2010 Awards Compendium

Cycle 16

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 $8 million for research projects being performed at 17 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 by our volunteer Breast Cancer Research Council, which sets program priorities and recommends the grants to be funded. The council consists of 16 members: five are representatives of breast cancer survivor/advocacy groups; five are scientists/clinicians; two are members from nonprofit health organizations, one is a practicing breast cancer medical specialist, two are members from private industry, and one is an *ex officio* member from the California Department of Health Services breast cancer early detection program, "Every Woman Counts."

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

Core Funding Overview & Award Types

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

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

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

Core Funding award types include:

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

Core Funding Submissions & Review

We received 163 submissions in response to our 2010 *Call for Applications* for new research grants on breast cancer. They were evaluated, discussed in review committee meetings, and rated for scientific merit by our out-of-state peer reviewers. Conference Award applications were reviewed directly by our Breast Cancer Research Council.

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

Table 1. 2010 Core Funding application submissions by award type and priority issue (research topic)

Award Types ↓	Priority Issues				Award Type Totals
	Etiology & Prevention	Community Impact	Detection, Prognosis & Treatment	Biology of the Breast Cell	
Postdoctoral Fellowship	0	1	18	15	34
Dissertation	1	1	9	1	12
IDEA	9	1	54	30	94
IDEA-competitive renewal	0	1	0	2	3
Translational	0	1	6	0	7
CRC Pilot	1	4	0	0	5
CRC Full	0	7	0	0	7
Conference	0	1	0	0	1
Priority Totals	11	17	87	48	**163**

Compared to the previous year (2009/Cycle 15) the application submission changes in award types and priority issues showed these trends:

- The total number of submissions was nearly unchanged (reduced by five)
- Postdoctoral and dissertation applications decreased by almost 20%
- Community collaboration (CRC) applications increased three-fold.
- In the basic science portion of the application portfolio there is a shift from more biology-oriented to treatment-oriented topics.

The CBCRP made several **changes to the review process in 2009** to reduce costs and increase efficiency, and this continued in 2010. First, we initiated a triage process to reduce the number of applications receiving a full review committee discussion. This resulted in the triage of 69 (43%) applications, such that they did not receive a scientific merit score and were not eligible for funding. Next, we eliminated the tertiary level of scientific review for most award types. Finally, we reduced the number of review committees from six in 2008 to four in 2009, and limited the meetings to one-day sessions. Taken together, these and other cost-cutting measures reduced the approximately $450,000/year spent for peer review in 2008 to about $125,000/year in 2009 and 2010.

Finally, the 93 fully-reviewed applications were evaluated for programmatic responsiveness by the CBCRP's 16 member Breast Cancer Research Council. There are seven programmatic criteria for each award type. To select applications to recommend for funding, the council balanced the scientific merit and programmatic ratings. **All funded applications represent projects of high scientific merit that also address the priorities of the Program**.

Core Funding Summary

Applications offered and accepting funding = **35**
Applications offered funding, but declined = **6**
Overall success rate (35/163) = **21%**
Amount awarded in 2010 = $8,181,898

The two tables below summarize the 2010 Core Funding grant distribution by award type and priority issue.

Table 2. 2010 Core Funding portfolio distribution by award type

Award Type	Number of Applications	Grants Funded (Success Rate)	Amount Awarded	Percentage of Total Funding
Dissertation	12	5 (42%)	$380,000	4.6%
Postdoctoral Fellowship	34	6 (18%)	$538,467	6.6%
IDEA	94	18 (19%)	$3,957,995	48.4%
IDEA-Competitive Renewal	3	1 (33%)	$239,673	2.9%
Translational	7	2 (33%)	$1,958,190	23.9%
Community Research Collaboration (CRC)	12	2 (17%)	$1,229,181	15.0%
Conference	1	1 (100%)	$25,000	0.3%

Table 3. 2010 Core Funding portfolio distribution by priority issue

Priority Issue	Number of Applications	Grants Funded (Success Rate)	Amount Awarded	Percentage of Total Funding
Community Impact	17	4 (24%)	$1,493,454	18.3%
Etiology & Prevention	11	2 (18%)	$419,575	5.1%
Biology of the Breast Cell	48	10 (21%)	$1,671,431	20.4%
Detection, Prognosis & Treatment	87	19 (22%)	$4,597,438	56.2%

Comparing the 2010 and 2009 portfolios reveals a number of changes. First, the amount available for “investigator initiated” core funding grants decreased by about $500,000. In addition, the amount of funding for CRC large awards increased by a similar amount. Thus, the number of overall grants fell from 44 in 2009 to 35 in 2010, and the overall success rate decreased by about 5%. In terms of award types, the total number of dissertation and postdoctoral grants decreased from 18 in 2009 to 11 in 2010. Funding for other CBCRP award types remained about the same with the IDEA representing about 50% of the portfolio in terms of both award types and total funding amount.

In terms of research topics (CBCRP priority issues), the basic science areas of Detection, Prognosis & Treatment and Biology of the Breast Cell received less than 75% of the 2010 funding. There continues to be a shift in both application volume and funding away from tumor biology topics towards more detection and treatment-oriented research topics.

Four 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 **Allison Kurian**, Stanford University School of Medicine for *Measuring Real-World Breast Cancer Outcomes*; an IDEA grant to **Peggy Reynolds**, Cancer Prevention Institute of California investigate *Light at Night and Breast Cancer Risk in California Teachers*; an IDEA grant to **Mihaela Lorger**, The Scripps Research Institute for *Targeting Brain Metastasis with a Cell-based Approach*; and an IDEA grant to **Lei Zhang**, University of California, Los Angeles to identify *Salivary Biomarkers for Early Detection of Breast Cancer*.

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 **2010 Faith Fancher Research Award** are **Jeffrey Belkora** (University of California, San Francisco) and **Sara O'Donnell** (Mendocino Cancer Resource Center) for their community collaborative project, **Recording Medical Visits for People with Breast Cancer**. Women diagnosed with breast cancer often struggle to ask questions and absorb, understand, and act upon the information they get from doctors. The aim of this project is to help patients develop a list of questions prior to major medical visits, and providing audio-recordings and/or plain language summaries of consultations. Although based in rural Mendocino County, this study will address barriers to the broader adoption of interventions that help patients and doctors exchange information more effectively. The findings will be relevant to support programs focused on improving educational and quality of life outcomes for over 250,000 people making breast cancer treatment decisions every year.

