

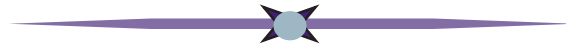
CALIFORNIA  
Breast  
Cancer  
Research  
PROGRAM

## Cycle VIII 2002 Awards Compendium

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# Introduction



The California Breast Cancer Research Program (CBCRP) is pleased to announce the funding of 67 new research grants that will advance our knowledge about the causes, prevention, biology, detection, and treatment of breast cancer. With these new awards, the State is investing nearly \$15 million to impact the lives of California women. These research projects are being performed at 22 institutions across the state, including universities both public (e.g., University of California campuses) and private (e.g., Stanford University); national laboratories (e.g., Lawrence Berkeley National Laboratory); research institutes (e.g., The Burnham Institute); and medical centers (e.g., California Pacific Medical Center).

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

- 1) A portion of a 2 cents per pack State cigarette tax
- 2) Contributions from individuals using the State's income tax check-off option
- 3) Other generous contributions from concerned community members dedicated to defeating breast cancer


This is our eighth year (or cycle) of grant funding, and through 2002 we have distributed or encumbered approximately \$131 million to fund 518 research projects. The CBCRP is administered by the University of California, Office of the President-Division of Health Affairs, in Oakland. The overall objectives, strategies, and priorities of the CBCRP are set by a volunteer advisory Council, which actively participates in overseeing the program and making final recommendations on the grant applications 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 non-profit 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.

## The Challenge:

With a budget only about 0.1% that of the NIH, the challenge the CBCRP faces is to make the most impact on breast cancer and address the specific concerns of our California stakeholders. Our stated mission is:

*“...to reduce the impact of breast cancer in California by supporting research on breast cancer and facilitating the dissemination of research findings and their translation into public health practice.”*

We realize that both the task to accomplish this mission and the opportunities for success are enormous. Working alongside our advisory Council, we designated nine specific topics, which we call Priority Issues, for invited research in 2002. In addition, we offer a variety of award types that are tailored to the needs of both researchers and the CBCRP's mission. The reason we detail our funding interests so carefully is to: (1) encourage multi-disciplinary collaborative and community-oriented participatory research, (2) allow researchers to explore innovative, “high reward” opportunities, (3) bring new researchers into breast cancer at all levels, and (4) focus on underserved communities and special topics not well covered by other funding agencies. We have seen that our interests and goals have attracted the highest-quality California researchers and institutions to apply. There are two primary reasons for this. First, we maintain the focus of California researchers towards breast cancer by hosting a statewide, biennial CBCRP Research Symposium. This meeting brings the general public, Program stakeholders, and our funded researchers together and serves to motivate and generate a common purpose. We encourage breast cancer activists to express their concerns, so that the research community comes face-to-face with the human issues of the disease. Second, we offer an objective, competitive grant application



evaluation and funding process. In summary, we keep the challenge of defeating breast cancer squarely in the path of researchers in California, and we become active partners in their efforts.

How do we see our mission being accomplished? Our thinking is that the successful enterprise to impact breast cancer will emerge from a combination of: (1) individual creativity, (2) the coalescence of talent from different fields, (3) integrating the social and political components of the disease, (4) involving communities as equal partners in research aims, and (5) an overall vision of purpose. To the extent that encouraging research and funding grants can accomplish these ends, the CBCRP is taking up the challenge.

## The CBCRP Funding Process:

In January–February 2002 we received 198 grant applications in response to our “Call” for new research on breast cancer. This was a more than 20% increase in applications compared to 2001. They were evaluated for scientific excellence in a “study section”, or peer review process. Our review committee membership and a description of this process are found at the end of this booklet. What we feel makes our system special is the input of our advisory Council in a well-defined “programmatic review”, which complements the scientific review to ensure that funded grants match the goals of the CBCRP. The Council members consider several aspects of the responsiveness of the applications to programmatic criteria independently before seeing the scientific peer review merit scores. Thus programmatic interest is rated as a separate item. Finally, the advisory Council and Program staff combine the scientific merit and programmatic interest elements to arrive at a funding decision for each application. The end result is that the successful applicant has responded both in terms of presenting a high quality research project **and** by meeting the interests of the CBCRP stakeholders.

## The Outcome:

In the remainder of this introduction and the detailed sections to follow, we present a summary and listing of funded CBCRP grants for 2002 including:

1. Statistics related to funding CBCRP Priority Issue topics and Award Types
2. Highlights of 2002 funding
3. Portfolio summary and detailed list of funded grants for each of our Priority Issue groups
4. List of funded institutions
5. Detailed description of the review and funding process and review committee membership

We have organized our nine research topic Priority Issues into four groups that have a common theme. We feel that this best integrates the pieces of the puzzle that each grant represents in the breast cancer research landscape. The full abstracts of these newly funded grants, as well as those from previous CBCRP funding cycles, can be found on our Web site: <http://cbcrp.ucop.edu/>. We welcome your thoughts and feedback either via our Web site link “CBCRP Listens” or by e-mail: [cbcrp@ucop.edu](mailto:cbcrp@ucop.edu).

# 1. Statistical Summary:

## A. New CBCRP Funding in 2002:

- ◆ Total applications reviewed = 198
- ◆ Success rate = 33.8%
- ◆ Total new grants awarded = 67
- ◆ Amount awarded for new grants = \$14,809,103

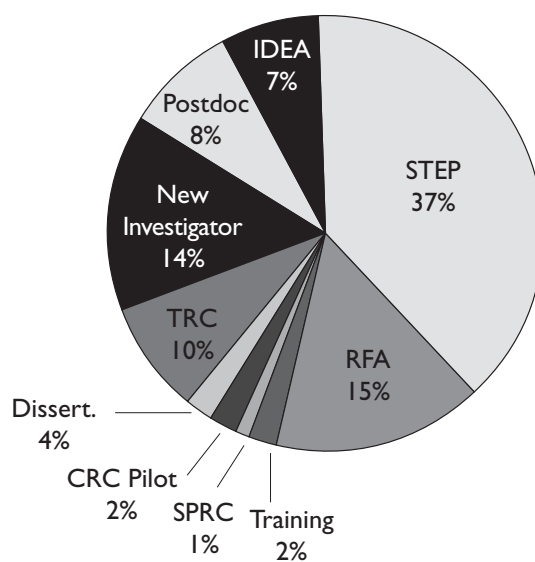
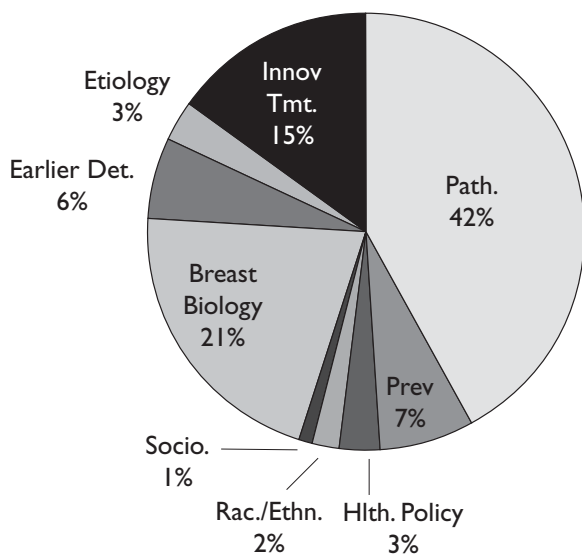
### Diversity supplements to previous CBCRP grants:

