Annual Report to the Legislature
2008

CALIFORNIA
Breast Cancer
Research Program

Executive Summary

Designed to push breast cancer research in new, creative directions, the CBCRP is funded primarily by a California state tax on tobacco. Since 1993, the CBCRP has provided nearly $195 million in research funds.

Women with breast cancer and survivors of the disease are involved in all levels of the CBCRP's decision making, including decisions about which projects get funded. With input from these advocates, the CBCRP has established a record for funding cutting-edge studies and jump-starting new areas of research.

During 2008, the California Breast Cancer Research Program (CBCRP) funded 52 new single- and multiple year research projects that will advance scientific knowledge about breast cancer. With these new awards, we are investing almost $14 million at 24 California institutions. These pages list the studies funded this year, the studies in progress, and summaries of 56 studies funded in previous years that were completed during 2008.

Designed to push breast cancer research in new, creative directions, the CBCRP is funded primarily by a California state tax on tobacco. Since 1993, the CBCRP has provided nearly $195 million in research funds.

The need is urgent. Every two hours, on average, a California woman dies of breast cancer. More than 275,000 Californians are living with the disease, and over 21,000 more will be diagnosed this year. Over the past three decades, some progress has been made. Between 1988 and 2005, the breast cancer death rate in California dropped by 29 percent. While some argue that this is the result of earlier detection, there has been no significant drop in diagnosis of cancers that have spread to other parts of the body. Thus, it is more likely that the lower death rate is due to improvements in treatment, or to more women receiving appropriate treatment.

The rate at which California women get breast cancer, after climbing steeply from 1973-1988 and staying near the 1988 rate for more than a decade, has dropped by eight percent. While some attribute this to a drop in detecting breast tumors because women are receiving fewer mammograms, others observe that even women who receive mammograms are being diagnosed with breast cancer at a lower rate. This leads many researchers to believe that the current decrease in breast cancer cases is due to fewer women receiving hormone replacement therapy. This welcome decrease in breast cancer underscores the need to move beyond just stopping a harmful medical intervention; research is needed to find out why so many women still get breast cancer and to develop positive interventions that prevent the disease.

Breast cancer activists have played a leading role in the CBCRP from the beginning. They helped write and pass the statewide legislation that created the Program in 1993.

Table 1. Grants Awarded in 2008 by Subject Area

	Number of Grants	Amount	Percentage of Total Funding
Community Impact of Breast Cancer	23	$3,485,596	24.9%
Etiology and Prevention	9	$6,137,311	43.8%
Detection, Prognosis and Treatment	11	$3,356,365	24%
Biology of the Breast Cell	9	$1,016,985	7.3%
Totals	52	$13,996,257	100%

Women with breast cancer and survivors of the disease are involved in all levels of the CBCRP's decision making, including decisions about which projects get funded. With input from these advocates, the CBCRP has established a record for funding cutting-edge studies and jump-starting new areas of research. The Program's goal is to fund the projects that will lead most rapidly to the end of the breast cancer epidemic.

This report has been prepared by the University of California pursuant to Article 1 of Chapter 2 of Part 1 of Division 103 of the California Health and Safety Code, Section 104145; and the Revenue and Taxation Code Sections 30461-30462.1 and 18791-18796 amended by AB-28 Oct. 11, 2008. The following required reporting elements will be addressed in this report:

1. The number and dollar amounts of research grants, including the amount allocated to indirect costs.
The CBCRP awarded almost $14 million for 52 single- and multiple-year research projects at 24 California institutions in 2008. A complete list of newly funded grants can be found in Table 2.

2. The institutions and campuses receiving grant awards.
All funded grants are listed with the recipient institutions in Table 2 (page V) and in the Research Funding and Results section of this report (pages 18–42).

3. The subject of research grants.
All of the investigator-initiated grants funded by the CBCRP involve key questions in one or more of the following research areas:

- Basic Biology of the Breast (normal breast biology and breast cancer pathogenesis)
- Breast Cancer Causes and Prevention
- Earlier Detection, Diagnosis, and Treatment of Breast Cancer
- Community Impact of Breast Cancer (Sociocultural behavioral studies and health policy)

The CBCRP is also devoting 30 percent of program funding to its Special Research Initiatives, which is a program-initiated endeavor to significantly advance understanding of factors that can contribute to breast cancer prevention. The Initiatives fund investigations into three of the most challenging and under-researched areas: the environmental links to breast cancer; ethnic, racial, and other disparities in breast cancer incidence and survival; and the combination of these and other factors that impact breast cancer.

4. The relationship between federal and state funding for breast cancer research.
The CBCRP takes several steps to avoid duplication of funding at the individual grant level and in the Program's research priorities. We identify and attempt to fill important gaps in knowledge about breast cancer. We review priorities yearly in light of changes in the research field, successes and failures of previous funding initiatives, and the results of previous funding. Additionally, as founding members of the International Cancer Research Portfolio and participating members of the Collaborative Summit on Breast Cancer Research, we are able to ensure that CBCRP funding complements rather than duplicates grants bestowed by other funding organizations.

The CBCRP's Breast Cancer Research Council sets the Program's funding priorities, taking into account:

- Opinions from national breast cancer experts
- Opinions from California advocates and activists, healthcare providers, public health practitioners, community leaders, biotechnology scientists, and academic researchers
- Current literature on breast cancer and current gaps in knowledge
- Comparisons with portfolios and programmatic goals of other funding agencies
- In-house evaluations of the efficacy of CBCRP grant mechanisms and topic areas in fulfilling program goals

5. The relationship between each project and the overall strategy of the research program.
The following ten criteria are used to set overall programmatic research priorities and calls for applications.

- **California Specific:** Fund research that utilizes resources particular to California and/or addresses a breast cancer need that is specific but not necessarily unique to the burden of breast cancer in California

- **Career Development:** Fund research that helps recruit, retain, and develop high-quality California-based investigators who engage in breast cancer research
- **Collaboration:** Fund research that uses multidisciplinary approaches and helps fosters collaboration among California scientists, clinicians, advocates, community members, patients, survivors and others
- **Disparities:** Fund research that addresses disparities, inequalities and/or underserved populations in California
- **Innovation:** Fund innovative research (i.e., new drugs, new strategies, new paradigms, new applications of tested strategies in new populations and contexts)
- **Non-duplicative:** Fund research that complements, builds on, and/or feeds into, but does not duplicate, other research programs
- **Outcome Driven:** Fund research that will improve public health outcomes (e.g. preventing breast cancer, detection of breast cancer, effective treatments and quality of life)
- **Policy:** Fund research and evaluation that will have policy implications for breast cancer in California
- **Responsive:** Fund research that is responsive to the perceived breast cancer research needs, opportunities and expectations of the CBCRP as identified by scientists and the public in California
- **Translation:** Fund research that is on a critical path for practical application and leads to more effective products, technologies, interventions, or policies and their application/delivery to Californians

The review of each individual grant application is also designed to ensure that the grants funded by the CBCRP have both high scientific merit and programmatic interest. Each individual application is evaluated by our scientific review committees for specific aspects of scientific merit including, but not limited to, impact on breast cancer, innovation, feasibility, and approach. All applications of sufficient scientific merit undergo a programmatic review by our advisory Breast Cancer Research Council for responsiveness to program priorities, including whether it's an underfunded research area, integrates advocacy issues, and is an underfunded research question.

6. A summary of research findings including discussion of promising new areas.

Summaries of all of research grants completed in 2008 are included in the body of this report. Listed below are just a few of the findings:

- **Roshan Bastani, Ph.D.,** and **Beth Glenn, Ph.D.,** at the **University of California, Los Angeles,** and **Zul Surani, B.S.,** at the **South Asian Cancer Foundation,** Mission Hills, assessed the needs of South Asian women with breast cancer, a segment of the California population that is growing but is rarely studied. Their study highlighted the need for intervention programs that use religious and community networks, promote healthy lifestyles, address the important role of spirituality in the breast cancer experience, and tackle the social stigma that surrounds South Asian breast cancer survivors. See page 20.
- **Yoshiko Umezawa, M.H.S.,** at the **University of California, Los Angeles,** investigated the role that social and religious support plays in helping minority women cope with their diagnosis. One of her findings was that Latinas and African American women were more likely to rely on social and religious support than white women. This study could help improve breast cancer patients' quality of life and help healthcare providers develop more culturally sensitive partnerships with their patients. See page 21.
- **Koie Chin, M.D., Ph.D.,** at the **University of California, San Francisco,** compared breast tumor tissue from African Americans to white women to see if they could identify genomic variations that could account for the 20 percent poorer prognosis observed in African Americans. An analysis of gene expression identified more than 40 genes that were turned on at a higher level in the African American women's tumors than in the white women's tumors. See page 23.
- **Peggy Reynolds, Ph.D.,** at the **Northern California Cancer Center,** Union City, used data from the U.S. census and the California

Cancer Registry to investigate whether they could identify birth characteristics that would be predictive of breast cancer risk in young women. Dr. Reynolds and her colleagues found, among other things, that maternal age and paternal age were the strongest predictors of breast cancer risk, and that women who were born post-term (42 weeks or later) had a significantly reduced risk of breast cancer. See page 26.

- **Christina Clarke Dur, Ph.D.,** at the **Northern California Cancer Center,** Union City, tested the "hygiene hypothesis", which is the theory that living in a sanitized environment hampers the development of a healthy immune system, thus weakening the immune response against tumors, increasing estrogen production, or both. Her preliminary analysis showed that certain markers of a weaker immune system were associated with an increased risk of postmenopausal breast cancer. See page 28.
- **Sean McAllister, Ph.D.,** at the **California Pacific Medical Center Research Institute,** San Francisco, and colleagues used a mouse model to investigate whether cannabidiol, a non-psychotropic component of the Cannabis sativa (marijuana) plant, could be used to treat breast cancer. They found that it was able to inhibit cancer growth and decrease production of a protein that is believed to make breast cancer more aggressive. See page 31.
- **Konstantin Stoletov, Ph.D.,** at the **Scripps Research Institute,** La Jolla, studied role of a metastatic gene called RhoC in metastasis by growing human cancer cells that RhoC in see-through Zebrafish and directly observing how tumors grow, invade, and develop new blood vessels. They found that RhoC causes the tumor cell to develop specific features that allow it to penetrate the blood vessel. See page 38.

7. Inclusion of women and minorities in research studies.

Forty-four percent (19 of 43) of the grants and initiatives that the CBCRP awarded in 2008 studied either women or tissues from women, while the remaining 58 percent were laboratory studies that did not directly involve women or tissues from women.

Of the 19 grants and initiatives that involved women or tissues from women, 79 percent (15) collected new information from and about women.

Out of the 15 studies that included women:

- Eighty-seven percent, (13) grants include minority women in the study.
- Forty-seven percent, (7) are focused on minority women.
- Sixty percent, (9) are focused on underserved women.

The CBCRP's activities, goals, and progress during 2008 are described in this report, along with the challenges that must be confronted in order to decrease the economic burden and human suffering caused by breast cancer in California.

Summary of New Research Funded in 2008

Table 2

Institution and Investigator		Years	Project Title	Direct Costs	Indirect Costs	Total Costs
Asian Health Services						
	Linda Okahara	1	Nail Salon Workers: Chemical Exposures in the Workplace	$25,000	$0	$25,000
Beckman Research Institute of the City of Hope						
	Kimlin Ashing-Giwa	1	Increasing the Voice of African Americans in Research	$25,000	$0	$25,000
A*	Leslie Bernstein	1	Women's CARE Study	$19,917	$13,145	$33,062
This is a sub-award of the SRI initiative, "Understanding Racial and Ethnic Differences in Stage-specific Breast Cancer Survival: A Pilot Study"						
	Rebecca Crane-Okada	1.5	Mindful Movement Program for Breast Cancer Survivors	$75,000	$49,625	$124,625
This is a collaborative grant with Holly Kiger of WISE & Healthy Aging.						
A*	Katherine Henderson	1	California Teachers Study	$19,853	$13,103	$32,956
This is a sub-award of the SRI initiative, "Understanding Racial and Ethnic Differences in Stage-specific Breast Cancer Survival: A Pilot Study"						
	Daniel Tamae	2	Prognostic Implications of DNA Glycation in Breast Cancer	$67,060	$0	$67,060
	Jeffrey Weitzel	1	Community Breast Cancer Screening & Prevention Conferences	$24,919	$0	$24,919
The Burnham Institute for Medical Research						
	Robert Oshima	1.5	Maternal Embryonic Leucine Zipper Kinase in Mammary Tumors	$150,000	$136,500	$286,500
T*	Gaurav Sharma	2	Nanotherapy for Breast Cancer Targeting Tumor Macrophages	$90,000	$0	$90,000
Golden Valley Health Centers						
	Christine Noguera	3	Increasing Mammography Screening in Latinas with Diabetes	$402,074	$91,592	$493,666
This is a collaborative grant with Stergios Roussos of San Diego State University Research Foundation.						
Kaiser Foundation Research Institute						
	Reina Haque	1.5	Antidepressants and Breast Cancer Treatment Interactions	$163,083	$0	$163,083
A*	Marilyn Kwan	1	Pathways: A Study of Breast Cancer Survivorship and Life after Cancer Epidemiology (LACE) Study	$19,953	$10,528	$30,480
This is a sub-award of the SRI initiative, "Understanding Racial and Ethnic Differences in Stage-specific Breast Cancer Survival: A Pilot Study"						
Lawrence Berkeley National Laboratory						
	Aaron Boudreau	2	Tumor Suppressor 14-3-3sigma in Breast Cancer Progression	$63,334	$0	$63,334

	Institution and Investigator	Years	Project Title	Direct Costs	Indirect Costs	Total Costs
Los Angeles Partnered for Progress						
	Brian Montano	1	Latina Breast Cancer Survivors…Our Experience	$0	$0	$0
This is a collaboration grant with Diane Tisnado at University of California, Los Angeles.						
Northern California Cancer Center						
	Scarlet Lin Gomez	*1*	Demographic Questions for California Breast Cancer Research	$299,994	$130,995	$430,989
A*	Esther John	1	San Francisco Bay Area Breast Cancer Study	$20,000	$9,000	$29,000
This is a sub-award of the SRI initiative, "Understanding Racial and Ethnic Differences in Stage-specific Breast Cancer Survival: A Pilot Study"						
A*	Peggy Reyn-olds	1	Exploring Diversity in an Environmental Study of California Teachers	$99,851	$29,399	$129,399
Public Health Institute						
A*	Barbara Cohn	5	Environmental Causes of Breast Cancer Across Generations	$4,564,314	$435,686	$5,000,000
San Diego State University						
	Vanessa Malcarne	3	Breast Cancer Clinical Trials Education Program	$139,570	$69,087	$208,657
This is a collaborative grant with Natasha Riley of Vista Community Clinic and Georgia Sadler of University of California, San Diego.						
San Diego State University Research Foundation						
	Stergios Roussos	3	Increasing Mammography Screening in Latinas with Diabetes	$169,099	$83,704	$252,803
This is a collaborative grant with Christine Noguera of Golden Valley Health Centers.						
Scripps Research Institute						
	Wolfram Ruf	1.5	Inhibition of TF Signaling as a Novel Breast Cancer Therapy	$150,000	$134,250	$284,250
Sidney Kimmel Cancer Center						
	Stefan Grotegut	3	Global Analysis of Protein Ubiquitina-tion in Breast Cancer	$135,000	$0	$135,000
	Barbara Mueller	1.5	Treating BC Brain Metastases with Cytotoxic Lymphocytes	$149,955	$142,457	$292,412
South Asian Cancer Foundation						
	Zul Surani	2	Adapting a Breast Cancer Education Program for South Asians	$0	$0	$0
This is a collaboration grant with Beth Glenn of California, Los Angeles.						
Stanford University						
	Zhen Cheng	1.5	Novel Small Proteins for PET Imaging of Breast Cancer	$166,626	$95,223	$261,849
	Rebecca Rakow-Penner	2	Functional Breast MRI with BOLD Contrast	$76,000	$0	$76,000
	Joseph Wu	1.5	Imaging of Novel Stem Cell Therapy Targeting Breast Cancer	$150,000	$89,243	$239,243

	Institution and Investigator	Years	Project Title	Direct Costs	Indirect Costs	Total Costs
Turtle Health Foundation						
	Linda Navarro	1	Breast Cancer Risk Reduction in American Indian Women	$10,000	$0	$10,000
This is a planning grant with Marlene vonFriedrichs-Fitzwater at University of California, Davis.						
University of California, Berkeley						
	John Balmes	1	California Chemicals Policy and Breast Cancer	$159,334	$0	$159,334
	Sara Fernandes-Taylor	2	Provider Communication and Health in Breast Cancer Survivors	$67,872	$0	$67,872
	Holly Hantz	2	Dietary Metabolite Inhibition of Breast Cancer Cell Survival	$76,000	$0	$76,000
University of California, Davis						
	Marlene von Friederichs-Fitzwater	1	Breast Cancer Risk Reduction in American Indian Women	$0	$0	$0
This is a planning grant with Linda Navarro at Turtle Health Foundation.						
	Paul Henderson	1.5	Nanolipoproteins to Study Breast Cancer Growth Receptors	$99,000	$0	$99,000
	Teresa Marple	3	Folate, DNA Methylation, and Breast Cancer Metastasis	$135,000	$0	$135,000
University of California, Irvine						
	Mikhail Geyfman	2	Role of Estrogen-modulated Protein AGR2 in Breast Cancer	$71,491	$0	$71,491
	Bingnan Gu	3	Regulation of Breast Stem-Progenitor Cell Chromatin by Pygo2	$135,000	$0	$135,000
	Ke Nie		Development of a Breast MRI Computer-Aided Diagnosis System	$76,000	$0	$76,000
University of California, Los Angeles						
	Patricia Ganz	1	APOS 5th Annual Conference	$15,000	$0	$15,000
	Beth Glenn	2	Adapting a Breast Cancer Education Program for South Asians	$150,000	$0	$150,000
This is a collaboration grant with Zul Surani of SouthAsian Cancer Foundation						
	Diane Tisnado	1	Latina Breast Cancer Survivors...Our Experience	$168,421	$0	$168,421
This is a collaborative grant with Brian Montano of Los Angeles Partnered for Progress.						
	Shannon Sirk	2	Novel Anti-HER2 Fragments for Better Detection and Therapy	$76,000	$0	$76,000
	Yoshiko Umezawa	3	An Ecological Study of Quality of Life in Low-Income Women	$115,960	$0	$115,960

	Institution and Investigator	Years	Project Title	Direct Costs	Indirect Costs	Total Costs
University of California, San Diego						
	Daniel Donoghue	1.5	FGFR2 Signaling in Human Breast Cancer Cells	$100,000	$0	$100,000
T*	Jessica Gorman	1	Reproductive Concerns and Depression among Younger Survivors	$35,492	$0	$35,492
	Janine Low-Marchelli	2	Dissecting the Role of Twist in Breast Cancer Metastasis	$76,000	$0	$76,000
	Morgan O'Hayre	2	Chemokine Receptor Signaling in Breast Cancer	$74,660	$0	$74,660
	Georgia Sadler	3	Breast Cancer Clinical Trials Education Program	$158,140	$0	$158,140
This is a collaborative grant with Natasha Riley of Vista Community Clinic and Vanessa Malcarne of San Diego State University.						
University of California, San Francisco						
	Lauren Goldman	1.5	Quality of Mammography Facilities Serving Vulnerable Women	$150,000	$0	$150,000
T*	Paul Mills	1.5	Pesticide and Gene Interactions in Latina Farm Workers	$163,667	$0	$163,667
T*	Thea Tlsty	3	Stratifying DCIS Biopsies for Risk of Future Tumor Formation	$750,000	$0	$750,000
	Irene Yen	2	Neighborhoods and Obesity in Preadolescent Girls: Part II	$214,406	$0	$214,406
	Elad Ziv	3	Genetics of Tamoxifen Response	$803,111	$0	$803,111
University of Southern California						
	Eunjung Lee	3	Genes in Hormone Metabolism Pathway and Breast Cancer	$134,996	$0	$134,996
C*	Kristine Monroe	1	Grapefruit, Hormones, and Postmenopausal Breast Cancer Risk	$149,758	$94,348	$244,106
A*	Kristine Monroe	1	Multiethnic Cohort Study	$19,045	$11,998	$31,043
This is a sub-award of the SRI initiative, "Understanding Racial and Ethnic Differences in Stage-specific Breast Cancer Survival: A Pilot Study"						
	Michael Press	2	Topoisomerase-IIa as a Predictor of Anthracycline Response	$250,000	$157,500	$407,500
A*	Anna Wu	1	Los Angeles County Asian American Breast Cancer Study	$20,000	$12,600	$32,600
Vista Community Clinic						
	Natasha Riley	3	Breast Cancer Clinical Trials Education Program	$302,290	$70,131	$372,421
This is a collaborative grant with Georgia Sadler of University of California, San Diego, and Vanessa Malcarne of San Diego State University.						
WISE & Healthy Aging						
	Holly Kiger	1.5	Mindful Movement Program for Breast Cancer Survivors	$75,000	$18,750	$93,750
This is a collaborative grant with Rebecca Crane-Okada at Beckman Research Institute of the City of Hope.						
Totals				**$12,097,393**	**$1,898,864**	**$13,996,257**

T* = Funded in part by Tax Check-off: voluntary donations from individual taxpayers' income tax forms
C* = Funded in part by a grant from the California Community Foundation
A* = Funded in part by a grant from the Avon Foundation

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California Breast Cancer Research Program

Annual Report to the State of California Legislature 2008

Report prepared by the University of California, Office of the President pursuant to Article 1 of Chapter 2 of Part 1 of Division 103 of the California Health and Safety Code

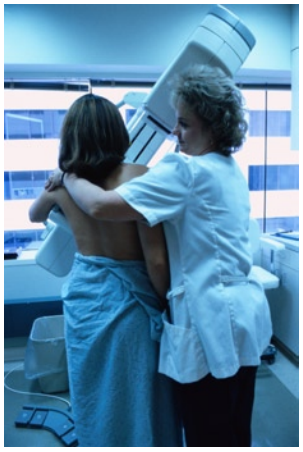
Marion H. E. Kavanaugh-Lynch, M.D., M.P.H.
Director, California Breast Cancer Research Program

Steven Beckwith, Ph.D.
Vice President for Research and Graduate Studies

California Breast Cancer Research Program
University of California, Office of the President
300 Lakeside Drive, 6th Floor
Oakland, CA 94612-3550

Phone: 510 987-9884
Toll-free: (888) 313-BCRP
Fax: 510 587-6325
Email: cbcrp@ucop.edu
Web: www.CABreastCancer.org

About the California Breast Cancer Research Program



The CBCRP has made California a leader among states by becoming the largest, most stable state-funded breast cancer research effort in the nation.

