

# 2003 Cycle IX Awards Compendium



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# 2003 CBCRP New Awards Compendium

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## Introduction

The California Breast Cancer Research Program (CBCRP) is pleased to announce the funding of 50 new research grants that will advance our knowledge about the causes, prevention, biology, detection, and treatment of breast cancer. With these new awards we are investing \$11.5 million to improve the lives of California women. These research projects are being performed at 21 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); medical centers (e.g., Childrens Hospital Los Angeles); and community organizations (e.g., Women's Cancer Resource Center).

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

- A portion of a 2 cents 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

This is our ninth year (or cycle) of grant funding, and through 2003 we have awarded nearly \$150 million to fund 569 research projects. The CBCRP is administered by the University of California, Office of the President, in Oakland. Our overall objectives, strategies, and priorities are developed with the assistance of a volunteer advisory Council, which also makes recommendations on the 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 nonprofit health organizations, one is a practicing breast cancer medical specialist, two are members from private industry, and one is an *ex officio* member from the DHS Breast Cancer Early Detection Program: "Every Women Counts".

## The Challenge:

*“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 challenge and barriers to address this mission are tremendous. Although CBCRP is the largest breast cancer research funder in the world, we work with a budget less than 0.05% of the NIH (\$23B) and 0.2% of the NCI (\$4.6B). We seek to fund a unique grant portfolio and reduce overlap with other agencies. Our funded research is broken down into categories by both breast cancer-specific research topics that we call Priority Issues and by project- and investigator-specific award types.

To **establish the CBCRP’s priorities and advance our mission**, our advisory Council identified these key criteria for the research CBCRP funds:

- **Nurture collaboration** and synergy between California scientists, clinicians, advocates, community members, and others.
- **Recruit, retain, and develop high-quality California-based investigators** who focus on breast cancer research.
- Foster **innovative ideas** (i.e., new drugs, new strategies and new paradigms).
- **Address the public health outcomes** of prevention, earliest detection, effective treatments, and quality of life.
- **Translate research** to more effective products, technologies, or interventions and their **application/delivery to Californians**.
- **Drive policy** in both the private and public sectors on breast cancer in California.
- **Reduce disparities** and/or **address the needs of the underserved** in California.
- Complement, build on, and/or feed into, but **do not duplicate the research programs of other funding agencies** interested in breast cancer.
- Respond to feedback and breast cancer research needs and **expectations of the CBCRP as identified by scientists and the public** in California.

We are constantly evaluating our granting efforts to better meet the needs of both the research and the breast cancer advocacy communities in California. This year marks our tenth anniversary, and we are planning for the future. The increasing human cost and suffering due to breast cancer in California reminds us of how much is yet to be accomplished. We welcome your thoughts and feedback either via our Web site link “CBCRP Listens” or by e-mail: [cbrp@ucop.edu](mailto:cbrp@ucop.edu).

## The CBCRP Funding Process:

In this Compendium we present the outcome of our 2003 grant application evaluation and funding process. In early 2003 we received grant applications in response to our “Call” for new research on breast cancer. During the period from 2001 through this year our application volume has increased by almost 40%, but our available budget has remained constant. In this funding cycle we evaluated 221 applications for scientific merit using a peer-review process. Our review committee membership and a description of this process are found at the end of this booklet. After the peer review scores were tabulated, the upper two-thirds of applications having “sufficient scientific merit” were considered by our advisory Council for funding in a programmatic review process. The Council members rate the applications for responsiveness to stated CBCRP criteria. The end result is that the CBCRP’s advisory Council and Program staff balance the scientific merit and programmatic ratings to arrive at a funding decision for each application. Thus, 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 sections to follow we present a summary, discussion, and listing of newly funded CBCRP grants for 2003 including:

- New awards broken down by CBCRP Priority Issue topics and Award Types
- Highlights of 2003 funding
- Portfolio summary, discussion, and list of grants for each of our Priority Issue groups
- Funded institutions
- Description of the review process and review committee membership

We have organized our nine research topic Priority Issues into four groups that have a related 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: [www.cbcrp.org](http://www.cbcrp.org).

### 1. Statistical Summary:

#### A. New CBCRP Funding in 2003:

- Total applications reviewed = **223**
- Applications offered funding = **51**
- Success rate = **22.8%**
- Grants accepted = **50**
- Amount awarded for new grants = **\$11,529,618**
- Grant supplements awarded in 2003 = **1, \$10,000**

<b>Total of new grants and supplements awarded in 2003 = \$11,539,618</b>
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#### B. Applications and Awards by CBCRP Priority Issues:

<u>Priority Issue</u>	<u># Applications</u>	<u># Grants Awarded</u>	<u>Awarded Amount</u>
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##### Community Impact:

Health Policy & Health Services	7	1	\$315,198
Sociocultural	20	6	\$1,447,888
Racial & Ethnic Differences	7	4	\$1,866,302
<b>Total</b>	<b>34</b>	<b>11</b>	<b>\$3,629,388</b>

##### Prevention & Risk Reduction:

Etiology	9	4	\$1,338,399
Prevention	24	4	\$1,348,860
<b>Total</b>	<b>33</b>	<b>8</b>	<b>\$2,687,259</b>

##### Diagnosis & Treatment:

Earlier Detection	9	2	\$83,304
Innovative Treatments	54	9	\$1,800,044
<b>Total</b>	<b>63</b>	<b>11</b>	<b>\$1,883,348</b>

##### Biology of the Breast Cell:


Biology of the Normal Breast	19	8	\$1,463,162
Pathogenesis	74	12	\$1,866,461
<b>Total</b>	<b>93</b>	<b>20</b>	<b>\$3,329,623</b>