Community Impact of Breast Cancer:
portfolio summary

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 14 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 Impact Portfolio

The CBCRP funded four new grants that address the "community impact" topic. Two of these were Community Research Collaborations.

First, it is important for patients, who often lack resources and skills, to gain a full understanding of their cancer diagnosis and the treatment options open to them. This becomes even more critical with the expansion of Health Information Technology to streamline and make health care systems more effective and cost-efficient in delivery. **Jeffrey Belkora** from the **University of California, San Francisco** and **Sara O'Donnell** at the **Mendocino Cancer Resource Center** address patient-provider communication in their project, *Recording Medical Visits for People with Breast Cancer*. The aim of this project is to help patients develop a list of questions prior to medical visits, and make audio-recordings and/or plain language summaries of consultations. Although based in rural Mendocino County, this study will address barriers to the broader adoption of interventions that help patients and doctors exchange information more effectively. The findings will be relevant to patient support programs focused on improving educational and quality of life outcomes for over 250,000 people making breast cancer treatment decisions every year.

American Indian/Alaska Native (AI/AN) women have the poorest cancer screening rates (42% in 2007) of any ethnic group in California, and AI/AN women with breast cancer have the lowest 5-year survival rate when compared to other ethnic groups. To tackle this disparity **Marlene von Friederichs-Fitzwater** at the **University of California, Davis** will partner with **Linda Navarro** from the **Turtle Health Foundation** to deliver the Mother's Wisdom Breast Health Program to 320 American Indian/Alaska Native women in California, ages 41 and older, who have not had a mammogram within the past two years. The Mother's Wisdom program uses a DVD to provide consistent, culturally sensitive information to women, regardless of their literacy; and combines traditional values, beliefs, and philosophy with Western medical information. The goal of Dr. von Friederichs-Fitzwater's and Ms. Navarro's study is to increase breast cancer screening rates among non-compliant American Indian/Alaska Native (AI/AN) women in California.

A key unanswered question underlying disparities in detection and treatment is the degree to which medical facilities treating underserved (i.e., vulnerable) women offer inferior services that compromise disease outcomes. **Lauren Goldman** from the **University of California, San Francisco** completed a CBCRP IDEA project funded in 2008 and found that diagnostic mammograms interpretations at facilities serving vulnerable women are more likely to recommend biopsy for women who did not subsequently receive a cancer diagnosis, without any difference in cancer detection among women who were diagnosed with cancer. To continue these studies, Dr. Goldman received an additional two year grant to validate these findings using two new databases, (1) the 2009 Breast Cancer Surveillance Consortium (BCSC) Facility Survey, a national survey of mammography facilities, and (2) a new linkage to Medicare Claims data to study facility characteristics. The potential of this research is to translate the influence of the patient, provider, and facility-level system factors to change modifiable factors of diagnostic mammography accuracy to neutralize the differences for vulnerable populations.

The CBCRP provided partial funding for the *2nd National Latino Cancer Summit* in San Francisco, CA on July 27-29, 2010. This conference is organized by the community group, **Latinas Contra Cancer**, with **Ysabel Duron** as the Founder & Executive Director. A study by MD Anderson published in June 2009 in the Journal of Clinical Oncology finds that cancer in the Latino community will likely increase by 142% over the next two decades. The Summit conference addressed cancer issues in the Latino community, along the cancer continuum - prevention, diagnosis, treatment, survivorship and end of life with special focus on prevention, intervention and innovation.

Community Impact Grants Listing

Recording Medical Visits for People with Breast Cancer
Award Type: CRC-Full
Belkora, Jeffrey, Ph.D. (co-PI)
University of California, San Francisco
$450,000
O'Donnell, Sara (co-PI)
Mendocino Cancer Resource Center
$187,500

2010 National Latino Cancer Summit
Award Type: Conference
Duron, Ysabel
Latinas Contra Cancer
$25,000

Quality of Mammography Facilities Serving Vulnerable Women
Award Type: IDEA, renewal
Goldman, Lauren, M.D.
University of California, San Francisco
$239,673

Increasing Mammography Screening Among Native Women
Award Type: CRC-Full
von Friederichs-Fitzwater, Marlene, Ph.D. (co-PI)
University of California, Davis
$217,281
Navarro, Linda (co-PI)
Turtle Health Foundation
$374,400

Etiology & Prevention: portfolio summary

Overview: Risks associated with breast cancer are often classified into: family history factors, hormonal and reproductive factors, and lifestyle and environmental factors. Some estimates place more than 70% of breast cancers as likely attributable to environmental factors. Since over 75% of breast cancers occur in postmenopausal women, this late onset is consistent with the long latency periods usually related with chemical carcinogenesis in humans. Thus, effective preventive strategies for breast cancer must take into account individual risks to reduce exposure to environmental chemicals and other agents, combined with lifestyle changes (diet, exercise, alcohol consumption, and hormonal exposure).

Etiology & Prevention Portfolio

The CBCRP funded two new IDEA grants to address the etiology and prevention (risk reduction) topic. It has been proposed that exposure to light at night (LAN) can increase the risk of breast cancer by disrupting normal circadian rhythms. A number of possible mechanisms have been suggested to explain how such an exposure could result in an increased risk of breast cancer. **Peggy Reynolds** at the **Cancer Prevention Institute of California** will take advantage of a unique resource, the California Teachers Study (CTS) cohort, and newly-available satellite data on night-time illumination, to develop methods of estimating individual LAN exposure levels. Dr. Reynolds will then evaluate the relationship between LAN exposure and breast cancer risk, taking into account existing data on established risk factors. The primary purpose is to determine whether LAN is associated with an increased risk of breast cancer, independent of night shift work and/or other factors associated with night shift work (e.g., stress, sleep disruption, or type of occupation).

As recently reported in the New York Times, vitamin D will be the "most talked-about and written-about supplement of the decade." Deficiencies in this vitamin include an elevated risk of cancers of the colon, breast and prostate; high blood pressure and cardiovascular disease; osteoarthritis; and immune-system abnormalities. These deficiencies are thought to be attributable to people limiting their sun exposure, which reduces the natural mechanism of producing Vitamin D in the skin. In addition, African Americans (AA) average less circulating Vitamin D compared to Caucasians, and they are below a critical circulating minimal threshold 10-fold more frequently. **Wei Wang** also at the **Cancer Prevention Institute of California** will utilize data from 2,244 women with breast cancer (541 AA, 1,107 Hispanics, 596 non-Hispanic Whites) to examine the relationship between the chance of dying after breast cancer diagnosis and several measures of an individual's vitamin D status. Dr. Wang will also examine genetic variations (polymorphisms) in the vitamin D receptor to determine how these might be associated with breast cancer outcome and ethnic variations in survival.