- ◆ Number of supplements = 6
- ◆ Amount awarded = \$199,990

**Total of new grants and supplements awarded in 2002 = \$15,009,003**

## B. Applications and Awards by CBCRP Priority Issues:

Priority Issue	# Applications	# Grants Awarded	Awarded Amount
Health Policy & Health Services	3	2	\$432,055
Sociocultural	9	2	\$205,028
Racial & Ethnic Differences	3	2	\$289,563
Etiology	6	3	\$389,696
Prevention	18	4	\$1,087,573
Earlier Detection	10	3	\$955,959
Innovative Treatments	38	10	\$2,293,421
Biology of the Normal Breast	28	11	\$3,076,254
Pathogenesis	83	30	\$6,079,554



Pie charts showing relative distribution of 2002 CBCRP grants by Priority Issues (left) and Award Types (right). Data is for dollar amount.


## C. Applications and Awards by CBCRP Award Types:

Award Type	# Applications	# Grants Awarded	Award Amount
<b>Collaboration awards:</b>			
Community (CRC)	6	2	\$266,889
Translational (TRC)	8	4	\$1,512,755
Sci. Perspectives (SPRC)	4	1	\$100,000
<b>Investigator-initiated Awards:</b>			
RFA	11	3	\$2,282,399
STEP	64	19	\$5,618,764
IDEA	32	8	\$1,085,670
<b>Career Development Awards:</b>			
Dissertation	15	11	\$551,729
Postdoctoral	40	13	\$1,092,544
New Investigator	16	5	\$2,028,655
Training Program	2	1	\$269,698

## 2. Funding Highlights:

### 2002 CBCRP funding featured:

- ◆ Eleven grants to expand our knowledge of normal breast development, function, aging, and separating abnormal breast structures from normal ones. These projects lay the groundwork for explaining the source of breast cancer and how **normal breast biology** might be influenced to prevent breast cancer.
- ◆ Seven awards that focus on **prevention/risk reduction and etiology**, including state-of-the-art genetic analysis, exploring ethnic differences, and continuing a training program to focus on these issues
- ◆ Two projects to **improve health services** by investigating bone density and access and delivery issues for African American women
- ◆ Three projects investigate the underlying reasons behind **racial and ethnic disparities** associated with breast cancer
- ◆ Two awards deal with **sociocultural/psychological issues** related to weight loss and the physiological effects of breast cancer diagnosis
- ◆ Ten grants will further our understanding of **how the disease progresses** at the basic science level
- ◆ Thirteen grants to explore novel methods to **detect breast cancer and explore novel approaches to treatments**. Many of these projects involve cross-disciplinary collaboration teams.
- ◆ Twenty-seven projects for **innovative, exploratory, and high-risk/high reward research** projects to push boundaries, challenge existing paradigms, and initiate new research programs
- ◆ Thirty awards provide opportunities in **career development** at the levels of graduate training, postdoctoral fellowships, and newly independent investigators. These researchers bring fresh thinking to their respective disciplines.

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- ◆ Three grants in **special-topic RFAs**, which we have identified as under-funded and allow the CBCRP to maximize its overall impact in breast cancer research
  - ◆ Seven projects involve **collaborative teams** that include community groups and cross-disciplinary efforts of traditional researchers
  - ◆ Three awards and the 6 diversity supplements to previously-funded CBCRP grants are of special interest, because they are funded, in part, by revenue from the California **State Income Tax Check-off**. These projects are great examples of our research commitment.

# The Community Impact of Breast Cancer: The Social Context



A woman determined to be “at high risk”, diagnosed with, or surviving breast cancer is changed forever. The CBCRP supports research and formulation of public policy alternatives that would contribute to breast cancer prevention and improve outcome. The CBCRP recognizes the need for reducing inequities in access to prevention, detection, treatment, and survivorship services for underserved populations. Finally, we encourage sociocultural, psychological, and behavioral research to reduce the impact of breast cancer on each woman.

Three of CBCRP’s Priority Issues are represented in this section:

- ◆ Health Policy and Health Services: Better Serving Women’s Needs
- ◆ Sociocultural, Behavioral & Psychological Issues Relevant to Breast Cancer: The Human Side
- ◆ Racial/Ethnic Differences in Breast Cancer: Eliminating Disparity

## Funding Data:

	Proportion of CBCRP’s Total	
<b>Community Impact grants awarded in 2002:</b>	6	9%
<b>Funded amount:</b>	\$926,646	6%

## Community Impact Portfolio Summary:

Concerned women and scientists alike have long been puzzled by differences in breast cancer incidence and mortality outcomes among racial/ethnic populations. For example, while African American women have a lower incidence of breast cancer, they have a higher mortality rate. Three grants in the community impact section of this year’s research portfolio are looking at both health care system and biological factors that may shed light on this issue.

**Priscilla Banks with the African American Advisory Committee and Carol Somkin with the Kaiser Foundation Research Institute** will carry out a qualitative study to investigate what it is about the health care settings and interactions with providers and staff that promotes and inhibits the delivery of care for African American women. They will explore issues of cultural sensitivity in patient-provider/staff communications and the physical and social environment of the health care settings in which the communications take place. They intend to develop testable hypotheses not only about each of these areas separately but also about their interrelationships.

**Barbara Cohn of the Public Health Institute** is following up her very recent, exciting findings (that certain placental factors during pregnancy seem to be protective factors for breast cancer later in life) for the first time among African American, Asian, and Hispanic women. **Sally Glaser of the Northern California Cancer Center**, in view of the fact that known risk factors do not explain the majority of the racial/ethnic variation in occurrence, is looking at a novel factor, human leukocyte antigen (HLA), as a new possible genetic factor underlying incidence differences between African American, Hispanic, and white women.