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

<u>Award Type</u>	<u># Applications</u>	<u># Grants Awarded</u>	<u>Award Amount</u>
<b>Collaboration Awards:</b>			
Community (CRC)	6	2	\$232,264
Translational (TRC)	13	2	\$288,800
Sci. Perspectives (SPRC)	2	0	0
Joining Forces Conference	2	2	\$50,000
<b>Total</b>	<b>23</b>	<b>6</b>	<b>\$571,064</b>
<b>Investigator-initiated Awards:</b>			
RFA	26	7	\$4,125,804
STEP	55	13	\$3,393,662
IDEA	43	7	\$ 884,863
<b>Total</b>	<b>124</b>	<b>27</b>	<b>\$8,404,329</b>
<b>Career Development Awards:</b>			
Dissertation	3	2	\$118,304
Postdoctoral	47	11	\$858,024
New Investigator	23	3	\$1,422,488
Career Enrichment	1	1	\$155,409
Mentored Scholar	2	0	0
<b>Total</b>	<b>76</b>	<b>17</b>	<b>\$2,554,225</b>

### 2. Funding Highlights:

- Eight grants expand our **knowledge of normal breast biology**, 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.
- Eight awards focus on **prevention/risk reduction and etiology**, including state-of-the-art genetic analysis, exploring dietary and viral causes associated with risk and risk factors for African Americans.
- One project **improves health policy** by investigating the cost of breast cancer in California.
- Four grants investigate the underlying reasons behind **racial and ethnic disparities** associated with breast cancer.
- Six awards deal with **sociocultural/psychological issues** related to underserved communities, ethnic factors, and access to clinical trials.
- Twelve grants further our understanding of **tumor biology**.
- Eleven projects explore novel methods to **detect breast cancer and develop novel approaches to treatments**.
- Twenty projects for **innovative, exploratory, and high-risk/high reward research** projects push boundaries, challenge existing paradigms, and initiate new research programs.
- Seventeen awards provide opportunities in **career development** at the levels of graduate training, postdoctoral fellowships, career enrichment, and newly independent investigators. These researchers bring fresh thinking to their respective disciplines.
- Seven grants in **special-topic RFAs**, which we have identified as under-funded, allow the CBCRP to maximize its overall impact in breast cancer research
- Four projects involve **collaborative teams** that include either community groups and researchers or cross-disciplinary efforts between researchers

-  **Five awards are of special interest**, because they are funded, in part, by revenue from the **California State Income Tax Check-off**. These grants are indicated in the following sections.

# The Community Impact of Breast Cancer: The Social Context

**Overview:** The CBCRP supports research into 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. 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**
- **Racial/Ethnic Differences in Breast Cancer: Eliminating Disparity**
- **Sociocultural, Behavioral, and Psychological Issues Relevant to Breast Cancer: The Human Side**

## Funding Data:

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		<u>Proportion of Total</u>
Community Impact grants awarded in 2003:	11	22%
Funded amount:	\$3,629,388	31%
Supplements Funded	1 (\$10,000)	

## Community Impact Portfolio Summary:

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One newly funded CBCRP grant was awarded under the *Health Policy and Health Services* priority issue to **Wendy Max** at the **University of California, San Francisco**. Dr. Max will be studying the economic cost of breast cancer in California; this research will allow policy-makers to understand the impact that breast cancer has on both the entire state and in various counties and regions.

Six new awards were to initiate research projects in our *Sociocultural, Behavioral and Psychological Issues* priority issue. First, **Rebecca Rausch** at the **University of California, Los Angeles** will follow-up on a previous CBCRP award and continue to examine the effects of chemotherapy and/or antiestrogen therapy on the mental functioning of breast cancer patients. The term "chemo brain" has long been an issue of concern among women undergoing cancer therapy, but only fairly recently has there been systematic investigation into this problem. Dr. Rausch's study will measure long-term deficits in memory, attention and concentration among a small group breast cancer patients, and they will use MRI (magnetic resonance imaging) to study specific structural changes in the brain associated with these mental deficits. Next, **Beth Glenn** also at the **University of California, Los Angeles** will examine the communication style, structure, and the anticipated impact of BRCA1 and 2 testing on the family. The idea is that the family context in which a woman considers genetic evaluation and testing may represent an important influence on her decision whether to be evaluated and tested. Furthermore, this family context may differ by ethnicity that may explain the low level of minority participation in genetic testing. Next, psychosocial support for women with breast cancer is an innovative and understudied field of research. **Kate**

**Collie** is a postdoctoral fellow in the **Stanford University** School of Medicine working with **Cheryl Koopman** in the Department of Psychiatry and Behavioral Sciences. Dr. Collie's project, 'Art for Recovery', is based at the UCSF Comprehensive Cancer Center, which offers a variety of support services for breast cancer patients that involve visual creative expression. This support does not rely on verbal expression, and Dr. Collie will study how well the program is meeting the emotional, psychological, and social support needs of women, especially underserved women. Next, **Janine Giese-Davis** also at **Stanford University** will examine the possible role of guilt in affecting psychological and emotional recovery from breast cancer. Women may feel guilt because they have not been able to spend as much time with their children or families, mistakenly believe that they have caused their cancer, think that their children may be at greater risk for cancer, or fear dying prematurely, thereby abandoning children and family members. Dr. Giese-Davis' team will be the first researchers using recently developed methods (e.g., questionnaires and coding from videotapes of counseling sessions) to measure shame and guilt, as well as embarrassment and pride in women with breast cancer. **John Park** and **Morton Lieberman** (co-PIs) at the **University of California, San Francisco** will study the effectiveness of BreastCancerTrials.org (BCT.org), an Internet-based tool for matching breast cancer patients to clinical trials. This secure and confidential online registry enables comparison of patient self-reported medical histories with clinical trial eligibility requirements. The hypothesis of this study is that BCT.org can shorten the duration of clinical trials and promote participation among underserved women including seniors, racial and ethnic minorities, rural residents, and lower income families. Finally, **Celia Kaplan** also from the **University of California, San Francisco** will compare treatment decision-making processes, quality of life issues, and the receipt of follow-up care among 300 Latinas and 300 white women diagnosed with DCIS in diverse regions in California. Women with DCIS have a unique disease profile, since their prognosis is often very good, and many of the discovered lesions would not have resulted in invasive cancer if left untreated. Still, many DCIS patients will undergo treatment essentially the same as women with invasive breast cancer.