Etiology & Prevention Grants Listing

Light at Night and Breast Cancer Risk in California Teachers
Award Type: IDEA
Reynolds, Peggy, Ph.D
Cancer Prevention Institute of California
$199,080

Vitamin D and Breast Cancer Survival
Award Type: IDEA
Wang, Wei, M.D.
Cancer Prevention Institute of California
$220,495

Detection, Prognosis & Treatment:
portfolio summary

Overview: Most CBCRP-funded projects that focus on the detection, prognosis, and treatment of breast cancer represent a "bridge" between new basic science discoveries and their practical application in the clinical setting. Earlier detection and staging/prognosis for breast cancer often fails to distinguish aggressive disease requiring therapy from early, pre-invasive DCIS that often need less aggressive intervention strategies. Thus, new information from tumor biology, stem cell biology, immunology, and advanced knowledge of cellular processes, such as DNA repair and hormone signaling, are continually being studied for new detection, prognosis, patient stratification, and treatment potential.

Detection, Prognosis & Treatment Portfolio

Two newly funded grants are **translational projects** that aim to directly impact patient care. First, little research effort has been directed to analyze novel treatments for breast cancer, and their dissemination and use in clinical practice for an average patient, outside of clinical trials- the so-called "real world setting." Factors that influence this phase of translation may have the biggest practical impact. **Alison Kurian** from **Stanford University** will employ a unique database approach, called OncoShare, to extract "de-identified data" from the electronic health records of all patients receiving breast cancer care at Stanford and the Palo Alto Medical Foundation (PAMF) from 2006-2009. The key data elements include: demographics, chemotherapy drug orders, laboratory, radiologic, and pathologic test results. A unique innovation in OncoShare is its ability to mine physician's clinical notes through "Natural Language Processing" technology, in order to obtain insights into clinical decision-making. Dr. Kurian's team will enhance OncoShare with patient-reported data, and develop a survey instrument in partnership with breast cancer advocates. Then, they will administer it to a prospective cohort of women starting therapy at Stanford and PAMF. They will use classification and regression trees (CART) analysis to evaluate patterns of care in the retrospective (N=2520) and prospective (target N=320) cohorts, and to determine the impact of patient-reported information on care.

Next, the success of new targeted therapies depends on the ability to administer them to specific patient groups in terms of dosing and other factors to maximize the changes for success. Lapatinib (GlaxoSmithKline) is an orally active drug for breast cancer and other solid tumors. It is a "dual tyrosine kinase inhibitor", which interrupts the HER2 growth receptor pathway, and is often used in combination therapy in HER2-positive patients, especially when patients have progressed on Herceptin. **Mark Moasser** at the **University of California, San Francisco** plans a phase I clinical trial to enhance lapatinib effectiveness by employing higher, intermittent dosing, increasing dietary fat intake, and using ketoconazole (an antifungal drug that inhibits the enzyme, cytochrome P450). The aim is to achieve better drug absorption and higher blood levels in patients, hopefully to better inactivate tumor HER2-HER3 signaling and induce more clinical remissions. An innovative element of this study is the use of CT imaging to evaluate potential cardiac toxicity in the treatment regimen.

Five newly funded grants focus on either earlier detection of breast cancer through imaging technologies or novel biomarker approaches.

The use of blood samples as a source of biomarkers has had limited success. Examples of tumor markers include: prostate-specific antigen (PSA) for prostate cancer, cancer antigen 125 (CA 125) for ovarian cancer, and alpha-fetoprotein (AFP) for liver cancer. In particular, the PSA test, introduced in 1987, has been found to save few lives in recent reports of long term studies. More recent approaches, such as mass spectrometry for broadband metabolic profiling of ovarian cancer have not yet come into clinical use. In the past 1-2 years much interest is focused on microRNAs (MiRs) for blood detection of breast cancer. **David Hoon** from the **John Wayne Cancer Institute** is funded thought an IDEA grant to explore a *Multimarker miR Blood Assay for Breast Cancer Detection.* MiRs are non-coding RNA molecules (18~22 nucleotides) expressed in a tissue-specific manner, and are stable in the circulation. Dr. Hoon's team has developed a direct PCR assay (no extraction from blood samples) that will be applied to detect early-stage breast cancer with greater sensitivity and accuracy than standard screening/detection. Thus, the objective is to develop a miR biomarker panel for clinically relevant assessment of serum in patients at risk of new or recurrent breast cancer.

In a similar manner, **Lei Zhang** from the **University of California, Los Angeles** will investigate salivary transcriptomic (mRNA) biomarkers for the non-invasive early detection of breast cancer. In previous work Dr. Zhang has validated this approach for pancreatic cancer, and identified a panel of promising mRNA biomarkers for breast cancer. The CBCRP funding will test these biomarkers for their potential to detect and discriminate DCIS and Stage I/ IIA invasive ductal carcinomas that Dr. Zhang's collaborators at the Cedars-Sinai Medical Center have collected and classified. In addition, this group has initiated a "Saliva Drive" to collect samples at the waiting area of the UCLA hospital system to increase awareness of salivary diagnostics and its potential for diagnosing breast cancer and other cancers non-invasively.

Three newly funded projects focus on novel imaging technologies. Often, the images obtained during breast cancer screenings are able to detect tumors that are non-palpable (i.e., cannot be felt to the touch). Because these tumors are non-palpable, the surgeon requires a physical marker in order to find the tumor during surgery. The current method is image-guided wire placement. It is a multistep process where ultrasound, mammography, or MRI, is used to image the tumor, then a thin wire is placed into the approximate center of the tumor. However, wire localization is not precise, and often results in residual cancer tissue left in the breast after surgery. **Rachel Bitton** from **Stanford University** is funded to explore the use of MR-Image guided Focused Ultrasound (MR-FUS) to thermally create palpable lesions, and circumscribe an otherwise non-palpable tumor. Working in the lab of her mentor, Bruce Daniel, this approach non-invasively creates a small thermal hot spot (about the size of a grain of rice) that kills cells at targets deep within the body, while completely sparing healthy adjacent tissues. The mechanical properties of the tissue change due to heating, and can become stiffer while the patient is inside the MRI scanner, so that surgeons can accurately feel the tumor's location.