Until the disease is prevented, quality of life issues will continue to be important, especially as new treatment options lengthen survival. Three grants are looking at this issue: two considering various physiological and hormonal aspects of quality of life and one looking at the psychological dimensions. **Carolyn Crandall, a clinician practicing at the University of California, Los Angeles**, will use a new investigator award to help her in transition to a clinical research career by looking at the quality-of-life impact of treatment on bone density and osteoporosis in breast cancer survivors. **Rowan Chlebowski at the Harbor-UCLA Research and Education Institute** will test the feasibility of an intervention to achieve weight loss sufficient to show a reduction in fasting insulin levels in a racially and ethnically diverse population of breast cancer patients in a public hospital setting. He is hoping to eventually be able to show not only an increase in quality of life, but also perhaps a reduction in rates of recurrence.

Finally, **Jill Mitchell, a doctoral student at the University of California, Los Angeles**, will look at what can be learned from the meaning women give to their breast cancer experience, the processes through which they achieve meaning, and what the differences are among women who achieve positive meaning and those who do not. She will also look at how different themes of meaning correspond to cortisol profiles, which is a physiological measure of stress and a potential indicator of disease progression.

### Community Impact Grants Funded in 2002:

#### **African American Women and Breast Cancer:**

##### **What Works?**

Banks, Priscilla  
 African American Advisory Committee  
 Somkin, Carol  
 Kaiser Foundation Research Institute  
 Community Research Collaboration, Pilot Award  
 1.5 years, \$132,055

*TaxCheck-off*

#### **Weight Loss in Public Hospital Breast Cancer Patients**

Chlebowski, Rowan  
 Harbor-UCLA Research & Education Institute  
 IDEA Award  
 1.5 years, \$140,941

#### **Can Placenta Factors Explain Race Patterns of Breast Cancer?**

Cohn, Barbara  
 Public Health Institute  
 IDEA Award  
 1 year, \$86,175

#### **Impact of Breast Cancer and its Therapy on Bone Density**

Crandall, Carolyn  
 University of California, Los Angeles  
 New Investigator Award  
 3 years, \$300,000

#### **Immune-Function Genes and Race Differences in Breast Cancer**

Glaser, Sally  
 Northern California Cancer Center  
 STEP Award  
 2 years, \$203,388

#### **Constructed Meaning and Stress in Breast Cancer Experience**

Mitchell, Jill  
 University of California, Los Angeles  
 Dissertation Award  
 2 years, \$64,087



# Prevention and Risk Reduction: The Environment of the Disease



Despite the identification of breast cancer genes and other risk factors, the disease strikes women seemingly at random. There are causes of the disease that cannot be explained by studying tumors in the laboratory setting. What are environmental and biological factors that interact to increase a woman's risk of developing breast cancer? How do these factors increase the risk and impact different communities of women in California? Knowing what causes breast cancer will allow us to take steps to prevent it.

Two of CBCRP's Priority Issues are represented in this section:

- ◆ Etiology: Finding the Causes
- ◆ Prevention and Risk Reduction: Ending the Danger of Breast Cancer

## Funding Data:


	Proportion of CBCRP's Total	
<b>Prevention &amp; Risk Reduction grants awarded in 2002:</b>	7	10%
<b>Funded amount:</b>	\$1,477,269	10%

## Prevention & Risk Reduction Portfolio Summary:

**Catherine Blake, a doctoral student at the University of California, Irvine**, was funded to develop a computer program to help scientists rapidly identify new risk factors associated with breast cancer. She intends to semi-automate both the extraction of data from the breast cancer medical literature and the meta-analysis by which conclusions are drawn from multiple studies on the same topic. If scientists are able to explore secondary information in the literature faster and more comprehensively, then they may also be able to reduce publication bias by including articles that were not specifically studying a given risk factor.

Two grants will examine the role of the androgen receptor (AR) in breast cancer. The AR is a steroid hormone receptor that mediates the affects of the steroid hormones testosterone and 5 $\alpha$ -dihydrotestosterone. There are contradictory studies in cell line, animal, and human studies about the role of androgen in affecting breast cancer risk. **Elizabeth Lillie, a doctoral student at the University of Southern California**, proposes to test the hypothesis that there is an association between AR activity, as measured by genotyping variations in the AR gene (AR polymorphism), and percent mammographic density, which is a known risk factor for breast cancer, and to determine whether the AR polymorphism is associated with more advanced forms of breast cancer. **Wei Wang, also a doctoral student at the University of Southern California**, will undertake a human population study that will incorporate genetic markers to study differences among individuals in one specific androgen pathway (the PSA pathway) in order to try to determine how androgens act to influence breast cancer risk. The molecular epidemiologic approach he will use is a powerful method that may overcome some of the deficiencies in the previous human studies on this topic.

**Bradley Ekstrand, a postdoctoral fellow at Stanford University**, will investigate a novel approach to the prediction and prevention of breast cancer. Cells from women with and without breast cancer will be exposed to X-rays and the genetic response to the X-rays will be measured using a microarray. The resulting data from women without breast cancer



will be compared to those with breast cancer. A computer-based statistical method will be used to identify the genes whose responses to X-rays predict the patients with breast cancer. If successful, this strategy would allow breast cancer risk assessments to be based on genetic factors specific to each woman.

There is a large and compelling body of evidence implicating estrogen in human breast cancer. Diet is also thought important, although its role is less clear; however, dietary fiber may play an important role in estrogen metabolism and may therefore be an important determinant of circulating estrogen levels in the body, and thus affect breast cancer risk.

**Malcolm Pike at the University of Southern California** will conduct a study into this issue, which is innovative in that it: (1) utilizes an ideal population where the traditional diet is rich in dietary fiber, (2) comprises two generations of Mexican-origin women where differences in breast cancer rates provide powerful evidence on the extent to which the causes are due to changes in environmental factors, and (3) utilizes two methods of quantifying fiber intake—that of a food frequency questionnaire as well as a biochemical marker.

A full term pregnancy (FTP) before age 20 reduces breast cancer risk in women. It does the same in rats and mice exposed to potent chemical carcinogens, perhaps by permanently reducing secretion (in parous animals who have given birth) of some hormones associated with breast cancer. **Satyabrata Nandi at the University of California, Berkeley**, intends to optimize and analyze the physiological and molecular bases of a short-term (7–21 days) protective hormone treatment (PHT) that he has developed using pregnancy levels of estrogen. In rats who have never given birth, this treatment reduced mammary cancer incidence by over 80% and multiplicity of tumors by over 90%. The eventual goal is for this PHT to serve as a paradigm for safe and efficient human breast cancer prevention.

Part of CBCRP's goal is to continually bring fresh ideas and new approaches into breast cancer research. One way of doing this is to support the training of highly qualified students. **Ronald Ross at the University of Southern California** will continue with the third cycle of CBCRP support for a training program emphasizing multidisciplinary interests, which include pathology, molecular biology, cell biology, and cancer control. Trainees are matched to an appropriate faculty mentor with an active breast cancer research program.