During its fifteen-year history, the CBCRP has established a record for filling gaps not covered by other research funders, jump-starting new areas of research, and fostering new types of collaboration.

The CBCRP has provided a total of nearly $195 million in research funds since 1993. In 2008, the CBCRP awarded nearly $14 million for 52 single- and multiple-year research projects at 24 California institutions.

Making California a Leader among States

In 1993, California breast cancer activists joined forces with scientists, clinicians, state legislators, and University of California officials to propel the state into national leadership for breast cancer research.

The activists, most of them women who had survived or currently had breast cancer, were impatient with the slow pace of progress against the disease. With their allies, they wrote and won passage of statewide legislation to push breast cancer research in new, creative directions. The California Breast Cancer Act, sponsored by then-Assemblywoman Barbara Friedman, raised the tobacco tax by two cents a pack, with 45 percent of the proceeds going to the California Breast Cancer Research Program (CBCRP), which is administered as a public service by the University of California.

Since then, the CBCRP has continued to make California a leader among states by becoming the largest, most stable state-funded breast cancer research effort in the nation.

The mission of the CBCRP is to eliminate breast cancer by leading innovation in research, communication, and collaboration among California's lay and scientific communities.

The CBCRP has provided a total of nearly $195 million in research funds since 1993. In 2008, the CBCRP awarded nearly $14 million for 52 single- and multiple-year research projects at 24 California institutions.

The CBCRP is funded primarily by the tobacco tax, a steadily declining source of revenue due to decreasing consumption of tobacco products. This funding is supplemented with taxpayer donations contributed through state income tax forms. The CBCRP also receives private contributions.

Pushing the Research Boundaries

During its fifteen-year history, the CBCRP has established a record for filling gaps not covered by other research funders, jump-starting new areas of research, and fostering new types of collaboration. Now the Program is challenging itself to focus its resources on questions that could change the face of breast cancer research.

The CBCRP's Special Research Initiatives (SRI) are investigating three interconnected research areas that have long received little attention from traditional private and federal research funding sources:

- Environmental links to breast cancer
- The reasons why some groups of women are more likely to get or die from breast cancer, based on characteristics that include race and ethnicity
- Combinations of factors—including those within the first two research areas—that impact breast cancer

The CBCRP is investing 30 percent of its funds in the SRI. In April 2008, the ten ground-breaking initiatives were announced to the media and the public. Five of the ten studies were funded during 2008:

- Environmental Causes of Breast Cancer Across Generations
- Chemicals Policy and Breast Cancer
- Demographic Questions for California Breast Cancer Research

- Understanding Racial and Ethnic Differences in Stage-Specific Breast Cancer Survival: a Pilot Study
- Exploring Diversity in an Environmental Study of California Teachers

To assure that the Special Research Initiatives will have the most impact on breast cancer and avoid duplication, the CBCRP drafted a review of previous research in the areas to be covered. This document, titled "Identifying Gaps in Breast Cancer Research," is available at the CBCRP Web site, www.CABreastCancer.org. Two committees composed of national experts are providing leadership for this research effort. The six-member steering committee (see page 13) guided the Special Research Initiatives. The 33-member strategy team (see Appendix A) developed specific recommendations for research to be funded. The final selection of the ten initiatives was made by the CBCRP's highest decision-making body, the Breast Cancer Research Council. The Special Research Initiatives are discussed more fully in the section of this report titled "The CBCRP's Strategy for Funding Research."

A Structure That Encourages Public Input

The CBCRP's structure has set a standard for community involvement that has inspired similar changes in other research funding agencies around the nation. Through example, the CBCRP is encouraging other agencies to include community advocates in the review of research proposals and to involve community members in the design and conduct of research. Breast cancer advocates play a critical role in every aspect of the CBCRP's work, from setting research priorities to recommending grants for funding to getting out the word about research results.

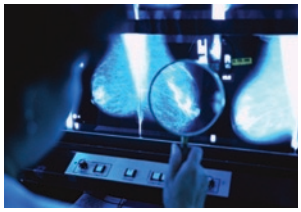
The CBCRP is under the administration of the University of California, Office of the President, in Oakland, with a staff managing the solicitation, review, award, and oversight of grants and dissemination of research results.

The CBCRP's 17-member advisory Breast Cancer Research Council includes scientists, clinicians, representatives of industry and nonprofit health organizations, and breast cancer advocates. The council provides vision, sets research priorities, and determines how the CBCRP invests its funds in research. It also conducts one of the two reviews that every proposal must pass to receive funding. The council reviews research proposals for relevance to the CBCRP's goals, while teams of research scientists and breast cancer advocates from outside California review all proposals for scientific merit.

In addition, all Californians concerned about breast cancer have opportunities to help set the research agenda via several avenues of feedback created by the Program. The Program's research symposia bring the scientific and treatment communities into dialog with a broader range of the public than is common at such conferences. Each symposium includes a session for members of the public to provide feedback on the Program's work and suggest research priorities. The Program's Special Research Initiatives included several opportunities for the public to take part in identifying and prioritizing the questions to be investigated. These opportunities included town hall meetings, teleconferences, and a special section on the CBCRP Web site. The CBCRP also encourages public review of its funded research through its annual reports and the Program's Web site (www.CABreastCancer.org), where members of the public can leave written comments.

By bringing the research, advocacy, and treatment communities into closer collaboration, the California Breast Cancer Research Program pushes the boundaries of research, mobilizing greater creativity and resources toward decreasing—and ending—the suffering and death caused by breast cancer.

Sharing Research With Scientists and the Public



If research is going to be effective, then people need to know the results.

The scientific community needs to know, to make progress against the disease.

The medical community needs to know, to improve prevention and treatment. People with breast cancer need the opportunity to learn about new prevention and treatment options.

Breast cancer activists and policy makers need information about research results to shape their advocacy agenda.

Communities affected by breast cancer need to know what's been proven to work in other communities.

And the taxpayers of California need to know what their taxes are funding.

The legislation that established the California Breast Cancer Research Program calls on the Program to disseminate the results of its research. This is because the sponsors of the legislation recognized that funding high quality research is necessary but not sufficient to fulfill the Program's mission. If the research is going to be effective in reducing or ending the suffering caused by breast cancer, then people need to know the results. The scientific community needs to know, to make progress against the disease. The medical community needs to know, to improve prevention and treatment. People with breast cancer need the opportunity to learn about new prevention and treatment options. Breast cancer activists and policy makers need information about research results to shape their advocacy agenda. Communities affected by breast cancer need to know what's been proven to work in other communities. And the taxpayers of California need to know what their taxes are funding.

The scientists whose projects are funded by the CBCRP publish their results in peer-reviewed scientific journals and present them at scientific conferences. The California Breast Cancer Research Program is committed to going beyond this venue, and makes the results and progress of research it funds available to a much wider audience. The CBCRP publishes and distributes summaries of Program-funded research widely, in print and over the Internet. The CBCRP is one of the few research funding programs in the world to publish annual summaries of research while the studies are still in progress, so that scientists and other interested people can make use of the information as soon as possible. Research results and research progress are disseminated in a variety of ways:

Research Symposia

The CBCRP regularly hosts a research symposium, a statewide conference presenting the results of the research the CBCRP funds. A research symposium typically draws 500 or more attendees.

The CBCRP's most recent symposium, "From Research to Action: Breaking New Ground," was held in Los Angeles, September 7-9, 2007.

These statewide conferences provide a forum where research scientists present their findings to a concerned public. Equally important, women whose lives have been affected by the disease share their priorities and hopes with researchers. The CBCRP makes a special effort to bring women who have, had, or are at risk for breast cancer to the Program's symposia. Scholarships that cover travel and accommodations are provided. Artwork that portrays the breast cancer experience is on display. California community organizations also send representatives who provide information on their breast-cancer related programs. In addition, scientists can get information on how to obtain CBCRP funding for their investigations.

Reports, free to the public in book form and available on the CBCRP Web site, provide summaries of presentations made at the 2005 and 2007 symposia. The next symposium, the CBCRP's seventh, will be held in 2010.

Web site

The CBCRP Web site (www.CABreastCancer.org) has summaries of all completed research projects and annual progress reports for ongoing projects, in language accessible to

the general reader. All research on the CBCRP Web site is fully searchable, and visitors who want to keep up with the latest research can search to access the most recently posted findings. A featured researcher section, which changes three times per year, profiles one researcher and her or his findings. Visitors to the Web site can ask this expert questions, and receive answers, via email. Progress on the development of the CBCRP's Special Research Initiatives is also reported on the Web site.

Publication abstracts supported by CBCRP funding have links to the National Institutes of Health's PubMed, a public-access database of biomedical journals. The CBCRP Web site also contains a list of each year's awards and information on applying for grants. In addition, all CBCRP publications are available and downloadable. Another feature allows visitors to listen to a presentation made at the CBCRP's 2007 symposium.

The Web site includes an opportunity to join the Program's volunteer team, request specific information from the CBCRP, and make online donations to the CBCRP.

Publications

All CBCRP publications are available free to the public in printed form and on the CBCRP Web site. Multiple copies are available free of charge to organizations.

Compendium of Awards: To make it easy for scientists and the public to follow CBCRP-funded research from the beginning, a description of newly funded projects is published each year.

Formal Evaluations of the CBCRP: Formal evaluations let the public understand the success and improvement efforts of CBCRP work.

Community Research Collaboration Awards Abstract Booklet: The CBCRP's Community Research Collaboration awards bring together members of community groups and academic scientists to conduct breast cancer research. This booklet, with abstracts of many past community research collaboration projects funded by the CBCRP, is designed to make community groups aware of this opportunity.

Newsletter: The CBCRP's newsletters report on new awards, research results, scientific meetings where the CBCRP is presenting an exhibit of Program work, and other Program news.

Breast Cancer in California: A Closer Look/El Cancer de Seno en California: Una Mirada Mas de Cerca: This 40-page booklet provides a picture of breast cancer's effect on the lives of California women. It is available in both English and Spanish.

Identifying Gaps in Breast Cancer Research: This research paper reviews previous research in the areas covered under the CBCRP's Special Research Initiatives: environmental links to breast cancer, the reasons why some groups of women bear a greater burden of the disease, and the intersections of complex factors that impact breast cancer. The draft is available on the CBCRP Web site. During 2009, the CBCRP will publish a booklet that will include a summary of the most important findings from this research paper. The booklet will also include ideas for breakthrough breast cancer research that were developed by teams of experts who used "Identifying Gaps in Breast Cancer Research" as a starting point.

California Breast Cancer Research Program brochure: An overview of the CBCRP, our philosophy, and opportunities to get involved. The brochure is available in English and Spanish.

Further Methods of Sharing Research

Scientific Presentations at Conferences: The CBCRP and CBCRP-funded researchers present research results at scientific conferences. During 2008, the CBCRP gave presentations at the international meeting of the American Association of Cancer Researchers and the Canadian Breast Cancer Research Association on the Program's Special Research Initiatives and the methods used to develop the research questions for the initiatives. The CBCRP also gave presentations on community based participatory research at the Association of Asian Pacific Community Health Organizations.

E-Newsletter: The CBCRP's email newsletter gives subscribers timely announcements of funding opportunities, early notification of new research resources and breast cancer conferenc-

es, and avenues to stay involved, informed, and active in the fight against breast cancer. It is distributed to over 2,000 stakeholders each month.

Expressions: The Art of Healing Breast Cancer: The CBCRP owns a collection of wearable breast art created by California artists to reflect on the breast cancer epidemic. The entire collection is on exhibit at CBCRP symposia. During 2008, portions of *Expressions: the Art of Healing Breast Cancer* were displayed, along with the CBCRP's exhibit, at scientific meetings. An art catalog of this collection is available online at the CBCRP Web site.

Exhibits at Scientific and Community Meetings: The CBCRP presented displays of the Program's work at a number of scientific and community meetings during 2008. The meetings included:

- Zero Breast Cancer 3rd Annual Town Hall Meeting, Oakland
- Northern California Cancer Center 7th Annual Allison Taylor Holbrooks Breast Cancer Conference, San Francisco
- 20th Anniversary: Cultivating Traditions of Wellness National Technical Assistance Conference, Washington, D.C.
- Young Women's Breast Health Summit, San Francisco
- Cancer – Challenges & Solutions for Confronting the Disease of Our Time, San Francisco
- American Association for Cancer Research (AACR) Annual Meeting, San Diego
- American Cancer Society "Reducing Cancer Disparities through Research: A Community Forum" Oakland
- Intercultural Cancer Council 11th Biennial Symposium on Minorities, the Medically Underserved & Cancer, Washington, DC
- Professional Business Women's Conference, San Francisco
- Northern California Cancer Center's Annual African American Breast Cancer Conference, Oakland
- Latino Cancer Conference, San Francisco
- Annual San Francisco Marathon / A Cause to Run, San Francisco
- Center of Community Alliance for Research & Education (CCCARE) / City of Hope "A Dialogue between Advocates and Researchers," Duarte
- The North Face 1st Annual Benefits & Resources Fair, San Leandro
- Breast Cancer Connections 5th Annual Breast Cancer Conference, Palo Alto

Serving the Media: The CBCRP does regular outreach to the media about the Program and about CBCRP-funded research projects that are of interest to the general public. When reporters from TV, newspapers, magazines, or other media need information on breast cancer research, the CBCRP links them with the appropriate experts.

Speakers and Educational Bureau: When community organizations want speakers on breast cancer research for meetings and public events, the CBCRP provides referrals from the Program's network of researchers and advocates. The Program also refers research experts to teach continuing education classes for healthcare professionals.

Collaborating with Breast Cancer Advocates and California Communities

Having breast cancer advocates in a wide variety of leadership positions ensures that the CBCRP funds research important to people who face the disease in their day-to-day lives.

Research involving community organizations as active partners is gaining credibility in the United States, and the CBCRP has been a prime mover in extending and supporting the use of this kind of research.

People with breast cancer and survivors of the disease are involved in every level of the California Breast Cancer Research Program, from deciding which research the Program funds to actually carrying out some of the CBCRP's research. Non-scientist advocates have played a leadership role in the CBCRP right from the start. The CBCRP has been in the forefront of a nationwide trend among research funding agencies toward a greater voice for the people breast cancer affects most, and the CBCRP still sets the standard for including advocates at all levels of leadership.

Breast Cancer Advocates in Leadership

Breast cancer advocates comprise one-third of the CBCRP's highest leadership body, the advisory council. The council recommends the research proposals that best fit the CBCRP's funding strategy. Throughout the CBCRP's fifteen-year history, an advocate has also always served as the council's Chair or Vice-Chair. In addition, out-of-state panels of scientists and advocates review all CBCRP research proposals for scientific merit. Out-of-state breast cancer advocates are full voting members of these review panels and a California advocate observes each one. Advocates are also involved in the development and leadership of the CBCRP's Special Research Initiatives, a multi-year effort to investigate the environmental causes of breast cancer, the reasons why some groups of women bear a greater burden of the disease, and the intersections of complex factors that impact breast cancer.

Having breast cancer advocates in a wide variety of leadership positions ensures that the CBCRP funds research important to people who face the disease in their day-to-day lives.

Communities Conducting Research

Breast cancer advocates are also investigators on a rising number of the CBCRP's research projects. In 1997, the CBCRP pioneered a new type of research grant that allows community groups and breast cancer advocacy organizations to team up with experienced scientists to pursue a research idea of importance to the community in a scientifically rigorous way. These Community Research Collaboration (CRC) awards are open to nonprofit organizations or ad-hoc community groups in any California community affected by breast cancer. The majority of community collaborators funded by the CBCRP to date have been breast cancer survivors.

Research involving community organizations as active partners is gaining credibility in the United States, and the CBCRP has been a prime mover in extending and supporting the use of this kind of research to breast cancer in California. The Community Research Collaboration awards have provided nearly $16 million in funding to 60 collaborative projects. Projects funded over the years include the following:

- Determining whether Vietnamese nail salon workers have higher breast cancer rates and whether this group of women's workplace exposures to toxic substances exceed health-based standards
- Investigating immigrant Afghan women's concerns, knowledge, attitudes, behaviors, and sources of information about breast care, and perceived barriers to care

- Educating African American and Hispanic women about the importance of participating in breast cancer clinical trials and developing tools for an educational program entitled *Scientific Literacy and Breast Cancer Clinical Trials Education Program*
- Development of effective breast cancer education tools for South Asian immigrant women
- Determining the benefits of peer-led African American support groups to address the unmet needs of African American women with breast cancer in a geographically underserved area
- Assessing the benefits and acceptability of a videoconferencing support group for rural and isolated women
- Evaluating an ethical will intervention for underserved women at end of life
- Identifying barriers to survivorship in the Latina population by assessing knowledge, attitudes, beliefs, experiences, and needs in terms of planning for and accessing medical care for surveillance, monitoring, and management of cancer and non-cancer medical issues
- Testing complementary and alternative medicine approaches to improving the quality of life of breast cancer survivors through mindful movement programs
- Breast cancer risk factors of lesbians and heterosexual women
- Culturally-appropriate breast cancer health care for Samoan American and Korean American women
- The effectiveness of "peer navigators," trained volunteer breast cancer survivors who work with newly-diagnosed women to understand decisions about treatment and to cope with the disease
- Testing of a culturally-sensitive DVD to increase knowledge of breast health and breast cancer risk among Native American women
- The breast cancer experience of Slavic American women
- The barriers to older Thai American women participating in breast cancer screening.

The CBCRP's Community Research Collaboration awards are designed to have an impact on breast cancer health care:

- Lay health workers, also known as promotoras, are widely used in community clinics as a valuable link between the health care system and the Latino community. However, promotora programs vary significantly, and there is little research that identifies common challenges and synthesizes their solutions. Rena Pasick, Dr.P.H., at the University of California, San Francisco, and Peggy McGuire at the Women's Cancer Resource Center, Oakland, conducted a preliminary study of promotora programs in Alameda County. They found that lay health worker programs empower promotoras, increase community awareness of specific health issues and access to health care, and foster social change. The research team will now develop, implement, and evaluate breast cancer promotora programs at two primary care clinics in Alameda serving Latinos.
- It is not enough to help patients prepare a list of questions before meeting with a breast care specialist, because the answers they receive can be overwhelming. Jeffrey Belkora, Ph.D., at the University of California, San Francisco, Sara O'Donnell, at the Mendocino Cancer Resource Center, Mendocino, and Dawn Elsbree, at the Humboldt Community Breast Health Project, Arcata, investigated which procedures best help patients absorb, remember, and act upon the information and advice they get from breast specialists. Their survey included doctors, community health agency staff, and diverse (Native American, Latina, and white) breast cancer survivors. It revealed that specific changes to the physical infrastructure; institutional policies; and patient, doctor, or accompanier practices or behaviors could improve interactions. This work could lead to new programs that help patients, accompaniers, and their doctors make the most of consultations leading to major treatment decisions.

Fostering Community-Based Research

The CBCRP has taken major steps over the past five years to enable diverse populations in California to take part in quality scientific research into breast cancer issues of interest to their communities. These efforts resulted in 2008 with the CBCRP continuing to receive a high number of applications for Community Research Collaboration grants. The scientific quality of these applications was also very high. The CBCRP funded six community research collaboration projects which cover a wide range of under-studied research topics.

The effort that led to this success began in 2003. That year, the CBCRP began a series of changes to make the process of applying for CRC grants and conducting CRC research more user-friendly to both the community organizations and scientific researchers who make up the research teams.

Beginning in 2003, the CBCRP has offered a technical assistance program geared to interested community agencies and prospective applicants. The application process and application evaluation process were also changed to better suit the community participation research model. During 2005, the CBCRP added teleconference training for community groups and academic researchers interested in applying for CRC awards.

During 2006 through Spring of 2008, the CBCRP held outreach workshops and outreach teleconferences about the opportunity to apply for CRC awards, and also made presentations at community events across the state. Funded CRC teams participated in the outreach workshops, sharing their experiences and the challenges they faced working together. Attendees gave positive feedback about the funded research teams' role in the outreach workshops and reported that they learned from these funded teams. Over two dozen teleconferences and site visits also provided training and assistance both to research teams who had been awarded grants to plan future research projects, and to teams conducting research. In addition, during 2007 and 2008, at major national and international conferences, the CBCRP presented results of the Program's research into the effectiveness of community-based participatory breast cancer research.

Beginning in June 2008 training and outreach were conducted only via teleconference, a modification made necessary by changes in the CBCRP's staff. The CBCRP also streamlined the CRC application process. Some parts of this process were found helpful by only a portion of applicants, so those parts have been made optional.

In recognition of her leadership in community breast cancer research, the CBCRP's Director, Dr. Marion H.E. Kavanaugh-Lynch, received the Bay Area-based nonprofit organization Zero Breast Cancer's 2008 Honor Thy Healer Award.

