhibit tumor suppressors, in particular p53. The mechanism being tested is that the estrogen receptor and beta-catenin recruit ADA2 and ADA3 away from p53.

Finally, two new projects seek to understand events involved in tumor progression. Cancer cells are surrounded by a complex mixture of blood vessels, inflammatory cells, and different types of connective tissue cells. These stromal cells are themselves not cancerous, but have been shown to play a crucial role in cancer development and progression. An alternative avenue of therapy focuses on targeting various non-neoplastic cells that are associated with the tumor microenvironment. **Robert West** from the **Palo Alto Institute for Research & Education** will study the gene expression of soft tissue tumors (STT, including the malignant variants called sarcomas) to dissect and understand the gene expression of normal connective tissue cells, using these SSTs as surrogates for normal connective tissue cells. Dr. West's initial studies show that genes differentially expressed in STTs vary among groups of breast cancers. They plan to confirm and extend these observations to find breast cancer "stromal reaction patterns" as a novel tumor classification scheme. In addition to their use as prognostic markers, potential therapeutic targets may also be discovered in the group of SST genes, if confirmed in breast cancers. Lastly, BRCA1 gene mutations account for 50% of hereditary breast cancers. In sporadic breast cancers, although the BRCA1 gene is intact, its protein expression is often reduced. BRCA1 is known to play an essential role in maintaining genomic integrity mainly through direct involvement in repairing damaged DNA and monitoring cell proliferation. However, these functions of BRCA1 do not adequately explain how its deficiency accelerates breast cancer progression. **Connie Tsai** at the **University of California, Irvine,** recently demonstrated that BRCA1 has a direct role in regulating the expression of an array of genes involved in tumor progression, one of which is HMGA2 (i.e., one of the high mobility group chromosomal proteins with an AT-hook DNA-binding motif that is frequently associated with benign and malignant tumors). Her dissertation award project will study the regulation of HMGA2 expression by BRCA1 and the effects of altering HMGA2 amounts in breast cancer cells and in mouse tumor models.

Biology of the Breast Cell Grants Funded in 2007

Telomerase, Mammary Stem Cells, and Breast Cancer
Steven Artandi, M.D., Ph.D.
Stanford University
Award type: IDEA-competitive renewal
$419,400

Novel Regulation of the Rb Pathway in Breast Epithelium
Deborah Burkhart
Stanford University
Award type: Dissertation
$76,000

Breast Tumor Responses to Novel TGF-beta Inhibitors
Kelly Harradine, Ph.D.
University of California, San Francisco
Award type: Postdoctoral Fellowship
$90,000

Cytoskeletal Regulation of Invading Breast Cells
Catherine Jacobson, Ph.D
University of California, San Francisco
Award type: Postdoctoral Fellowship
$90,000

Lipid Raft Composition in Deregulated ERBB2 Signaling
Ralf Landgraf , Ph.D.
University of California, Los Angeles
Award type: IDEA
$100,000

Indole (I3C) Control of Breast Cancer by ER Downregulation
Crystal Marconett
University of California, Berkeley
Award type: Dissertation
$76,000

Mechanisms of Daxx-Mediated Apoptosis in Breast Cancer
Lorena Puto
The Burnham Institute of Medical Research
Award type: Dissertation
$76,000

Targeting Tissue Factor in Breast Cancer
Florence Schaffner, Ph.D.
Scripps Research Institute
Award type: Postdoctoral Fellowship
$90,000

 **The Relationship of BRCA1 and HMGA2 in Breast Cancer**
Connie Tsai
University of California, Irvine
Award type: Dissertation
$76,000

Determination of Stromal Gene Expression in Breast Cancer
Robert West, M.D., Ph.D.
Palo Alto Institute for Research & Education
Award type: IDEA
$139,441

Trask, a Candidate Breast Cancer Metastasis Protein
Ching Hang Wong, Ph.D.
University of California, San Francisco
Award type: Postdoctoral Fellowship
$90,000

Competition for ADA2 and 3 to Inhibit p53 in Breast Cancer
Min Yang, M.D.
University of California, Irvine
Award type: Dissertation
$76,000

A New Mouse Model of PI3-Kinase Induced Breast Cancer
Jun Zhang, Ph.D.
University of California, San Francisco
Award type: Postdoctoral Fellowship
$90,000

2007 CBCRP Funding by Institution

The following 21 California research institutions and community organizations were awarded new CBCRP funding in 2007. Some community collaborative (CRC) grants were structured as separate awards that are split between institutions.