The CBCRP awarded four new grants in our *Racial/Ethnic Differences* priority issue. Two of these projects are for Community Research Collaboration (CRC) Pilot awards to support teams of community organizations and university researchers. First, **Soo-Young Chin** at the **Korean Health, Education, Information & Research Center** (KHEIR) and **Annette Maxwell** from the **University of California, Los Angeles** will explore misconceptions and barriers to regular mammographic screening among Korean-American women. The aims are to address cultural barriers to encourage these women to be screened on a regular basis and to learn how best to disseminate this information to Korean-American women. Using information obtained in focus groups, they will develop one or more interventions and pilot test them in women who are due for re-screening. Next, **Diane Estrin** at the **Women's Cancer Resource Center**, **Linda Wardlaw** from the **Charlotte Maxwell Complementary Clinic**, and **Rani Eversley** at the **University of California, San Francisco** will study the problems of lymphedema among breast cancer surgery patients. This university-community team will test the feasibility issues surrounding the development, testing and standardization of a low-cost intervention to prevent or reduce the severity of secondary arm lymphedema among breast cancer patients. They anticipate developing a full-scale intervention to test the efficacy of this approach in the future.

Two of the *Racial/Ethnic Differences* grants are epidemiology-based. First, **Rebecca Smith-Bindman** at **University of California, San Francisco** will investigate the basis for different rates of breast cancer death between women from different racial and ethnic groups. Dr. Smith-Bindman will use two large, population-based sources with data on 5,880 African Americans, 3,240 Hispanics, and 2,573 Asian women diagnosed with breast cancer from 1992 through 2001. In addition, they will augment this information with person-to-person interviews. Next, **Anna H. Wu** at the **University of Southern California** will examine whether pre-and post-diagnostic dietary (especially green tea and soy) and other lifestyle factors (e.g., physical activity, body size) are associated with breast cancer outcome in Asian American women. The data will be gathered from 1,200 Asian-American women diagnosed from 1995 through 2000.

The CBCRP also awarded a supplement to an existing Community Research Collaboration grant. This funding will enable a community based organization, the **Chamorro Community Council of California**, to gain experience in participatory research with a mentor organization, the **Guam Communications Network**. The aim is to develop and evaluate a culturally tailored, lay health advocate intervention to increase breast cancer screening rates among Chamorro women aged 50 years and older in Los Angeles and Orange counties.

### Community Impact Grants Funded in 2003:

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#### Health Policy and Health Services Priority Issue

##### ***The Cost of Breast Cancer in California***

Wendy Max  
University of California, San Francisco  
Request for Applications Award  
2 years; \$315,198

#### Racial/Ethnic Differences Priority Issue

##### ***Reducing Disparities Among Korean Women***

Soo-Young Chin and Annette Maxwell (co-PIs)  
Korean Health, Education, Information and Research Center and University of California, Los Angeles  
Community Research Collaboration—Pilot Award  
1.5 years, \$107,264

##### ***Correlates of Lymphedema Severity and Access to Intervention***

Diane Estrin, Linda Wardlaw and Rani Eversley (co-PIs)  
Women's Cancer Resource Center, Charlotte Maxwell Complementary Clinic and the University of California, San Francisco  
Community Research Collaboration—Pilot Award  
1.5 years; \$125,000



***Racial Disparity in Breast Cancer Mortality***

Rebecca Smith-Bindman  
University of California, San Francisco  
Request for Applications Award  
3 years; \$583,287

***Lifestyle Factors & Breast Cancer Prognosis in Asian Americans***

Anna Wu  
University of Southern California  
Request for Applications Award  
3 years; \$1,050,751

**Sociocultural, Behavioral, and Psychological Priority Issue**

***'Art for Recovery': Expanding Access for the Underserved***

Kate Collie  
Stanford University  
Postdoctoral Fellowship Award  
2 years; \$86,138

***Assessing the Impact of Shame and Guilt in Recovery***

Janine Giese-Davis  
Stanford University  
IDEA  
1.5 years; \$157,576

***Interplay of Family Context and Ethnicity in BRCA1/2 Testing***

Beth Glenn  
University of California, Los Angeles  
Postdoctoral Fellowship Award  
2 years; \$80,000

***Latinas and DCIS: Treatment Decisions and Quality of Life***

Celia Kaplan  
University of California, San Francisco  
Request for Applications award  
3 years; \$774,174

***BCT.org: Feasibility of a Clinical Trial Matching Tool***

Morton Lieberman and John Park (co-PIs)  
University of California, San Francisco  
Translational Research Collaboration—Pilot Award  
1 year; \$100,000

***Late Cognitive and Brain Changes After Breast Cancer Therapy***

Helen Rebecca Rausch  
University of California, Los Angeles  
STEP Award  
2 years; \$250,000

Community Research Collaboration Supplement Award (CRCAS)

***A Network Based Intervention for Chamorros in Southern California***

Mentor Group: Guam Communications Network

Trainee Group: Chamorro Community Council of California

1 year; \$10,000

## Prevention and Risk Reduction: The Environment of the Disease

**Overview:** Despite our knowledge of breast cancer genes and other risk factors, the cause of breast cancer in most women is unknown. There are causes of the disease that cannot be explained by the analysis of 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 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:

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		<u>Proportion of Total</u>
Prevention & Risk Reduction grants awarded in 2003:	8	16%
Funded amount:	\$2,687,259	23%