During 2009, the CBCRP will continue to facilitate diverse communities in California taking part in quality scientific breast cancer research and to take leadership in community-based participatory research.

The CBCRP's Strategy for Allocating Research Funds

One goal underlying the CBCRP's funding strategy is the leveraging of Program funds to influence the research system nationwide.

Another major goal is to increase the number of talented scientists engaged in breast cancer research.

An additional goal of the CBCRP's research strategy is encouraging and inspiring other research funding agencies to support cutting-edge research.

The CBCRP's Breast Cancer Research Council and staff set the priorities for allocating the Program's research funds. The following ten criteria are used by the Breast Cancer Research Council to set priorities.

- **California Specific:** Fund research that utilizes resources particular to California and/or addresses a breast cancer need that is specific but not necessarily unique to the burden of breast cancer in California.
- **Career Development:** Fund research that helps recruit, retain, and develop high-quality California-based investigators who engage in breast cancer research.
- **Collaboration:** Fund research that uses multi-disciplinary approaches and helps fosters collaboration among California scientists, clinicians, advocates, community members, patients, survivors, and others.
- **Disparities:** Fund research that addresses disparities, inequalities, and/or underserved populations in California.
- **Innovation:** Fund innovative research (i.e., new drugs, new strategies, new paradigms, new applications of tested strategies in new populations and contexts).
- **Non-duplicative:** Fund research that complements, builds on, and/or feeds into, but does not duplicate, other research programs.
- **Outcome Driven:** Fund research that will improve public health outcomes (e.g. preventing breast cancer, detection of breast cancer, effective treatments, and quality of life).
- **Policy:** Fund research and evaluation that will have policy implications for breast cancer in California.
- **Responsive:** Fund research that is responsive to the perceived breast cancer research needs, opportunities, and expectations of the CBCRP as identified by scientists and the public in California.
- **Translation:** Fund research that is on a critical path for practical application and leads to more effective products, technologies, interventions, or policies and their application/delivery to Californians.

To ensure that the CBCRP fulfills all of the criteria, the Council devised a two-part funding strategy, the Special Research Initiatives and Core Funding.

Special Research Initiatives

Investigate Crucial, Neglected Questions

The CBCRP is investing 30 percent of its research funds in the Program's Special Research Initiatives. The initiatives utilize California's diverse populations and extensive research infrastructure to focus on challenging questions that have thwarted traditional research approaches. The initiatives investigate two interconnected research areas:

- Environmental links to breast cancer;
- The reasons why some groups of women are more likely to get or die from breast cancer, based on characteristics that include geographic location, race, and ethnicity.

In April 2008, the ten groundbreaking initiatives were announced to the media and the public. Three

are concerned with environmental links to breast cancer:

- **Chemicals Policy and Breast Cancer** convenes an expert working group to identify biological pathways through which chemicals contribute to breast cancer and to identify the best currently available chemical safety tests. The results will be used to bring breast cancer to the forefront in the California government's statewide development of a new green policy on chemicals. The CBCRP has set aside $160,000 plus indirect costs to fund one award.
- **Making Chemicals Testing Relevant to Breast Cancer** will invite researchers to submit proposals to develop the most comprehensive battery of accurate, reliable, rapid, and cost-effective existing tests that can be performed on chemicals to see if they cause changes in the body that contribute to breast cancer. The CBCRP will issue a request for proposals and fund up to nine awards at $300,000 in direct costs each and up to six awards at $450,000 in direct costs each.
- **Environmental Causes of Breast Cancer across Generations** will test tissue samples collected 40-50 years ago to find out whether exposure to certain chemicals during pregnancy increases the child's risk for breast cancer in later life. The CBCRP allocated up to $5 million for the Child Health and Development Study (Barbara Cohn, Principal Investigator) to carry out a study on the relationship of pre-natal exposures to PCBs and DDT to breast cancer rates in women who are in their 40s today.

Three initiatives investigate the reasons why some groups of women are more likely to get or die from breast cancer, based on characteristics that include geographic location, race, and ethnicity:

- **An Integrated Approach to Understanding Behavioral, Social, and Physical Environment Factors and Breast Cancer among Immigrants** investigates a trend among women who immigrate to the U.S. from countries with lower breast cancer rates. The longer the women live here, the higher their rates of the disease. Their daughters born here have higher rates still. Researchers will be invited to submit proposals for pilot studies that describe changes in California immigrant women's behavior, social lives, and physical environment that may cause their increase in breast cancer. The CBCRP allocated funds for up to three awards for up to $400,000 in direct costs each.
- **Demographic Questions for California Breast Cancer Research** is designed to remedy a current problem, where researchers seeking to understand ethnic differences in breast cancer need demographic information that is often not standardized or available. The CBCRP allocated up to $300,000 to convene an expert panel to identify the demographic measures that will best allow better health predications among diverse populations.
- **Understanding Racial and Ethnic Differences in Stage-Specific Breast Cancer Survival: A Pilot Study**. In general, the lower the stage of a breast tumor when a woman is diagnosed, the more likely she is to survive. However, women from some racial and ethnic groups are less likely to survive than women from other racial and ethnic groups diagnosed at the same stage. To find out why, this feasibility study will determine whether data from existing California studies can be combined to provide a more complete picture. If so, the CBCRP will fund a major study combining the data for up to $3.9 million in total costs. The CBCRP allocated funds to support up to six researchers for up to $20,000 in direct costs each and one convener for up to $80,000 in direct costs for the feasibility study. If the pilot is successful, the CBCRP will fund a major study to combine and analyze the data for up to $3.9 million in total costs.

Four Special Research Initiatives investigate intersections of multiple factors that impact breast cancer:

- **New Statistical Models to Address Disease Complexity.** Environmental exposures, such as contact with toxic chemicals, can contribute to breast cancer. So can social exposures, such as living with the stress of racism. Researchers will be invited to submit

proposals to develop and test new statistical analysis strategies to better address how multiple exposures across a woman's life course may cause breast cancer. The CBCRP allocated funding for up to five awards of $150,000 to $300,000 in direct costs.

- **Toward a New Paradigm of Breast Cancer Breast Cancer Causation and Prevention** will convene a diverse, interdisciplinary panel that includes social scientists, environmental scientists, and experts on ethnic and other disparities in breast cancer. The panel will develop a model of breast cancer causation based on complexity theory that takes into account many events, on many levels, over the life course. The CBCRP allocated funds for one award for up to $230,000 in direct costs.
- **Environmental Exposures and Breast Cancer among a Large, Diverse Cohort of Women** funds **two pilot studies** to find the most promising research cohort to use for investigating California women's environmental exposures and breast cancer.
  - > One considers the statewide California Teachers Study, where over 133,000 women periodically provide biological samples (such as blood) and information about their lives to the study's researchers at several universities. The CBCRP will award $100,000 in direct costs to support this pilot.
  - > The second pilot study considers Kaiser Permanente Northern California's study of over 200,000 women, the Research Program on Genes, Environment and Health (RPGEH). If one of these pilot studies yields promising results, a larger study will be funded in 2010. The CBCRP will award up to $100,000 in direct costs for this pilot.

If one of these pilot studies yields promising results, a larger study will be funded in 2010 at up to $6 million in total costs.

The CBCRP launched the Special Research Initiatives in 2005 because the Program's previous efforts to increase research addressing these questions had not led to enough progress. California is an ideal laboratory for these under-researched questions. The state has varied geography, heavily industrialized areas, and a large agricultural area. It has a mix of urban, suburban, small town, and rural communities. The state's population is ethnically and racially diverse. California also has communities with some of the highest rates of breast cancer in the nation.

The initiatives are the result of a thoughtful, thorough planning process that included analyzing years of nationwide and CBCRP-funded breast cancer research, and collecting feedback from breast cancer advocates, researchers, healthcare providers, policy makers, other funders, and the public.

To select the research that will lead to the most progress against breast cancer, the Program followed a carefully-crafted, two-year, publicly-accessible strategy development process. A steering committee of researchers and advocates from across the nation guided this process of developing strategy. The members of this committee include:

- **Olufunmilayo I. Olopade, M.D., Walter L. Palmer Distinguished Service Professor of Medicine, University of Chicago Medical Center,** who recently received a MacArthur fellowship for her work translating findings on the molecular genetics of breast cancer in African American and African women into innovative clinical practices in the United States and abroad.
- **Susan Shinagawa, co-founder/co-chair of the Asian & Pacific Islander National Cancer Survivors Network,** is widely recognized as the nation's leading Asian American cancer and chronic pain advocate and activist.
- **David R. Williams, Ph.D., Norman Professor of Public Health at the Harvard School of Public Health and a Professor of African American Studies and Sociology at Harvard University, is** a leader in research into how racial discrimination affects heart disease and other health conditions.
- **Julia G. Brody, Ph.D., Executive Director, Silent Spring Institute,** is one of the world's experts on breast cancer and the environment.

- **Sandra Steingraber, Ph.D., is** author of the book *Living Downstream: An Ecologist Looks at Cancer and the Environment,* and an environmental activist with a national reputation.

The CBCRP's director, Marion H.E. Kavanaugh-Lynch, also serves on the steering committee.

A major step in selecting the topics to be studied under the CBCRP's Special Research Initiatives was the drafting of a review of previous research into the impact of the environment on breast cancer and the reasons why some groups of women bear a greater burden of the disease. This document, titled "Identifying Gaps in Breast Cancer Research," runs to hundreds of pages, considers the results of thousands of research studies, summarizes the latest thinking on these questions, and makes recommendations for research to be pursued. "Identifying Gaps in Breast Cancer Research" is available to the public on the CBCRP Web site. A panel of science advisors, composed of experts from California and across the nation, reviewed and shaped "Identifying Gaps in Breast Cancer Research." A list of the science advisors, staff, and consultants who wrote and shaped "Identifying Gaps in Breast Cancer Research" is found in Appendix A.

The CBCRP also gathered ideas for research to be conducted under the Special Research Initiatives from a variety of sources. Town hall stakeholder meetings, teleconferences, online brainstorming, and a session at the CBCRP's most recent symposium all encouraged the California public and breast cancer experts to submit ideas. Those who participated in this process were later able to rate the ideas submitted. Participants included women affected by breast cancer, investigators, clinicians, government officials, and interested members of the public across California and the nation.

During 2008, a 33-member strategy team of scientists, advocates, and clinicians from California and across the nation made specific recommendations for the ten research initiatives. The strategy team members are listed in Appendix B.

As a result of the CBCRP's leadership in research into the role of the environment in breast cancer, the Program's director, Marion H.E. Kavanaugh-Lynch, has been appointed to the nine-member California Environmental Contaminant Biomonitoring Program Scientific Guidance Panel. The panel assists the Department of Health Services and California Environmental Protections Agency by providing scientific peer reviews and making recommendations regarding the design and implementation of the California Environmental Contaminant Biomonitoring Program.

Core Funding

After setting aside 30 percent of CBCRP research funds for the Special Research Initiatives, the CBCRP dedicates the remaining 70 percent to challenging investigators to use the funds to maximum effect. During its fifteen-year history, the CBCRP has developed and fine-tuned a funding strategy designed to stimulate innovative research.

Each core funding research project must fall under one of the CBCRP's Priority Issue areas:

- The Community Impact of Breast Cancer
- Etiology and Prevention
- Biology of the Breast Cell
- Detection, Prognosis, and Treatment

Each core funding research project must also qualify as one of the CBCRP types of awards:

- **Community Research Collaboration (CRC) award:** Brings community organizations—such as breast cancer advocacy organizations, community clinics, or organizations serving under-represented women—together with experienced scientists to investigate breast cancer problems that are important to that community, using culturally-appropriate research methods. Pilot CRC awards are funded up to 18 months and up to $150,000 in direct costs. Full CRC awards are funded up to three years for up to $600,000 in direct costs.
- **Innovative Developmental and Exploratory Award (IDEA):** Funds promising high-risk/high-reward research to "road test" innovative concepts. Applicants must show how their project is part of a step-by-step research process that will lead to practical applications. IDEAs are funded for up to 18 months and up to $100,000—and for stud-

ies using animals or humans, $150,000—in direct costs.

- **IDEA–competitive renewal**: Allows recently-funded recipients of CBCRP IDEA grants to compete for additional funding, if the project has succeeded in meeting key milestones in a research process that will lead to practical applications. IDEA-competitive renewal awards are available for up to two years and up to $200,000—and for studies using animals or humans, $250,000—in direct costs.
- **Postdoctoral Fellowship award:** Funds advanced training under a breast cancer mentor. Total postdoctoral tenure (prior training plus new CBCRP funding) is limited to five years, and the maximum award duration is three years at $45,000 per year.
- **Dissertation award:** Supports the completion of dissertation research by masters or doctoral degree candidates. Dissertations are funded up to $38,000 per year for up to two years.
- **Joining Forces Conference award:** Supports a conference, symposium, retreat, or other meeting to link breast cancer researchers, non-breast cancer investigators, and community members for the purpose of stimulating new ideas and collaborations.
- **Translational Research award:** Funds research that will take basic science findings quickly toward treatment, diagnosis, prevention or another application that can directly impact breast cancer, either in a medical clinic setting or through a public health measure.

Core Funding by Priority Issue and by Award Type

Below, two tables present statistics on the 42 projects funded during 2008 by Priority Issue and by Award Type.

Table 3. 2008 Core Funding Grants Awarded by Priority Issue

Grant Type	Number of Grants	Amount	Percentage of Total Funding
Community Impact of Breast Cancer	15	$2,706,131	33.5%
Etiology and Prevention	7	$1,007,913	12.5%
Detection, Prognosis and Treatment	11	$3,356,365	41.5%
Biology of the Breast Cell	9	$1,016,985	12.6%
Totals	42	$8,087,394	100%

Table 4. 2008 Core Funding Grants Awarded by Award Type

Award Type	Number of Grants	Amount	Percentage of Total Funding
Dissertation	11	$759,909	9.4%
Postdoctoral Fellowship	6	$745,956	9.2%
Innovative Developmental and Exploratory (IDEA)	11	$2,284,111	28.2%
IDEA-Competitive Renewal	2	$621,906	7.7%
Community Research Collaboration (CRC) Pilot Award	2	$386,796	4.8%
Community Research Collaboration (CRC) Full Award	4	$1,645,686	20.4%
Joining Forces Conference Award	4	$89,919	1.1%
Translational Research Award	2	$1,553,111	19.2%
Totals	42	$8,087,394	100%

Influencing the Research System Nationwide

One goal underlying the CBCRP's funding strategy is the leveraging of Program funds to influence the research system nationwide. The CBCRP is part of a much larger research system. The federal government funds breast cancer research through agencies like the National Cancer Institute and the Department of Defense. Nonprofit organizations and for-profit corporations also fund breast cancer research. Although the CBCRP is the largest state funding source for breast cancer research in California, these funds make up only a small part of the funds granted through the larger system. The CBCRP tries to influence this larger research system to move in new, creative directions.

An example is the CBCRP's Innovative, Developmental, and Exploratory Awards (IDEAs). These awards were specifically designed to fund research that has a high potential for scientific payoff—and also a high potential for failure. When the CBCRP began funding breast cancer research in 1995, less than 10 percent of research proposals submitted to the nation's funding agencies were successful. This led the people who decided what got funded—panels of research experts—to look for proposals that seemed most likely to succeed. Research scientists had to have done a significant portion of the research, and have strong preliminary data, before they could even get a grant. This made it hard for anyone to get funding in order to try out a high-risk idea. However, high-risk ideas are often the source of scientific breakthroughs. The CBCRP's IDEAs meet a need by funding creative new research approaches.

If the research funded by an IDEA succeeds, the researcher may well be able to get another research funding agency to fund the next step. For example, John Boone, Ph.D., and Karen Lindfors, M.D., of the University of California, Davis, received a CBCRP IDEA award that allowed them to build the first dedicated computerized tomography (CT) breast scanner. CT scanners are a special type of x-ray machine that produce three-dimensional pictures. In contrast, mammogram x-rays produce a two-dimensional picture and may not show a tumor obscured by other breast tissue. Standard mammography detects tumors at an average size of about 11 millimeters in diameter, about the size of a garbanzo bean (or chick pea). Breast CT aims to detect tumors at an average diameter of 5 millimeters, about the size of a small pea. The smaller a tumor is when it is discovered, the more treatment options a woman has—and the better her odds of surviving breast cancer. CBCRP funding allowed the researchers to solve problems that included lowering the previously unacceptably high radiation dose involved in breast CT scanning. As a result, Boone and Lindfors have received $6 million from the National Institutes of Health to further develop their CT scanner, which is currently being tested in clinical trials.

The CBCRP uses additional methods to get creative new research going. These include encouraging researchers in California to submit exciting new ideas. The CBCRP also developed a new scoring system to help reviewers read proposals with a perspective toward rewarding high-risk research. In addition, the Program's Special Research Initiatives are a multi-year effort to stimulate new research in previously under-investigated areas that have a high potential to lead to breakthroughs in breast cancer causes and prevention.

Enlarging the Pool of Breast Cancer Researchers

Another major goal of the CBCRP is to increase the number of talented scientists engaged in breast cancer research. Some of the Program's grants have allowed investigators to specialize in, or concentrate much of their efforts on, breast cancer research. For example, Anastasia Kralli, Ph.D., of the Scripps Research Institute, has been interested in investigating mechanisms of action of estrogen-related receptors in the muscle and central nervous system. CBCRP funding has encouraged her to expand her investigations to include breast cancer. Using her 2006 CBCRP IDEA grant, Dr. Kralli was able to demonstrate that when the activity of these proteins is selectively increased in breast tumor cells, it keeps these cells from growing and forming tumors. Dr. Kralli's findings also suggest that compounds based on parts of the molecular structure of estrogen-related receptors could be used to treat breast cancer.

Leveraging Funds for Promising Research

An additional goal of the CBCRP's research strategy is encouraging and inspiring other research funding agencies to support cutting-edge research. For example, in 2008, the Avon Foundation, which funds breast cancer research nationwide, joined the CBCRP in supporting the Program's ground-breaking Special Research Initiatives. The foundation, long a funder of breast cancer research, agreed that not enough has been done in the areas of environmental links to breast cancer and the reasons why some groups of women bear a greater burden of the disease. The Avon Foundation awarded the CBCRP a $500,000 grant earmarked for three of the ten CBCRP Special Research Initiatives. Two of the initiatives support research exploring environmental exposures and breast cancer among large and diverse groups of women at several points through their life. The third project will combine data from multiple California studies to explore answers to why people from different racial and ethnic groups have different survival outcomes, despite being diagnosed with breast cancer at the same stage.

Research Funding and Results

Special Research Initiatives

Environmental links to breast cancer

The reasons why some groups of women are more likely to get or die from breast cancer, based on characteristics that include geographic location, race, and ethnicity.

Special Research Initiatives

Unlike the procedure used with previous CBCRP-funded research studies, and the majority of scientific research funded in the nation today, the scientists involved in the Special Research Initiatives are not selecting the topics to be studied. To select topics for the initiatives, the CBCRP worked with over 300 leading breast cancer experts and advocates from across the nation.

The CBCRP invited California scientists to submit their proposals and qualifications for investigating the selected Special Research Investigation topics. Requests for Qualifications (RFQs) announcements were sent out to the entire CBCRP mailing list, people identified during the course of the SRI development, relevant organizations and researchers, and investigators and organizations recommended by the Strategy Team and Steering Committee members for four of the initiatives. The responses to the RFQs were evaluated and scored for innovation, impact and approach and feasibility (and in the case of the Survival RFQ, the quality of the study and the comparability to other studies) by external scientific and advocate peer reviewers. The advisory Breast Cancer Research Council funded the following investigators:

- **California Chemicals Policy and Breast Cancer**

  > John Balmes, M.D.
  Northern California Center for Occupational and Environmental Health
  University of California, Berkeley
  $159,334

- **Demographic Questions for California Breast Cancer Research**

  > Scarlet Lin Gomez, Ph.D.
  Northern California Cancer Center
  $430,989

- **Understanding Racial and Ethnic Differences in Stage-Specific Breast Cancer Survival: A Pilot Study**

  > California Teacher's Study
  Katherine Henderson, Ph.D.
  Beckman Research Institute, City of Hope
  $32,956

  > Los Angeles County Asian American Breast Cancer Study
  Anna Wu, Ph.D.
  University of Southern California
  $32,600

  > Multiethnic Cohort Study
  Kristine Monroe, Ph.D.
  University of Southern California
  $31,043

  > Pathways: A Study of Breast Cancer Survivorship and Life After Cancer Epidemiology (LACE) Study
  Marilyn Kwan, Ph.D.
  Kaiser Foundation Research Institute
  $30,480

  > San Francisco Bay Area Breast Cancer Study
  Esther John, Ph.D.
  Northern California Cancer Center
  $29,000

  > Women's CARE Study
  Leslie Bernstein, Ph.D.
  Beckman Research Institute, City of Hope
  $33,062

Several California data resources were determined to be particularly unique and useful for investigating Special Research Initiative topics. Three cohorts were identified in the course of the SRI development by the Strategy Team and Steering Committee members. These groups then generated ideas for advancing environmental and disparities research through exceptional resources and worked together to elaborate the research concepts and goals. These were evaluated by experts who offered suggestions for improving the potential for significant advances. The advisory Breast Cancer Research Council funded the following investigators:

- **Environmental Causes of Breast Cancer Across Generations**

  > Barbara Cohn, Ph.D.
  Public Health Institute, Berkeley
  $5,000,000

- **Exploring Diversity in an Environmental Study of California Teachers**

  > Peggy Reynolds, Ph.D.
  Northern California Cancer Center, Berkeley
  $129,399

Core Funding Investigator Initiated Awards

On the following pages, the results of investigator-initiated research funded by the California Breast Cancer Research Program and completed during 2008 are presented. Listings of research in progress and research Core-funding grants awarded this year are also presented.