Institution (city)	**# Awards**	**Amount**
Afghan Coalition (Fremont)	1	$99,255
Alta Bates Summit Medical Foundation (Berkeley)	1	$15,000
Asian Health Services (Oakland)	1	$317,610
Beckman Research Institute of the City of Hope (Duarte)	2	$236,871
California Institute of Technology (Pasadena)	1	$76,000
Burnham Institute for Medical Research (La Jolla)	1	$76,000
Charlotte Maxwell Complementary Clinic (Oakland)	1	$337,500
Dr. Susan Love Research Foundation (Pacific Palisades)	2	$876,559
Northern California Cancer Center (Berkeley)	1	$349,303
Northern Sierra Rural Health Network (Nevada City)	1	$405,000
Palo Alto Institute for Research & Education	1	$139,441
Scripps Research Institute (La Jolla)	2	$450,277
Stanford University	7	$1,397,013
University of California, Berkeley	2	$146,481
University of California, Irvine	2	$152,000
University of California, Los Angeles	2	$250,000
University of California, San Diego	3	$419,003
University of California, San Francisco	7	$929,927
University of Southern California	1	$244,500
Vista Community Clinic	1	$121,402
Women of Essence (Lynwood)	1	$62,500

2007 CBCRP Evaluation Process and Review Committees

The CBCRP thanks the participants in our 2007 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 in a "study section" format 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 in breast cancer areas associated with the committee's central topics (e.g., etiology and prevention). Committee Members have broad expertise in topics associated with individual applications. Breast cancer Advocate reviewers are women and men active in breast cancer issues and many of whom are also living with the disease. Advocates bring their personal knowledge and commitment to the review process. Often they have specialized training in grant review, such as the NBCC's Project LEAD. Each committee also includes a California Advocate Observer, who does not review or vote, but represents the California advocacy community. The observer gains insight into our process and provides feedback to the Program. Ad Hoc members participate by teleconference and bring their specialized expertise to the review of individual applications.

The majority of research funding agencies rate proposals with a single scientific merit score. In contrast, the CBCRP uses a merit scoring system that separates scientific merit into individual components (e.g., approach, innovativeness, impact). This allows our expert reviewers and the Program to better differentiate applications that might otherwise appear identical. For example, we can now pick the most innovative applications, or those that have the highest career development potential. Depending on the award type, we use four or five scientific merit components in the peer review process.

After the completion of all review committees, the CBCRP ranks the application pool by **average scientific merit**. Applications in the upper two-thirds of average scientific merit are rated by the CBCRP's advisory council for **programmatic responsiveness**. The following criteria are used:

- Responsiveness to the CBCRP's priority issues and award types
- Strength of individual scientific merit component scores (e.g., "innovation" for IDEA applications)
- CBCRP balance or an 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 & Translational Research Award), career plan/mentoring (dissertation, postdoc), or dissemination and translation potential (CRC)

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

CRC Concept Paper & CRC-Sociocultural Review Committees

►Chair:

Suzanne M. Miller, Ph.D.
Senior Member
Fox Chase Cancer Center
Philadelphia, PA

►Members:

Deborah Bowen, Ph.D.
Member and Professor
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Charles Wiggins, Ph.D.
Director and Principal Investigator
New Mexico Tumor Registry
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Mayumi A. Willgerodt, Ph.D.
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Etiology & Prevention Committee

►**Chair:**

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Mount Sinai Medical School
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►**Members:**

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Susan Pelletier
Vermont Breast Cancer Coalition
Stockbridge, VT

Rosemary Rosso, JD
National Breast Cancer Coalition
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Njara Stout, MBA
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Ithaca, NY

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►**Ad-Hoc Member:**
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Kapil Dhingra, M.D.
Vice President, Oncology
Hoffmann-La Roche
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The mission of the California Breast Cancer Research Program is to eliminate breast cancer by leading innovation in research, communication, and collaboration in the California scientific and lay communities.

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