# Annual Report

# 2006

California Breast Cancer Research Program

# EXECUTIVE SUMMARY

During 2006, the California Breast Cancer Research Program (CBCRP) awarded $9.8 million for 53 single- and multiple-year research projects at 34 California institutions. These pages list the studies funded this year, the studies in progress, and summaries of 55 studies funded in previous years that were completed during 2006.

**Table 1. Grants Awarded in 2006 by Subject Area**

| | Number of Grants | Amount | Percentage of Total Funding |
|---|---|---|---|
| **Community Impact of Breast Cancer** | **18** | **$3,172,432** | **32.3%** |
| **Etiology and Prevention** | **3** | **$797,337** | **8.1%** |
| **Biology of the Breast Cell** | **15** | **$2,331,263** | **23.7%** |
| **Detection, Prognosis and Treatment** | **17** | **$3,527,297** | **35.9%** |
| **Totals** | **53** | **$9,828,329** | **100%** |

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 over $174 million in research funds.

The need is urgent. Every two hours, on average, a California woman dies of breast cancer. More than 220,000 California women are living with the disease, and close to 19,000 more will be diagnosed this year. Over the past two decades, some progress has been made. Between 1988 and 2003, the breast cancer death rate for California women dropped 28%. 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.

Although the death rate is down, the rate at which California women get breast cancer climbed steeply between 1973 and 1988, and has only dropped slightly over the past few years. There is currently no scientific way to assure any woman that she will not get breast cancer, and every woman who has had breast cancer knows that it can return at any time. Further research is needed to find out why so many women get breast cancer and how to prevent it.

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. 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. 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 $9.8 million for 53 single- and multiple-year research projects at 34 California institutions in 2006. 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 the Research and Results section of this report (pages 27 – 63).

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 (Socio-cultural behavioral studies, and health policy)

   We also are setting aside $18 over five years to fund our Special Research Initiatives, which is a program-initiated endeavor to identify and support research strategies to understand and address both the environmental causes of breast cancer and the unequal burden of the disease.

4. **The relationship between federal and state funding for breast cancer research.**
   The CBCRP avoids 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 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
   - 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 priorities that push the boundaries of research.

   1. The research helps form and nurture collaboration among California scientists, clinicians, advocates, community members, and others.
   2. The research helps recruit, retain, and develop high-quality California-based investigators who engage in breast cancer research.
   3. The research embodies innovative ideas (i.e., new drugs, new strategies, new paradigms).
   4. The research addresses the public health outcomes of prevention, earliest detection, effective treatments, and quality of life.
   5. The research leads quickly to more effective products, technologies, or interventions and their application/delivery to Californians.
   6. The research helps drive policy in both the private and public sectors on breast cancer in California.
   7. The research reduces disparities and/or addresses the needs of the underserved in California.
   8. The research complements, builds on, feeds into, but does not duplicate the research programs of other organizations interested in breast cancer.
   9. The research addresses a breast cancer need that is specific but not necessarily unique to the burden of breast cancer in California.
   10. The research is responsive to the perceived breast cancer research needs and expectations of the CBCRP as identified by scientists and the public in California.

   Each individual grant is evaluated by our scientific review committees and our advisory BCRC for essential criteria for addressing these goals, including innovativeness, impact on breast cancer, responsiveness to program priorities, whether it's an underfunded research area and integration of advocacy issues.

6. **A summary of research findings including discussion of promising new areas.**
   Summaries of all of the completed research grants are included in the body of this report. Listed below are just a few of the findings:
   - John Park and Morton Lieberman of the University of California, San Francisco developed and evaluated an internet tool to match breast cancer patients to clinical trials, bct.org. They are now preparing for a nation-wide launch.
   - Soo-Young Chin at the Korean Health, Education, Information and Research Center (KHEIR), Los Angeles and Annette Maxwell at the University of California, Los Angeles have identified strategies to improve access to breast cancer education and services in the Korean community
   - Kristen Kulp at the Lawrence Livermore National Laboratory found that essiac tea, an herbal extract used by many breast cancer patients as a complementary therapy to traditional treatment, does not protect against DNA damage or tumor formation in animals.