### Prevention & Risk Reduction Portfolio Summary:

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Four new grants were awarded in the CBCRP priority issue of *Etiology* to study the causes of breast cancer. Women who are obese may be more or less likely to develop breast cancer depending upon the age their obesity occurs. Obese women during the menstrual years have a lower risk, while risk increases for women who are obese after menopause. **Catherine Carpenter** at the **University of California, Los Angeles**, will study different forms of genes in relationship to breast cancer, the hypothesis being that genes that increase the likelihood of obesity may also increase women's chances of developing breast cancer. Several candidate genes (e.g., the leptin-receptor gene OB-R, which has never been studied in relationship to breast cancer) will be genotyped to see if various forms of these genes are related to chances of developing breast cancer or obesity. Next, **Christina Clarke Dur** at the **Northern California Cancer Center** received a New Investigator Award to examine "The Hygiene Hypothesis and Breast Cancer Risk." Dr. Clarke Dur will contact women with and without breast cancer to find out about their exposures relevant to hygiene. Dr. Clarke Dur will then use statistical analysis to determine if breast cancer cases have a different profile of immunodevelopmental exposures than control groups. The hypothesis to be tested is whether reduced or delayed exposure to microbes, or living in a mostly disease-free, sanitized environment hampers development of a healthy immune system. An underdeveloped immune system might subsequently influence breast cancer development by weakening responses against tumors, increasing estrogen production, or both. Next, **Sally Glaser** also from the **Northern California Cancer Center** is using an innovative, STEP award to examine a suggested link between EBV (Epstein-Barr Virus) and breast cancer. She will use a powerful gene amplification technique called "real-time PCR" to determine how much, if any, EBV is present in very small tissue samples provided by breast cancer patients. Another method, called "laser capture microdissection", will be used to

determine whether EBV is inside cancer cells or merely in the surrounding normal cells. Dr. Glaser will then begin identifying the characteristics of women (e.g., age, race/ethnicity, socioeconomic status, extent of disease spread, prognosis) who have EBV-associated breast cancers. Finally, prolactin is important to breast development both during puberty and pregnancy, and is the primary hormone responsible for milk production after pregnancy. Human and animal studies have supported the role of prolactin as a possible hormonal risk factor for breast cancer. **Brian Henderson** at the **University of Southern California** will take advantage of the multiethnic Hawaii/LA cohort, and, using an IDEA award study the breast cancer risk association between genetic variations in prolactin and the prolactin receptor. Using high-throughput laboratory techniques and novel statistical methods, this project will be the first to comprehensively evaluate genetic variations in PRL and the prolactin receptor in relation to breast cancer risk.

Four new CBCRP grants focus on the priority issue of *Prevention and Risk Reduction*. Two grants involve animal studies of novel breast cancer chemoprevention agents. **Michael DeGregorio** at the **University of California, Davis** received a STEP award to assess the ability of ginseng, a natural remedy that has been used to treat numerous ailments for several thousand years in the Orient, to prevent the development of breast cancer. In another STEP award, **Kristen Kulp** at the **Lawrence Livermore National Laboratory** will investigate whether Essiac® Herbal Tea, a commercially available complementary therapy, has protective properties that may have an effect on breast cancer risk. Dr. Kulp will study breast cell damage caused by PhIP, which is an ubiquitous food mutagen formed during high-temperature cooking of protein rich foods, especially meat. She will use cell lines and rat models treated with Essiac® Herbal Tea to see whether this prevents cell DNA damage or tumor formation caused by PhIP. Next, **Christopher Haiman** from the **University of Southern California** received a New Investigator award to study subtle variations in the BRCA1 and BRCA2 familial breast cancer genes that might be associated with sporadic breast cancer risk. It is also not known what percentage, if any, of the racial/ethnic variation in breast cancer risk may be explained by subtle variations in these genes. Dr. Haiman will use a novel genetic haplotype (i.e., a combination of genotypes on the same chromosome that tend to be inherited as a group) approach that exploits the ancestral relationship between common variations in the DNA to identify genetic markers of sporadic breast cancer risk in a large-scale multiethnic epidemiologic study of African-Americans, Latinas, Japanese, Whites and Hawaiians in Los Angeles and Hawaii. Finally, **Susan Neuhausen** at the **University of California, Irvine** will examine African American breast cancer mortality, employing a molecular epidemiology approach. The aim is to identify genes in the insulin-like growth factor (IGF) pathway that are important for breast cancer occurrence and progression. Dr. Neuhausen will compare specific genetic changes in DNA from African American women with and without breast cancer, and then analyze the data for the effects of genetic changes, for gene-gene interactions and lifestyle factors. She will correlate these lifestyle factors, such as body mass index, with breast cancer risk, age at which it was diagnosed, and tumor characteristics.

## Prevention & Risk Reduction Grants Funded in 2003:

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### Etiology Priority Issue



#### ***Genetics, Obesity, and Breast Cancer Risk***

Catherine Carpenter  
University of California, Irvine  
Request for Applications Award  
3 years; \$533,527

#### ***The Hygiene Hypothesis and Breast Cancer Risk***

Christina Clarke Dur  
Northern California Cancer Center  
New Investigator Award  
3 years; \$366,997

#### ***Epstein-Barr Virus in Breast Cancer Tissues***

Sally Glaser  
Northern California Cancer Center  
STEP Award  
2 years; \$275,564

#### ***Prolactin and Breast Cancer Risk in a Multiethnic Cohort***

Brian Henderson  
University of Southern California  
IDEA  
1.5 years; \$162,311

### Prevention Priority Issue

#### ***Preventing Breast Cancer with Ginseng***

Michael DeGregorio  
University of California, Davis  
STEP Award  
1 year; \$99,708

#### ***Common Genetic Variation & Breast Cancer: A Genomic Approach***

Christopher Haiman  
University of Southern California  
New Investigator Award  
3 years; \$462,925

#### ***Studying the interaction of an Essiac Tea and Food Mutagen***

Kristen Kulp  
Lawrence Livermore National Laboratory  
STEP Award  
2 years; \$363,760

***The IGF Pathway & Breast Cancer Risk in African Americans***

Susan Neuhausen

University of California, Irvine

Request for Applications Award

3 years; \$422,467

# Diagnosis and Treatment: Delivering Clinical Solutions

**Overview:** Early detection does not guarantee a cure. 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 patient-individualized therapies require investigation. The CBCRP encourages lab researchers and clinicians 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:

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		<u>Proportion of Total</u>
Diagnosis & Treatment grants awarded in 2003:	11	20%
Funded amount:	\$1,883,348	16%