During neoadjuvant (pre-surgery) chemotherapy, one of the challenges is to be able to visualize the tumor bed and detect residual disease in the breast. However, breast deformation and re-positioning present critical challenges for accurate delineation of tumors and visualization to measure the effect of therapy and presence of residual disease. **Muqing Lin** at the **University of California, Irvine** will develop image registration algorithms for MRI applied to neoadjuvent chemotherapy and also to develop 4D algorithms (with time as the 4th dimension) for proper tissue registration. The goal is to better measure and compare the "tumor bed" before and after treatment.

Finally, breast PET (positron emission tomography) is not yet an accepted method for screening, but it has significant potential for breast cancer staging and for assessing treatment. PET is constantly evolving with higher resolution and sensitivity, but there is still room for improvement. The combined use of PET, such as PET-CT is not routine, and PET-MRI has also been developed and it is under investigation at a few centers around the world. However, the intrinsic poor resolution of PET remains as the weak link, and this is being addressed in a new dissertation grant to **Frances Lau** from **Stanford University**. This research in the mentor's (Craig Levin) lab focuses on only one component in PET design, the signal processing module to improve image quality. Their approach will use an innovative architecture that enables the multiple analog circuits in current PET instruments that will be combined with the analog-to-digital converter into a single integrated circuit. They expect that this approach will consume much less power with a much smaller "electronic footprint." The long term goal is to develop a high-resolution (~1mm), portable, breast-dedicated PET camera.

Nine newly funded grants focus on improving chemotherapy of hormone therapy for breast, or address issues of drug resistance and failed drug response.
First, women with HER2-positive breast cancers are reported to be resistant to treatment with anti-estrogen therapies, such as tamoxifen, and more responsive to certain forms of chemotherapy, such as anthracycline-containing chemotherapy and taxane-containing chemotherapy. In addition, many HER2-positive breast cancer patients benefit greatly from the use of targeted therapies that interfere with signaling through the HER2 receptor protein, such as trastuzumab and lapatinib. However, a significant portion of women do not respond to these treatments and the genetic/molecular basis is not known. **Michael Press** from **University of Southern California** will test the hypothesis that treatment responsiveness in HER2-positive breast cancer is modulated by other genes, most of which are co-amplified with HER2, either as part of the same amplicon (i.e., pieces of genomic DNA formed as the products of natural or artificial amplification events), or at remote locations from the HER2 amplicon. Dr. Press will evaluate both HER2 gene amplification and co-amplification of selected candidate genes in a pilot "test set" study of 976 breast cancer specimens from women whose detailed clinical treatment and outcome is known. In addition, they will identify genes co-amplified with HER2 in a series of 45 human breast cancer cell lines and in a series of 107 tissue specimens on a genome-wide basis using single nucleotide polymorphism (SNP) arrays.

Monoclonal (mAb) antibody technology has prolonged the survival of thousands of patients with cancer. Despite the promising activity of monoclonal antibodies, including trastuzumab (Herceptin), the response rates among patients with either refractory or advanced cancer are usually suboptimal at less than 25%. One of the primary mechanisms of mAb antitumor action is through antibody dependent cell-mediated cytotoxicity (ADCC), whereby a natural killer (NK) cell bearing an Fc receptor binds to the antibody-targeted tumor cell and mediates the actual killing function. **Ronald Levy** from **Stanford University** will investigate whether administration of anti-CD137 mAb will synergize with trasntuzumab in enhancing ADCC-dependent elimination of breast cancer cells using a mouse model. Comparable studies on lymphoma have shown promising results.

Aromatase inhibitors (AI) are currently the most commonly used endocrine therapy agents to treat ER-positive breast tumors. However, increasing evidence shows that tumors eventually acquire resistance to AI therapies. **Karineh Petrossian** at the **Beckman Research Institute of the City of Hope** is funded for her dissertation research to identify novel kinases/growth factors involved in endocrine resistance via the approach of of kinomics (i.e.,

cataloging and understanding protein phosphorylation by protein kinases). They will further study for the role of a specific kinase, called Cdk7, in acquired endocrine resistance in tumors. A long-term estrogen deprived cell line (LTEDaro) is available for these studies, and additional cell lines are in the process of being generated in the mentor's lab (Shiuan Chen).

Two newly funded grants deal with endocrine (SERM) drug resistance. Approximately 70% of breast cancers express estrogen receptor alpha (ERα) and these tumors tend to respond favorably to anti-hormones, such as tamoxifen (TAM), which targets the ER and blocks its activation by 17β-estradiol and related estrogens. Despite its effectiveness, however, ER positive tumors generally acquire resistance to TAM, and this results in a very poor prognosis when the cancer recurs. In the first newly funded grant, **Nicolas Andrews** at the **University of California, Davis** will study ANCCA, an ATP-dependent transcription regulator that functions as a co-activator of several other transcription factors including estrogen receptor, E2F1 (control of cell cycle), and c-MYC (regulate expression of 15% of all genes). Dr. Andrews will explore the growth properties of MCF-7 cells engineered to increase ANCCA in the presence of estrogen or tamoxifen using mouse models. In additional work in the mentor's laboratory (Dr. Hongwu Chen), he will identify target genes of ANCCA and investigate whether ANCCA can be used as a biomarker of disease progression by studying archived 200 breast cancer samples. Using a different approach, **Richard Pietras** from the **University of California, Los Angeles** will design a new class of compounds (drugs) to specifically bind ER, but that also disrupt and destabilize ER, which should lead to ER loss in tumors and a blockade of tumor growth. Once these compounds are identified, they will be tested using both endocrine-sensitive and endocrine-resistant breast tumor cells. Potential synergy of these novel SERMs with the HER2 inhibitor, trastuzumab (Herceptin) will be considered as a possible dual treatment strategy.

It is estimated that 20-30% of women diagnosed with breast cancer in the California will have hormone receptor-negative (HRN) invasive breast cancer, an aggressive subtype of breast cancer that also disproportionately affects young women, African Americans, and Latinas. A growing body of pre-clinical evidence implicates excessive histone deacetylation (HDAC, epigenetic regulation) as a primary mechanism responsible for loss of ER, and possibly PR gene expression, in breast cancer. **Dennis Holmes** from the **University of Southern California** will treat patients (tumors > 2cm) with triple-negative breast cancer for 21 days with an HDAC inhibitor, called SAHA, prior to surgery and tumor samples will be obtained pre and post treatment to determine ER, PR and HER/2 expression. If successful, then this novel approach would enable the use of more effective SERMs for treatment of initially-diagnosed HRN women.