The Research Progress and Results section is organized by the CBCRP's four major Priority Issues:

The Community Impact of Breast Cancer

Etiology and Prevention

Detection, Prognosis, and Treatment

Biology of the Breast Cell

The Community Impact of Breast Cancer

California is comprised of diverse communities differing by multiple characteristics such as ethnicity, culture, language, sexual identity, immigration history, and socioeconomic status. This diversity offers the unique opportunity to investigate disparities and the unequal burden of breast cancer among underserved groups. Critical questions to be addressed include:

- How do poverty, race/ethnicity, and social factors impact incidence and mortality for breast cancer?
- What are the sociocultural, behavioral, and psychological issues faced by women at risk for or diagnosed with breast cancer?
- What services are needed to improve access to care in order to improve quality of life and reduce suffering?

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

The CBCRP has been supporting Community Research Collaborations (CRC) for over 11 years. These partnerships are based on the established principles of community-based participatory research (CBPR) whereby academic and community investigators work together to identify the research question, develop the study design, carry out the research, analyze results, and disseminate information to scientific and lay communities.

Core Funding Investigator-initiated Awards

The Community Impact of Breast Cancer

Etiology and Prevention

Detection, Prognosis, and Treatment

Biology of the Breast Cell

The CBCRP offers pre-application teleconferences to provide information on CRC application requirements and tips for successful grant applications. We are encouraged that many CRC grants focus on the underlying disparities of underserved populations through innovative and understudied research areas. We feel that addressing these gaps in our knowledge will lead to promising solutions for underserved communities disproportionately affected by breast cancer.

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

Three research topics are represented in this section:

- Health Policy and Health Services: Better Serving Women's Needs
- Disparities: Eliminating the Unequal Burden of Breast Cancer
- Sociocultural, Behavioral, and Psychological Issues Relevant to Breast Cancer: The Human Side

Research Conclusions

South Asian Women with Breast Cancer: What are Their Needs?
Increasing numbers of South Asian women are diagnosed with breast cancer each year; however, little is known about their psychosocial and practical needs. **Roshan Bastani, Ph.D.,** and **Beth Glenn, Ph.D.,** at the **University of California, Los Angeles,** and **Zul Surani, B.S.,** at the **South Asian Cancer Foundation,** Mission Hills, conducted a pilot study to assess the needs of South Asian women with breast cancer and outline the essential components of an intervention to meet these needs. Their semi-structured interviews with 40 South Asian breast cancer survivors and 10 other community members highlighted the need for intervention programs that use religious and community networks; promote healthy lifestyles; address the important role of spirituality in the breast cancer experience; and tackle the social stigma that surrounds South Asian breast cancer survivors. The research team is currently disseminating its results as well as pursuing funding to implement the intervention developed during the pilot project.

Informal and Formal Support and Needs Among Samoan Survivors
Breast cancer is the leading cause of cancer for Samoan women, yet there is no information on the relative importance informal and formal support play in their long-term survival and quality of life. **Sora Park Tanjasiri, Dr.P.H., M.P.H.,** at **California State University, Fullerton,** and **Sala Mataalii,** at the **Samoan National Nurses Association,** conducted a pilot project that expored the formal and informal social support needs of Samoan women diagnosed with breast cancer. Through interviews with 20 Samoan survivors and 40 members of their informal support network, Dr. Tanjasiri and Ms. Mataalii identified important themes related to women's social support needs and experiences. They have shared these findings with the community and are now working with community members to refine an existing community-based social support program so that it better meets Samoan survivors' needs. The researchers intend to publish their findings as well as present them at professional conferences.

Hormone, Psychologic and Immunologic Factors & Breast Cancer Survivorship
Researchers have theorized that the timing of breast cancer surgery may affect a woman's risk for recurrence. **Hillary Klonoff-Cohen, Ph.D.,** at the **University of California, San Diego,** and colleagues are exploring this question in a study entitled "Looking Forward to LIFE," which will investigate the role that hormone levels at the time of surgery, stress, and the immune system play on breast cancer survivorship. Earlier this year, the CBCRP decided to end this project due to limited progress in recruitment for the study. The researchers have submitted their proposal to other funding agencies and hope to have the opportunity to conduct the fully proposed study.

Latinas and DCIS: Treatment Decisions and Quality of Life
Widespread mammography screening has resulted in an increase in the number of women diagnosed with ductal carcinoma in situ (DCIS), a non-invasive form of breast cancer. However, little is known about treatment decision-making and

follow-up care among women with DCIS, particularly Latinas. **Celia Kaplan, Dr.P.H.,** at the **University of California, San Francisco,** and colleagues interviewed English- and Spanish-speaking Latinas and white women diagnosed with DCIS. They then developed, tested, and implemented a telephone survey to assess and compare treatment selection, decision-making, quality of life, and the receipt of follow-up care. Dr. Kaplan and her team found, among other things, that the vast majority of the respondents (67%) chose breast-conserving surgery; that English-speaking Latinas (87%) and Spanish-speaking Latinas (82%) were more likely to receive radiation than white women (72%); and that Spanish-speaking Latinas were less likely to have reconstruction than the other two groups of women. Dr. Kaplan intends to use these research findings to develop culturally sensitive approaches to treatment decision-making and follow-up care for women diagnosed with DCIS.

Social Support and Quality of Life in Older Minority Women with Breast Cancer
Breast cancer care typically fails to acknowledge the role of cultural diversity in social support. Such cultural insensitivity may hinder the development of trusting partnerships between the patient, family, and providers. This, in turn, may exacerbate disparities in breast cancer treatment and survival. **Yoshiko Umezawa, M.H.S.,** at the **University of California, Los Angeles,** surveyed 99 Latina, 66 African American, and 92 white women newly diagnosed with breast cancer to gain insight into the role social and religious support plays in helping minority women cope with their diagnosis. Ms. Umezawa found that, overall, Latinas and African American women were more likely to rely on social and religious support than white women. She also found that minority women, especially Latinas, were more likely than white women to receive support from children; that less-acculturated Latinas were more worried about being a burden on their support network; and that minority patients received more information from doctors if their companions asked questions. These findings could help health care providers develop more culturally sensitive partnerships with their patients that can help improve quality of life after a breast cancer diagnosis.

Fresno Breast Cancer Navigator Pilot Program
A complex health care system awaits women diagnosed with breast cancer. The many different types of doctors and multiple types of treatments that patients must pursue often contribute to disparities in breast cancer care and survival. Breast Cancer Navigator programs have been identified as a practical solution to improving care for underserved women. However, it is not known which type of Breast Cancer Navigator program is best. **Mary Wallace** at the **San Joaquin Valley Health Consortium, John Zweifler, M.D.,** at the **University of California, San Francisco,** and **John Capitman, Ph.D,** at **California State University, Fresno Foundation** designed, pilot tested, and evaluated a Breast Cancer Navigator service designed to help address racial/ethnic and insurance-related disparities in breast cancer care at a Fresno safety-net hospital. This work involved identifying points of service breakdown and determining if insurance or race were related to service breakdown, conducting survivor interviews, determining the best way a Breast Cancer Navigator program could address the problems they had identified, hiring and training Breast Cancer Navigators, and conducting patient exit satisfaction interviews. The research team has submitted a grant to conduct a three-year comparative study of the effectiveness of the Breast Cancer Navigator Model. This study would examine the differences in timing and completion of care between patients that receive care at the Fresno's safety-net hospital, and those that receive care at a private hospital within the same Community Medical Center system.

Breast Health Literacy and Health Care Decision Making
Resources that address healthcare services specific for each Asian sub-population, specifically the Filipina, Laotian, and Chinese communities, are scarce. **Joel San Juan, M.S.,** at **Operation Samahan Inc.,** a primary care health clinic, and **Suzanne Lindsay, Ph.D., M.P.H.,** at the **San Diego State University Research Foundation,** received a planning grant to strengthen the scientific and community elements of a research project that would explore the effect cultural factors have on the breast health beliefs and behaviors and to develop an intervention that would addresses the specific health needs of women in the Chinese,

Filipina, and Laotian communities. As part of this effort, the collaborators conducted four focus groups in the Chinese, Filipina, and Laotian communities and held eleven partnership meetings to discuss the project. The partners are pursuing additional funding to continue this work.

The Breast Cancer Experience of Slavic Women
The greater Sacramento area is home to the largest Slavic community in the country (close to 100,000 persons). Little is known about this population's understanding of and experiences with breast cancer. **Debora Paterniti, Ph.D.,** at the **University of California, Davis,** and **Roman Romaso,** at the **Slavic Assistance Center, Sacramento,** conducted six focus groups with first and second generation Slavic women in Sacramento and Yolo counties to learn about their breast cancer and breast health experiences. They also conducted a focus group with health professionals and leaders in the Sacramento Slavic community. Dr. Paterniti and Mr. Romaso found that Slavic immigrant women in these areas have a need for culturally appropriate accessible information about breast health and cancer prevention. Their research also indicated that it would be important for this information to come from a trusted source; be designed to empower women in their interactions with U.S. physicians; and offer strategies for maintaining breast health and preventing cancer. These findings have been presented at national, state, and local meetings of social scientists and cancer researchers. Dr. Paterniti and Mr. Romaso intend to seek additional funding to develop and test print, radio, and face-to-face educational intervention programs for Slavic women.

Introducing Acupuncture to Black Survivors for Wellness
Studies have shown that acupuncture can help improve wellness in breast cancer survivors by reducing symptoms and improving quality of life. African Americans are much less likely than members of other racial groups to utilize acupuncture health services. **Carolyn Tapp,** of the **Women of Color Breast Cancer Survivors Support Project,** and Michael **Johnston, Ph.D.,** at the **University of California, Los Angeles,** received a planning grant to help them strengthen the research design and methodology of a study that would discover the reasons why African American breast cancer survivors are less likely to seek out acupuncture. As part of that effort, the researchers conducted interviews with African American breast cancer survivors and worked together to obtain funding to continue the work.

Factors Influencing Breast Cancer Screening Among Older Thai
Asian women have a lower incidence of breast cancer than white women. Whether this reflects a lower rate of participation in mammography screening is not known. **Mary Jo Clark, Ph.D., RN,** at the **University of San Diego,** and **Bulaporn Natipagon-Shah, Ph.D., R.N.,** at the **Thai Health and Information Service, Los Angeles,** conducted focus groups with Thai women to learn more about why they have, or have not, gotten a mammogram. They then used this information to develop a telephone questionnaire about mammography screening that was used in interviews conducted with 360 Thai women aged 40 to 81 living in Los Angeles, Riverside, Orange, San Bernardino, and San Diego counties. Drs. Clark and Natipagon-Shah found that while a majority of the women (84%) had had a mammogram at some time, almost half (44%) did not get a mammogram annually, as is recommended by the American Cancer Society. They also found that although most of women were knowledgeable about breast cancer, they perceived Thai women, particularly young women, to be at low risk. Major factors impeding screening included lack of health insurance, cost of screening, and language difficulties. Other barriers included lack of time either due to family or work responsibilities and distance to services. These findings suggest avenues for intervention to increase mammography screening in this population and they are the focus of a follow-up study the researchers have proposed.

Increasing Mammography Among Latinas with Disabilities
Both women with disabilities and Latinas are less likely to obtain mammograms than other women. **H. Stephen Kaye, Ph.D.,** at the **University of California, San Francisco,** and **Elsa Quezada,** at the **Central Coast Center for Independent Living,** Salinas, investigated whether a breast cancer peer education program designed specifically for Latinas with disabilities could increase mammography screening. Dr. Kaye and Ms. Quezada hired Lati-

nas from the Central Coast as community health workers (promotoras) and trained them to provide breast cancer and mammography peer education classes. The promotoras provided classes to 350 women. Ninety-five of these women were Latinas with disabilities who were over 40 and who had not recently, if ever, had a mammogram. The participants were tested before and after the peer education program to assess their knowledge of mammography. The test results showed that the peer education program increased the women's awareness of breast cancer and mammography and boosted their confidence in their ability to obtain a mammogram. In addition, a follow-up questionnaire found that a majority of the participants either obtained a mammogram or attempted to do so during the two months following the class. Dr. Kaye and Ms. Quezada are currently developing a more broadly focused promotora health promotion program for Latinas with disabilities that will include multiple components, including breast cancer and mammography.

Assessing Recurrent Genomic Aberrations Linked to Ethnicity

In the U.S., the incidence of breast cancer in African Americans is about 20 percent lower than it is in white women. However, the prognosis in African Americans with breast cancer is 20 percent poorer. Studies have shown that African American women tend to have tumors that are larger and more advanced in stage than white women. They also tend to have higher lymph node involvement and more distant metastasis. The reasons for these differences remain unclear. **Koie Chin, M.D., Ph.D., at the University of California, San Francisco,** and colleagues compared breast tumor tissue from 122 African Americans and 106 white women to see if they could identify genomic variations that could account for these differences. First, they classified the tumors into three genomic subtypes; then, they measured disease-free survival according to genomic subtype. This analysis showed no significant differences between African American and white women's tumors. A second analysis of gene expression identified more than 40 genes that were turned on at a higher level in the African American women's tumors than in the white women's tumors. To follow up on these findings, Dr. Chin and his team intend to conduct a combined analysis of genomic copy number and gene expression. This work could lead to a better understanding of why African American women have a poorer prognosis than white women.

Grants in Progress: 2008

Addressing Cultural & Tribal Issues in Breast Cancer

Linda Navarro and Marlene von Friedrichs-Fitzwater

Turtle Health Foundation and University of California, Davis

A Blueprint for Advancing Quality in Breast Cancer

Laura Esserman

University of California, San Francisco

Breast Health Behaviors of Immigrant Afghan Women

Aida Shirazi and Joan Bloom

Afghan Coalition and University of California, Berkeley

Breast Cancer Education for Deaf and Hard-of-Hearing Women

Heidi Kleiger and Barbara Berman

Greater Los Angeles Council on Deafness, Inc. and University of California, Los Angeles

Expanding Rural Access: Distance Delivery of Support Groups

Jim Perkins, Mary Anne Kreshka, and Cheryl Koopman

Northern Sierra Rural Health Network and Stanford University

Mammography Screening for Latinas with Diabetes

Christine Noguera and Stergios Roussos

Golden Valley Health Centers and California State University, Fullerton

Neighborhood Environment and Obesity in Preadolescent Girls

Irene Yen

University of California, San Francisco

Networking Breast Cancer Navigator Programs in Northern California

Lisa Bailey

Alta Bates Summit Medical Foundation

Science Literacy & Breast Cancer Clinical Trials Education
Natasha Riley, Vanessa Malcarne, and Georgia Sadler
Vista Community Clinic, San Diego State University Research Foundation, and University of California, San Diego

Sister Survivor: African American Breast Cancer Coalition
Gloria Harmon and Kimlin Ashing-Giwa
Women of Essence and Beckman Research Institute of the City of Hope

Social Capital, Social Support and Long-Term Quality of Life
Dana Peterson
University of California, Berkeley

Southeast Asian Breast Health Navigation
Mary Ann Foo and Marjorie Kagawa-Singer
Orange County Asian & Pacific Islander Community Alliance and University of California, Los Angeles

Telephone-based Decision Support for Rural Patients
Sara O'Donnell and Jeff Belkora
Mendocino Cancer Resource Center and University of California, San Francisco

Underserved Women with Breast Cancer at End of Life
Beverly Burns and Shelley Adler
Charlotte Maxwell Complementary Clinic and University of California, San Francisco

Young Breast Cancer Survivors: Ten Years Later
Joan Bloom
University of California, Berkeley

Research Initiated in 2008

Adapting a Breast Cancer Education Program for South Asians
Zul Surani, Roshan Bastani, and Beth Glenn

South Asian Cancer Foundation and University of California, Los Angeles

APOS 5th Annual Conference
Patricia Ganz
University of California, Los Angeles

Breast Cancer Clinical Trials Education Program
Natasha Riley, Vanessa Malcarne, and Georgia Sadler
Vista Community Clinic, San Diego State University Research Foundation, and University of California, San Diego

Breast Cancer Risk Reduction in American Indian Women
Linda Navarro and Marlene von Friederichs-Fitzwater
Turtle Health Foundation and University of California, Davis

Community Breast Cancer Screening & Prevention Conferences
Jeffrey Weitzel
Beckman Research Institute of the City of Hope

An Ecological Study of Quality of Life in Low-Income Women
Yoshiko Umezawa
University of California, Los Angeles

Increasing Mammography Screening in Latinas with Diabetes
Christine Noguera and Steve Roussos
Golden Valley Health Centers and San Diego State Research Foundation

Increasing the Voice of African American Women in Research
Kimlin Ashing-Giwa
Beckman Research Institute of the City of Hope

Latina Breast Cancer Survivors…Our Experience
Brian Montaño and Diana Tisnado
Partnered for Progress and University of California, Los Angeles

Mindful Movement Program for Breast Cancer Survivors
Holly Kiger and Rebecca Crane-Okada
WISE and Healthy Aging and Beckman Research Institute of the City of Hope

Nail Salon Workers: Chemical Exposures in the Workplace
Linda Okahara
Asian Health Services

Neighborhoods and Obesity in Pre-adolescent Girls: Part II
Irene Yen
University of California, San Francisco

Provider Communication and Health in Breast Cancer Survivors
Sara Fernandes-Taylor
University of California, Berkeley

Quality of Mammography Facilities Serving Vulnerable Women
Lauren Goldman
University of California, San Francisco

Reproductive Concerns and Depression among Younger Survivors
Jessica Gorman
University of California, San Diego

Etiology and Prevention

Although our foundation of knowledge for the basic science aspects of breast cancer has expanded greatly over the past decade, gaps still remain in our strategies for large-scale prevention due to uncertainties over the underlying causes of the disease and their relative importance. There is an extensive list of factors associated with increased and decreased risk for breast cancer. However, the relative importance of diet, exercise, family history, pregnancy, alcohol, hormone replacement therapy, and other factors remains controversial.

Two research topics are represented in this section:

- Etiology: The Role of the Environment and Lifestyle
- Prevention and Risk Reduction: Ending the Danger of Breast Cancer

Research Conclusions

Structural Characterization of Aromatase
Aromatase is the enzyme that converts androgen into estrogen. Aromatase inhibitors, which block this synthesis of estrogen, are now widely used to treat hormone-responsive breast cancer in postmenopausal women. They are also being studied in the breast cancer prevention setting in high-risk women. **Yanyan Hong, M.S.,** at the **Beckman Research Institute** of the City of Hope, Duarte, and colleagues are attempting to ascertain the three-dimensional structure of the aromatase enzyme. This will allow them to gain insight into the precise way in which these drugs bind to and block the aromatase enzyme. This work could lead to the development of a more potent fourth-generation of aromatase inhibitors that could be used for the prevention and the treatment of hormone-responsive breast cancer. Findings from this research were published in *New York Academy of Sciences* 2006(1089)237; *Molecular Endocrinology 2007*(21)401; and *Journal of Steroid Biochemistry and Molecular Biology* 2007(106)8.

Breast Cancer Prevention with Phytochemicals in Mushrooms
Aromatase is a protein that makes estrogen, which plays a key role in the development of hormone-sensitive breast cancer. Oncologists use a class of drug called aromatase inhibitors to treat these types of tumors. **Shiuan Chen, Ph.D,** at the **Beckman Research Institute** of the City of Hope, Duarte, and colleagues previously showed that white button mushrooms (species *Agaricus bisporus*) contain chemicals that can suppress human aromatase activity. Dr. Chen and his team have now shown that, in a mouse model, these mushroom can turn off the genes that are involved in cell growth and energy production, and that they are able to do so even after the mushrooms are cooked. In addition, Dr. Chen and his team showed that white button mushrooms contain a type of fatty acid, called conjugated linoleic acid, which is an aromatase inhibitor; and that oral intake of mushroom extract decreases both tumor cell proliferation and tumor weight in mice. Based on these findings, a clinical trial that will test whether mushroom intake can inhibit estrogen production in postmenopausal breast cancer survivors will soon get underway at the City of Hope. Findings from this research were published in *Cancer Research* 2006(66)12026

Grape Seed as a Natural Breast Cancer Chemopreventive Agent
Aromatsase inhibitors are now widely used to treat hormone-response breast cancer in postmenopausal women; they are also being studied in the breast cancer prevention setting. Their effectiveness had led researchers to look for other

chemicals that can also suppress aromatase. **Melanie Ruth Palomares, M.D., M.S.,** at the **Beckman Research Institute of the City of Hope,** Duarte, previously demonstrated that grape seed extract acts like an aromatase inhibitor in mice. This grant allowed her to conduct a clinical trial that would investigate whether grape seed extract also acts like an aromatase inhibitor in healthy postmenopausal women. Dr. Palomares and her team enrolled 25 women in their trial and tested four different doses of grape seed extract, ranging from 50mg/day to 2,000mg/day. They are currently analyzing their data, and intend to present their findings when their work is completed. If Dr. Palomares finds that grape seed extract acts like an aromatase inhibitor in women, this research could lead to the introduction of a safe, inexpensive option for reducing breast cancer risk.

Targeted Chemoprevention in a Mouse Model for DCIS

Anti-estrogen treatments are currently used to reduce breast cancer risk in high-risk women. But anti-estrogen therapy is not effective in all patients. **Jeffrey Gregg, M.D,** at the **University of California, Davis,** investigated whether combining anti-estrogen therapy with an agent that promotes cell death would be more effective than anti-estrogen therapy alone. Dr. Gregg used a mouse model for DCIS to study the effect of the anti-estrogen treatment tamoxifen. This research indicated that tamoxifen reduced pre-neoplastic growth and decreased tumor incidence. It also showed that tamoxifen worked by decreasing cell proliferation. Next, Dr. Gregg used a mouse model for DCIS to study an agent that promotes cell death called rapamycin. This work showed that rapamycin reduces tumor incidence by inducing cell death. These findings suggest that this type of combination therapy might work better than an anti-estrogen therapy alone as a breast cancer prevention treatment. Findings from this research were published in *Breast Cancer Research* 2005(7)R881, *Clinical Cancer Research* 2006(12)2613, and *BMC Cancer* 2006(6)275.