- Stefanie Jeffrey at Stanford University and Thea Tlsty at the University of California, San Francisco have identified a distinct molecular signature in non-tumor cells near breast tumors that can be used to detect pre-cancerous cells.
- Jeffrey Smith at the Burnham Institute of Medical Research has determined that a protein called maspin is key player in regulating breast cancer metastasis.
- Dave S.B. Hoon, Armando E. Giuliano and Lori L. Wilson at the John Wayne Cancer Institute used a new technology called proteomics to identify proteins that predict which tumors are likely to spread to the lymph nodes.
- Ana Krtolica at the Lawrence Berkeley National Laboratory found the critical genetic changes occurring in the aging breast that can contribute to cancer development.

7. **Inclusion of women and minorities in research studies.**
   Sixty percent (32 of 53) of the grants awarded by the CBCRP in 2006 studied either women or tissues from women, while the remaining 40% were laboratory studies that did not directly involve women or tissues from women.

   Of the 32 grants that involved women or tissues from women, all of the grants involved women as participants and four of the grants (13%) also used tissues or tumor samples.

   One-hundred percent (32) of these studies included minority women in the study.
   - Fifty-three percent (17) are focused on underserved women.
   - Fifty-three percent (17) are focused on minority women.

This report describes the CBCRP's recent activities, goals, progress, and plans for the challenges that lie ahead on the road to decreasing the human and economic cost of breast cancer for the people of California.

# Table 2. Summary of Research Funded in 2006

| Institution and Investigator | Yrs | Project Title | Direct Costs | Indirect Costs | Total |
|---|---|---|---|---|---|
| **Alameda County Health Care Foundation** | | | | | |
| Linda Engelstad | 1 | Multilingual Access to Breast Cancer Early Detection | $5,000 | 0 | $5,000 |
| *This is a planning grant with Susan Stewart of University of California, San Francisco* | | | | | |
| **Beckman Research Institute of the City of Hope** | | | | | |
| Linda Weitzel | 1.5 | Hereditary Breast Cancer and Novel Hispanic BRCA Mutations | $150,000 | 103,500 | $253,500 |
| **California Pacific Medical Center Research Institute** | | | | | |
| Shanaz Dairkee | 1.5 | A Novel Biological Framework for the Role of Xenoestrogens | $183,200 | 96,042 | $279,242 |
| Sean McAllister | 1 | Inhibition of Breast Cancer Aggressiveness by Cannabidiol | $100,000 | 83,000 | $183,000 |
| **California State University, Fresno Foundation** | | | | | |
| John Capitman | 1.5 | Fresno Breast Cancer Navigator Pilot Program | $40,000 | 10,400 | $50,400 |
| *This is a collaborative grant with Mary Wallace and John Zweifler of San Joaquin Valley Health Consortium* | | | | | |
| **California State University, Fullerton** | | | | | |
| Stergios Roussos | 1.5 | Mammography Screening for Latinas with Diabetes | $61,735 | 30,559 | $92,294 |
| *This is a collaborative grant with Christine Noguera of Golden Valley Health Centers* | | | | | |
| Sora Tanjasiri | 1.5 | Informal and Formal Support and Needs Among Samoan Survivors | $49,954 | 19,732 | $69,686 |
| *This is a collaborative grant with Sala Mataalii of Samoan National Nurses Association* | | | | | |
| **Central Coast Center for Independent Living** | | | | | |
| Elsa Quezada | 1.5 | Increasing Mammography Among Latinas with Disabilities | $100,000 | 25,000 | $125,000 |
| *This is a collaborative grant with H. Stephen Kaye at University of California, San Francisco* | | | | | |
| **Golden Valley Health Centers** | | | | | |
| Christine Noguera | 1.5 | Mammography Screening for Latinas with Diabetes | $88,265 | 22,067 | $110,332 |
| *This is a collaborative grant with Stergios Roussos of San Diego State University -Research Foundation* | | | | | |
| **Greater Los Angeles Council on Deafness, Inc.** | | | | | |
| Heidi Kleiger | 3 | Breast Cancer Education for Deaf and Hard-of-Hearing Women | $300,000 | 75,000 | $375,000 |
| *This is a collaborative grant with Barbara Berman of University of California, Los Angeles* | | | | | |
| **John Wayne Cancer Institute** | | | | | |
| Armando Giuliano | 1.5 | Intraoperative Assessment of Surgical Lumpectomy Margins | $150,000 | 133,200 | $283,200 |
| **La Jolla Institute for Molecular Medicine** | | | | | |
| Barbara Mueller | 1.5 | Identification of Metastasis Competent Breast Cancer Cells | $149,964 | 177,408 | $327,372 |
| **Mendocino Cancer Resource Center** | | | | | |
| Sara O'Donnell | 3 | Telephone-Based Decision Support for Rural Patients | $289,086 | 72,272 | $361,358 |
| *This is a collaborative grant with Jeff Belkora of University of California, San Francisco* | | | | | |
| **Northern California Cancer Center** | | | | | |
| Susan Hurley and Peggy Reynolds | 1 | Special Research Initiatives State of the Science Lit Review | $195,123 | 0 | $195,123 |
| **Operation Samahan Inc.** | | | | | |
| Joel San Juan | 1 | Breast Health Literacy and Health Care Decision Making | $6,000 | 0 | $6,000 |
| *This is a planning grant with Suzanne Lindsay of San Diego State University Research Foundation* | | | | | |
| **Orange County Asian and Pacific Islander Community Alliance** | | | | | |
| Mary Anne Foo | 2 | Southeast Asian Breast Health Navigation | $75,000 | 37,500 | $112,500 |
| *This is a collaborative grant with Marjorie Kagawa-Singer of University of California, Los Angeles* | | | | | |
| **Samoan National Nurses Association** | | | | | |
| Sala Mataalii | 1.5 | Informal and Formal Support and Needs Among Samoan Survivors | $100,031 | 25,008 | $125,039 |
| *This is a collaborative grant with Sora Tanjasiri of California State University - Fullerton, Auxilary Services Corp.* | | | | | |
| **San Diego State University Research Foundation** | | | | | |
| Suzanne Lindsay | 1 | Breast Health Literacy and Health Care Decision Making | $4,000 | 0 | $4,000 |
| *This is a planning grant with Joel San Juan of Operation Samahan Health Clinic* | | | | | |
| **San Francisco State University** | | | | | |
| Grace Yoo | 1 | Dialogue with Breast Cancer Survivors | $27,000 | 0 | $27,000 |
| **San Joaquin Valley Health Consortium** | | | | | |
| Mary Wallace and John Zweifler | 1.5 | Fresno Breast Cancer Navigator Pilot Program | | | $0 |
| *This is a collaborative grant with John Capitman of California State University-Fullerton Foundation* | | | | | |