## Diagnosis & Treatment Portfolio Summary:

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The past decade has offered many challenges for researchers working in the fields of breast cancer early detection and treatment. Screening mammography has been a success in terms of access with annual screening rates of 70–80%. Despite this, there is debate and uncertainty over the degree of benefit and what technology might replace mammography in the future. The screening mantra of “smaller is better” has reached practical limits. We know that many breast cancers as small as 1–2 mm already have the physiological means to metastasize. Conversely the number of biopsies that turn out to be things other than cancer needs to be reduced to spare women the trauma of a “suspect lesion.” The CBCRP funded two grants in 2003 that address the *Earlier Detection* priority issue. First, we teamed with the **Susan Love MD Breast Cancer Foundation** to co-sponsor their **3rd Symposium on the Intraductal Approach to Breast Cancer** in Santa Barbara held in March 2003. This symposium brought together more than 120 researchers, scientists, doctors, and advocates from throughout the world, including many from California. The meetings were multidisciplinary, including clinicians, bench scientists, and the lay public. Pilot grants were funded to further support and encourage research on fluids and cells collected from the breast ducts to allow earlier detection and analysis of breast cancer. Next, we funded a dissertation project at the Beckman Laser Institute, **University California, Irvine**, to **Sean Merritt** in **Bruce Tromberg**'s laboratory to explore the potential of combining ultrasound with their pre-clinical development of an infrared, optical imaging of breast cancer. This technology employs a portable, hand-held device that allows tumor detection without radiation or breast compression.

The discovery and development of effective new treatments for breast cancer remains an elusive goal. Seven of our newly funded grants focus in two areas that have

attracted advocacy attention, (1) less toxic treatments that might also be useful in chemoprevention, and (2) harnessing the immune response. Indole 3-carbinols (I3C) are compounds derived from certain vegetables (e.g. Brussels spouts) that were initially studied for prevention of cancer cell growth through modulation of the cell cycle, but are now being studied for possible inhibition of cell invasion properties. **Christine Brew** and her mentor **Gary Firestone** at the **University of California, Berkeley**, are funded through separate grants to study I3C's role in regulation of metalloproteinase genes and to identify the cellular target for the I3C derivative DIM, respectively. **Ling Jong** from **SRI International** received an award to evaluate novel I3C derivatives using assays for cell signaling pathways associated with apoptosis (programmed cell death) and angiogenesis. By understanding the mechanism of action and cellular targets, these natural compounds have the potential to become anti-cancer agents.

There is the concern that widespread use of alternative and complementary therapies might alter the effectiveness of Western medicines. **Michael Campbell** at the **University of California, San Francisco**, was awarded an innovative STEP grant to investigate how Chinese medicinal herbal preparations work in combination with the traditional chemotherapeutic drugs, doxorubicin and paclitaxel. Dr. Campbell's study will be done in cell culture systems, but promising results might quickly be translated to human trials.

Three newly-funded CBCRP awards focus on research questions related to immunotherapy of breast cancer. First, **Joseph Lustgarten** at the **Sidney Kimmel Cancer Center** is funded to study a novel group of "non-self" protein fragments (peptides) for their potential to establish immune responses against the Her-2 oncogene. The normal immune response to Her-2 is weak, so Dr. Lustgarten's approach of directly activating T-cells might circumvent the immune tolerance exhibited by most patients. **Edward Nelson** at the **University of California, Irvine**, received an IDEA (innovative) award to explore a novel immunophototherapy approach. This is based on the injection of a precursor molecule, uptake by tumor cells, and metabolic production of a "photosensitive" killer compound. The "photo" element involves "activation" by laser light focused on the tumor. Dr. Nelson is evaluating whether marrow-derived dendritic cells might work to enhance this therapy. **Margaret Huflejt** also from the **Sidney Kimmel Cancer Center** received an IDEA award to explore how best to neutralize immunosuppressive "galectins" produced by tumor cells. Galectins are carbohydrate-rich cell surface proteins that are thought to mask tumor cells from immune detection.

**Peter Vogt** from the **Scripps Research Institute** will explore a new approach to screen drugs targeting Myc, an oncogene that is elevated in most breast cancers and serves to "de-regulate" many genes that are associated with aggressive tumors. Dr. Vogt is searching for compounds that block the key Myc-Max protein interaction, and he plans to evaluate lead compounds by their potential to block anti-estrogen resistance in cultured cells. Finally, **Robert Cardiff** at the **University of California, Davis**, received Joining Forces Conference Award to support a special conference on improving animal models in pre-clinical research on breast cancer. Too many drug discovery efforts either fail at the stage of animal studies or yield promising results that do not translate into successful human trials.

## Diagnosis & Treatment Grants Funded in 2003:

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### Earlier Detection Priority Issue

#### ***3rd Symposium on the Intraductal Approach to Breast Cancer***

Susan Love  
Susan Love MD Breast Cancer Foundation  
Joining Forces Conference Award  
1 year; \$25,000

#### ***Combined Optical and Ultrasound Imaging for Breast Cancer***

Sean Merritt  
University of California, Irvine  
Dissertation Award  
2 years; \$58,304

### Innovative Treatment Modalities Priority Issue

#### ***Inhibition of Breast Cancer Cell Invasion by Natural Indoles***

Christine Brew  
Postdoctoral Fellowship Award  
2 years; \$80,000

#### ***Chinese Herb/Chemotherapy Interactions in Breast Cancer***

Michael Campbell  
University of California, San Francisco  
STEP Award  
2 years; \$200,000

#### ***Preclinical Trials for Breast Cancer***

Robert Cardiff  
University of California, Davis  
Joining Forces Conference Award  
1 year; \$25,000

#### ***Novel I3C Regulated Cell Cycle Factor in Breast Cancer Cells***

Gary Firestone  
University of California, Berkeley  
STEP Award  
2 years; \$150,000