## Prevention & Risk Reduction Grants Funded in 2002:

### **Using Scientific Text to Identify Breast Cancer Risk-Factors**

Blake, Catherine  
University of California, Irvine  
Dissertation Award  
1 year, \$29,136

### **Using Microarrays to Estimate Breast Cancer Risk**

Ekstrand, Bradley  
Stanford University  
Postdoctoral Fellowship  
2 years, \$86,400

### **The Androgen Receptor and Mammographic Density**

Lillie, Elizabeth  
University of Southern California  
Dissertation Award  
2 years, \$59,998

### **Breast Cancer Prevention with Estrogen**

Nandi, Satyabrata  
University of California, Berkeley  
Prevention RFA Award  
3 years, \$812,340

### **Fiber, Estrogen and Breast Cancer in Mexican American Women**

Pike, Malcolm  
University of Southern California  
STEP award  
2 years, \$159,697

*TaxCheck-off*

### **USC/NCCC Breast Cancer Research Training Program**

Ross, Ronald  
University of Southern California  
Training Program  
3 years, \$269,698

### **Androgen Receptor Gene and PSA Gene in Breast Cancer Risk**

Wang, Wei  
University of Southern California  
Dissertation Award  
2 years, \$60,000

# Diagnosis and Treatment: Delivering Clinical Solutions



Early detection does not guarantee a cure. And the limitations of mammography require women to undergo unnecessary biopsies and emotional strain. Ultimately patients and physicians have too few options for treatment. New breast cancer specific and individualized therapies require investigation. Lab researchers and clinicians are encouraged to engage in more cross-disciplinary research projects to link discovery efforts with the clinical issues important to breast cancer.

Two of CBCRP's Priority Issues are represented in this section:

- ◆ Earlier Detection: Improving the Chances for a Cure
- ◆ Innovative Treatment Modalities: Search for a Cure

## Funding Data:


	Proportion of CBCRP's Total	
<b>Diagnosis &amp; Treatment grants awarded in 2002:</b>	13	19%
<b>Funded amount:</b>	\$3,249,380	21%

## Diagnosis & Treatment Portfolio Summary:

We are pleased that several of the newly funded grants in the Diagnosis & Treatment topics are collaborative efforts between scientists from different fields. Starting with the earliest development of the disease, **Thea Tlsty at University of California, San Francisco, and Stefanie Jeffrey at Sanford University** are funded for a Translational Research Collaboration award to examine the role of the connective tissues and stromal cells of the breast. Their research will examine the underlying genetic profile of tissue and cells immediately adjacent to breast tumors and pre-neoplastic lesions to see whether there are changes relative to normal stromal tissue. Detection of cancer, thus, might occur indirectly via biomarkers in the breast stroma, and this research could lead to new thinking on how breast tumors might be arrested by inhibiting the ability of non-cancerous cells to become permissive and support the tumor.

**Steven Cummings, Karla Kerlikowske, and John Shepherd at the University of California, San Francisco**, are funded for a Scientific Perspectives Research Collaboration exploratory award to employ novel X-ray approaches to study breast density. This project brings new technology to bear on breast cancer. This approach, if successful, also has the potential to be used as an adjunct to mammography to screen high-risk women and monitor preventive treatments. **Kai Vetter and Christine Hartmann Siantar at Lawrence Livermore National Laboratory** are collaborating with **Gerald DeNardo at the University of California, Davis**, in a TRC pilot award to develop a fundamental improvement in visualizing tumors that are "tagged" with radioactive isotopes. If successful, this approach will reduce the radiation needed and improve image quality to bring this method of diagnosis a step closer to the clinic.

**Lucy Berlin with her community group, Young Moms with Breast Cancer, and Hope Rugo at the University of California, San Francisco**, are sharing a Community Research Collaboration pilot award with **Lynn Westphal at Stanford University**. They are funded to develop a new approach to spare younger women diagnosed with breast cancer possible ovarian damage and infertility that often results from chemotherapy treatment. This grant is aimed at



developing the information needed to advance this concept to a clinical trial. Taken together, the four collaboration awards described above allow researchers to combine critical, cross-disciplinary expertise on innovative, “high risk/high reward” projects.

Other grants funded by the CBCRP in 2002 are focused on issues related to immune therapy, new drug targets and tumor-selective agents, chemotherapy and drug resistance, and the application of novel methodologies to address treatment issues. **John Reed, Xiao-Kun Zhang, and Marcia Dawson at The Burnham Institute** and **Francisco Piedrafita at the Sidney Kimmel Cancer Center** are funded for separate innovative STEP grants to study key issues in programmed cell death (apoptosis). Breast cancer cells survive drug treatments, and one aspect of drug resistance is the alterations in cellular pathways that might otherwise respond to DNA damage and immune attack. **Jennifer Murray at the Beckman Research Institute of the City of Hope** is funded for a dissertation award to study a gene involved in expression of the key multi-drug resistance protein that often foils treatments with chemotherapy. Another dissertation award to **Christine Case Lo at the University of California, San Francisco**, involves the new discipline of pharmacogenomics to examine the individual response of patients to chemotherapy drugs, so that the tumor exposure and response might be optimized. **Jack Youngren at the University of California, San Francisco**, received funding to explore the insulin-like growth factor and small molecule inhibitors as possible anti-breast cancer agents.

Finally, two new grants focus on cell movement and angiogenesis. Clinical development of MMP (matrix metalloproteinase) inhibitors has lagged, because these enzymes are widespread in the body and have several related forms. Thus, MMP inhibitors usually have too severe side-effects that preclude clinical development. **Vito Quaranta at the Scripps Research Institute** will be using new CBCRP funding in collaboration with a recent Nobel Prize laureate to employ a novel chemistry method to use a specific breast cancer MMP itself to “instruct” the synthesis of a selective inhibitor. **Michael Samoszuk at University of California, Irvine**, is funded for to see if a normal blood clotting mechanism can be activated in the tumor blood supply to starve breast cancer.