| Institution and Investigator | Yrs | Project Title | Direct Costs | Indirect Costs | Total |
|---|---|---|---|---|---|
| **Scripps Research Institute** | | | | | |
| Brunhilde Felding-Habermann | 2 | Inhibition of Brain Metastases in Breast Cancer | $250,000 | 214,750 | $464,750 |
| Brunhilde Felding-Habermann | 1.5 | Neural Stem Cell Therapy for Breast Cancer Brain Metastases | $181,395 | 120,690 | $302,085 |
| Anastasia Kralli | 1.5 | The Role of Estrogen-Related Receptors in Breast Cancer | $150,000 | 128,850 | $278,850 |
| Sherry Niessen | 2 | The Role of Serine and Metallo-Hydrolase's in Breast Cancer | $76,000 | 0 | $76,000 |
| Jennifer Scorah | 2 | The Role Chk1 in Breast Cancer DNA Damage Repair | $90,000 | 0 | $90,000 |
| Aaron Wright | 3 | Profiling Drug Metabolism (P450) Proteins in Breast Cancer | $135,000 | 0 | $135,000 |
| **Sidney Kimmel Cancer Center** | | | | | |
| Albert Deisseroth | 1.5 | Vascular Targeting Therapy for Breast Cancer | $150,000 | 139,500 | $289,500 |
| **Slavic Assistance Center** | | | | | |
| Roman Romaso | 1.5 | The Breast Cancer Experience of Slavic Women | $93,750 | 0 | $93,750 |
| *This is a collaborative grant with Debora Paterniti of University of California, Davis* | | | | | |
| **Stanford University** | | | | | |
| Adam Adler | 2 | MYC and CSN5 in the Breast Cancer "Wound Signature" Profile | $76,000 | 0 | $76,000 |
| Michael Bax | 2 | Real-Time 3D Ultrasound Image-Guidance for Breast Surgery | $66,641 | 0 | $66,641 |
| Howard Chang | 1 | A Targeted Therapy for Wound-like Breast Cancers | $148,313 | 84,621 | $232,934 |
| David Feldman | 1.5 | Breast Tumor Inhibition by Vitamin D in a Mouse Model | $150,000 | 84,388 | $234,388 |
| Craig Levin | 1 | New Technology to Enhance PET Imaging of Breast Cancer | $100,000 | 55,502 | $155,502 |
| Yohei Shimono | 3 | Analysis of MicroRNA Expression in Breast Cancer Stem Cells | $135,000 | 0 | $135,000 |
| Alice Whittemore | 1.5 | Breast Cancer Metastasis: a Heritable Trait? | $149,984 | 114,611 | $264,595 |
| **Thai Health and Information Service** | | | | | |
| Bulaporn Natpagon-Shah | 1.5 | Factors Influencing Breast Cancer Screening Among Older Thai | $70,741 | 17,686 | $88,427 |
| *This is a collaborative grant with Mary Jo Clark of University of San Diego* | | | | | |
| **The Burnham Institute of Medical Research** | | | | | |
| Barbara Blouw | 3 | The Role of Podosomes in Breast Cancer Metastasis | $135,000 | 0 | $135,000 |
| Robert Oshima | 1 | A New Marker for Mammary Epithelial Stem Cells? | $100,000 | 91,000 | $191,000 |
| Chung-Wai Shiau | 3 | Chemical Inhibitors of Hsp70 for Breast Cancer | $135,000 | 0 | $135,000 |
| Alexey Terskikh | 1.5 | A Candidate Marker of Mammary Tumor Initiating Cells | $150,000 | 136,500 | $286,500 |
| Chen Yang | 2 | Modeling, Targeting Acetyl-CoA Metabolism in Breast Cancer | $90,000 | 0 | $90,000 |
| Xiao-Kun Zhang | 2 | Nur77-derived Peptides as a Novel Breast Cancer Therapy | $150,000 | 136,500 | $286,500 |
| **Turtle Health Foundation** | | | | | |
| Linda Navarro | 1.5 | Addressing Cultural & Tribal Issues in Breast Cancer | $70,900 | 17,725 | $88,625 |
| *This is a collaborative grant with Marlene von Friedrichs-Fitzwater of University of California, Davis* | | | | | |
| **University of California, Berkeley** | | | | | |
| Gary Firestone | 1.5 | Artemisinin Disrupts Estrogen Receptor-Alpha and Cell Growth | $100,000 | 0 | $100,000 |
| Dana Petersen | 2 | Social Capital, Social Support and Long-Term Quality of Life | $67,540 | 0 | $67,540 |
| **University of California, Davis** | | | | | |
| Debora Paterniti | 1.5 | The Breast Cancer Experience of Slavic Women | $73,609 | 0 | $73,609 |
| *This is a collaborative grant with Roman Romaso of Slavic Assistance Center* | | | | | |
| Marlene von Friederichs-Fitzwater | 1.5 | Addressing Cultural & Tribal Issues in Breast Cancer | $79,100 | 0 | $79,100 |
| *This is a collaborative grant with Linda Navarro of Turtle Health Foundation* | | | | | |
| **University of California, Irvine** | | | | | |
| Hyeon-Man Baek | 2 | In Vivo MRS for Cancer Diagnosis and Treatment Monitoring | $90,000 | 0 | $90,000 |
| Gultekin Gulsen | 1.5 | Combined Imaging Modalities for Breast Cancer | $149,382 | 0 | $149,382 |
| **University of California, Los Angeles** | | | | | |
| Barbara Berman | 3 | Breast Cancer Education for Deaf and Hard-of-Hearing Women | $300,000 | 0 | $300,000 |
| *This is a collaborative grant with Heidi Kleiger of Greater Los Angeles Council on Deafness* | | | | | |
| Michael Johnston | 1 | Introducing Acupuncture to Black Survivors for Wellness | $5,000 | 0 | $5,000 |
| *This is a planning grant with Carolyn Tapp of Women of Color Breast Cancer Survivors Support Project* | | | | | |
| Marjorie Kagawa-Singer | 2 | Southeast Asian Breast Health Navigation | $75,000 | 0 | $75,000 |
| *This is a collaborative grant with Mary Anne Foo of Orange County Asian and Pacific Islander Community Alliance* | | | | | |
| Yoshiko Umezawa | 2 | Social Support and QOL in Older Minority Women with BC | $70,838 | 0 | $70,838 |
| **University of California, San Diego** | | | | | |
| Eliot Bourk | 2 | Inflammation Alters Transcription by ER in Breast Cancer | $75,551 | 0 | $75,551 |
| Jing Yang | 1.5 | Twist Activation in Breast Cancer Metastasis | $150,000 | 0 | $150,000 |