#### ***Lactulosamines: Novel, Non-toxic Therapies for Breast Cancer***

Margaret Huflejt  
Sidney Kimmel Cancer Center  
IDEA  
1 year; \$192,600

#### ***Dietary Indole Analogs Inhibit Breast Cancer Cell Invasion***

Ling Jong  
SRI International  
STEP Award  
2 years; \$388,491

***Cryptic Peptides-Based Vaccines for Breast Tumor Treatment***

Joseph Lustgarten  
Sidney Kimmel Cancer Center  
STEP Award  
2 years; \$385,200

***Pilot Studies of Breast Cancer Immunophototherapy***

Edward Nelson  
University of California, Irvine  
IDEA  
1 year; \$99,834

***Inhibitors of Myc: Novel Drugs for Breast Cancer***

Peter Vogt  
Scripps Research Institute  
STEP Award  
2 years; \$278,919



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

**Overview:** Breast cancers originate from normal breast epithelial cells, so critical research is needed to understand the pre-cancerous, causative events of the disease. The underlying genetics of disease heterogeneity seen in the clinic need clarification at the basic science level. We need better and more relevant cell and pre-clinical animal models of breast cancer. The key genetic and molecular signatures of the disease may provide useful biomarkers for better diagnosis and prognosis, so treatments can be individualized and women spared the use of non-effective drugs. The underlying cellular signaling pathways for growth control, cell death, DNA repair, and cell migration/metastasis require exploration to develop into targets for therapy and prevention.

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:**

		<b><u>Proportion of CBCRP's Total</u></b>
<b>Grants awarded in 2003:</b>	<b>8</b>	<b>16%</b>
<b>Funded amount:</b>	<b>\$1,463,162</b>	<b>13%</b>

### **Biology of the Normal Breast Portfolio Summary:**

The biology of the normal breast is a greatly understudied area. 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 eight newly funded grants in the biology of the normal breast priority area investigate various pathways that contribute to breast cell growth, maturation, and death.

The earliest stage of *embryonic breast development* involves the migration of the breast epithelial cells to the location on the body where the breast will eventually form. **Saverio Bellusci** of the **Childrens Hospital Los Angeles** received a three-year RFA to investigate this process. He will study how the interactions between the growth factor FGF10 and the WNT gene family direct breast epithelial cell migration. Ultimately this research may give us insights into the metastatic process of breast tumors.

Three investigators were granted awards to study the *regulation of gene activation and inactivation in the normal breast cell*. First, **John Conboy** of the **Lawrence Berkeley National Laboratory** will use an IDEA award to investigate the changes in cell behavior due to “alternate splicing”— when one gene produces different proteins from the same code. Dr. Conboy will study the mechanism for the determining which protein is produced under different cellular conditions. Next, **Peter Kaiser** of the **University of California, Irvine**, will also use an IDEA award to study the genetic regulation of the breast cancer susceptibility gene BRCA1 through a process of protein degradation, called ubiquitylation. Finally, **Yuehai Ke** at **The Burnham Institute** was awarded a postdoctoral fellowship to determine the role of a set of proteins call tyrosine phosphatases, which are known to regulate the activation of other proteins, in the development and normal functioning of the mammary gland.

The *aging of breast cells and supporting stroma* results in changes that may contribute to breast cancer. Two newly funded CBCRP grants will investigate the role of DNA integrity in the function of normal breast cells. First, **Kimberly McDermott** of the **University of California, San Francisco**, will undertake a postdoctoral fellowship to investigate the how the cellular structures that regulate DNA replication (centrosomes) function to protect it from mutations and chromosomal abnormalities. Next, **Paul Yaswen** of the **Lawrence Berkeley National Laboratory** received a STEP award to investigate a newly discovered gene, called BORIS, for its role in controlling the integrity of DNA and to determine whether it plays a role in the early transformation of breast cells.

The *early changes in the transition from a normal breast cell to a breast tumor cell* are subtle, but it is the goal of two studies funded this year to define the key genetic changes in this transition. **Thea Tlsty** of the **University of California, San Francisco** developed an early precursor model of breast cancer, called the variant Human Mammary Epithelial Cell (vHMEC) that has specific genetic characteristics. Dr. Tlsty will determine whether these same characteristics can be found in early pre-cancer breast lesions, and therefore be used to distinguish them from normal breast tissue. Finally, the “information age” has opened new avenues for characterizing and understanding important changes to tissues at the protein level. One new technology is called “proteomics”, which is the simultaneous comparison of presence or absence of a panel of proteins in tissues under different physiological conditions. **Dave Hoon, Armando Giuliano, and Lori Wilson** (co-PIs) at the **John Wayne Cancer Institute** were awarded a Translational Research Collaboration Pilot Award (TRC pilot) to apply this new technology to the breast. The two major goals of the project are to: (1) determine whether it is possible to develop a proteomic profile “signature” of normal breast tissue during different stages of breast physiology, and (2) to determine if proteomic profile signatures of various types of breast lesions can be used to identify early pre-cancerous breast disease.

## **Biology of the Normal Breast Grants Funded in 2003:**

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### **FGF10 and Mammary Placode Induction in Mouse**

Saverio Bellusci  
Childrens Hospital, Los Angeles  
Request for Applications Award  
3 years; \$446,400

### ***Alternative pre-mRNA Splicing in Mammary Epithelial Cells***

John Conboy  
Lawrence Berkeley National Laboratory  
IDEA  
1.5 years; \$122,542



### ***Translational Proteomics of Normal to Benign Breast Disease***

Dave Hoon, Lori Wilson and Armando Giuliano (co-PIs)  
John Wayne Cancer Institute  
Translational Research Collaboration—Pilot Award  
1.5 years; \$188,800

### ***Identification of BRCA1 Ubiquitylation Targets***

Peter Kaiser  
University of California, Irvine  
IDEA  
1.5 years; \$75,000

### ***Dissection of Signaling Events in the Mammary Gland in vivo***

Yuehai Ke  
The Burnham Institute  
Postdoctoral Fellowship Award  
2 years; \$86,400

### ***Does Disregulation of Centrosomes Cause Breast Cancer?***

Kimberly McDermott  
University of California, San Francisco  
Postdoctoral Fellowship Award  
2 years; \$80,000