Birth Characteristics and Breast Cancer in Young Women

Currently, only about 50% of breast cancer can be explained by known risk factors. Most of these risk factors are related to exposures to estrogens during adult life. Very little, however, is known about how factors experienced earlier in life affect later breast cancer risk. **Peggy Reynolds, Ph.D.,** at the **Northern California Cancer Center, Union City,** used data from the U.S. census and the California Cancer Registry to investigate whether certain birth characteristics that are considered to be markers for high levels of *in utero* estrogen exposures are related to breast cancer risk in young women. Dr. Reynolds and her colleagues found, among other things, that maternal age and paternal age were the strongest predictors of breast cancer risk, and that women who were born post-term (42 weeks or later) had a significantly reduced risk of breast cancer. Dr. Reynolds and her team also found that women born to mothers living in higher socioeconomic neighborhoods had an increased risk of developing breast cancer, while region at birth was not associated with breast cancer risk. These findings were presented at the International Society for Environmental Epidemiology and International Society for Exposure Analysis (ISEE/ISEA) 2008 Joint Annual Conference and are in preparation for publication.

Androgen Receptor Gene and p21 Gene in Breast Cancer

Androgens, which are usually thought of as male hormones, have many important functions in the female body. These functions are both indirect (acting as a source of estrogen production) and direct (binding to the androgen receptor). Accumulating evidence suggests that the indirect effect (acting as a source of estrogen production) contributes to increased breast cancer risk, while the direct effect (binding to the androgen receptor) may reduce risk, with the overall effect being the balance between the two. **Wei Wang, M.D.,** at the **University of Southern California, Los Angeles,** and colleagues previously found a relationship between a stronger type of androgen receptor and reduced breast cancer risk in a small group of African American women who had a mother or sister with breast cancer. This project allowed Dr. Wang and her team to study genetic variations in the androgen receptor in 1724 African American, Hispanic, and non-Hispanic white women and to investigate the relationship between a protein called p21 and breast cancer risk. They studied this protein because it is regu-

lated by androgens and because it helps control normal and cancer cell growth. Dr. Wang and her team are now completing their data analysis. Their findings have the potential to pave the way toward the development of new breast cancer prevention treatments.

Lifestyle Factors & Breast Cancer Prognosis in Asian Americans

Little is known about the influence of lifestyle factors on a woman's breast cancer prognosis. **Anna Wu, Ph.D.,** at the **University of Southern California, Los Angeles,** and colleagues conducted interviews with 1,463 Asian women who had taken part in a case-control study of breast cancer in Los Angeles to investigate whether pre-diagnostic dietary and non-dietary lifestyle factors were associated with breast cancer prognosis. Preliminary analyses of pre-diagnostic lifestyle factors found that the risk of mortality was not associated with intake of green tea or black tea. However, there was an increased risk seen in the women who had the highest weight and the lowest soy intake. Additional telephone interviews were conducted with 780 breast cancer patients to investigate whether there was a relationship between post-diagnostic dietary habits and the risk of recurrence or a second cancer. Preliminary analyses of these data suggest that the risk of recurrence or a second cancer is not associated with post-diagnostic body weight or intake of green tea or black tea. However, risk was lower among women who had a high intake of soy and seafood, and it was higher among those who ate a lot of red meat. Dr. Wu and her team are continuing to examine the role of soy as well as the combined effects of soy intake and use of tamoxifen on recurrence risk. This work will shed light on the relationship between dietary factors and breast cancer and could help identify dietary elements that may improve breast cancer outcomes. Results of this research were published in *Nutrition and Cancer* 2006(56)128.

Hereditary Breast Cancer and Novel Hispanic BRCA Mutations

Inherited mutations in the BRCA (BReast CAncer) genes are associated with 5-10% of breast cancer cases. Women with these mutations have up to an 85% risk of developing breast cancer in their lifetime. Little is known about the prevalence of the BRCA mutation in the Hispanic population. **Jeffrey Weitzel, M.D.,** at the **Beckham Research Institute of the City of Hope, Duarte,** and colleagues developed a prototype genetic test for 18 different BRCA mutations common in the Hispanic population. Dr. Weitzel and his team found that a specific mutation called BRCA1 185delAG accounted for 11% of all the positive test results in this population. They are now revising the genetic test so that it can screen for 56 different common Hispanic BRCA mutations. The new test should be able to rapidly and inexpensively identify up to 90% of all BRCA mutations among high-risk Hispanic women undergoing genetic testing. Dr. Weitzel intends to use this test to pre-screen high-risk Hispanic patients at his clinic. If no mutation is found, a woman will go on to have the more expensive full BRCA gene test. By utilizing this unique Hispanic BRCA mutation panel, Dr. Weitzel and his colleagues will be able to reduce the cost associated with testing high-risk Hispanic individuals for BRCA mutations and be able to provide more extensive information to Hispanic women about their individual breast cancer risk. This research was published in *Cancer, Epidemiology, Biomarkers and Prevention* 2007(16)1615-20

A Novel Biological Framework for the Role of Xenoestrogens

Exposure to estrogen mimicking compounds, called xenoestrogens, appears to play a role in cancer development. **Shanaz Dairkee, Ph.D.,** at the **California Pacific Medical Center Research Institute, San Francisco,** developed a human cell model system to study the role of the xenoestrogen bisphenol A in malignant breast disease. Bisphenol A directly enters the human body by leaching out from polycarbonate plastic containers of food and beverages, and from epoxy resins used as dental sealants. Dr. Dairkee and her team identified gene signatures that reflect distinctive patterns of response to estrogen, progesterone, and bisphenol A; demonstrated that bisphenol A-induced genetic changes are similar to that of estrogen exposure; and showed that these changes promote cell survival. They also found that the genetic signature of bisphenol A was most often seen in aggressive, high-grade tumors. These findings suggest that analyzing this genetic signature in clinical tumor tissue

could provide a reliable way to identify individuals who have been exposed to excessive xenoestrogen levels. It also could lead to the development of new breast cancer prevention treatments for women whose breast cells contain a genetic signature linked to bisphenol A exposure. Findings from this research were published in *Cancer Research* 2008(68)2076.

Breast Cancer Metastasis: A Heritable Trait?
Scientists have discovered a gene in mice that, when altered, causes their mammary cancers to spread to other organs (metastasize). **Alice Whittemore, Ph.D.**, at **Stanford University, Palo Alto,** and colleagues used retrospective data from 743 female breast cancer patients in 242 families registered with the Fox Chase Cancer Center in Philadelphia and the Huntsman Cancer Institute in Salt Lake City to investigate whether humans can also inherit genetic mutations that increase their risk of having a breast cancer metastasize. Their research did not find any evidence to suggest that a family history of metastatic breast cancer contributes substantially to a breast cancer patient's risk of metastasis.

The Hygiene Hypothesis and Breast Cancer Risk
Microbial exposures have been studied previously as part of the "hygiene hypothesis" to explain the causes of allergic and autoimmune diseases. This idea holds that reduced or delayed exposures to microbes, or living in a mostly disease-free, sanitized environment, hampers development of a healthy immune system. It is possible that an underdeveloped immune response might also influence breast cancer development by weakening immune responses against tumors, increasing estrogen production, or both. **Christina Clarke Dur, Ph.D.,** at the **Northern California Cancer Center,** Union City, investigated whether women with breast cancer were less likely than healthy women to report certain exposures known to positively influence healthy immune system development. Preliminary analyses indicated an association between a history of mastitis and an increased risk of postmenopausal breast cancer. Dr. Clarke Dur and her colleagues intend to investigate this association further using data from the California Teachers Study. This research could help to jumpstart new efforts to study the role of immune system factors in breast cancer.

Grants in Progress: 2008

Breast Cancer Lymphedema: Role of Insulin Resistance/FOXC2
Stanley Rockson
Stanford University

Breast Cancer Risks in California Nail Salon Workers
Peggy Reynolds and Linda Okahara
Northern California Cancer Center and Asian Health Services

Circuit Training to Lower Breast Cancer Risk in Latina Teens
Jaimie Davis
University of Southern California

Structural Characterization of Aromatase
Yanyan Hong
Beckman Research Institute of the City of Hope

Tea, Genes, and Their Interactions on Breast Cancer
Anna H. Wu
University of Southern California

Research Initiated in 2008

Antidepressant and Breast Cancer Drug Interactions
Reina Haque
Kaiser Foundation Research Institute

FGFR2 Signaling in Human Breast Cancer Cells
Daniel Donoghue
University of California, San Diego

Folate, DNA Methylation and Breast Cancer Metastasis
Teresa Marple
University of California, Davis

Genes in Hormone Metabolism Pathway and Breast Cancer
Eunjung Lee
University of Southern California

Grapefruit, Hormones, and Postmenopausal Breast Cancer Risk
Kristine Monroe
University of Southern California

Pesticide and Gene Interactions in Latina Farm Workers
Paul Mills
University of California, San Francisco

Prognostic Implications of DNA Glycation in Breast Cancer
Daniel Tamae
Beckman Research Institute of the City of Hope

Detection, Prognosis, and Treatment

Until we learn how to prevent all breast cancers, detection, prognosis and treatment are research areas that need to be pursued. The detection, prognosis, and treatment topics funded by the CBCRP continue to change as novel technologies and approaches come under investigation. Breast cancer detection technology is moving past traditional mammography; diagnosis is depending on understanding the genetic profile of tumors rather than the anatomy; and treatment is moving toward more tailored and personalized approaches. Alternative therapies and drugs, especially those derived from plants, engender intriguing areas of investigation. Taken together these advances are leading to patient care that treats women appropriately and spares them unnecessary side effects.

Two research topics are represented in this section:

- Imaging, Biomarkers, and Molecular Pathology: Improving Detection and Diagnosis
- Innovative Treatment Modalities: Search for a Cure

Research Conclusions

Breast Cancer Functional Imaging with Optics and MRI
Researchers are trying to develop new imaging techniques that can identify breast cancers better than mammography, which is currently the best tool available. **Nola Hylton, Ph.D.,** at the **University of California, San Francisco** and **John Butler, M.D,** and **Bruce Tromberg, Ph.D.,** at the **University of California, Irvine,** are developing a laser breast scanner that, like mammography, could be used for breast cancer screening and detection. The research team previously demonstrated that their hand-held laser breast scanner, which uses diffuse optical spectroscopy (DOS), was able to detect both cancerous and non-cancerous tumors. They have now developed a new technique that combines MRI and DOS information to assess breast density. Drs. Butler, Hylton, and Tromberg demonstrated that DOS can find breast tumors in both pre-menopausal and post-menopausal women; generated maps of tumor biochemistry; and developed ways to identify absorption patterns that differentiate malignant tumors from normal tissue. They also demonstrated that DOS can measure a tumor's response to chemotherapy given prior to surgery. This work could lead to the introduction of new tools for breast cancer screening and diagnosis. Findings from this research were published in *Journal of Biomedical Optics* 2004(9)230 and 534, 2005(10)5150; *Disease Markers* 2004(19)95; *Technology in Cancer Research and Treatment* 4(2005)549; and *Breast Cancer Research* 2005(7)279.

Early Breast Cancer Detection Using 3D Ultrasound Tomography
Early detection is one of the main tools we currently have to improve breast cancer survival. Mammography is the current "gold standard" for diagnosing breast disease. But it doesn't work well in women with dense breast tissue, and is not adequate for those who are high-risk. For these women, ultrasound is an important adjunct to mammography. However, ultrasound is operator dependent and the lack of consistency between centers limits widespread acceptance. To address this problem, **Thomas Nelson, Ph.D.,** at the **University of California, San Diego,** and colleagues constructed and tested a prototype volume breast ultrasound scanner that can standardize the acquisition of ultrasound data from the breast. This work has the potential to improve early detection of breast disease, especially in women with dense breast tissue. Findings from this research were published in *IEEE Transactions on Biomedical Engineering* 2007(54)1885 and *Medical Physics* 2008(35)1078.

New Technology to Enhance PET Imaging of Breast Cancer
Currently, Positron Emission Tomography (PET) is impractical for routine breast imaging. This is because the PET system is large, expensive, and requires a long scan time. Furthermore, it is

unable to detect very small lesions. **Craig Levin, Ph.D.,** at **Stanford University, Palo Alto,** is working in collaboration with Dr. James Matteson, at the University of California San Diego Center for Astrophysics and Space Studies, to develop a high-performance, compact, cost effective PET system dedicated to breast imaging. They are trying to develop a system that can see smaller lesions, that will have a shorter scan time, and that will cost significantly less than the currently available machine. If successful, this work could increase the role of PET in breast cancer management as well as bring PET to smaller clinics nationwide. Findings from this research were published in *PET Clinics* 2007(2)125 and *IEEE Transactions in Nuclear Science* 2007(M19-35)3700.

Combined Imaging Modalities for Breast Cancer
Dynamic contrast enhanced (DCE) MRI has become the most popular imaging technique for screening young women for breast cancer. DCE-MRI is also considered the best method available for screening women who have breast implants or scar tissue. However, DCE-MRI also detects many benign lesions, which can lead to unnecessary anxiety, biopsies, or over-treatment. **Gultekin Gulsen, Ph.D.,** at the **University of California, Irvine,** is developing a novel type of MRI that will improve upon the current DCE-MRI screening technology. The final version of this new imaging device is expected to be ready soon, and Dr. Gulsen and his colleagues have received funding from another source to continue their clinical research studies. This work has the potential to bring a new imaging device that surpasses what is currently available into the clinic setting. Results from this study were published in *Physics in Medicine and Biology* 2008(53)3189-200.

In Vivo MRS for Cancer Diagnosis and Treatment Monitoring
Magnetic resonance spectroscopy (MRS) is a non-invasive technique that can provide information about a tumor's metabolism. This information may be able to improve a doctor's ability to diagnose and treat breast cancer. **Hyeon-Man Baek, Ph.D.,** at the **University of California, Irvine,** investigated whether MRS improves the ability of dynamic contrast enhanced MRI (DCE-MRI) both to diagnosis breast cancer and to evaluate a tumor's response to chemotherapy given prior to surgery. Dr. Baek's team found that MRS did not improve the sensitivity (the false negative rate) of DCE-MRI in detecting breast cancer tumors. It did, however, improve the specificity (the false positive rate), which is consistent with previously published research. Dr. Baek also found that MRS appears to be better at detecting a tumor's response to chemotherapy than the current method, which involves physically measuring the tumor's size. Dr. Baek intends to conduct additional research on MRS in conjunction with DCE-MRI. This work could lead to improvements in how MRI is used to guide breast cancer treatment. Three papers were published with this grant support, including *Annals of Oncology* 2008(19)1022-4.

Removing Respiratory Artifacts in Nuclide Breast Imaging
Positron emission tomography (PET) breast exams typically require several minutes to acquire data, and the resulting image represents an averaging of tumor motion over several breathing cycles. This can make the picture of the breast cancer tumor blurry; it can also make it easy to miss a tumor. **Brian Thorndyke, Ph.D.,** at **Stanford University, Palo Alto,** explored ways to separate and the recombine the data acquired during a PET scan to reduce the impact breathing has on breast cancer PET imaging. His initial studies suggested that the technique he developed could have the potential to reveal small tumors that would otherwise have been missed. This work could lead to the development of data collection methods that improve the ability of PET scans to find breast cancer tumors.

rADDs: Novel Disintegrins Targeting Breast Cancer
Breast cancer cells have proteins on their surface that can be used as targets for anti-cancer treatments. These proteins can also be detected with special imaging agents. **Stephen Swenson, Ph.D.,** at the **University of Southern California, Los Angeles,** is exploring whether a fragment of a type of protein called natural human ADAM (A Disintegrin And Metalloproteinase) can bind to breast cancer cells and stop both tumor and blood vessel growth. Dr. Swenson and his team produced

a recombinant ADAM-Derived Disintegrin (rADD) protein, and studied the effect it had on breast cancer cell lines and the extracellular matrix (the scaffolding that surrounds and supports cells). They then used a mouse model to evaluate whether the rADD protein could limit cancer cell growth and stop tumors from making the blood vessels they need to grow and spread. In addition, they put an imaging agent on rADD proteins so that they could be identified on primary and metastatic tumors during a Positron Emission Tomography (PET) scan. This work could lead to the development of new ways of diagnosing and treating breast cancer.

Inhibition of the BRCA2-RAD51 Interaction in Breast Cancer

Women who inherit a mutation in the gene called BRCA2 (BReast CAncer 2) are at increased risk of developing breast cancer. BRCA2 works with a protein, called Rad51, to repair DNA breaks. If this BRCA2-Rad51 interaction is disrupted in a breast cancer cell, the cell will be more likely to respond to anti-cancer drugs. **Jiewen Zhu, Ph.D.,** at the **University of California, Irvine,** and colleagues had previously identified two small compounds, IBR1 and IBR2, which disrupt the BRCA2-Ra51 interaction, inhibit breast cancer cell growth, and make breast cancer cells more likely to respond to radiation or the chemotherapy drug cisplatin. In this project, Dr. Zhu tried to modify these two compounds to improve their effectiveness. So far, the new compounds Dr. Zhu and his team have developed have not proven to be more effective than IBR1 and IBR2. However, they have found compounds that are more soluble and stable, which is important for new drug development. Dr. Zhu and colleagues are continuing to search for a new, more effective IBR compound. This work could lead to the development of new treatments specifically for women with breast cancer who carry a BRCA2 mutation.

Breast Tumor Inhibition by Vitamin D in a Mouse Model

Clinical trials have demonstrated that the active form of vitamin D, called calcitriol, can delay cancer progression and prolong survival in prostate cancer patients without causing serious side effects. **David Feldman, M.D.,** at **Stanford University, Palo Alto,** used a mouse model to examine whether calcitriol is an effective breast cancer treatment when combined with non-steroidal anti-inflammatory drugs (NSAIDs) or an aromatase inhibitor. (Aromatase inhibitors are used to treat hormone-responsive tumors.) Dr. Feldman and his team found that when given alone, calcitriol decreased levels of COX-2, an enzyme that helps prostaglandins stimulate aromatase. It also decreased levels of aromatase and estrogen receptor alpha. A follow-up study found that when calcitriol and an aromatase inhibitor were given together, it was more effective in inhibiting tumor growth than either calcitriol or an aromatase inhibitor alone. These findings could pave the way for clinical trials that would evaluate whether a combination of calcitriol and an aromatase inhibitor were more effective than an aromatase inhibitor alone in treating women with breast cancer.

Inhibition of Breast Cancer Aggressiveness by Cannabidiol

Investigators are continually trying to identify effective cancer treatments that do not cause serious side effects. **Sean McAllister, Ph.D.,** at the **California Pacific Medical Center Research Institute,** San Francisco, and colleagues previously discovered that cannabidiol, a non-psychotropic component of the Cannabis sativa (marijuana) plant, can inhibit aggressive breast cancer cells from growing and spreading. This research project allowed Dr. McAllister and his team to conduct additional studies on cannabidiol's effectiveness in treating breast cancer. The research team discovered that cannabidiol was able to slow breast cancer growth in both a cell model and a mouse model. They also demonstrated, for the first time, that cannabidiol is able to decrease production of a protein, called Id-1, which is believed to make breast cancer more aggressive. Building on these findings, Dr. McAllister and his team made small structural changes to cannabidiol that could make it even better at inhibiting Id-1 and aggressive breast cancers. These findings could lead to the development of cannabinoid compound-based treatments for aggressive types of breast cancer. Findings from this research were published in *Molecular Cancer Therapeutics* 2007(6)2921.

Artemisinin Disrupts Estrogen Receptor-Alpha and Cell Growth

Breast cancer treatments that have fewer side effects than those currently available are widely needed. Natural plant compounds provide a potential source for these treatments. One promising natural compound is Artemisinin, which has been used by Chinese traditional medicine practitioners for at least two thousand years to treat fever. It has also been used since the 1970s as an anti-malaria drug. **Gary Firestone, Ph.D.,** at the **University of California, Berkeley,** and colleagues discovered that artemisinin is able to disrupt estrogen responsiveness in human hormone-responsive breast cancer cell lines. They also observed that artemisinin inhibits estrogen receptor-alpha (ER-alpha) without having any effect on estrogen receptor-beta (ER-beta). Following up on this finding, Dr. Firestone and his team uncovered an artemisinin-regulated region of ER-alpha that makes the ER-alpha gene sensitive to artemisinin. In addition, they demonstrated that not only does artemisinin disrupt estrogen responsiveness and the growth of human breast cancer cells, but that artemisinin and anti-estrogens work together to slow the growth of estrogen responsive breast cancer cells. This work could lead to the development of new artemisinin-based cancer treatments.

A Targeted Therapy for Wound-like Breast Cancers

When an injury occurs, cells that are normally dormant begin to divide rapidly in an effort to close up the wound. The cells' work includes remodeling the extracellular matrix that surrounds them, migrating across tissue planes, and sending out chemical signals to recruit new blood vessels. **Howard Chang, Ph.D.,** at **Stanford University, Palo Alto,** and colleagues previously discovered that some breast cancers exhibit wound-like features that can be distinguished by a specific pattern of 512 genes, which they call a "wound signature." They also showed that this wound signature is found primarily in tumors that are likely to metastasize. This project allowed Dr. Chang and his colleagues to identify cancer treatments that are able to target the breast cancer cells that exhibit this wound signature. One of the drugs they studied was bortezomib. It is an FDA-approved drug that is the first in a new class of medicines called proteasome inhibitors. Dr. Chang and his team found that bortezomib has the potential to be effective in treating breast tumors that have this wound signature. Dr. Chang and his team also were able to identify how bortezomib is able to block human breast cancer cell growth. This work could lead to new treatments for the subset of breast cancers that have the genetic pattern known as the wound signature.