| Institution and Investigator | Yrs | Project Title | Direct Costs | Indirect Costs | Total |
|---|---|---|---|---|---|
| **University of California, San Francisco** | | | | | |
| Jeffrey Belkora | 3 | Telephone-Based Decision Support for Rural Patients | $310,914 | 0 | $310,914 |
| *This is a collaborative grant with Sara O'Donnell of Mendocino Cancer Resource Center* | | | | | |
| Nancy Burke | 1 | Filipina Breast Cancer Support: What Model is Meaningful? | $5,000 | 0 | $5,000 |
| *This is a planning grant with Edwin Jocson of West Bay Pilipino Multi-Service Center* | | | | | |
| H. Stephen Kaye | 1.5 | Increasing Mammography Among Latinas with Disabilities | $50,000 | 0 | $50,000 |
| *This is a collaborative grant with Elsa Quezada of Central Coast Center for Independent Living* | | | | | |
| Bob Liu | 3 | Isolation of Cancer Precursors from Normal Human Breasts | $135,000 | 0 | $135,000 |
| Claudia Petritsch | 1.5 | Role of Cell Division Asymmetry in Breast Cancer Stem Cells | $149,990 | 0 | $149,990 |
| Susan Stewart | 1 | Multilingual Access to Breast Cancer Early Detection | $5,000 | | $5,000 |
| *This is a planning grant with Linda Englestad at Alameda County Health Care Foundation* | | | | | |
| Irene Yen | 1.5 | Neighborhood Environment and Obesity in Pre-adolescent Girls | $162,847 | 0 | $162,847 |
| **University of California, Santa Barbara** | | | | | |
| Olga Azarenko | 2 | Sulforaphane: Its Potential for Treatment of Breast Cancer | $65,415 | 0 | $65,415 |
| **University of San Diego** | | | | | |
| Mary Jo Clark | 1.5 | Factors Influencing Breast Cancer Screening Among Older Thai | $63,333 | 23,640 | $86,973 |
| *This is a collaborative grant with Bulapom Natpagon-Shah of Thai Health and Information Service* | | | | | |
| **University of Southern California** | | | | | |
| Michael Press | 1.5 | Topoisomerase-IIa as a Predictor of Anthracycline Response | $150,000 | 94,500 | $244,500 |
| Stephen Swenson | 1.5 | rADDs: Novel Disintegrins Targeting Breast Cancer | $150,000 | 94,500 | $244,500 |
| **West Bay Pilipino Multi-Service Center** | | | | | |
| Edwin Jocson | 1 | Filipina Breast Cancer Support: What Model is Meaningful? | $5,000 | 0 | $5,000 |
| *This is a planning grant with Nancy Burke at University of California, San Francisco* | | | | | |
| **Women of Color Breast Cancer Survivors Support Project** | | | | | |
| Carolyn Tapp | 1 | Introducing Acupuncture to Black Survivors for Wellness | $5,000 | 0 | $5,000 |
| *This is a planning grant with Michael Johnston of University of California, Los Angeles* | | | | | |