Two newly funded grants explore the potential use of microRNAs (MiRs) with a focus on the treatment setting. First, neoadjuvant chemotherapy (NCT) is used prior to surgery in patients with locally advanced breast cancers. The response to NCT varies between 30–60%, and is correlated with improved survival. **Shizhen Emily Wang** at the **Beckman Research Institute of the City of Hope** will determine circulating microRNAs (miRs) profiles from breast cancer patients and correlate these MiR profiles with NCT response. The goal is to characterize individual breast cancer patients by their miR profiles and determine if changes in miRs in tumors and/or in circulation will best measure the tumor-shrinking effects of NCT. Dr. Wang's project could lead to a simple, low-cost blood test. Next, the oncoprotein c-MYC is one of the key effectors of estrogen signaling and overexpression of c-MYC has been observed in the development of endocrine-resistant breast cancer cells. ATM (ataxia telangiectasia mutated) is the major transducer in DNA damage response and alteration of ATM expression or its activity

has been shown to modulate cellular radiosensitivity (including cancer stem cells), thus providing a molecular target for developing new sensitizers. **Hailang Hu** from the **University of California, Los Angeles** will study the miR-374b/421 cluster for its ability to increase the sensitivity of breast cancer cells to anti-estrogens, chemotherapeutic compounds, or radiation by the ability of the MiR cluster to target c-MYC and ATM concurrently. This type of MiR therapy could reduce doses of radiation and drugs, thereby easing the burden of treatment.

Mitotic inhibitors, such as taxol, have proven to be effective anti-cancer agents; however, these agents are associated with toxicity issues due to non-specific effects on non-malignant cells. **Erin Goldblatt** from the **University of California, Irvine** will study Hec1 (Highly Expressed in Cancer 1), which is essential for chromosome condensation, migration, and cell mitosis. Importantly, increased amounts of Hec1 are associated with poor prognosis of primary breast cancers in humans, and Hec1 also initiates tumor formation in a mouse model, suggesting that Hec1 functions as an oncogene. Dr. Goldblatt's mentor (Wen-Hwa Lee) has identified, developed, and characterized a small molecule inhibitor of Hec1 function, called INH1, which increases mitotic index, spindle abnormalities, chromosome segregation errors, and induces cell death. The research hypothesis is that mitotic disruption through combined treatment with INH41 and paclitaxel will inhibit the ability of cancer cells to maintain genomic stability, thereby increasing cell killing and enhancing the efficacy of therapeutic regimens.

Three newly funded grants focus on metastasis of breast cancer to the brain or breast cancer stem cells.

Breast cancers are made up of phenotypically distinct populations of cells, including a subset of stem cell-like cells referred to as breast cancer stem cells (BCSCs). BCSCs are associated with a more aggressive phenotype, resistant to conventional chemotherapies, and are thought to be responsible for recurrence of metastatic disease. Cancer stem cells have genetic properties similar to that of embryonic stem (ES) cells in terms a common transcriptional profile (mRNAs) driven by the MYC oncogene/transcription factor. **Noelle Husky** from the **University of California, San Francisco** will investigate a novel approach to specifically target the sub-population of BCSCs within breast tumors. Working in Andrei Goga's (mentor) lab, they will study cyclin-dependent kinase inhibitors (CDKs) for their ability to induce apoptosis (programmed cell death) in BCSCs, and determine whether this effect is MYC-dependent.

The metastasis of breast cancer to the brain is a critical clinical problem, particularly with patients surviving longer with targeted therapies, such as Herceptin. Brain microglial cells, which originate from hematopoietic stem cells (HSC), surround brain metastases and appear to provide a microenvironment essential for growth. Since microglial cells are of hematopoietic origin, they can also be used as gene therapy vehicle to deliver drugs or anti-tumor agents to brain due to an ability to cross the blood-brain barrier. **Mihaela Lorger** from the **Scripps Research Institute** will test whether suppression of microglial activation can inhibit the proliferation of metastatic brain lesions using a mouse model. Further, Dr. Lorger will explore the potential of using HSC for therapy by testing their specific homing potential to breast tumor metastatic sites in the brain. In a separate grant to the same laboratory, **Brunhilde Felding-Habermann** also at the **Scripps Research Institute** has previously identified a cell adhesion receptor, called $\alpha v\beta 3$, as key player in tumor metastasis. Furthermore, $\alpha v\beta 3$ binds the RGD peptide sequence found on adhesion molecules (e.g., vitronectin and fibronectin). Such discoveries aided in the development of Cilengitide (cyclic peptide cyclo(-RGDfV-), a small molecule inhibitor of integrin, $\alpha v\beta 3$. Cilengitide, a Merck Company product, is currently in Phase

3 trials to assess its effectiveness against primary glioblastoma in man. As brain metastasis is more common in HER2-positive patients, Dr. Felding-Habermann plans to evaluate a combination of Cilengitide and lapatinib to concurrently interrupt HER2/EGFR1 signaling and tumor cell adhesion as a novel therapeutic approach for brain metastasis. This study is also performed in mouse models.

Detection, Prognosis & Treatment Grants Listing

The Role of ANCCA in Tamoxifen Resistant Breast Cancer
Award Type: Postdoctoral fellowship
Andrews, Nicolas, Ph.D.
University of California, Davis
$90,000

MRI Guided Focused Ultrasound in Breast Cancer Treatment
Award Type: Postdoctoral fellowship
Bitton, Rachel, Ph.D.
Stanford University
$88,467

Inhibiting Breast Cancer Brain Metastasis with Cilengitide
Award Type: IDEA
Felding-Habermann, Brunhilde, Ph.D.
Scripps Research Institute
$284,850

Hec1 Inhibitor Synergizes With Taxol in Breast Cancer
Award Type: Postdoctoral fellowship
Goldblatt, Erin, Ph.D.
University of California, Irvine
$90,000

Receptor Re-expression in ER and PR Negative Breast Cancer
Award Type: IDEA
Holmes, Dennis, M.D.
University of Southern California
$243,000

Multimarker miR Blood Assay for Breast Cancer Detection
Award Type: IDEA
Hoon, David, Ph.D.
John Wayne Cancer Institute
$282,900

Targeting Drug Resistant Breast Cancer by microRNAs
Award Type: IDEA
Hu, Hailang, Ph.D.
University of California, Los Angeles
$100,000

Targeting Breast Tumor Stem Cells with Cell Cycle Inhibitors
Award Type: Dissertation
Huskey, Noelle
University of California, San Francisco
$76,000