Neural Stem Cell Therapy for Breast Cancer Brain Metastases

Breast cancer is the main source of metastatic brain disease in women, and nearly 30% of all women with advanced breast cancer will be diagnosed with brain metastasis. **Brunhilde Felding-Habermann, Ph.D.,** at the **Scripps Research Institute, La Jolla,** is exploring whether breast cancer brain cells can be targeted with neural stem cells, which are the body's own mechanism for healing and regeneration in the brain. Dr. Felding-Habermann and her colleagues previously showed that neural stem cells seek out cancerous areas in the brain and follow spreading breast cancer lesions within the brain tissue. In this research project, Dr. Felding-Habermann and her team used human and mouse tumor cell systems to follow the progression of metastasis development and observe how neural stem cells track the tumor cells in real time. This work showed that implanted neural stem cells seek out even widespread metastatic breast cancer lesions within the brain tissue. Dr. Felding-Habermann was funded by the CBCRP to continue to explore the safety and effectiveness of neural stem cell based treatments. This work could lead to new treatments for metastatic breast cancer that has spread to the brain.

Vascular Targeting Therapy for Breast Cancer

Women whose tumors express a large amount of a protein called Her-2/neu are at increased risk of having their cancer recur or of developing metastatic disease. The immune response does not respond to Her-2/neu because the protein is naturally present on the body's epithelial cells. **Albert Deisseroth, M.D., Ph.D.,** at the **Sidney Kimmel Cancer Center, San Diego,** and colleagues have developed a vaccine that can trick the immune system into responding to both Her-2/neu and the blood vessels that breast tumors develop as if they were a viral infection. In this project,

which used an animal model, Dr. Deisseroth and his team found that combining their vaccine with conventional chemotherapy resulted in a greater levels of immune response and cancer suppression than either the their vaccine or chemotherapy alone. Dr. Deisseroth and his team intend to conduct additional research on this new vaccine. This work could lead to new breast cancer treatments that are more effective than traditional chemotherapy regimens. Results from this research were published in *Molecular Therapy* 2008(16)1753-60.

Symposium on the Intraductal Approach to Breast Cancer

The Dr. Susan Love Research Foundation is committed to advancing research and developing resources that explore the intraductal approach to the breast. As part of this effort, **Susan Love, M.D., M.B.A.,** at the **Dr. Susan Love Research Foundation,** Santa Monica, and colleagues hosted The 5th International Symposium on the Intraductal Approach to Breast Cancer in Santa Monica, California, March 1-4, 2008. In attendance were more than 120 oncologists, epidemiologists, biostatisticians, surgeons, biochemists, pathologists, radiologists, endocrinologists, and breast cancer advocates who are currently conducting, or are interested in, research utilizing the intraductal approach.

The Symposium addressed topics ranging from "Anatomy of the Breast," and "Ductoscopy and Imaging," to "Intraductal Therapy," and "Nipple Aspirate Fluid: The Optimal Approach to Screening?" It also provided participants with the opportunity to observe demonstrations of ductoscopy and ductal lavage with ultrasound. A Public Panel provided the community with information about ongoing intraductal research. At the close of the Symposium, the Foundation awarded $100,000 in pilot grants to 12 research studies.

Grants in Progress: 2008

An Approach to Antiestrogen Resistance in Breast Cancer
Oksana Tyurina
University of California, San Diego

Breast Cancer Treatment Monitoring Combining MRI and Optics
Catherine Klifa
University of California, San Francisco

Chemical Inhibitors of Hsp70 for Breast Cancer
Chung-Wai Shiau
The Burnham Institute of Medical Research

Determinants of Response to Microtubule Stabilizing Drugs
Tatana Spicakova
Stanford University

Differential Optical Mammography
Gregory Faris and Christopher Comstock
SRI International and University of California, San Diego

Engineering EGFR Antagonists for Breast Tumor Targeting
Jennifer Lahti
Stanford University

Exploring the Role of PARP Inhibitors in Breast Cancer
Karlene Cimprich
Stanford University

Factors Influencing Breast Cancer Screening Among Older Thai
Bulaporn Natipagon-Shah and Mary Jo Clark
Thai Health and Information Service and University of California, San Diego

ID4: A Prognostic Factor of Breast Cancer Metastasis
Dave Hoon
John Wayne Cancer Institute

Inhibition of Brain Metastases in Breast Cancer
Brunhilde Felding-Habermann
Scripps Research Institute

Intraductal Therapy of DCIS: a Presurgery Study
Susan Love
Dr. Susan Love Research Foundation

Intraoperative Assessment of Surgical Lumpectomy Margins
Armando Giuliano
John Wayne Cancer Institute

Mechanisms of HSP90 Inhibitor Action in Breast Cancer
Cynthie Wong
Beckman Research Institute of the City of Hope

Modulation of Breast Cancer Stem Cell Response to Radiation
Frank Pajonk
University of California, Los Angeles

Molecular Imaging of Breast Cancer Using Breast PET/CT
John Boone
University of California, Davis

Molecular Imaging of Metastatic Lymph Nodes in Breast Cancer
Ella Jones
University of California, San Francisco

Multinuclear MRI of Breast Tumors
Brian Hargreaves
Stanford University

Neural Stem Cell Therapy for Breast Cancer Brain Metastases
Brunhilde Felding-Habermann
Scripps Research Institute

Novel Cytokine Immunotherapy for Breast Cancer
Ananda Goldrath
University of California, San Diego

Nur77-derived Peptides as a Novel Breast Cancer Therapy
Xiao-kun Zhang
The Burnham Institute of Medical Research

Polyamide HIF Inhibitors to Block Breast Cancer Metastasis
John Phillips
California Institute of Technology

Real-Time 3D Ultrasound Image-Guidance for Breast Surgery
Michael Bax
Stanford University

Sulforaphane: Its Potential for Treatment of Breast Cancer
Olga Azarenko
University of California, Santa Barbara

Topoisomerase-IIa as a Predictor of Anthracycline Response
Michael Press
University of Southern California

Research Initiated in 2008

Development of a Breast MRI Computer-Aided Diagnosis System
Ke Nie
University of California, Irvine

Functional Breast MRI with BOLD Contrast
Rebecca Rakow-Penner
Stanford University

Genetics of Tamoxifen Response
Elad Ziv
University of California, San Francisco

Imaging of Novel Stem Cell Therapy Targeting Breast Cancer
Joseph Wu, M.D.
Stanford University

Inhibition of TF Signaling as Novel Breast Cancer Therapy
Wolfram Ruf
The Scripps Research Institute

Nanotherapy for Breast Cancer Targeting Tumor Macrophages
Gaurav Sarma
The Burnham Institute for Medical Research

Novel Anti-HER2 Fragments for Better Detection and Therapy
Shannon Sirk
University of California, Los Angeles

Novel Small Proteins for PET Imaging of Breast Cancer
Zhen Cheng
Stanford University

Stratifying DCIS Biopsies for Risk of Future Tumor Formation
Thea Tlsty
University of California, San Francisco

Topoisomerase-IIa as a Predictor of Anthracycline Response
Michael Press
University of Southern California

Treating BC Brain Metastasis with Cytotoxic Lymphocytes
Barbara Mueller
Sidney Kimmel Cancer Center

The Biology of the Breast Cell

To understand the origin of breast cancers, more research is needed on the architecture, cell interactions, and molecular pathways in the normal breast. Understanding how cells coordinate migration, maturation, proliferation, and cell death over space and time gives us the foundation from which to learn what it is that makes a tumor cell. The CBCRP funded studies that model normal pre-cancer and tumor breast to learn how cancer develops, and moves to other parts of the body. Important basic science topics represented in CBCRP's portfolio include: exploring the role of stem cells in normal and tumor breast; cell proliferation control mechanisms through the estrogen receptor and growth factor receptors (e.g., Her-2); alterations in DNA repair processes that permit genetic damage to accumulate in cancer cells; cell cycle changes that permit division under conditions where normal cells would undergo programmed cell death (apoptosis); novel biomarkers to distinguish pre-cancerous and cancerous cells from normal breast epithelium and their validation as potential new detection and therapy targets, and developing methods for accounting for the complexity of the interplay of all of these factors in breast cancer.

Two research topics are presented in this section.

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

Research Conclusions

Normal Mammary Biology of Phosphorylated Prolactin
The hormone prolactin has two major forms, an unmodified form that promotes cell proliferation and a phosphorylated form that inhibits cell proliferation. **Ameae Walker, Ph.D.,** at the **University of California, Riverside,** and colleagues explored the effect of both types of prolactin on the breast. Ms. Walker and her team demonstrated that prolactin turns into the phosphorylated form that inhibits cell proliferation when the mammary gland. They also showed that unmodified prolactin makes changes in the cells that favor proliferation, whereas phosphorylated prolactin makes changes that reduce cell proliferation and, under some circumstances, lead to cell death. These findings suggest that phosphorylated prolactin is beneficial to breast health, and may help explain why breastfeeding reduces breast cancer risk. While conducting this research, Dr. Walker identified a new molecule inside breast cells. She also found that the ratio of this molecule to another molecule is associated with the absence or presence of breast cancer, and that breast cells grow faster when exposed to more of this molecule. This work could lead to new methods of assessing breast cancer risk that involve measuring prolactin levels. It also could lead to the development of new treatments that use phosphorylated prolactin (or a molecular mimic of it) to prevent or treat breast cancer.

Axon Guidance Proteins in Mammary Gland Development
The Slits are a protein family found in many organs, including the breast. Some studies have suggested that Slits are a tumor suppressor gene that can stop cancer cells from growing and spreading, but others have found that the Slit gene does not function in breast cancer cells. Using a mouse model, **Lindsay Hinck, Ph.D.,** at the **University of California, Santa Cruz,** and colleagues showed that the Slit gene stops functioning in breast cells that have increased levels of the protein Cxcr4 and a molecule related to it called Sdfe1. They also discovered that high levels of Slit are correlated with lower levels of Cxcr4 and decreased tumor growth, and that there is a similar inverse correlation between Slit and Cxcr4 expression in human breast tumor tissue. These findings support previous research that has demonstrated that Cxcr4 and Sdf1 play a pivotal role in breast cancer growth and metastasis. It also suggests that Slit may be a marker of whether a cancer cell has the potential

to become invasive. Dr. Hinck received a grant from the National Cancer Institute that will allow her to further investigate how Slit functions. This work could lead to the development of new treatment strategies to prevent invasive breast cancer. Findings from this research were published in *Development* 2006(133)823 and *Cancer Research* 2008(68)7919.

A Candidate Marker of Mammary Tumor Initiating Cells

Researchers have shown that only a small number of breast cancer cells are able to produce tumors when they are transplanted into an animal model. These cells, called cancer stem cells, may be good targets for drug treatments. However, no one has yet identified a functional marker on these cells. **Alexey Terskikh, Ph.D.,** at **The Burnham Institute for Medical Research,** La Jolla, and colleagues investigated whether a newly discovered gene, called MELK (maternal embryonic leucine-zipper kinase), might be a functional marker for breast cancer stem cells. Studies have shown that MELK is turned on in a number of different cancer cell lines, but the exact role it plays is not known. This project allowed Dr. Terskikh and his team to complete the animal breeding necessary to develop mice with the proper genetic structure needed for their experiments. The studies they conducted with these mice found that MELK appears to be a marker for breast cancer stem cells. This work suggests that the small molecule inhibitors of MELK that Dr. Terskikh's colleagues at the Burnham Institute for Medical Research are developing may make effective breast cancer treatments.

A New Marker for Mammary Epithelial Stem Cells?

Scientists believe that it is the breast epithelial stem cells that give the breast the ability to grow and start making milk after each pregnancy. **Robert Oshima, Ph.D.,** at **The Burnham Institute for Medical Research,** La Jolla, discovered a new marker gene, called maternal embryonic leucine-zipper kinase (Melk), on several types of stem cells. This research project allowed Dr. Oshima to explore in both cell and animal models whether Melk is also present in breast epithelial stem cells. Dr. Oshima and his team found that the dividing cells that contribute to the interior lining of the breast ducts are the breast cells that express the most Melk protein. But even though these cells increase rapidly, they do not have same ability that stem cells do to generate a new mammary gland. Dr. Oshima is continuing to explore the relationship between Melk-producing cells and cancer stem cells.

The Role of the ECM in Breast Cancer DNA Damage Repair

The extracellular matrix (ECM) provides structural support to cells. It also gives chemical cues that can stop cells from becoming cancerous. **Albert Davalos, Ph.D.,** at the **Lawrence Berkeley National Laboratory,** used 3-D breast cell and animal models to investigate the role the ECM's basement membrane plays in breast cancer progression. Dr. Davalos and his team found that exposing epithelial cells that lack a BRCA1 gene to drugs that disrupt cell replication causes them to develop a mutation in a key tumor suppressor protein called p53. In addition, they grow more rapidly and fail to die. Their research also showed that exposing cells that are missing the BRCA1 gene and the p53 protein to drugs that disrupt cell replication causes them to fail to die and to divide with numerous DNA breaks. Dr. Davalos and his team observed the same result when they turned off the special proteins in cells that "unwind" double-stranded DNA for replications and repair processes. These findings suggest that loss of a "caretaker" and "gatekeeper" protein, like p53, allows breast epithelial cells to evade cell death and divide with more DNA damage. While doing this work, Dr. Davalos and his team discovered that a protein called HMGB1 is secreted when other repair proteins are missing. Dr. Davalos and his team are now exploring whether HMBG1 is as an early biomarker of genetic instability in breast cancer. Findings from this research were published in *Cell* 2007(128)97.

Stem Cells of Molecularly Diverse ER-negative Breast Cancers

Cancer stem cells comprise only a small fraction of a tumor, but they play a critical role in tumor growth. In fact, 100 cancer stem cells implanted into a mouse can reproduce a large breast tumor, whereas 20,000 malignant epithelial cells will not generate a breast tumor at all. **Stefanie Jeffrey, M.D.,** at **Stanford University,** Palo Alto, used a

mouse implanted with human tissue to investigate whether two subtypes of estrogen receptor negative breast cancer have different cancer stem cell populations and to explore whether cancer stem cells are the same as circulating tumor cells. Dr. Jeffrey and her team found that circulating tumor cell gene expression could vary in a single human blood sample. They also found that, in some instances, the circulating tumor cells were similar to those seen in the primary tumor, whereas in other instances they were similar to the cells in the biopsy taken from the metastases. These findings advance our understanding of the cancer stem cells and circulating tumor cells and could help lead to the development of treatments targeted at specific types of tumor cells. Findings from this research were published in *BMC Genomics* 2006(7)231, *Bioinformatics* 2007(23) 957, *Breast Cancer Research* 9(2007) R30, *Molecular Biology* 2007(8)118, *Oncogene* 2007(26)6269, and *Radiology* 2008(246)367.

A Novel Epithelial-Stromal Model of Metastatic Breast Cancer

Identifying the genes that directly regulate cell physiology and architecture in the breast can help researchers understand how breast cancer tumors spread to other organs (metastasize). **Richard Neve, Ph.D.,** at the **Lawrence Berkeley National Laboratory,** and colleagues used an animal model to study the role a receptor, called EPHA2, and its protein, EFNA1, play in breast biology. They were interested in EPHA2 because it is seen in a subset of breast cancers that scientists have learned are predisposed to metastasis. Dr. Neve and his team found that reducing the EPHA2 protein keeps the cancer cells in triple-negative breast tumors from becoming invasive. (They are called triple negative because they are estrogen receptor, progesterone receptor, and Her-2 negative.) They also found that a malignant cell will not become invasive when it is adjacent to a cell with EFNA1 on its surface. This suggests that stromal cells (connective tissue cells) with EFNA1 on their surface may be able to stop breast tumors from becoming invasive. Dr. Neve and his team developed a screening system that mimics the stromal cells to study cell-to-cell interactions of EPHA2 and EFNA1 in a variety of breast tumor cell lines. These experiments indicated that this interaction has the potential to slow the growth of cancer cells. These findings provide evidence that EPHA2 plays a role in breast cancer metastasis and could lead to the development of new treatments for metastatic breast cancer.

MYC and CSN5 in the Breast Cancer "Wound Signature" Profile

In normal wound healing, as in cancer growth, there is rapid cell proliferation, cell migration, and new blood vessel development. For this reason, cancer is sometimes referred to as "wounds that do not heal." **Adam Adler, B.A.,** at **Stanford University,** Palo Alto, and colleagues previously found that when two genes, called CSN5 and MYC, are turned on, they induce a genetic process referred to as a "wound signature." Furthermore, when this "wound signature" is present, a breast cancer is more likely to become invasive. To investigate these findings, Mr. Adler and his team developed human and mouse cell models that would allow them to explore the role of CSN5 and MYC in promoting breast cancer progression. Mr. Adler and this team found that when CSN5 or MYC is turned off in this model, cancer does not progress. This means that both genes are necessary for cancer to develop. Additional animal model studies confirmed that CSN5 is required for MYC-induced breast cancer growth. These findings show that MYC and CSN5 play a critical role in regulating breast cancer progression, and they could lead to the development of new breast cancer treatments that target CSN5. Results of this research were published in *PLoS Genetics* 2007(3)91e and in *Cancer Research* 2008(68)369 and 506.

Role of Cell Division Asymmetry in Breast Cancer Stem Cells

Breast cancers contain a small population of breast cancer stem cells that appear to be more resistant to existing treatments than other tumor cells. **Claudia Petritsch, Ph.D.,** at the **University of California, San Francisco,** attempted to discover the very first changes normal stem cells undergo when they turn into breast cancer stem cells. Dr. Petritsch and her team began by developing a cell-based test to analyze the rate and nature of asymmetric cell division in mouse mammary stem cells. This test allowed them to show that normal breast stem cells undergoing asymmetric cell division generate another stem cell and a differentiating cell. They also showed that breast stem cells

that do not perform this asymmetric cell division properly generate too many breast cancer stem cells. Dr. Petritsch is now exploring what occurs when she disrupts asymmetric cell division by taking out the gene Lgl-1, which regulates asymmetric cell division in the developing breast. She is studying Lgl-1 because the human equivalent of this gene, called Hugl-1, is missing in 76% of breast cancers. Dr. Petritsch and her team also intend to investigate how Lgl-1 prevents cancer from developing by preserving normal asymmetric cell divisions. This work could lead to new treatments that more specifically target breast cancer stem cells and could lead to the development of tools for the early diagnosis of breast cancer.

Role of Integrins in Lymphangiogenesis During Breast Cancer

Breast cancer spreads predominantly through lymphatic vessels and lymph nodes. The lymphatic vessels that surround breast tissue consist of a single layer of cells, called lymphatic endothelium. **Barbara Susini, Ph.D.,** at the **University of California, San Diego,** previously found that the number of lymphatic vessels in breast tissue increases dramatically during breast tumor development, a process called lymphangiogenesis. Now, she is exploring the mechanisms that drive this increase in lymphatic endothelial cells or promote breast tumor cell invasion of the lymphatic vessels. Dr. Susini and her team found that growing lymphatic vessels and cells express only one protein; it is called alpha4/beta1, and it works with a molecule called VCAM in the metastatic process. They also found that the CCL21 protein and its receptor, called CCR7, help tumor cells get to the lymph nodes by making it easier for the tumor cells to attach to the lymphatic endothelium. Furthermore, they were able to identify which molecules interact with alpha4/beta1 to induce lymphatic endothelial cell migration. In addition, they discovered that tumor cells cause lymphatic vessels to grow both in the tumor and in the lymph nodes. This research advances our understanding of breast cancer metastasis and could lead to the development of new breast cancer treatments. Three papers were published on this research, including a summary in *Nature Reviews Cancer* 2008(8)604-17.

Imaging RhoC-induced Breast Cancer Invasion and Angiogenesis

Metastasis—the spread of cancer cells to other parts of the body—is the major cause of death in breast cancer patients. Metastasis is a highly dynamic process that occurs in several distinct steps. **Konstantin Stoletov, Ph.D.,** at the **Scripps Research Institute,** La Jolla, and colleagues grew human cancer cells that contained a metastatic gene, called RhoC, in optically clear Zebrafish so that they could directly observe how tumors grow, invade, and develop new blood vessels, a process called angiogenesis. Dr. Stoletov and his team found that a gene, called RhoC, causes the tumor cell to develop specific features that allow it to penetrate the blood vessel. They also found that tumor cells only penetrate the blood vessels in places where new vessels are currently developing, and that continuous secretion of the growth factor called VEGF is necessary to create an opening in the blood vessel for the cancer cell to pass through. These findings could lead to the development of new drug treatments that target these processes. Dr. Stoletov and his team are continuing to investigate how tumor cells and blood vessels interact during metastasis. Three papers were published on this research, including a summary in *Oncogene* 2008(8)604-17.

Identifying Metastatic Breast Cells from Peripheral Blood

Surgeons examine the lymph nodes of breast cancer patients to assess whether metastases has occurred. But this method is not perfect, and new approaches are needed. Studies have shown that tumors shed cancer cells into the blood when they become invasive. **Kristen Kulp, Ph.D.,** at the **Lawrence Livermore National Laboratory,** and colleagues are attempting to develop a blood test that could determine whether circulating tumor cells are present in the blood and, in turn, whether metastases has occurred. Dr. Kulp and her team identified a way to prepare cells for this type of analysis. However, the methods currently available to isolate circulating tumor cells are not able to detect as few as 10 cells in 15 milliliters of human blood, which is what would be necessary to identify metastases. As a result, they were not able to implement this new technique. Dr. Kulp and her team intend to monitor the development of new methods for cell isolation

and will continue to attempt to develop a blood test for breast cancer metastasis. Three publications resulted from this funding, including *Analytical Chemistry* 2006(78)3651-8 and *Journal of the American Society of Mass Spectrometry* 2008(19)1230-6.