# Table of Contents

# California Breast Cancer Research Program
## Annual Report to the State of California Legislature 2006

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

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# About the California Breast Cancer Research Program

## 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). The CBCRP has since become the largest state-funded breast cancer research effort in the nation, and the fourth largest funder of breast cancer research in the world.

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 more than $174 million in research funds since 1993. In 2006, the CBCRP awarded $9.8 million for 53 single- and multiple-year research projects at 34 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 selected on state income tax returns. The CBCRP also receives private contributions.

## Pushing the Research Boundaries

During its thirteen-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 find ways to focus Program resources on questions that could change the face of breast cancer research.

The CBCRP's five-year Special Research Initiatives will investigate the role of the environment in breast cancer and the reasons why breast cancer affects some groups of Californians more than others. The CBCRP is investing 30 percent of its funds in these initiatives. During 2006, to assure that the research will have the most impact on breast cancer and to avoid duplication, the CBCRP drafted a review of previous research in the areas to be covered under the Special Research Initiatives. This year, the CBCRP also recruited experts of national stature to two leadership bodies for this research effort. The 6-member steering committee will guide the Special Research Initiatives. The 30-member strategy team will develop specific recommendations for research to be funded. During 2007, the public will have an opportunity to help shape the Special Research Initiatives through a series statewide stakeholder town hall meetings and through comments on a special section of the CBCRP Web

site. 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 leading 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 direction of the University of California, Office of the President, in Oakland, with a staff managing the solicitation, review, award, and oversight of grants.