Measuring Real-World Breast Cancer Outcomes
Award Type: Translational
Kurian, Allison, M.D.
Stanford University, School of Medicine
$1,066,225

Electronics for High Resolution Breast-Dedicated PET
Award Type: Dissertation
Lau, Frances
Stanford University
$76,000

Enhancing Trastuzumab Therapy with an NK Activating Antibody
Award Type: IDEA
Levy, Ronald, M.D.
Stanford University
$225,389

MRI Registration for Therapy Evaluation and Annual Screening
Award Type: Dissertation
Lin, Muqing
University of California, Irvine
$76,000

Targeting Brain Metastasis with a Cell-based Approach
Award Type: IDEA
Lorger, Mihaela, Ph.D.
Scripps Research Institute
$284,850

Towards Highly Effective Inactivation of HER2-HER3 Signaling
Award Type: Translational
Moasser, Mark, M.D.
University of California, San Francisco
$745,757

A Novel Mediator of AI Resistance in Breast Cancer
Award Type: Dissertation
Petrossian, Karineh
Beckman Research Institute of the City of Hope
$76,000

New Estrogen Receptor Downregulators for Breast Cancer
Award Type: IDEA
Pietras, Richard, M.D., Ph.D.
University of California, Los Angeles
$150,000

HER2 Co-Amplified Genes and Treatment Response
Award Type: IDEA
Press, Michael, M.D., Ph.D.
University of Southern California
$243,000

Breast Cancer Neoadjuvant Chemotherapy Response with miRNA
Award Type: IDEA
Wang, Shizhen Emily, Ph.D.
Beckman Research Institute of the City of Hope
$249,000

Salivary Biomarkers for Early Detection of Breast Cancer
Award Type: IDEA
Zhang, Lei, Ph.D.
University of California, Los Angeles
$150,000

Biology of the Breast Cell: portfolio summary

Overview: It has now been a decade since the publication of Hanahan and Weinberg's influential "six hallmarks of cancer" review in Nature, and these critical distinctions (self-sufficiency in growth signals, evading apoptosis, insensitivity to antigrowth signals, limitless replicative potential, sustained angiogenesis, and tissue invasion and metastasis) between normal and tumor cells remain at the core of current basic science research efforts. Likewise, we are a decade removed from the landmark paper by Perou and colleagues that classifies breast tumors by patterns of gene expression into five major subtypes. Researchers can now use cell and animal models to better reflect variations in breast cancer seen at the clinical level. Finally, we are nearly a decade into the "post genomic era" and approaching the time when each person's genome (or tumor DNA) might be sequenced for under $1,000 as new technologies emerge. Still, despite the vast amount of new research, there remains a substantial gap between reductionist knowledge ("pieces of the puzzle") at the molecular, biochemical, cellular and animal model levels versus. "real world" breast cancer in the clinical setting influenced by each patient's unique genetics, life history, and environmental factors that underlie disease initiation and progression.

Biology of the Breast Cell Portfolio

Five newly funded projects focus on either metastasis or the breast tumor's microenvironment in terms of its ability to regulate tumor progression. These are related to an "endothelial-to-mesenchymal transition" (EMT) that involves "global shifts" in cell phenotype that occurs in tissue formation and cell migrations during embryogenesis. Twist1 is a basic helix-loop-helix transcription factor (protein) that was initially identified as a critical inducer of EMT during mesoderm formation in development. Studying EMT remains challenging, due in part to its rare occurrence. Therefore, the majority of studies on EMT are performed using established epithelial cell lines grown in two-dimensions, which do not accurately recapitulate the EMT program in the body. **Jeff Tsai** at the **University of California, San Diego** will use a three-dimensional mammary "organoid" culture system to visualize and study EMT. Normal mammary ducts are bilayered, with basal myoepithelial cells surrounding the luminal epithelial cells, and Dr. Tsai, working in the laboratory of his mentor (Jing Yang) will reproduce this morphology in his organoid system to study the role of Twist1.

Increasing evidence supports the concept that cancer cells cannot develop into a lethal tumor without the cooperation of other neighboring cells, such as fat cells. Adipocytes are present in the tumor micro-environment, and they produce angiogenic, inflammatory, and endocrine factors to affect neighboring breast cancer cells. **Barbara Mueller** at the **Torrey Pines Institute for Molecular Studies** received IDEA funding to explore the role of *Local Adipocyte Function in Breast Cancer*. The aim is to develop a new mouse model to study interactions between fat and breast cancer cells and to understand the mechanism by which fat cells enable growth of hormone-dependent breast cancer (focusing on leptin and its regulation of aromatase activity). This novel animal model will not rely on the endogenous fat, but rather on transplanted fat cells (i.e., fat cells from obese mice) or fat tissues from donor mice into recipient mice.

It has been suggested that breast tumors are like "wounds that never heal." Processes involved in wound healing, such as activation of matrix remodeling, inflammation, and cell motility and angiogenesis, are also common features of tumor progression. For example,

rheumatoid arthritis patients who regularly take NSAIDs (which fight inflammation) almost never get colon cancer. Mesenchymal stem cells (MSC), which are thought to expedite healing by "homing" to wounded tissue, have been shown to be recruited to the stroma of the developing breast cancers. However, in this setting MSC turn into tumor-associated fibroblasts and contribute to tumor growth and metastasis. The complement cascade (i.e., blood proteins that "complements" the ability of antibodies to clear pathogens) may play a role in this process, and persistent complement activation occurs in breast cancer. **Ingrid Schraufstatter** also from the **Torrey Pines Institute for Molecular Studies** has previously shown that MSC express receptors for the complement factors C3a and C5a. Together, with evidence that breast tumor cells secrete C3a and C5a, Dr. Schraufstatter will test whether C3a and C5a are responsible for breast tumor-dependent recruitment of MSC and how this affects tumor progression.

Reelin is a protein that regulates neuron migration and positioning in the developing brain. Its name comes from the abnormal reeling gait of mice deficient in this protein. **Ellen Carpenter** at the **University of California, Los Angeles** is funded though an IDEA to study how in mammary epithelial, Dab-1, the intracellular adaptor protein that links reelin the migratory cytoskeleton functions in mammary development and tumor metastasis. In other studies, Dr. Carpenter will utilize tumor cell lines and relate reelin/Dab-1 normal and altered functions to metastatic behavior.