The Role of Serine and Metallo-hydrolases in Breast Cancer

Extracellular and cell-surface enzymes (a type of protein made by cells) from the serine and metallo-hydrolase family are believed to play a role in breast cancer metastases. **Sherry Niessen, M.S.,** at **Scripps Research Institute,** La Jolla, and colleagues used the most advanced techniques available to identify and characterize novel serine and metallo-hydrolase enzymes that play a role in breast cancer biology. Ms. Niessen and her team found that a serine hydrolase called KIAA1363 was increased in tumors and aggressive cell lines. Additional studies showed that KIAA1363 regulated levels of a family of lipids known as monoalkylglycerol ethers (MAGEs); had an impact on a larger lipid signaling network that included lysophosphatidylcholine (alkyl¬LPC) and lysophosphatidic acid (alkyl-LPA); and suggested that KIAA1363 has an effect on these lipids. Ms. Niessen and her team were able to define an aggressive gene signature regulated by KIAA1363. This signature included a protein called Fra-1, which they demonstrated is regulated by both alkyl-LPC and alkyl-LPA. These findings indicate that KIAA1363 is an important molecule in human cancer biology, and contribute to our understanding of the role enzymes play in breast cancer progression.

Twist Activation in Breast Cancer Metastasis

Metastasis occurs when tumor cells spread from a primary site to distant organs and establish secondary tumors. During metastasis, tumor cells obtain the ability to break away from their neighbor cells and migrate. **Jing Yang, Ph.D.,** at the **University of California, San Diego,** previously showed that tumor cells activate a gene called Twist to begin this process. She is now using a mouse model to investigate how Twist gets breast tumor cells to spread to distant organs. Dr. Yang found that turning the Twist gene "on" alters the form and structure of the breast. She also found that turning on Twist is sufficient to get certain human breast cancer cells to spread to distant organs, such as the lung. Using human tumor cells, Dr. Yang and her team demonstrated that Twist appears to facilitate metastasis. However, continued Twist expression appears to inhibit proliferation at metastatic sites, like the liver and lung. Dr. Yang and her team have generated new mouse models that will allow them to learn more about the impact Twist has on breast tissue. This work could establish Twist as an important prognostic marker. It could also lead to the development of new drug treatments for metastatic breast cancers.

Identification of Metastasis Competent Breast Cancer Cells

It currently is not possible to diagnose the earliest stages of metastasis. As a result, many women undergo chemotherapy and radiation to kill metastatic cells, even though it's not known whether they are present. These post surgical treatments undoubtedly save lives, but they have no medical benefit if the cancer has not spread. **Barbara Mueller, Ph.D.,** at the **La Jolla Institute for Molecular Medicine,** is developing tools that can measure a cancer cell's ability to cause metastasis before metastasis actually occurs. Dr. Mueller and her team have identified four specific molecules that, when present, appear to indicate that a breast cancer cell has the capability to metastasize. Dr. Mueller is currently seeking funding from the National Institutes of Health to conduct the additional studies necessary to validate these findings. The ability to identify cells with metastatic potential could result in more effective use of existing treatment options. It could also lead to the development of new treatments for early stage metastatic disease.

Modeling, Targeting Acetyl-CoA Metabolism in Breast Cancer

Cancer cells differ from normal cells in that they grow uncontrollably, require increased energy, and withstand low pH and low oxygen conditions. In addition, cancer cells use glucose as an energy source in ways that normal cells do not. **Chen Yang, Ph.D.,** at **The Burnham Institute for Medical Research,** La Jolla, studied how breast cancer cells metabolize glucose in an attempt to develop an anticancer drug that would interrupt this process. By comparing normal and breast cancer

cells, Dr. Yang was able to pinpoint tumor-specific metabolism and characterize the metabolic changes that occur during cancer development. He was also able to select a set of prospective drug targets. Dr. Yang is continuing to study the genetic patterns in breast cell metabolism to determine the best ways to target this process. The research was published in *Breast Cancer Research* and *Treatment* 2008(100)297-307 and *Metabolomics* 2008(4)13-29.

The Role of Estrogen-Related Receptors in Breast Cancer

The small family of estrogen-related receptors consists of three proteins that control the expression of many genes important in maintaining normal cell growth. The three estrogen-related receptors are similar to the estrogen receptors, but they are not activated by natural estrogens. This similarity has led researchers to hypothesize that estrogen-related receptors, like estrogen receptors, play a role in breast cancer development or growth. **Anastasia Kralli, Ph.D.,** at the **Scripps Research Institute,** La Jolla, used human breast cancer cells to study estrogen-related receptors and the role they play in breast cancer growth, metastasis, and response to drugs. Dr. Kralli and her team found that cells with higher levels of estrogen-related receptor activity responded as expected to chemotherapy drugs in cell culture studies. However, these cells were not able to grow and develop when transplanted into the breast area of mice. These findings demonstrate that certain changes in estrogen-related receptor activity appear to keep breast cancer tumors from growing in animal models. This work could lead to the development of new treatments that use estrogen-related receptor molecules to slow breast cancer growth.

The Role of LMO4 in Breast Cancer

Cancer cells have acquired genetic mutations that give them the ability to grow and divide uncontrollably. **Zhengquan Yu, Ph.D.,** at the **University of California, Irvine,** and colleagues investigated whether a protein called LMO4, which is found in breast epithelial cells (the cells in which breast cancer begins), helps to regulate cell proliferation and cell death. Dr. Yu and his team also explored whether cells that have too much of this protein begin to grow and divide uncontrollably. Using a mouse model, Dr. Yu and his team showed that mammary epithelial cells that lack an LMO4 gene are less likely to divide and more likely to die. While conducting these studies, the research team found that another gene, called BMP7, is regulated by LMO4 in breast cancer cells. Dr. Yu and his team intend to continue to study the role of BMP7 in mammary gland development and breast cancer. This work could advance our understanding of how breast cancer develops. Results from this research were published in *Oncogene* 2007(26)6431-41.

Grants in Progress: 2008

Analysis of MicroRNA Expression in Breast Cancer Stem Cells
Yohei Shimono
Stanford University

Breast Cancer Studies in a 3-D Cell Culture System
Robert Abraham
The Burnham Institute of Medical Research

Breast Tumor Responses to Novel TGF-beta Inhibitors
Kelly Harradine
University of California, San Francisco

Competition for ADA2 and 3 to Inhibit p53 in Breast Cancer
Min Yang
University of California, Irvine

Cytoskeletal Regulation of Invading Breast Cells
Catherine Jacobson
University of California, San Francisco

Defining Mammary Cancer Origins in a Mouse Model of DCIS
Alexander Borowski
University of California, Davis

Determination of Stromal Gene Expression in Breast Cancer
Robert West
Palo Alto Institute for Research & Education

Functional Analysis of BORIS, A Novel DNA-binding Protein
Paul Yaswen
Lawrence Berkeley National Laboratory

Indole (I3C) Control of Breast Cancer by ER Downregulation
Crystal Marconett
University of California, Berkeley

Inflammation Alters Transcription by ER in Breast Cancer
Eliot Bourk
University of California, San Diego

Lipid Raft Composition in Deregulated ERBB2 Signaling
Ralf Landgraf
University of California, Los Angeles

Mechanisms of Daxx-mediated Apoptosis in Breast Cancer
Lorena Puto
The Burnham Institute for Medical Research

A New Mouse Model of PI3-kinase Induced Breast Cancer
Jun Zhang
University of California, San Francisco

Novel Approach to Analyze Estrogen Action in Breast Cancer
Brian Elicieri
La Jolla Institute for Molecular Medicine

Novel Regulation of the Rb Pathway in Breast Epithelium
Deborah Burkhart
Stanford University

Profiling Drug Metabolism (P450) Proteins in Breast Cancer
Aaron Wright
Scripps Research Institute

Reactivation of the Inactive X Chromosome and Breast Cancer
Angela Anderson
University of California, San Francisco

Regulation of Mammary Epithelial Invasion by MMPs and FGFs
Andrew Ewald
University of California, San Francisco

The Relationship of BRCA1 and HMGA2 in Breast Cancer
Connie Tsai
University of California, Irvine

The Role Chk1 in Breast Cancer DNA Damage Repair
Jennifer Scorah
Scripps Research Institute

The Role of Podosomes in Breast Cancer Metastasis
Barbara Blouw
The Burnham Institute of Medical Research

Stem Cells in Breast Cancer Metastasis
Brunhilde Felding-Habermann, John Yates & Evan Snyder
Scripps Research Institute and The Burnham Institute of Medical Research

Structural Analysis of Cancer-relevant BCRA2 Mutations
Henning Stahlberg
University of California, Davis

Targeting Tissue Factor in Breast Cancer
Florence Schaffner
Scripps Research Institute

Telomerase, Mammary Stem Cells, and Breast Cancer
Steven Artandi
Stanford University

Trask, a Candidate Breast Cancer Metastasis Protein
Ching Hang Wong
University of California, San Francisco

Research Initiated in 2008

Chemokine Receptor Signaling in Breast Cancer
Morgan O'Hayre
University of California, San Diego

Dietary Metabolite Inhibition of Breast Cancer Cell Survival
Holly Hantz
University of California, Berkeley

Dissecting the Role of Twist in Breast Cancer Metastasis
Janine Low-Marchelli
University of California, San Diego

Global Analysis of Protein Ubiquitination in Breast Cancer
Stefan Grotegut
Sidney Kimmel Cancer Center

Maternal Embryonic Leucine Zipper Kinase in Mammary Tumors
Robert Oshima
The Burnham Institute for Medical Research

Nanolipoproteins to Study Breast Cancer Growth Receptors
Paul Henderson
University of California, Davis

Regulation of Breast Stem-progenitor Cell Chromatin by Pygo2
Bingnan Gu
University of California, Irvine

Role of Estrogen-modulated Protein AGR2 in Breast Cancer
Mikhail Geyfman
University of California, Irvine

Tumor Suppressor 14-3-3sigma in Breast Cancer Progression
Aaron Boudreau
Lawrence Berkeley National Laboratory

Improving the CBCRP through Evaluation

One third of those receiving CBCRP Postdoctoral Fellowships used their grant to switch to breast cancer from another field.

California taxpayers deserve to have the funds they provide for breast cancer research spent wisely. That's why the California Breast Cancer Research Program is conducting a multi-year, formal evaluation of the entire program. Evaluation helps the program target research dollars where they will do the most to reduce and end the suffering caused by breast cancer.

Over the past several years, the CBCRP has evaluated several of its award types: the Community Research Collaboration awards, the Postdoctoral Fellowship awards, the New Investigator awards, and the Innovative, Developmental, Exploratory Awards (IDEAs). The results of these evaluations were used by the CBCRP's advisory Breast Cancer Research Council to set priorities. These evaluations are available in print to the public and can also be viewed on the Program Web site.

Dissertation Awards Evaluation. During 2008, the CBCRP evaluated the Program's Dissertation Awards, which fund research performed by graduate students as part of the requirements they complete to receive a Ph.D. degree. The evaluation found that these awards are meeting several goals they were established to achieve. Receiving a CBCRP Dissertation Award helped develop the students' careers. The CBCRP funding was also used by the students' mentors to leverage large amounts of additional funding for breast cancer research. However, an important goal of the Dissertation Awards is to train the breast cancer researchers of tomorrow. Only a minority—26 percent—of those who received CBCRP Dissertation Awards are staying in the breast cancer research field.

Postdoctoral Awards Evaluation. This year, the CBCRP also conducted the second evaluation of the Program's Postdoctoral Fellowship Awards. These fellows—including graduates having recently completed their Ph.D.s, physicians continuing research activity, and individuals in transition to breast cancer research from another field—receive CBCRP financial support to obtain their postdoctoral training under a designated mentor experienced in breast cancer research. The evaluation found that these awards are meeting important goals set by the CBCRP. The majority (63 percent) of those who received these fellowships continued to be involved in breast cancer research after their fellowships ended, and a total of 84 percent were involved in some type of work related to breast cancer. One third of those receiving CBCRP Postdoctoral Fellowships used their grant to switch to breast cancer research from another field. These awards also allowed the fellows to leverage millions in additional funding for breast cancer research, assuring that the lines of inquiry they are pursuing will go forward in the future. In addition, almost three quarters of CBCRP Postdoctoral Fellows said the award gave them the opportunity to do relevant breast cancer research that they would otherwise not have been able to do.

The results from these evaluations will contribute to the CBCRP's current three-year priority setting process, which will be completed in 2010. Previous priority-setting evaluation processes have led to major improvements in the type of research the CBCRP funds.

Evaluation Leading to Improvement

Formal evaluations are used to improve the CBCRP. Examples of changes in the program made as a result of evaluations include:

- The CBCRP's first formal evaluation of the program's Community Research Collaborations, in 2000, led to a multi-year effort that has increased the number of community organizations and scientific researchers collaborating on breast cancer research questions of interest to communities of California women. This effort is discussed more fully in this report in the section titled "Collaborating with Breast Cancer Activists and California Communities."
- The CBCRP's second formal evaluation of the Community Research Collaborations, conducted in 2005, highlighted a problem facing the research teams. Once they had successfully tested an intervention, they encountered difficulty applying their research results because of lack of funds. This led to the CBCRP providing a new grant opportunity, where successful research teams can apply for an additional grant to make their results available to other programs, apply their results to changing public policy, or make the public more aware of their results. The evaluation also resulted in the CRC grant amount being increased to $150,000 for pilot awards and $600,000 for full awards.
- The CBCRP's third formal evaluation of the Community Research Collaborations, conducted in 2007, led to the Program modifying the application process for these grants. Some parts of the application process were helpful to only a portion of the applicants, and these parts have been made optional.
- A previous three-year priority-setting process led the CBCRP to discontinue award types that were not meeting the program's goals. It also led to the CBCRP investing 30 percent of its funds in the Program's Special Research Initiatives, in order to answer crucial questions about the influence of the environment on breast cancer, and to uncover the reasons why some groups in California bear more of the burden of the disease. For more on the CBCRP's Special Research Initiatives, see the previous section of this report titled, "The CBCRP's Strategy for Allocating Research Funds."
- CBCRP staff and the Program's advisory council informally evaluated how CBCRP-funded research gets translated into new medications, new detection methods, new programs to support patients, policy changes, or other actions that have an impact on breast cancer. As a result, applicants for CBCRP research grants are now required to describe the steps necessary to translate their research project into action that impacts the disease. This has enabled the Program to target its limited funds toward research most likely to lead to progress against breast cancer.

Relationship between Federal and State Funding for Breast Cancer Research

The California Breast Cancer Research Program's primary source of funds, from a State tax on cigarettes, is unique among agencies that fund breast cancer research across the nation—and is declining and temporary.

The California Breast Cancer Research Program is distinct from research programs funded by the federal government in both the CBCRP's sources of funding and in the types of research funded.

The CBCRP's Source of Funding: Unique Among The Nation's Breast Cancer Research Agencies

The primary source of funding for the CBCRP is a 45 percent share of revenue from a two-cent State tax on cigarettes. This source of funding is unique among agencies that fund breast cancer research across the nation.

In contrast, funding for breast cancer research at other programs in the U.S. comes from a variety of different sources:

- **Federal Agencies** (National Institutes of Health, Department of Defense) receive funding through Congress from the national budget and from the public's voluntary purchase of more expensive postage stamps
- **National Voluntary Health Organizations** (such as the American Cancer Society, Komen Foundation, Breast Cancer Research Foundation, Avon Foundation) receive funding through charitable contributions from individuals, corporations, and foundations
- **Regional Nonprofit Organizations** (such as the Entertainment Industry Foundation, The Wellness Foundation) also receive funding through charitable contributions
- **State Agencies** (such as the New Jersey Breast Cancer Research Fund, Illinois Ticket for the Cure State Lottery, and the Cancer Prevention and Research Institute of Texas, the latter a new program that includes breast cancer) receive funding from state general funds, auto license fees, lottery ticket sales and voluntary donations on individual state income tax returns

The California Breast Cancer Research Program's primary source of funds, from a State tax on cigarettes, is declining and temporary. In the past, measures were proposed in the California State Legislature that would have had the indirect effect of decreasing funding for the CBCRP by $5 million; similar measures may be proposed, and may pass, in the future.

The CBCRP also receives some funding from the income tax check-off program, which allows individuals the opportunity to make voluntary donations on state income tax returns. Voluntary tax contribution funding is a result of legislation passed by the California State Legislature that authorizes donations for five years. During 2007, AB28, a bill authored by Assembly Member Jared Huffman, became law. This legislation provides individuals the opportunity to make donations to the CBCRP through voluntary tax contributions through 2012.

To increase these sources of revenue, the CBCRP conducts a public outreach and fundraising effort, the Community Partners Program. This effort, begun in 2002, has led to an increase in donations to the CBCRP from individuals, businesses, and foundations. The CBCRP's Community Partners Program is discussed more fully in the section of this report titled "Increasing Funding for and Awareness of Breast Cancer Research."

Types of Research Funded by the CBCRP: Complementing, Not Duplicating, Federal Efforts

The CBCRP has a deep commitment to using the funds provided by the State of California in the most efficient and cost-effective manner, and to adhering to the Program's mandate as defined by the California Legislature. One of the CBCRP's mandates is to "fund innovative and creative research, with a special emphasis on research that complements, rather than duplicates, the research funded by the federal government." The CBCRP fulfills this mandate in three ways:

1. By funding breast cancer research areas that could have a major impact on breast cancer—including leading to prevention and cure—that are not getting sufficient attention from the federal government;

2. By having expert reviewers from across the U.S. review grant applications for their innovation and impact;

3. Before funding a grant application, reviewing it for overlap with current and pending funding from other agencies;

4. By taking leadership to reduce barriers and waste in state, federal, and international breast cancer research funding.

Funding Promising Areas of Research That Have Not Received Sufficient Attention

The federal government's method for funding research has led to some promising areas of breast cancer research being under-funded. The federal government funds most health-related research through the National Institutes of Health (NIH). The NIH view is on "capitalizing…investigator-initiated research." The primary basis on which the NIH chooses grants for funding is their scientific merit, not their relevance to a particular disease. As a result, most research proposals submitted to the NIH address scientific questions in which the investigators have theoretical and empirical interest, even though there may be no clear relevance to particular diseases.

Only a small percentage of NIH funds go to research in issues the NIH has identified as particularly important to specified diseases (i.e., Requests for Applications). The majority of NIH funds support the most scientifically meritorious research regardless of the applicability of the research to particular diseases.

In contrast, a fundamental priority for the CBCRP is to fund research that will speed progress in preventing and curing breast cancer. The CBCRP's advisory Breast Cancer Research Council sets the Program's funding priorities, taking into account:

- Opinions from national breast cancer experts
- Opinions from California advocates and activists, healthcare providers, public health practitioners, community leaders, biotechnology scientists, and academic researchers
- Current literature on breast cancer and current gaps in knowledge

The council attempts to identify and fill important gaps in knowledge about breast cancer and reviews priorities yearly in light of changes in the research field, successes and failures of previous funding initiatives, and the results of previous funding.

The CBCRP is conducting a program initiative begun in 2005 to fill a significant gap in breast cancer research. The Special Research Initiatives addresses three overlapping research questions that California is uniquely positioned to address. They are environmental links to breast cancer, the reasons for the unequal burden of breast cancer among various populations of women, and the intersections of multiple factors that impact breast cancer. More information on these Special Research Initiatives may be found in a previous section of this report, "The CBCRP Strategy for Allocating Research Funds."

Choosing Research for Innovation and Impact

The CBCRP created its own scoring system to allow the Program's expert reviewers to differentiate applications that are especially innovative and that have the most potential impact on breast

cancer. The scoring system has improved the Program's 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 National Institutes of Health, scored funding proposals with a single score based solely on scientific merit. With this method, 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 a flawed research plan to test a novel idea. The CBCRP's scoring method, based on the recommendations of an NIH Advisory Committee, can distinguish these two applications. The CBCRP scores applications separately for innovation, impact, approach, and feasibility. The CBCRP's advisory Breast Cancer Research Council uses these separate scores to inform their funding recommendations. Under the CBCRP's "impact" criterion, researchers are required to describe the steps necessary to turn their research into products, technologies, or interventions that will have an impact on breast cancer, and describe where their study fits into this critical path.

Reviewing Grant Proposals for Overlap with Federal Funding

As a final step to ensure that CBCRP-funded research doesn't duplicate federally-funded research, breast cancer science experts in other states and Program staff scientists review all grants recommended for funding for overlap with current and pending federal grants. If overlap with federal funding is found, the overlapping grant (or portion of the grant) is not funded.

Taking Leadership to Reduce Barriers and Waste In Federal, State, and International Funding

The CBCRP is part of a nationwide effort to reduce barriers and waste in research toward the goal of ending breast cancer. Along with other U.S. breast cancer research funding agencies, industry representatives, regulators, advocates, and social scientists, the CBCRP participates in the National Breast Cancer Planning Committee, which is reviewing the national breast cancer research agenda and assisting U.S. breast cancer organizations in identifying gaps, opportunities, and overlaps in research into the disease. The committee will also produce a report to the general public on how key breast cancer organizations use donations to fund research.

In addition, the CBCRP has joined with seven other cancer research funding organizations in the U.S., 15 of the largest government and charitable cancer research funders in the United Kingdom, and the key government and non-government cancer research funders in Canada in the International Cancer Research Portfolio (ICRP). The organizations that make up the ICRP are working to make it easier to avoid duplication among research funding agencies and to speed progress in breast cancer research by increasing communication among agencies that fund breast cancer research.