The CBCRP's 16-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 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 also review all proposals for scientific merit.

The following ten criteria are used by the Breast Cancer Research Council to set priorities that push the boundaries of research.

1. The research helps form and nurture collaboration among California scientists, clinicians, advocates, community members, and others.
2. The research helps recruit, retain, and develop high-quality California-based investigators who engage in breast cancer research.
3. The research embodies innovative ideas (i.e., new drugs, new strategies, new paradigms).
4. The research addresses the public health outcomes of prevention, earliest detection, effective treatments, and quality of life.
5. The research leads quickly to more effective products, technologies, or interventions and their application/delivery to Californians.
6. The research helps drive policy in both the private and public sectors on breast cancer in California.
7. The research reduces disparities and/or addresses the needs of the underserved in California.
8. The research complements, builds on, feeds into, but does not duplicate the research programs of other organizations interested in breast cancer.
9. The research addresses a breast cancer need that is specific but not necessarily unique to the burden of breast cancer in California.
10. The research is responsive to the perceived breast cancer research needs and expectations of the CBCRP as identified by scientists and the public in California.

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 biennial 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 CBCRP also encourages public review of its funded research through its *Advances in Breast Cancer Research* report 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

The sponsors of the legislation that established the California Breast Cancer Research Program recognized that funding high quality research is necessary but not sufficient to fulfill the Program's mission. Therefore the statutory language calls on the CBCRP to disseminate the results of the research it funds. 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 treatment options. Breast cancer activists 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 making the 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

Every other year, the CBCRP 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: Seeking Solutions," was held in Sacramento, September 9–11, 2005.

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.

The next symposium, the CBCRP's sixth, will be held at the Westin Bonaventure in downtown Los Angeles, September 7-9, 2007. A plenary session will focus on recent advances in breast cancer treatment.

# 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. Publication abstracts supported by CBCRP funding have links to the NIH'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. The Web site includes an opportunity to make online donations to the CBCRP.

During 2006, the CBCRP Web site became more interactive, with the addition of several new features.

- A five-minute video overview of the CBCRP is now available for viewing on the Web site. The video is narrated by TV host, breast cancer survivor, and former Olympic figure skater Peggy Fleming.
- Visitors to the site who want to keep up with the latest research progress can now conduct a search to access the most recently posted findings.
- The new featured researcher section at the Web site, which changes 8-12 times per year, profiles one researcher and her or his findings. Visitors can ask this expert questions, and receive answers, via email. The inaugural featured expert was Anna Wu, Ph.D., who found a reduction in the rate of breast cancer among Asian women who ate soy products and drank green tea.
- On the CBCRP Web site home page, two short summaries of interesting research are posted, with links to further information. These short summaries change daily.
- Progress on the development of the CBCRP's Special Research Initiatives is reported on the Web site.

# 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.

**Advances in Breast Cancer Research:** Every other year, the CBCRP publishes *Advances in Breast Cancer Research,* with summaries of completed research for the previous two years.

**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 CBCRP:** Formal evaluations let the public understand the success and need for improvement 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 all

community research collaboration research funded by the CBCRP to date, is designed to make community groups aware of this opportunity.

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

## Further Methods of Sharing Research

**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. During 2006, portions of *Expressions: the Art of Healing Breast Cancer* were displayed along with the CBCRP's exhibit at scientific meetings. The next exhibit of the entire collection is planned for the CBCRP's 2007 symposium. An art catalog of this collection is available online at the CBCRP Web site.

**Exhibits at Scientific and Community Meetings:** The CBCRP presented an exhibit of the Program's work at a number of scientific and community meetings during 2006. The meetings included:

- Charlotte Maxwell Complementary Clinic's 15th Year Annivesary Gala, San Francisco
- Professional Businesswomen of California's 17th Annual Conference, San Francisco
- Northern California Cancer Center's Each One Reach One, Oakland
- Bay Area Business Women's Expo, Oakland
- Kaiser Permanente Women's Health Check Up Day, West Los Angeles
- Sisters Network Luncheon and Fashion Show, San Francisco
- California Governor and First Lady's Conference for Women and Children, Long Beach
- Career Development Workshop to Increase Diversity in Research Funding, Palm Desert
- Women of Color 8th Annual Loving Each Other Luncheon, Torrance
- Sisters Network Gift for Life Black Walk & Health Fair, San Francisco
- Cancer In Our Lives—Raising Awareness in the LGBTQI Community, San Francisco
- Breast Cancer and the Creative Impulse Women's Conference and Health Fair, Long Beach
- Community Health Partnership Cancer Symposium, Santa Clara
- Breast Cancer Survivors' Breakfast, Fremont
- Professional Businesswomen of California Conference, Sacramento

**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. Requests for speakers and educators rose during 2006.

# Collaborating with Breast Cancer Advocates and California Communities

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 having 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 thirteen-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 five-year effort to investigate the environmental causes of breast cancer and the reasons why some groups of women bear a greater burden of the disease.