The AAA protein family ("Triple A", ATPases Associated with various cellular Activities) is widespread through evolution, but a fairly recent discovery in terms of cancer biology. One member of this family, called p97 (also called VCP for valosin-containing protein), is key player in many cellular protein degradation and protein remodeling pathways. **Martin Latterich** from the **Proteomics Research Institute for Systems Medicine** will study a mouse model of p97 to see whether its activity is responsible for aggressive metastatic behavior. The overall aim of this study is that a molecular switch controls metastasis and that this switch might provide a target for new therapeutic approaches to delay breast cancer metastasis.

Other newly funded grants consider a range of topics in normal mammary and tumor biology. Novel paradigms for breast cancer etiology arise from studies on other epithelial and proliferating cell populations. For example, transcriptional control (i.e. selective gene expression) mechanisms that underlie normal development of epidermis and hair follicles may provide insights into mammary gland carcinogenesis. **Suman Verma** at the **University of California, Irvine** will study whether the up-regulation of the Clim proteins results in an increase in breast cancer stem cell characteristics. Related research in the mentor's (Bogi Andersen) lab clearly indicate a linkage of Clim proteins in the maintenance of hair follicle stem cells and cornea homeostasis. Clim serves to regulate another factor, called LMO4 that affects proliferation of mammary epithelial cells. Dr. Verma will identify the cellular mechanism by which Clims regulate the normal mammary stem cell population and their role in breast tumor development.

Tumor progression is a multi-step process involving genetic alterations, such as activation of tumor promoting oncogenes and the inactivation of tumor suppressor genes. Cancer-promoting mutations occur via biochemical pathways that may have evolved to facilitate the completion of replication in the presence of DNA defects that occur in normal cells, especially as a result of aging. The previously known pathway of induced mutation in humans relies on a group of proteins that function in 'post replication repair' (PRR) and ultimately leads to the induction of specialized DNA polymerases that perform 'translesion synthesis' across the

damaged DNA. In an effort to identify pathways of induced mutations associate with breast cancer, **Floyd Romesberg** at the **Scripps Research Institute** screened the entire yeast genome for gene deletions that render the cell less mutable in response to different types of DNA damage. This major pathway of induced mutation in yeast and involves the enzyme ribonucleotide reductase, which supplies the building blocks of DNA (dNTPs), and a polymerase enzyme that normally copies DNA without errors. Dr. Romesberg will extend these observations to human breast cancer cells to determine whether one of the regulatory subunits of ribonucleotide reductase effectively inhibits mutation in cultured human breast epithelial cells.

The triple-negative (Her2, ER/PR negative) subclass of breast cancer represents the most aggressive genetic subset and is usually associated with poor prognosis. It is diagnosed more frequently in younger women, those with BRCA1 mutations, and African-American and Hispanic ethnic groups. Since these tumors do not respond to hormonal therapy (tamoxifen or aromatase inhibitors) or therapies that target HER2 receptors, such as Herceptin, there is an intensive effort to uncover new treatment strategies. **Leonard Kusdra** from the **University of California, San Francisco** will take a novel approach using information gained in his mentor's (Andrei Goga) lab showing that triple-negative cancers tend to have high levels of a protein called Myc. For reasons not yet clear, overexpression of Myc appears to make cells sensitive to cell death by inhibition of another protein called CDK1, a regulator of cell division. Dr Kusdra will test whether changes in the expression of a microRNA, called mir-19a, and other related MiRs may contribute to sensitivity of triple-negative cells to cell death induced by CDK1. MiRs are molecules that are naturally occurring in cells, and it has been shown that one MiR can control the expression of hundreds of gene targets. In addition, Dr. Kusrda will test whether MiRs are the basis for resistance to a common therapeutic drug, Taxol, frequently used to treat triple-negative breast cancer.

The transformation of normal breast cells into a cancerous state is accompanied by alterations of specific cell signaling and metabolic pathways. The identification of dysregulated pathways vital to disease progression may potentially lead to new diagnostic markers and therapeutic targets. **Daniel Bachovin** at the **Scripps Research Institute** will explore how inactivation of protein phosphatase 2A (PP2A) may be required for a fully transformed phenotype in breast cancer. Consequently, pharmacological "activation" of PP2A may represent a novel strategy to combat breast cancer. One enzyme thought to contribute to the deactivation of PP2A is protein methylesterase-1 (PME-1), a serine hydrolase that removes an activating post-translational methylation on the C-terminus of PP2A. This, working in Dr. Benjamin Cravatt's (mentor) lab Mr. Bachovin will globally profile phosphorylation and proteolytic events differentially regulated in breast cancer cells by PP2A, and evaluate of the role of PME-1 in breast cancer pathogenesis using cell and mouse model systems.

Oxidative stress (i.e., an imbalance between the production of reactive oxygen species and a cell's ability to readily detoxify reactive intermediates or to repair the resulting damage) contributes to major diseases of aging, including atherosclerosis, neurodegenerative disease, and cancer. Myeloperoxidase (MPO), studied in astrocytes for Alzheimer's disease and macrophages in atherosclerosis, leads to oxidative damage and cell death. In contrast, aberrant expression of MPO in breast cancer cells appears protective, reducing incidence of recurrence following chemotherapy. **Wanda Reynolds** from the **Sanford-Burnham Medical Research Institute** is funded to study the underlying mechanisms of why chemotherapy response is improved in patients with a -463G/A polymorphism in the myeloperoxidase gene. Experimental verification of the role of MPO using mouse models could convince physicians to advise patients

to avoid drugs that reduce MPO activity, and this may encourage pharmaceutical companies to develop drugs that enhance MPO activity or expression for breast cancer patients.