### ***Early Transitions in Breast Cancer***

Thea Tlsty  
University of California, San Francisco  
STEP Award  
2 years; \$199,999

### ***Functional Analysis of BORIS, A Novel DNA-binding Protein***

Paul Yaswen  
Lawrence Berkeley National Laboratory  
STEP Award  
2 years; \$264,021

## Pathogenesis: Understanding the Disease

### Pathogenesis Funding Data:

		<u>Proportion of CBCRP's Total</u>
Grants awarded in 2003:	12	24%
Funded amount:	\$1,866,461	16%

### Pathogenesis Portfolio Summary:

Although cancer is often described as a “genetic disease”, there are many competing theories to explain the gene alterations and mutations that initiate cancer and those that promote disease progression. W. Wayt Gibbs, writing in the July 2003 issue of *Scientific American*, summarized this cancer confusion as, “....it is more useful to think of cancer as the consequence of a chaotic process, a combination of Murphy's Law and Darwin's Law: anything that can go wrong will, and in a competitive environment, the best adapted survive and prosper.” In a more scientifically detailed fashion, William Hahn at Dana-Farber Cancer Institute in Boston and Robert Weinberg at MIT have pointed to six key cellular events that are “hallmarks of cancer” (recently reviewed in: *N Engl J Med.*, 2003 348:674). Taken together these cellular events attempt to account for the sporadic nature of cancer, the biological and pathological heterogeneity seen in patients, immortality of cancer cells, numerous gene and chromosomal alterations, uncontrolled growth, motility and metastasis events, and resistance to therapy. Since no single approach can successfully explain cancer, researchers are employing a variety of technologies and methods. These range from cell and animal models of breast cancer; complex genomic and proteomic techniques to identify and relate multiple genetic changes in various forms of the disease; and the application to cancer of new discoveries in basic cell biology, DNA repair, cell cycle, growth signaling, and gene regulation processes. Still, in breast cancer the response to hormones, especially estrogen, remains a key underlying theme. Researchers now think that estrogen may operate in ways outside the “classical” estrogen receptor pathway. New thinking is also emerging for the growth factor receptor EGFR and the Her oncogenes. There is much interest in “cross-talk” between signaling pathways, previously thought to be distinct. Finally, the inherited breast cancer risk genes, BRCA1 and 2, are being studied in more advanced ways to better explain how DNA defects, repair processes, and cell growth/death pathways are interrelated and become defective in cancer.

*Angiogenesis, invasion, and metastasis* continue to be areas of promising investigation, despite the reality that angiogenesis-blockers have not lived up to expectations. From a basic research perspective, there is still a tremendous amount of information needed on how cancer spreads to develop and use targeted therapies. **Min-Ying (Lydia) Su** from the **University of California, Irvine**, is funded for an innovative STEP award to use an MRI-based approach to study angiogenic markers in the earliest phases of breast cancer progression—from hyperplasia through DCIS. Dr. Su and colleagues hope to identify and classify the early cancers that are most likely to undergo angiogenesis and progress to life-threatening stages. **Verena Kallab** from the **University of California,**

**San Francisco**, is funded for a postdoctoral fellowship to study circulating tumor cells from patients with advanced disease. Dr. Kallab will study the cytotoxic effects of breast tumor therapy on circulating tumor cells and how key cancer biomarkers on these cells correspond with the primary tumor. Finally, **Nadim Jessani** from the **Scripps Research Institute** is a graduate student in the lab of CBCRP-funded investigator, **Benjamin Cravatt**. Mr. Jessani is funded through a dissertation award to apply a novel proteomics (i.e., study of the whole protein component profile of a cell or tissue) method to detect the “active” proteases present in human tumors grown in mice. Proteases, such as metalloproteinases, are key modulators of cell invasion, so knowing the active proteases is much more useful than cataloging them at the gene-level.

Cancer has long been characterized by *uncontrolled cell growth, responses to growth modulators* and, more recently, *resistance to cell death responses*. Even when an effective drug, such as Herceptin® is developed, the benefit to individual patients varies, because cancer cells differ in susceptibility and develop resistance. **Tsui-Ting Ching** at the **University of California, San Francisco**, is funded for a postdoctoral fellowship to study gene variation and gene methylation patterns in cell samples from patients with elevated Her-2. Dr. Ching hopes to identify gene/methylation patterns that underlie Herceptin resistance, since only about 30% of patients with elevated Her-2 respond well to this therapy. On the same general theme of drug resistance, **Kristiina Vuori** from **The Burnham Institute** is funded for a STEP award to investigate why about 40% of the patients treated with Tamoxifen have tumors that don't respond well to this therapy. Dr. Vuori and colleagues are focusing on a docking protein, called “Cas” that may function as an assembly point for anti-estrogen resistance signaling pathways. **Nola Hylton** at the **University of California, San Francisco**, is funded for a Career Enrichment award to study the role of p53 as a regulator of radiation-induced cell death in a mouse cancer model. Dr. Hylton will be trained in the techniques of basic science and transfer this knowledge to her current expertise in MRI and radiology. Finally, **Steven Martin** from the **University of California, Berkeley**, received an innovative IDEA award to investigate how an oncogene, called Src, regulates cell signaling through growth factors to influence the breast tissue architecture associated with early malignant events. Loss of cell polarity is a key morphological change in cancer development, and Dr. Martin will study the connection to Src by using specific inhibitors and a 3-D tissue culture system in the laboratory of his colleague, **Mina Bissell** at the **Lawrence Berkeley National Laboratory**.