One way the ICRP pursues these goals is by developing a research classification system to encourage agencies to report their funding in a way that is more accessible and meaningful to other agencies and the public. The ICRP also has a Web site (www.cancerportfolio.org) that includes research abstracts from more than 14,000 current and past research projects. The online database is searchable by cancer type, scientific area, funding organization, and other selected criteria. The Web site allows scientists to identify possible collaborators, plan their research based on current research, and facilitate dialogues among cancer researchers. Access to this information about ongoing research also aids research funding organizations in strategic planning for future spending. In addition, the Web site is a useful tool for other groups. Policy makers may use the database during the formulation of new health care and service delivery policies. Healthcare professionals, patients, survivors, and advocates may review the current status of funded research.

The CBCRP and the Program's partners in this effort are dedicated to making current research information available to funding agencies and the public, and to promoting scientific collaboration. To extend coordination further, the ICRP

partners invite representatives from the other organizations to attend their scientific meetings and review in person their funded research. During 2008, the ICRP took international coordination to a higher level by conducting an evaluation of the career development funding trends in the U.S. and U.K. In 2009, the ICRP will publish a review of cancer research funding patterns in the U.S., U.K., and Canada that will point to gaps in research and make recommendations for research priorities to fill those gaps.

Increasing Funding for and Awareness of Breast Cancer Research

Funding from the State cigarette tax decreases every year.

To increase its revenue, the CBCRP began its Community Partners Program in 2002. Its two goals are: (1) Increasing donations to the CBCRP through the California income tax voluntary contribution program and (2) Increasing public awareness of breast cancer, breast cancer research, and the California Breast Cancer Research Program.

Ensuring the CBCRP's present funding sources and increasing funds from new sources are necessary. CBCRP funding from the State cigarette tax decreases every year. Moreover, current funds are not sufficient to do all that needs to be done. During 2008, the CBCRP turned down grant applications requesting a total of $12,751,425 that were rated by expert reviewers as having sufficient scientific merit for funding.

To increase its revenue, the CBCRP began its Community Partners Program in 2002. The Community Partners Program pursues two goals:

- Increasing donations to the CBCRP through the California income tax voluntary contribution program and new sources;
- Increasing public awareness of breast cancer, breast cancer research, and the California Breast Cancer Research Program.

Community Partners: Increasing Voluntary Donations to the CBCRP

The Community Partners Program has led to growth and diversification in donations to the CBCRP. During 2008, the CBCRP received major funding from the California state income tax check-off program and from private foundations. In addition, the public took a number of other opportunities to donate to the CBCRP.

California State Income Tax Check-Off Program. More than 43,500 individuals donated over $568,000 to the CBCRP during 2008 through the state income tax check-off program. This made the CBCRP one of the check-off program's top beneficiary organizations for the year.

The following grants were funded in part through voluntary tax contributions in 2008:

Reproductive Concerns and Depression among Younger Survivors
Jessica Gorman, University of California, San Diego

Pesticide and Gene Interactions in Latina Farm Workers
Paul Mills, Ph.D., MPH, University of California, San Francisco

Nanotherapy for Breast Cancer Targeting Tumor Macrophages
Gaurav Sarma, Ph.D., The Burnham Institute for Medical Research

Stratifying DCIS Biopsies for Risk of Future Tumor Formation
Thea Tlsty, Ph.D., University of California, San Francisco

Faith Fancher Research Award
Faith Fancher was a long-time television news anchor and personality with KTVU (Oakland) who waged a very public battle against breast cancer. She also was the founding member of the CBCRP Executive Team, which formed in 2001 to help raise the visibility and fundraising profile of our program. Faith passed away in October 2003 after a six-year struggle with breast cancer. In Faith's honor we have created the annual Faith Fancher Research award, which is presented to a researcher, institution, or community-based organization whose work reflects those values that Faith held most closely and extends the work that Faith did for all women facing breast cancer. The advisory Breast Cancer Research Council named Georgia Sadler, Ph.D. M.B.A., University of California, San Diego, Natasha Riley, M.A., Vista Community Clinic and Vanessa Malcarne, Ph.D., San Diego State, Research Foundation the recipients of the Faith Fancher award for a grant,

entitled **Breast Cancer Clinical Trials Education Program.**

Foundations. During 2008, two foundations signaled their approval of the CBCRP's pioneering efforts by joining with the Program to support our leading-edge research.

- The Avon Foundation contributed $500,000 to support three of the CBCRP's groundbreaking Special Research Initiatives. The funds help support two studies examining long-term environmental exposures and breast cancer in large, diverse population groups and a third study investigating why women from some minority groups, once they are diagnosed with breast cancer, are less likely than others to be successfully treated
- The California Community Foundation contributed $31,000 to support a new CBCRP-funded study that explores emerging concerns about whether grapefruit increases breast cancer risk for post-menopausal women

United Way. The CBCRP is a participant organization in the Community Campaign of the United Way of California, which allows residents of the state to make donations at their place of work. During 2008, the CBCRP received donations from the United Way of the Bay Area, United Way of the Capitol Region, United Way Silicon Valley, United Way Southeastern Philadelphia, and the United Way State Employees Charitable Campaign.

Individual, Business, and Community Group Efforts. This year, the public demonstrated continued enthusiasm for the CBCRP's research. Runners participating in the San Francisco Marathon raised almost $11,000 for the CBCRP. The top fundraiser was runner Dipa Valambhia, who brought in $2,496; second was Christian Fitchett with $1,910; and third was Lauren Holmes, with $1,250. Businesses that made donations to the CBCRP included the Avon Foundation, Spectrum Clubs Inc., and Life Sera.

Business and Employee Giving Campaigns. Businesses that made the CBCRP the beneficiary of their community or employee fundraising efforts included: California State Employees Contribution Program, AT&T Employee Giving Program, Amgen Corporation Matching Gift Program, and Wells Fargo Community Support Campaign. In addition, the CBCRP received contributions from the Kaiser Permanente Community Giving Campaign, and the Superior Court of California - County of San Bernardino.

The public has also responded to the opportunity to make donations via the Program's Web site, www.CABreastCancer.org.

Community Partners: Increasing Awareness of Breast Cancer Research and of the CBCRP's Work

During 2008, the CBCRP's outreach campaign focused on raising awareness of breast cancer research results and the Program's work. The campaign also concentrated on increasing citizen contributions via their state income tax forms.

With the assistance and participation of Community Partners, individual donors to CBCRP, and breast cancer advocacy organizations, the CBCRP held public exhibits over the past year calling attention to the opportunity to donate to the CBCRP on state tax returns. During 2008, in addition, the CBCRP conducted a combined outreach effort, named Checkoff California, with other California nonprofit organizations who receive state tax return contributions. Together, the CBCRP and these nonprofit organizations created a radio and Internet marketing campaign to alert the public to the income tax check-off program. The campaign was conducted in partnership with the tax preparation firm Jackson Hewitt and California radio stations. It included radio public service announcements in English and Spanish, along with a Web site highlighting all nonprofit organizations included in the income tax check-off program. To augment this campaign, the CBCRP conducted its own on-air and Internet-based campaign alerting the public to the opportunity to make donations to the CBCRP via the income tax check-off. The campaign included radio spots on the Bay Area's Alice radio station. Targeted advertising was mailed to CBCRP and University of California contacts. Governor Arnold Schwarzenegger further boosted California's awareness of the opportunity to make donations through the tax check-off by issuing an official

proclamation declaring March as Check-off California Month.

The CBCRP's special Web site dedicated to the income tax check-off, www.endbreastcancer.org, informed stakeholders about fundraising progress. It also summarized progress researchers achieved with the grants funded via contributions made on state income tax returns.

The CBCRP gained exposure in a variety of media over 2008, including:

- CBCRP Director Dr. Marion H. E. Kavanaugh-Lynch was interviewed for a TV documentary to be aired in the nation of Kosovo
- Newspapers and TV and radio stations covered the CBCRP's Special Research Initiatives in the California cities of San Diego, Sacramento, San Francisco, and Eureka, and in places as far away as North Carolina, Canada, and the United Kingdom
- Information about CBCRP programs and research was selected for posting on highly-regarded Web sites dealing with health news.

Research on Women and Minorities

When breast tumors are diagnosed, they are often classified by stage. In general, the lower the stage, the more likely a woman is to survive.

However, women from some racial and ethnic groups are less likely to survive than women from other racial and ethnic groups diagnosed at the same stage.

The CBCRP is funding a $300,000 feasibility study to determine whether the data from existing California studies can be combined in order to provide a more complete, birds-eye picture of why this is so.

If it proves feasible to combine the studies and answer meaningful research questions, the CBCRP will provide $3.9 million for such a study.

Forty-four percent (19 of 43) of the grants and initiatives that the CBCRP awarded in 2008 studied either women or tissues from women, while the remaining 58 percent were laboratory studies that did not directly involve women or tissues from women.

Of the 19 grants and initiatives that involved women or tissues from women, 79 percent (15) collected new information from and about women.

Out of the 15 studies that included women:

- Eighty-seven percent, (13) grants include minority women in the study.
- Forty-seven percent, (7) are focused on minority women.
- Sixty percent, (9) are focused on underserved women.

A total of nine grants were funded with a primary emphasis on minority and/or underserved women:

Adapting a Breast Cancer Education Program for South Asians
Beth Glenn, Ph.D., University of California, Los Angeles
Zul Surani, B.S., South Asian Cancer Foundation, Mission Hills

Breast Cancer Clinical Trials Education Program
Georgia Sadler, Ph.D. M.B.A., University of California, San Diego
Natasha Riley, M.A., Vista Community Clinic
Vanessa Malcarne, San Diego State University

An Ecological Study of Quality of Life in Low-Income Women
Yoshiko Umezawa, M.H.S., University of California, Los Angeles

Increasing Mammography Screening in Latinas with Diabetes
Stergios Roussos, Ph.D., M.P.H., San Diego State University Research Foundation
Christine Noguera, M.S., Golden Valley Health Center

Latina Breast Cancer Survivors…Our Experience
Brian Montano, M.P.H., University of California, Los Angeles
Diana Tisnado , M.P.A., Ph.D., University of California, Los Angeles

Mindful Movement Program for Breast Cancer Survivors
Rebecca Crane-Okada, Ph.D., RN, AOCN, Beckman Research Institute
Holly Kiger, R.N., M.N., WISE & Healthy Aging

Pesticide and Gene Interactions in Latina Farm Workers
Paul Mills, Ph.D., M.P.H.
University of California, San Francisco

Quality of Mammography Facilities Serving Vulnerable Women
Lauren Goldman, M.D.
University of California, San Francisco

Reproductive Concerns and Depression among Younger Survivors
Jessica Gorman, M.P.H.
University of California, San Diego

Understanding Racial and Ethnic Differences in Stage-Specific Breast Cancer Survival: a Pilot Study
Katherine Henderson, Ph.D., Beckman Research Institute, City of Hope
Anna Wu, Ph.D., University of Southern California
Kristine Monroe, Ph.D., University of Southern California
Marilyn Kwan, Ph.D., Kaiser Foundation Research Institute
Esther John, Ph.D., Northern California Cancer Center
Leslie Bernstein, Ph.D., Beckman Research Institute, City of Hope

Advisory Council Members and Staff

Advisory Council (2008)

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Angela Lucia Padilla (2007-2008)
Klaus Porzig (2008-2009)

Vice-Chairs
Maria Wetzel (2007-2008)
Catherine Quinn (2008-2009)

Advocates
Roxanna Bautista, M.P.H, Asian & Pacific Islander American Health Forum (2007-2010)
Barbara Brenner, J.D., Breast Cancer Action (2008-2011)
Angela Lucia Padilla, Esq., Bay Area Young Survivors (BAYS) (2005-2009)
Karren Ganstwig, Los Angeles Breast Cancer Alliance (2007-2010)
Diane Griffiths, The Breast Cancer Fund (2006-2008)
Jeanne Rizzo, Breast Cancer Fund (2008-2011)
Maria Wetzel, Cancer Resource Center of Mendocino County (2005-2008)

Scientists/Clinicians
Moon Chen, Ph.D., University of California, Davis (2008-2011)
Laura Fenster, Ph.D., California Department of Public Health (2007-2010)
Jim Ford, M.D., Stanford University (2008-2009)
Larry Green, Dr.P.H., University of California, San Francisco (2008-2011)
Shelley Hwang, M.D., University of California, San Francisco Comprehensive Cancer Center (2007-2010)
Mary Alice Yund, Ph.D., University of California, Berkeley Extension (2007-2010)

Industry Representatives
Chris Bowden , Ph.D., Genentech (2007-2010)
Teresa Burgess, Ph.D., Amgen, Inc. (2008-2011)
Gordon Parry, Ph.D., Monogram Biosciences (2005-2008)

Nonprofit Health Representatives
Crystal D. Crawford, Esq., California Black Women's Health Project (2006-2009)
Catherine Quinn, California Health Collaborative (2006-2009)

Medical Specialist
Klaus Porzig, M.D., South Bay Oncology Hematology (2006-2009)

Ex Officio Member
Sherie Smalley, M.D., California Department of Public Health (ongoing)

Advisory Council Members and Staff

California Breast Cancer Research Program Staff

Marion H. E. Kavanaugh-Lynch M.D., M.P.H. — Director

Laurence Fitzgerald, Ph.D. — Manager: Core Funding; Biomedical Research Administrator

Katherine McKenzie, Ph.D. — Manager: External Relations; Biomedical Research Administrator

Catherine Thomsen, M.P.H. — Project Lead, Special Research Initiatives

DeShawn Boyd — External Relations Assistant

Sharon Cooper, M.P.A. — Research Analyst

Mary Daughtry — Core Funding Assistant

Elizabeth Day — Program Assistant

Brenda Dixon-Coby — Community Outreach & Special Events Coordinator

Lyn Dunagan — Communications Project Coordinator

Stella Gonzales — Administrative Assistant

Claudia Grossmann, Ph.D. — Program Evaluator

Lisa Minniefield — Assistant to the Director

Eric Noguchi — Senior Designer

Appendix A:
Special Research Initiatives
"Identifying Gaps in Breast Cancer Research"
Science Advisors, Staff, and Consultants

Science Advisors

Deborah Bowen, Ph.D., Professor, Social Behavioral Sciences, Boston University

Judy Bradford, Ph.D., Director, Community Health Research, Virginia Commonwealth University

Julia G. Brody, Ph.D., Executive Director of the Silent Spring Institute

Linda Burhansstipanov, MSPH, Dr.P.H., Grants Director, Native American Cancer Research

Christina A. Clark, Ph.D., Research Scientist, Northern California Cancer Center

Lisa Clarke, M.S., Research Associate, Northern California Cancer Center

Richard W. Clapp, D.Sc, M.PH., Professor, School of Public Health, Boston University

Melissa B. Davis, Ph.D., Postdoctoral Fellow/Scholar, Center for Interdisciplinary Health Disparities Research, University of Chicago

Suzanne E. Fenton, Ph.D., Research Biologist, Reproductive Toxicology Division, U.S. Environmental Protection Agency,

Maria Feychting, Ph.D., Professor, Institute of Environmental Medicine, Karolinska Institute

Scarlett Lin Gomez, Ph.D., Research Scientist, Northern California Cancer Center

Robert B. Gunier, M.P.H., Research Associate, Northern California Cancer Center

Dawn Hershman, M.D., Assistant Professor of Medicine, Columbia University

Chanita Hughes Halbert, Ph.D., Associate Professor University of Pennsylvania

Susan E. Hurley, M.P.H., Research Associate, Northern California Cancer Center

Esther M. John, Ph.D., Research Scientist, Northern California Cancer Center

Lovell Jones, Ph.D., Director, M.D. Anderson's Center for Research on Minority Health

Sue Joslyn, Ph.D., Professor of Epidemiology, Associate Dean of Graduate Academic Affairs, University of Northern Iowa

Marjorie Kagawa-Singer, Ph.D., RN, MN, MA, Professor, School of Public Health and School of Asian American Studies, University of California, Los Angeles

Marion H.E. Kavanaugh-Lynch, M.D., M.P.H., Director, California Breast Cancer Research Program

Judith Salmon Kaur, M.D., Medical Director, Professor of Oncology, Native American Programs, Mayo Comprehensive Cancer Center

Steve Kaye, Ph.D., Associate Professor, University of California, San Francisco

Charles Land, Ph.D., Senior Investigator, National Cancer Institute

Robert Millikan, Ph.D., Professor, University of North Carolina, Chapel Hill

Rachel Morello-Frosch, M.P.H., Ph.D., Assistant Professor, Department of Environmental Sciences, Policy, and Management, University of California, Berkeley

Kirsten Moysich, Ph.D., Associate Professor, Roswell Park Cancer Institute

Margaret Nosek, Ph.D., Professor, Baylor College of Medicine

Olufunmilayo I. Olopade, M.D., Professor of Medicine & Human Genetics at the University of Chicago

Sharon Perry, Ph.D., Senior Research Scientist, School of Medicine, Stanford University

Blase N. Polite, M.D. M.P.P., Instructor of Medicine, University of Chicago

Anh-Thu Quach, M.P.H., Research Associate, Northern California Cancer Center

Peggy Reynolds, Ph.D., Senior Research Scientist, Northern California Cancer Center

Stephanie Robert, Ph.D., Associate Professor, School of Social Work, University of Wisconsin-Madison

Ruthann Rudel, M.S., Senior Scientist, Toxicologist, Silent Spring Institute

Theresa M. Saunders, B.A., Research Program Manager, Northern California Cancer Center

Ted Schettler, M.D. M.P.H., Science Director, Science & Environmental Health Network

Susan Shinagawa, co-founder/co-chair of the Asian & Pacific Islander National Cancer Survivors

Sandra Steingraber, Ph.D., Distinguished Visiting Scholar at Ithaca College and author

Richard Stevens, Ph.D., Cancer Epidemiologist, Department of Community Medicine and Health Care, University of Connecticut

Joseph Thornton, Ph.D., Associate Professor, Center for Ecology & Evolutionary Biology, University of Oregon

Julie Von Behren, M.P.H., Research Associate, Northern California Cancer Center

David Wallinga, M.D., M.P.A., Director of the Food and Health Program, Institute for Agriculture and Trade Policy

Barbour Warren, Ph.D., Research Associate, Program on Breast Cancer & Environmental Risk Factors, Cornell University

Tom Webster, D.Sc., Associate Professor, Environmental Health, School of Public Health, Boston University

David R. Williams, Ph.D., Norman Professor of Public Health at Harvard University School of Public Health

Mary Wolff, Ph.D., Professor, Mount Sinai Medical Center

Staff and Consultants

Janna Cordeiro, M.P.H., Coordinator of Special Projects

Judy MacLean, B.A., Editorial Consultant

Katherine McKenzie, Ph.D., Manager of Research Dissemination and Outreach

Marj Plumb, Dr.PH., M.N.A., Senior Consultant, Plumbline Coaching and Consulting, Inc.

Patrice Sutton, M.P.H., Technical Consultant

Catherine Thomsen, M.P.H., Project Lead

Appendix B:
Special Research Initiatives Strategy Team

Nancy Adler, Ph.D., UC San Francisco, Health Psychology Program

Janice Barlow, B.S.N., N.P., Zero Breast Cancer

Leslie Bernstein, Ph.D., Beckman Research Institute, City of Hope

Vernal Branch, Virginia Breast Cancer Foundation

Barbara Brenner, J.D., Breast Cancer Action

Julia G. Brody, Ph.D., Executive Director of the Silent Spring Institute

Linda Burhansstipanov, M.S.P.H., Dr.PH., Native American Cancer Research, Corp.

Sarah Gehlert, Ph.D., University of Chicago, School of Social Service Administration

Joseph Guth, J.D., Ph.D., Science and Environmental Health Network

Robert Hiatt, M.D., Ph.D., UC San Francisco, Comprehensive Cancer Center

Marjorie Kagawa-Singer, Ph.D., RN, M.N., M.A., UC Los Angeles, School of Public Health; Community Health Sciences

Marion H.E. Kavanaugh-Lynch, M.D., M.P.H., Director, California Breast Cancer Research Program

Jean Latimer, Ph.D., University of Pittsburgh Cancer Institute, Center for Environmental Oncology

Michael Lerner, Commonweal

Michael Lipsett, M.D., J.D., California Department of Public Health, Environmental Health Investigations Branch

Bob Millikan, D.V.M., Ph.D., University of North Carolina School of Public Health

Rachel Morello-Frosch, PhD, MPH, UC Berkeley, Department of Environmental Science, Policy & Management

Kirsten Moysich, Ph.D., Roswell Park Cancer Institute, Cancer Prevention and Population Sciences

Olufunmilayo I. Olopade, M.D., Professor of Medicine & Human Genetics at the University of Chicago

Debra Oto-Kent, M.P.H., Health Education Council

Blaize Polite, M.D., M.P.P., University of Chicago, School of Medicine

Cathie Ragovin, M.D., Massachusetts Breast Cancer Coalition

Peggy Reynolds, **Ph.D., Northern California Cancer Center**

Jeanne Rizzo, RN, Breast Cancer Fund

Charmaine Royal, Ph.D., Duke University, Center for Genome Ethics, Law and Policy

Ted Schettler, M.D., M.P.H., Science and Environmental Health Network

Susan Shinagawa, co-founder/co-chair of the Asian & Pacific Islander National Cancer Survivors Network

Gina Solomon, M.D., M.P.H., Natural Resources Defense Council

Ana Soto, M.D., Tufts University, School of Medicine, Department of Anatomy & Cellular Biology

Sandra Steingraber, Ph.D., Distinguished Visiting Scholar at Ithaca College and author

JoAnn Tsark, M.P.H., Papa Ola Lökahi

Michelle Van Ryn, Ph.D., M.P.H., University of Minnesota, School of Public Health

David R. Williams, Ph.D., Norman Professor of Public Health at Harvard University School of Public Health

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I prefer to donate online by going to www.cbcrp.org/support and clicking on the "Donate online" link, or by clicking here.

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