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 Performing 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 for a research project. 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 over $11 million in funding to 49 collaborative projects. Projects funded over the years include:

- Investigation of problems women face returning to work after breast cancer surgery
- An examination of factors in health care settings and health care provider interactions that promote and inhibit the experience of culturally sensitive care for low-income African American women

- The breast cancer profile of Vietnamese nail salon workers
- Breast cancer risk factors of lesbians and heterosexual women
- Culturally-appropriate care for Samoan American and Korean American women
- The effectiveness of a community education project designed to increase participation by African American women in clinical trials of new breast cancer preventive drugs
- 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 women
- The barriers to older Thai women participating in breast cancer screening

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

- La Lobe, a grassroots breast cancer support group in Nevada County, teamed up with researchers from the Stanford University School of Medicine to form the Sierra-Stanford Partnership. This partnership created a user-friendly workbook-journal for isolated and rural women recently diagnosed with breast cancer. The workbook provides facts, figures, and personal experiences of other women diagnosed with the disease. The partnership evaluated the effectiveness of the workbook, titled "One in Eight," and found that women who were randomly selected to receive it showed a significant reduction in their traumatic stress symptoms related to having cancer, compared to women who did not receive the workbook. "One in Eight" has since been provided to other researchers and to community and state agencies for possible use in support programs. The workbook has drawn national and international interest.
- To understand and address the barriers faced by women with functional limitations in getting mammograms and other breast cancer screening services, Breast Health Access for Women with Disabilities (BHAWD) conducted a telephone survey of 320 women with physical disabilities in the San Francisco Bay Area's East Bay region. The data is being used to develop policies and programs to ensure that breast screening education and services are accessible for all women, regardless of disability. BHAWD has completed a manual that provides a practical resource to disseminate the program's successes, and to replicate it at disability and breast cancer screening programs.

## Fostering Community-Based Research

The CBCRP has taken major steps over the past four 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 2006 with the CBCRP receiving a record of 23 applications for CRC grants, the largest number in the ten years the Program has offered this type of grant. The scientific quality of these applications was also very high. The CBCRP funded ten of these applications, and also provided planning and development grants to four research teams whose applications had merit but needed strengthening. The funded research collaborations also extend across a wider geographic range of California than in any previous

year. Women whose breast cancer issues have been explored very little, or not at all, will now have their issues systematically addressed.

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, 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. Over two dozen teleconferences and site visits provided training and assistance both to research teams who had been awarded grants to plan future research projects, and to teams conducting research.

Over the past year, at major national conferences and in university courses in other states, the CBCRP has also presented results of the Program's research into the effectiveness of community-based breast cancer research. These presentations were based on an evaluation the CBCRP conducted in 2005, which found that the Community Research Collaboration awards empowered communities to address questions important to them. This contrasts with past research in underserved communities, which has often left community members feeling exploited by researchers who come in from the outside and conduct research that leaves the community with no lasting benefit. The evaluation further found that the CRC awards may be the most appropriate and effective way to perform breast cancer research within California’s diverse communities.

As a result of this evaluation, the CBCRP also made two changes during 2006 in the CRC awards:

- The CRC grant amount has been increased to $150,000 for pilot awards and $600,000 for full awards.
- Research teams who have conducted successful projects may now apply for an additional grant of up to $150,000 to disseminate and implement their research results, applying the results to programs, policy, or public awareness.

# The CBCRP's Strategy for Funding Research

The CBCRP's Breast Cancer Research Council and staff set the priorities for the Program's research funding. The CBCRP strategy for funding research has two parts, the Special Research Initiatives and Core Funding.