When breast cancer is detected clinically, it has already been present for many years; first in pre-neoplastic and then in small, developmental stages. We have too little information on what happens at the etiological (i.e, causative) and biological (i.e, genetic) levels during *breast cancer progression*. **Paul Henderson** at the **Lawrence Livermore National Laboratory** is funded for a novel approach to measure oxidative damage to DNA. Using breast cancer cell lines and tumors in animals, Dr. Henderson can feed cells or animals an oxidative damage-reporting marker for detecting and measuring DNA damage. This approach will enable the measurement of the ability of cells to either develop lesions or repair the damage. Another study will explore the role of BRCA1 in DNA repair. In recent years the role of the BRCA1 gene in DNA repair has become better defined, but we still need more information on its multiple roles in coordinating the cell cycle, protein degradation, and gene regulation. **Quan Zhu** at the **Salk Institute for Biological Studies** is funded as a postdoctoral fellow in the

laboratory of **Inder Verma**. Dr. Zhu will use new gene expression vectors to enable the many BRCA1 functional domains to be studied independently in a mouse model of breast cancer. A third study will explore a paradox in breast cancer biology and the clinic— why about 1/3 of patients at diagnosis are estrogen receptor negative (ER-). **Keon Wook Kang** has been awarded a postdoctoral fellowship to study the ER+ to ER- transformation using a special mouse model in his mentor's, **Eva Lee**, lab at the **University of California, Irvine**. Another perplexing issue in breast cancer is understanding the biological basis of why some DCIS progresses to invasive cancer and some does not. **Ruria Namba** from the **University of California, Davis**, is funded as a postdoc in the laboratory of **Jeffrey Gregg** to study DCIS-like hyperplastic outgrowths from pre-malignant mouse mammary tumors for the expression of altered genes and biomarkers of breast cancer. Finally, **Euan Slorach** from the **University of California, San Francisco**, was awarded a postdoctoral fellowship to study a novel gene, called Melb1, which is associated with embryonic and mammary development. Dr. Slorach will study this gene for its role in breast tumor development in the context of knockout mice lacking Melb1.

### **Pathogenesis Grants Funded in 2003:**

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#### ***Understanding Herceptin Resistance with Dual Function Array***

Tsui-Ting Ching  
University of California, San Francisco  
Postdoctoral Fellowship Award  
2 years; \$80,000

#### ***Role of Oxidative DNA Damage to Breast Tumor Progression***

Paul Henderson  
Lawrence Livermore National Laboratory  
New Investigator Award  
3 years; \$592,566

#### ***Study of the Apoptotic Phenotype as a Hallmark of Malignancy***

Nola Hylton  
University of California, San Francisco  
Career Enrichment Award  
1 year; \$155,409.00

#### ***Activity Based Profiling of Breast Cancer Xenografts***

Nadim Jessani  
Scripps Research Institute  
Dissertation Award  
2 years; \$60,000



#### ***Characterization of Circulating Tumor Cells in Breast Cancer***

Verena Kallab  
University of California, San Francisco  
Postdoctoral Fellowship Award  
2 years; \$80,000

***Mechanism of Estrogen Receptor Loss in Breast Cancer***

Keon Wook Kang  
University of California, Irvine  
Postdoctoral Fellowship Award  
1 years; \$39,086

***SRC Signaling in Breast Cancer***

Steven Martin  
University of California, Berkeley  
IDEA  
1 year; \$75,000

***Molecular Analysis of DCIS Progression in a Mouse Model***

Ruria Namba  
University of California, Davis  
Postdoctoral Fellowship Award  
2 years; \$80,000

***Novel Genes in Mammary Gland Development and Cancer***

Euan Slorach  
University of California, San Francisco  
Postdoctoral Fellowship Award  
2 years; \$80,000

***Angiogenesis in Hyperplasia to In-Situ Breast Cancers***

Min-Ying (Lydia) Su  
University of California, Irvine  
STEP Award  
2 years; \$250,000



***Overcoming Tamoxifen-Resistance in Breast Cancer***

Kristiina Vuori  
The Burnham Institute  
STEP Award  
2 years; \$288,0000

***Molecular Analysis of BRCA1 Function***

Quan Zhu  
Salk Institute for Biological Studies  
Postdoctoral Fellowship Award  
2 years; \$86,400

## 2003 CBCRP Funding by Institution

The following 21 California research institutions and community organizations were awarded new CBCRP grants in 2003. Some awards were split between institutions.

<b>Institution</b>	<b># Awards</b>	<b>Amount</b>
Chamorro Community Council of California, Carson	1	\$10,000
Childrens Hospital Los Angeles	1	\$446,400
John Wayne Cancer Institute, Santa Monica	1	\$188,800
Korean Health, Education, Information & Research Center Los Angeles	1	\$36,321
Lawrence Berkeley National Laboratory	2	\$386,563
Lawrence Livermore National Laboratory	2	\$956,326
Northern California Cancer Center, Union City	2	\$642,561
Salk Institute for Biological Studies, San Diego	1	\$86,400
Scripps Research Institute, La Jolla	2	\$338,919
Sidney Kimmel Cancer Center, San Diego	2	\$577,800
Susan Love MD Breast Cancer Foundation, Santa Barbara	1	\$25,000
SRI International, Menlo Park	1	\$388,491
Stanford University, Palo Alto	2	\$243,714
The Burnham Institute, La Jolla	2	\$374,400
University of California, Berkeley	3	\$305,000
University of California, Davis	3	\$204,708
University of California, Irvine	6	\$1,478,218
University of California, Los Angeles	4	\$934,470
University of California, San Francisco	11	\$2,648,067
University of Southern California, Los Angeles	3	\$1,675,987
Women's Cancer Resource Center, Oakland	1	\$125,000

# 2003 CBCRP Application Evaluation & Review Committees

Grant applications were initially reviewed and scored for scientific merit in six peer review committees. The CBCRP committees are composed of scientists and advocates from around the world. Grants are evaluated using a model that follows established practice at the National Institutes of Health (NIH). The committee 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 includes 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

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.

**The CBCRP wishes to thank the participants in our 2003 Review Committees for their service and dedication to our Program.**

## Basic Breast Biology Committee

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# **Community Resource Collaboration Concept Paper**

## **Chair**

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# **Community Resource Collaboration and Sociocultural, Behavioral, and Psychological Committee**

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***The mission of the California Breast Cancer Research Program is to eliminate breast cancer by leading innovation in research, communication, and collaboration in the California scientific and lay communities.***