## Diagnosis & Treatment Grants Funded in 2002:

### **Chemotherapy-Induced Ovarian Damage: Prevention & Impact**

Berlin, Lucy  
Young Moms with Breast Cancer, Sunnyvale  
Rugo, Hope  
University of California, San Francisco  
Lynn Westphal  
Stanford University  
Community Research Collaboration, Pilot Award  
1.5 years, \$82,479 (UCSF) and \$52,355 (Stanford/YMBC)

### **Drug Dose Tailoring Based on Patient-Specific Factors**

Case Lo, Christine  
University of California, San Francisco  
Dissertation Award  
2 years, \$50,572

### **Compositional Breast Density as a Risk Factor**

Cummings, Steven; Kerlikowske, Karla; and Shepherd, John  
University of California, San Francisco  
Scientific Perspectives Research Collaboration, Exploratory Award  
1.5 years, \$100,000

### **Novel Retinoids with Enhanced Anti-Breast Tumor Efficacy**

Dawson, Marcia  
The Burnham Institute  
STEP Award  
2 years, \$384,000

### **Regulation of SXR and Drug Resistance in Breast Cancer**

Murray, Jennifer  
Beckman Research Institute of the City of Hope  
Dissertation Award  
2 years, \$42,784

### **Retinoids in Combination Therapies Against Breast Cancer**

Piedrafita, Francisco  
Sidney Kimmel Cancer Center  
STEP Award  
2 years, \$396,800

### **MMP-Directed Synthesis of Invasive Breast Cancer Blockers**

Quaranta, Vito  
Scripps Research Institute  
IDEA Award  
1 year, \$136,224


### **PPAR $\gamma$ Modulators as Apoptosis Sensitizers for Breast Cancer**

Reed, John  
The Burnham Institute  
STEP Award  
2 years, \$465,373

### **Clotting Breast Cancer**

Samoszuk, Michael  
University of California, Irvine  
IDEA Award  
1 year, \$98,986

### **Breast Stromal Genes Act as Early Markers of Malignancy**

Tlsty, Thea & Jeffrey, Stefanie   
University of California, San Francisco and Stanford University  
Translational Research Collaboration, Full Award  
3 years, \$249,999 (UCSF) and \$392,498 (Stanford)

### **New Imager to Improve Specificity in Breast Cancer Detection**

Vetter, Kai; Hartmann Siantar, Christine; and DeNardo, Gerald  
Lawrence Livermore National Laboratory and University of California, Davis  
Translational Research Collaboration, Pilot Award  
1.5 years, \$213,462

### **Potential New Drug Therapy for Breast Cancer**

Youngren, Jack  
University of California, San Francisco  
STEP Award  
2 years, \$199,848

### **TR3-based Peptides for Apoptosis in Breast Cancer**

Zhang, Xiao-Kun  
The Burnham Institute  
STEP Award  
2 years, \$384,000

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



We need to move beyond the static picture of breast cancer in current tumor cell lines and animal models. We need new research to understand the pre-neoplastic, causative events of the disease at the tissue, cell, and genetic levels. Disease progression and the heterogeneity seen in the clinic need clarification at the basic science level. We must better understand the genetic and molecular signatures of the disease to treat it effectively.

Two of CBCRP's Priority Issues are represented, and the funding data, portfolio summaries, and funded grants are presented in separate sections:

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

## Biology of the Normal Breast: The Starting Point

### Biology of the Normal Breast Funding Data:

	Proportion of CBCRP's Total	
<b>Grants awarded in 2002:</b>	11	16%
<b>Funded amount:</b>	\$3,076,254	21%

### Biology of the Normal Breast Portfolio Summary:

The biology of the normal breast is a greatly understudied area. That is why the CBCRP has continued to support this priority issue. The breast is a complex structure composed of several cell types that function to generate milk or to support the cells that generate milk. We know that the milk-forming cells are the ones that are most likely to give rise to tumors, but there are many questions yet to be answered. How do the different types of cells interact in the breast under normal conditions? What normal changes are necessary for the breast to function properly? Without knowing the answers to these questions, it requires a leap of faith to be able to identify the abnormal changes associated with cancer.

What we do know about the breast is that it is an organ in constant flux. Researchers are finding that how the breast remodels itself under the influence of internal and external factors dictates how it functions. The production of milk depends on the maturity (differentiation) of the breast cells, which in turn is controlled by hormones and growth factors and the immediate environment of the cells, as well as the internal and external physical structure of the cells.

The eleven newly funded grants in the Biology of the Normal Breast priority area investigate various pathways that contribute to breast cell growth, maturation, and death. These include the:

- ◆ Influence of **breast structure** on growth and **maturation**
- ◆ **Influence of DNA structure on growth and cell growth and maturation**
- ◆ **Role of non-milk producing cells** in the breast
- ◆ Mechanisms of **action of hormones** and internal factors in breast cells
- ◆ Discrimination of normal **early changes in the breast** from abnormal ones

Several grants are examining how the non milk-producing cells and the environment that surround the milk-producing cells affect their behavior during growth, development, and aging. The role of cells such as those lining the blood vessels could affect breast cell growth potential. **Longchuan Chen of the La Jolla Institute for Molecular Medicine** received a one-year IDEA Award to determine whether blood vessel precursor cells can affect mammary cell growth. The extracellular matrix that surrounds the breast cells can also be a major factor in breast development. **Jamie Bascom at the Lawrence Berkeley National Laboratory** will use a one-year dissertation award to determine how an extracellular protein, called epimorphin, interacts with progesterone to influence breast development, while **Aylin Rizki from the Lawrence Berkeley National Laboratory** will use a two-year postdoctoral fellowship to determine the role of the extracellular matrix in protecting the milk-producing cells from DNA damage. **Ana Krtolica, also at the Lawrence Berkeley National Laboratory**, has a three-year new investigator award in which she will determine whether the age of fibroblasts—a type of breast cell that provides support for the milk-producing cells—effects the biological processes of the milk-producing cells. **Steven Artandi of Stanford University** is also going to study the affects of aging in the breast using a three-year RFA, but he will focus on the role of telomerase and telomere shortening in this process.

Several investigators will explore the role of hormones and growth factors on breast cell growth and breast development. Estrogen, progesterone, and prolactin have all been shown to regulate breast cell growth, but their process for doing so is still unclear. Three investigators will look at the effect of putative intermediate players in hormone growth regulation on breast growth by removing them from cells or adding excess amounts to cells. **Shi Huang of The Burnham Institute** will use a two-year STEP award to investigate the role of an estrogen-receptor related protein, called RIZ1, in mammary gland development; **Richard Price, Jr. from the University of California, San Francisco**, will use a two-year postdoctoral fellowship to investigate the effect of varying levels of estrogen receptor on mouse milk-producing cells; and **Hee Kwang Choi at The Burnham Institute** will use a two-year postdoctoral fellowship to investigate the effect of Rac/STAT5—a putative master switch for estrogen and prolactin action—on mammary growth. **Cindy Wilson of the University of California, Los Angeles**, will use a two-year STEP award to explore a slightly different aspect of normal mammary growth control. She will determine the effect of differing levels of the growth factor receptor called HER-2 on mammary growth inhibition.

An additional reason for studying normal breast biology is to devise ways to sort out normal changes in the breast from pre-cancerous changes. Two studies using different methods to advance this goal have been funded. **James Ford and Sylvia Plevritis at Stanford University** have been funded to perform a one-year Translational Research Collaboration pilot project, which will use MRI screening to detect changes in the breast and then genetic analysis to determine whether the normal structures can be differentiated from abnormal ones. **Saira Mian of the Lawrence Berkeley National Laboratory** will use a three-year RFA to develop statistical techniques to sort out which genetic changes in the breast are significant.