Biology of the Breast Cell Grants Listing

Pharmacological Modulation of PP2A Activity in Breast Cancer
Award type: Dissertation
Bachovchin, Daniel
Scripps Research Institute
$76,000

Reelin Signaling Involvement in Breast Cancer Cell Migration
Award type: IDEA
Carpenter, Ellen, Ph.D.
University of California, Los Angeles
$149,493

The Role of microRNAs in Triple-Negative Breast Cancer
Award type: Postdoctoral fellowship
Kusdra, Leonard, Ph.D.
University of California, San Francisco
$90,000

p97 as a Therapeutic Target in Breast Cancer Metastasis
Award type: IDEA
Latterich, Martin, Ph.D.
Proteomics Research Institute for Systems Medicine
$292,500

Local Adipocyte Function in Breast Cancer
Award type: IDEA
Mueller, Barbara, Ph.D.
Torrey Pines Institute for Molecular Studies
$273,000

Myeloperoxidase Mediated Protection in Breast Cancer
Award type: IDEA
Reynolds, Wanda, Ph.D.
Sanford-Burnham Medical Research Institute
$286,500

Inhibiting Mutation to Prevent and Treat Breast Cancer
Award type: IDEA
Romesberg, Floyd, Ph.D.
Scripps Research Institute
$187,438

Complement-mediated Stem Cell Recruitment to Breast Cancer
Award type: IDEA
Schraufstatter, Ingrid, M.D.
Torrey Pines Institute for Molecular Studies
$136,500

The Role of Twist1 in Epithelial-mesenchymal Transition
Award type: Postdoctoral fellowship
Tsai, Jeff, Ph.D.
University of California, San Diego
$90,000

The Role of Clim Proteins in Breast Cancer
Award type: Postdoctoral fellowship
Verma, Suman, Ph.D.
University of California, Irvine
$90,000

2010 CBCRP Funding by Institution

The following **17 California research institutions and community organizations were awarded new CBCRP funding in 2010** Community collaborative (CRC) grants are split between institutions.

Institution (city)	**# Awards**	**Amount**
Beckman Research Institute of the City of Hope (Duarte)	2	$325,000
Cancer Prevention Institute of California (Fremont)	2	$419,575
Cancer Resource Center of Mendocino County (Mendocino)	1	$187,500
John Wayne Cancer Institute (Santa Monica)	1	$282,900
Latinas Contra Cancer (San Jose)	1	$25,000
Proteomics Research Institute for Systems Medicine (San Diego)	1	$292,500
Sanford-Burnham Medical Research Institute (La Jolla)	1	$286,500
Scripps Research Institute (La Jolla)	4	$833,138
Stanford University	4	$1,456,081
Torrey Pines Institute for Molecular Studies (San Diego)	2	$409,500
Turtle Health Foundation, Inc. (Sacramento)	1	$374,400
University of California, Davis	2	$307,281
University of California, Irvine	3	$256,000
University of California, Los Angeles	4	$549,493
University of California, San Diego	1	$90,000
University of California, San Francisco	5	$1,601,430
University of Southern California (Los Angeles)	2	$486,000

2010 CBCRP Application Evaluation Process & Review Committee Rosters

The CBCRP thanks the participants in our 2010 review committees for their service and dedication to our Program!

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

In 2009 the CBCRP began **triaging** Core Funding most applications that scored in the lower 50% of a committee's portfolio using the preliminary scores of the assigned reviewers. Applications in the upper 50% of a committee's portfolio all received full committee discussion, as did any of the lower scoring applications requested by one of the reviewers.

Applications that were not triaged were rated by the Breast Cancer Research 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), career plan/mentoring (dissertation, postdoctoral fellowship), or dissemination and translation potential (CRC)

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

Community Impact Review Committee

►Chair:

Shiraz Mishra, M.B.B.S., Ph.D.
Associate Professor
Dept. Epidemiology & Preventive Medicine
University of Maryland, Baltimore - School of Medicine
Baltimore, MD

►Scientific Reviewers:

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Member and Professor
Social and Behavioral Sciences
Boston University
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Assistant Professor
Meharry Medical College
Nashville, TN

Carolyn Gotay, Ph.D.
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Mel Haberman, Ph.D.
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College of Nursing
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Margo Michaels, MPH
Executive Director
Education Network Access to Advance Clinical Trials
Bethesda, MD

Nalini Visvanathan, Ph.D.
Research Contractor, Editor
The Fenway Institute
Washington, DC

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Beverly Canin
Breast Cancer Option, Inc
Rhinebeck, NY

Christine Carpenter
Iowa Breast Cancer Edu-action
Cedar Falls, IA

►California Advocate Observer:

Ernesta Wright
The Green Foundation
Brea, CA

►Ad-Hoc Reviewers:

Dawn Hershman, M.D., M.S.
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New York, NY

Karen Meneses, Ph.D.
Professor & Associate Dean for Research
School of Nursing
University of Alabama at Birmingham
Birmingham, AL

George Wright, Ph.D.
Associate Professor
University of Washington
Seattle, WA

Detection and Prognosis Review Committee

►Chair:

Peggy Porter, M.D.
Head, Breast Cancer Research Program
Divisions of Human Biology and Public Health Sciences
Fred Hutchinson Cancer Research Center
Seattle, WA

►Scientific Reviewers:

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Vice President, Research
InterGenetics, Incorporated
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Scientist
Aparna Biosciences Corp.
Bethesda, MD

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

Beverly Parker, Ph.D.
Breast Cancer Network of Strength
Naperville, IL

► California Advocate Observer:

Sherrie Fasola Wilkins, Ph.D.
Breast Cancer Connections
Palo Alto, CA

Etiology and Prevention Review Committee

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The Annie Appleseed Project
Delray Beach, FL

Sara Williams
The Carolina Breast Cancer Study (UNC)
Mebane, NC

►California Advocate Observer:

Cindy Love
Albie Aware, Inc.
Sacramento, CA

Innovative Treatments Review Committee

►Chair:

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Karmanos Cancer Institute
Wayne State University
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Lily Yang, M.D., Ph.D.
Nancy Panoz Chair of Surgery in Cancer Research
Department of Surgery and Winship Cancer Institute
Emory University School of Medicine
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National Breast Cancer Coalition
Houston, TX

Marjorie Gallece
Breast Cancer Resource Centers of Texas
Austin, TX

Nancy Singleton
SHARE
Hoboken, NJ

Maria Wetzel
Michigan Breast Cancer Coalition
Baldwin, MI

►California Advocate Observer:

Carol Rose Schultz
Breast Cancer Connections
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►**Ad-Hoc Reviewers:**

Silvia Formenti, M.D.
Professor of Medicine
NYU School of Medicine
New York, NY

Eva Sevick-Muraca, Ph.D.
Professor and Director
The University of Texas
Brown Institute of Molecular Medicine
Houston, TX

Tumor Biology Review Committee

►**Chair:**

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Department of Pathology
University of Alabama - Birmingham
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Beth Israel Deaconess Medical Center
Harvard Medical School
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►**Advocate Reviewers:**

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Inflammatory Breast Cancer Research Foundation
Huntington Woods, MI

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Nancy Key
Susan G. Komen Foundation
Camano Island, WA

Theresa Martyka
Breast Cancer Network of Strength
Chicago Ridge, IL

►California Advocate Observer:
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Young Survival Coalition
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