## Biology of the Normal Breast Grants Funded in 2002:

### **Understanding Telomere Dynamics in the Breast**

Artandi, Steven  
Stanford University  
Request for Applications (RFA) Award  
3 years, \$675,691

### **Role of Epimorphin and Progesterone in Breast Development**

Bascom, Jamie  
Lawrence Berkeley National Laboratory  
Dissertation Award  
1 year, \$23,825

### **Defining a Role for Endothelial Precursor Cells in Breast**

Chen, Longchuan  
La Jolla Institute for Molecular medicine  
IDEA Award  
1 year, \$199,174

### **Rac/STAT5 Signaling**

Choi, Hee Kwang  
The Burnham Institute  
Postdoctoral Fellowship  
2 years, \$86,400

### **Genetic Alterations in MRI Screen-Detected Breast Lesions**

Ford, James & Plevritis, Sylvia  
Stanford University  
Translational Research Collaboration, Pilot Award  
1.5 years, \$157,000

### **Steroid Receptor Coactivators in Mammary Gland Development**

Huang, Shi  
The Burnham Institute  
STEP award  
2 years, \$394,020

### **Understanding Aging Effects in the Breast**

Krtolica, Ana  
Lawrence Berkeley National Laboratory  
New Investigator  
3 years, \$448,884

### **Statistical Techniques for Breast Biology & Cancer Research**

Mian, Saira  
Lawrence Berkeley National Laboratory  
Request for Applications Award  
3 years, \$794,368

### **Targeting Estrogen Receptors to Mouse Mammary Epithelium**

Price, Jr., Richard  
University of California, San Francisco  
Postdoctoral Fellowship  
2 years, \$80,000

### **Effect of Breast Cell Environment on Repair of DNA Damage**

Rizki, Aylin  
Lawrence Berkeley National Laboratory  
Postdoctoral Fellowship  
2 years, \$80,672

### **The Importance of Growth Inhibitory Signals in Normal Breast**

Wilson, Cindy  
University of California, Los Angeles  
STEP Award  
2 years, \$150,000

## Pathogenesis: Understanding the Disease

### Pathogenesis Funding Data:

	Proportion of CBCRP's Total	
Grants awarded in 2002	30	45%
Funded amount:	\$6,079,554	42%

### Pathogenesis Portfolio Summary:

The underlying cellular, genetic, and biological processes of breast cancer continue to be major topics of research interest and CBCRP funding for 2002. Some key questions that are being addressed in our funded research include:

- ◆ Why do cancer cells have the ability to divide beyond the point where normal breast cells become stable?
- ◆ What is the underlying biology that explains why many breast cancer cells do not respond well to drug treatment, or develop drug resistance?
- ◆ What are the genetic differences between various forms of breast cancer?
- ◆ Can a more detailed understanding of heterogeneity in breast cancer lead to better disease biomarkers and targeted, individualized therapies?
- ◆ What are the key genetic and protein biomarkers of disease status and risk for progression?

Because of the large number of Pathogenesis grants funded in 2002, we will provide highlights only for selected projects. **Gerry Boss and Anne Wallace at the University of California, San Diego**, are funded for a three-year Translational Research Collaboration to study whether a newly patented test for a key signaling protein, called Ras, might provide prognostic information on biopsy samples. Ras inhibitors are in clinical development, but there is not a validated assay to match patients with these drugs. **Jan Schnitzer from the Sidney Kimmel Cancer Center** is funded for an innovative STEP grant to discover new proteins on the blood vessel lining cells (endothelial cells) that are specific to breast cancer and might be the target of new therapeutics. This research would open new opportunities to target the tumor's blood supply. **Jonathan Pollack from Stanford University** is funded as a new investigator to use powerful DNA array technology to pinpoint DNA amplifications or deletions in clinical samples. Herceptin become most clinically useful when a test became available to determine those women having Her-2 gene amplifications. Dr. Pollack would greatly expand on this approach and simultaneously associate gene expression information and gene copy number.

Next, proteomics is an emerging discipline that complements genetic analysis by studying the protein content and abundance within cells and, in the case of breast cancer, determining how protein differences are associated with progression and key biological properties. **Benjamin Cravatt** and his postdoctoral fellow, **Arul Joseph at the Scripps Research Institute**, are funded in separate grants to apply a novel proteomics assay to analyze the invasive proteases of breast cancer cells. Their methods can catalog the active proteases and simultaneously point the way to inhibiting their activity.

The narrow focus in basic science's approach to breast cancer is illustrated best by the fact that the bulk of research is performed using less than ten model cell lines, and these model cells do not mirror key clinical aspects of the disease. **Shanaz Dairkee at the California Pacific Medical Center** is using CBCRP funding to think outside the box and develop a potential breakthrough technique to immortalize breast cancer cells directly from newly diagnosed patients. If successful, this method might bring individualized therapy a big step closer.

Finally, the CBCRP funds career development and allows researchers to bring approaches completely outside current breast cancer research to bear on our understanding the disease. **Patrick Lupardus at Stanford University** received a dissertation award to study a key DNA repair process using a frog model system. The inability of cancer cells to monitor their DNA properly is a key factor in allowing the massive genetic changes seen at diagnosis. A postdoctoral fellow, **Cheryl Van Buskirk at the California Institute of Technology**, is studying a nematode, called *C. elegans*, to see how the cellular processing of a key growth factor receptor (EGFR) is regulated. **Kelly Boatright at The Burnham Institute** received a dissertation award to enter breast cancer research by studying why chromosome separation is defective in breast cancer.

## Pathogenesis Grants Funded in 2002:

The newly funded grants for CBCRP's Pathogenesis priority issue are organized into five sub-topics.

### I. **Outbreak—How Cancer Spreads:Angiogenesis, Invasion, and Metastasis**

Breast tumors become life-threatening by acquiring the ability to stimulate blood vessel growth, initiating cell movement and invasion, and ultimately spreading to distant organs. The CBCRP funded four new grants in 2002 under this sub-topic.

#### **HOX Transcriptional Regulation of Angiogenesis**

Charboneau, Aubri  
University of California, San Francisco  
Postdoctoral Fellowship  
2 years, \$80,000

#### **The Role of Matrix Metalloproteinase 13 in Breast Cancer**

Egeblad, Mikala  
University of California, San Francisco  
Postdoctoral Fellowship  
2 years, \$80,000

#### **Method to Profile Active Metalloproteases in Breast Cancer**

Joseph, Arul  
Scripps Research Institute  
Postdoctoral Fellowship  
2 years, \$86,400

### **Identifying Accessible Targets in Human Breast Tumors**

Schnitzer, Jan  
Sidney Kimmel Cancer Center  
STEP Award  
2 years, \$496,000

### 2. **Too Much Cell Growth: Defective Messages and Internal Signaling**

Cancer is defined as the growth of abnormal cells. Therefore, much current research effort is directed at underlying growth processes of intracellular signaling, cell division control checkpoints, growth receptor function (e.g., Her-2 and EGFR), and programmed cell death (apoptosis). This research will give insight into tumor formation and the ability of cells to survive drug treatment and the immune response. The CBCRP funded eight new grants in 2002 under this sub-topic.

#### **Cell Killing Effect of Orphan Receptor TR3 in Breast Cancer**

Bruey-Sedano, Nathalie  
The Burnham Institute  
Postdoctoral Fellowship  
2 years, \$86,400

#### **Novel Ligands as Probes of Estrogen Receptor Signaling**

Clegg, Nicola  
University of California, San Francisco  
Dissertation Award  
2 years, \$50,941

**Cyclin E Affects Growth Arrest in Breast Cancer Cells**

Dhillon, Navdeep  
University of California, Davis  
Dissertation Award  
2 years, \$50,386

**A Novel Anti-estrogen Resistance Mechanism in Breast Cancer**

Ely, Kathryn  
The Burnham Institute  
IDEA Award  
1.5 years, \$144,000

**Structure and Function of the Bax Apoptosis Regulator**

Marassi, Francesca  
The Burnham Institute  
STEP Award  
2 years, \$297,000

**DNA Damage Response Pathways in Breast Cancer Cells**

Maroto, Beatriz  
Scripps Research Institute  
Postdoctoral Fellowship  
2 years, \$86,400

**Regulation of Estrogen Response by Corepressors**

Privalsky, Martin  
University of California, Davis  
STEP Award  
2 years, \$149,942

**Analysis of EGFR Transcript Splicing in *C. Elegans***

Van Buskirk, Cheryl  
California Institute of Technology  
Postdoctoral Fellowship  
2 years, \$86,400

**3. Mistakes on the Master Blueprint: Molecular Genetics and Gene Regulation**

Breast cancer is characterized by major chromosomal deletions, duplications, and rearrangements. These genetic mutations might someday form the basis of detection, treatment, and analysis of disease severity. Many of these genetic alterations are thought to accumulate as a result of defects in DNA monitoring functions and normal repair processes. The CBCRP funded four new grants in 2002 under this sub-topic.

**Alterations in the Separase/Securin Balance in Breast Cancer**

Boatright, Kelly  
The Burnham Institute  
Dissertation Award  
2 years, \$60,000

**Identifying Sources of Genomic Instability in Breast Cancer**

Cimprich, Karlene  
Stanford University  
IDEA Award  
1.5 years, \$118,432

**The Detailed Structure of a Model Breast Cancer Genome**

Collins, Colin  
University of California, San Francisco  
STEP Award  
2 years, \$194,840

**Global Gene Regulation by SATBI in Metastatic Breast Cancer**

Kohwi-Shigematsu, Terumi  
Lawrence Berkeley National Laboratory  
IDEA Award  
1 year, \$161,513

#### 4. **Searching the Unknown: Novel Breast Cancer Genes**

It has been estimated that up to 4,000 of the 30,000–35,000 human genes might represent causative agents for initiation and progression of various human diseases. The relevant number for breast cancer is thought to be 100–200, perhaps less. Each new suspected genetic piece of the puzzle needs to be validated as relevant to breast cancer and accurately placed with respect to the biology of the disease. The CBCRP funded four new grants in 2002 under this sub-topic.

##### **Profiling Enzyme Activities in Models of Human Breast Cancer**

Cravatt, Benjamin  
Scripps Research Institute  
STEP Award  
2 years, \$369,508

##### **Regulation of the Rad1 Checkpoint Complex in Breast Cancer**

Lupardus, Patrick  
Stanford University  
Dissertation Award  
2 years, \$60,000

##### **Cloning of the X Chromosome's Putative Tumor Suppressor Gene**

Malkhosyan, Sergei  
The Burnham Institute  
STEP Award  
2 years, \$297,000

##### **Locating Novel Breast Cancer Genes using DNA Microarrays**

Pollack, Jonathan  
Stanford University  
New Investigator Award  
3 years, \$470,796

#### 5. **Unraveling the Path to Breast Cancer: Tumor Progression**

Breast cancer develops through many stages for a decade or more before detection. What happens during this progression period, and are there new opportunities to arrest the disease? This topic also incorporates work on the biology of the normal breast and enables new treatment concepts based on an understanding of clinical heterogeneity of breast cancer. The CBCRP funded ten new grants in 2002 under this sub-topic.

##### **The Role of PTEN in Progression of Ductal Carcinoma *in Situ***

Bose, Shikha  
Cedars-Sinai Medical Center  
New Investigator  
2 years, \$306,000

##### **Prognostic Value of Ras Activation in Breast Cancer**

Boss, Gerry & Wallace, Anne  
University of California, San Diego  
Translational Research Collaboration, Full Award  
3 years, \$499,796

##### **Infinite Expansion of Breast Tumor Samples in Culture**

Dairkee, Shanaz  
California Pacific Medical Center  
STEP Award  
2 years, \$311,400

##### **Does the BLM Gene Co-regulate BRCA1 in DNA Damage Response?**

Davalos, Albert  
Lawrence Berkeley National Laboratory  
Postdoctoral Fellowship  
2 years, \$80,672

##### **Molecular Pathogenesis of Metastatic Breast Cancer**

Debs, Robert  
California Pacific Medical Center  
STEP Award  
2 years, \$311,400

**Studies of Telomere Capping Dysfunction in Breast Cancer**

Gilley, David  
Lawrence Berkeley National Laboratory  
New Investigator  
3 years, \$502,975

**Fatty Acid Synthase and Breast Cancer**

Knowles, Lynn  
The Burnham Institute  
Postdoctoral Fellowship  
2 years, \$86,400

**Identification and Prognostic Value of ER $\beta$  in Breast Cancer**

Leitman, Dale  
University of California, San Francisco  
STEP Award  
2 years, \$150,000

**Three-Dimensional Modeling of Breast Cancer Progression**

Ortiz de Solorzano, Carlos  
Lawrence Berkeley National Laboratory  
STEP Award  
2 years, \$336,328

**BRCA1-dependent Ubiquitin Ligase Activity in Breast Cancer**

Xia, Yan  
Salk Institute for Biological Studies  
Postdoctoral Fellowship  
2 years, \$86,400

# Diversity Supplements

In 2002 the CBCRP began offering award supplements to allow individuals and community organizations that face barriers to overcome these barriers and participate in CBCRP-funded research. We have two grant supplement categories.

First, the regular Diversity Supplements provide funds to CBCRP-supported Principal Investigators so that they may mentor a promising student who may not otherwise have the opportunity to continue in breast cancer research. The aim is to support students who are:

- ◆ Interested in pursuing careers in breast cancer research
- ◆ Facing barriers that may prevent them from realizing a career in breast cancer research or pursuing research in areas that are under-represented in breast cancer research or with

communities that are under-represented in breast cancer research

Second, we offer participatory research Community Research Collaboration (CRC) supplements (CRCAS) that focus in two distinct areas:

- ◆ **Academic:** To mentor students, research fellows, and early career (less than 3 years as an independent investigator) researchers.
- ◆ **Community:** To mentor new community groups to become part of an existing CBCRP-funded grant.

Note: The diversity supplements are supported by funds generated from Californians that donate to the CBCRP via the check-off line on the State income tax form.

## Funding Data:

<b>Diversity supplements awarded in 2002:</b>	6
<b>Funded amount:</b>	\$199,990

## Diversity Supplements Funded in 2002:

### The Impact of Structure on the Quality of Breast Cancer Care

Danielle Rose Ash  
University of California, Los Angeles  
PI and mentor: Katherine Kahn  
2 years, \$40,000

### Pathway-Specific Gene Expression in Breast Cancer Cells

Melanie Funes-Duran  
University of California, Davis  
PI and mentor: Colleen Sweeney  
2 years, \$40,000

### HER-2/neu Gene Variations and Breast Cancer Risk

Dorothy Hong  
University of Southern California  
PI and mentor: Michael Press  
2 years, \$40,000

### Determinants of Receiving Breast Cancer Treatment in the Underserved

Yoshiko Umezawa  
University of California, Los Angeles  
PI and mentor: Rose Maly  
2 years, \$40,000

### A Network-Based Intervention for Chamorros in Southern California

Tina Vacharkulksemsuk (CRCAS)  
University of California, Irvine  
Co-PIs and mentors: Sora Park Tanjasiri and Lola Sablan-Santos  
1 year, \$19,990

### Does a Peer Navigator Improve Quality of Life at Diagnosis?

Familia Center, Santa Cruz (CRCAS)  
Stanford University  
PI and mentor: Caroline Bliss-Isberg  
2 years, \$20,000

# 2002 CBCRP Funding by Institution



The following 22 California research institutions were awarded new CBCRP grants in 2002. Some awards were split between institutions.

Institution	# Awards	Award Amount
Beckman Research Institute of the City of Hope, Duarte	1	\$42,784
California Institute of Technology, Pasadena	1	\$86,400
California Pacific Medical Center Research Institute, San Francisco	2	\$622,800
Cedars-Sinai Medical Center, Los Angeles	1	\$306,000
Harbor-UCLA Research & Education Institute, Torrance	1	\$140,941
Kaiser Foundation Research Institute, Oakland	1	\$132,055
La Jolla Institute for Molecular Medicine	1	\$199,174
Lawrence Berkeley National Laboratory, Berkeley	9	\$2,642,699
Northern California Cancer Center, Union City	1	\$203,388
Public Health Institute, Berkeley	1	\$86,175
Salk Institute for Biological Studies, San Diego	1	\$86,400
Scripps Research Institute, La Jolla	4	\$678,532
Sidney Kimmel Cancer Center, San Diego	2	\$892,800
Stanford University, Palo Alto	8	\$2,013,397
The Burnham Institute, La Jolla	11	\$2,652,813
University of California, Berkeley	1	\$812,340
University of California, Davis	2	\$200,328
University of California, Irvine	2	\$128,122
University of California, Los Angeles	3	\$514,087
University of California, San Diego	1	\$499,796
University of California, San Francisco	11	\$1,318,679
University of Southern California, Los Angeles	4	\$549,393



# 2002 CBCRP Application Evaluation & Review Committees



Grant applications in 2002 were initially reviewed and scored for scientific merit in six peer review Committees. The Committees are composed of distinct types of reviewers, and they reviewed grants modeled on established practice at the National Institutes of Health (NIH). The Chair leads the review process and is a senior researcher in breast cancer areas associated with the Committee's central topic or priority issue. Committee members have broad expertise in topics associated with individual applications. Breast cancer Advocate reviewers are women active in breast cancer issues (many of whom are also living with the disease), and they bring their personal knowledge and commitment to the review process. Often the Advocates have specialized training in grant review, such as the NBCC's Project LEAD. Each committee also has a California Advocate Observer, who is not assigned applications for review and does not vote, but represents the California advocacy community. The Observer gains insight into the research evaluation process and provides feedback to the Program on this process. Ad Hoc members participate by teleconference and bring their specialized expertise to the review of individual applications.

Over the past five years, the CBCRP has developed, tested, and phased in a scoring system that allows our expert reviewers to better differentiate applications that are especially innovative and that have the most potential impact on breast cancer. This has improved our ability to choose the most innovative and creative research for funding. In the past, the majority of research funding agencies, including the CBCRP and the NIH, rated proposals with a single scientific merit score. With this method, for example, an application with an excellent research plan to test an idea that wasn't particularly novel could receive the same score as an application with an average research plan to test a very novel idea. CBCRP's new scoring method, which separates scientific merit into component elements specific for each award type, can better differentiate specific qualities in each application. Some key scientific merit components include:

- ◆ Innovativeness
- ◆ Impact
- ◆ Approach

- ◆ Feasibility
- ◆ Career Development
- ◆ Translational potential (TRC award type)
- ◆ Cross-disciplinary elements (TRC award type)
- ◆ Community Involvement (CRC award type)
- ◆ Community Benefit (CRC award type)

After the completion of all review committees, the CBCRP ranks the application pool by average scientific merit, which is the combined average of the scientific merit components for the application's award type. The lowest third (approximately) of applications ranked by average scientific merit are excluded from further consideration for funding.

Next, applications having sufficient scientific merit are then examined by the CBCRP's advisory Council for programmatic relevance. The following criteria are used:

- ◆ Responsiveness to the CBCRP's priority issues and award types
- ◆ Multidisciplinary approach
- ◆ Translational potential
- ◆ Focus on the underserved
- ◆ Strength of individual scientific merit component scores
- ◆ Balance of overall portfolio
- ◆ Emphasis on relatively underfunded areas
- ◆ Inclusion of advocates and sensitivity to advocacy issues/concerns

In addition, we place some of our Priority Issues and Award Types into a primary category, and these applications are given first consideration for funding.

Finally, the advisory Council recommends the grants to be funded, based upon (1) the review committee scientific average and component merit scores and (2) the programmatic relevance. This two-tiered process ensures both scientific excellence and relevance of the research to CBCRP's mission and goals.

# Basic Breast Biology Committee

## Chair:

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