## Five-Year Special Research Initiatives

The CBCRP's Special Research Initiatives address two overlapping questions:

- The impact of the environment on breast cancer
- The reasons why women from some ethnic groups, income levels, and geographic areas of the state of California bear more of the burden of breast cancer than others

The CBCRP launched the Special Research Initiatives in 2005 because the Program's previous efforts to increase research addressing these questions have not led to enough progress. The initiatives are the result of a long, thoughtful, thorough planning process that included analyzing years of nationwide and CBCRP-funded breast cancer research, and collecting feedback from breast cancer advocates, researchers, and the public.

The CBCRP is investing 30 percent of its research funds over five years, which will result in at least $18 million for these investigations.

To select the research that will lead to the most progress against breast cancer, the Program is following a carefully-crafted, two-year, publicly-accessible strategy development process. A steering committee of researchers and advocates from across the nation was recruited during 2006 and is guiding this process of developing strategy. The members of this committee include:

- **Olufunmilayo I. Olopade, M.D.,** 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,** who is widely recognized as the nation's leading Asian-American cancer and chronic pain advocate and activist.
- **David R. Williams, Ph.D.,** a leader in research into how racial discrimination affects heart disease and other health conditions.
- **Julia G. Brody, Ph.D.,** one of the world's experts on breast cancer and the environment.
- **Sandra Steingraber, Ph.D.,** 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.

The process of developing strategy moved forward during 2006. The CBCRP drafted 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. A 30-member strategy team of scientists, advocates and clinicians from California and across the nation was also recruited during 2006. During 2007, the CBCRP will gather input from women affected by breast cancer, investigators who may conduct future research under the initiatives, clinicians, government officials, and interested members of the public across California. The strategy team will use this input to make specific recommendations for research to be funded.

This two-year process for developing strategy is being followed because the questions selected for investigation hold great promise for progress against breast cancer, but they are also difficult to research. There's no scientific consensus on where to begin. Information about previous research into these questions is only available through widely scattered sources.

The CBCRP's strategy development process is designed to avoid duplicating previous research and to base the Program's efforts on the most up-to-date knowledge and on the opinions of experts nationwide. The process allows time to make the best use of the state's resources by identifying and involving California institutions and organizations who can join forces to make progress against breast cancer. The goal is an integrated, coordinated statewide approach that ensures statewide solutions. It is likely that these five-year Special Research Initiatives will unfold via some method other than grants to individual researchers who propose the topics of their research studies.

California is an ideal laboratory for research into the environment's role in breast cancer and the reasons why some groups of women bear an unequal burden of the disease. 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 diverse. California also has communities with the highest rates of breast cancer in the nation.

## Core Funding

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

Each 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
- Diagnosis, Prognosis and Treatment

Each 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 underrepresented women—together with experienced scientists to investigate breast cancer problems that are important to that community, using culturally-appropriate research methods. Pilot CRC awards were funded up to 18 months and up to $150,000 in direct costs. Full CRC awards were 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 were funded for up to 18 months and up to $100,000—and for studies 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 were

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 were 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.

During 2006, the CBCRP launched a new type of award, inviting applications for grants the Program will make during 2007. The **Translational Research Award** is an effort to stimulate 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. Translational Research is funded for a maximum of 3 years, for up to $750,000. This award replaces the CBCRP's previous Translational Research Collaboration Award, which was a mixed success. The requirements have been altered to stimulate research that moves most directly and quickly toward applications that will create progress against breast cancer.

Two goals underlying the CBCRP's funding strategy are the leveraging of Program funds to influence the research system nationwide, and enlarging the pool of breast cancer researchers.

## Influencing 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.

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, in 1997 and 1998 the CBCRP gave Silvia Formenti, M.D., at the University of Southern California, two grants to test a new treatment method for locally advanced breast cancer. With locally advanced breast cancer, the tumor has grown larger than an inch in diameter and spread to the lymph nodes. This diagnosis is more likely to be deadly and is common among minority women with little access to health care. Dr. Formenti's team gave chemotherapy and radiation before surgery to remove the

tumor, instead of after. Her research showed that tumors with certain characteristics are more likely to be treated successfully with chemotherapy and radiation first. The success of Dr. Formenti's original CBCRP-funded research led to her receiving grants to expand this treatment approach from the federal government's Centers for Disease Control and Department of Defense, as well as two nonprofit foundations, the New York-based Breast Cancer Research Foundation and the Avon Breast Cancer Foundation. She is now part of a much larger research team testing this new treatment in the U.S. and four other nations.

To get creative new research going, the CBCRP also encourages and trains researchers in California to submit exciting new ideas. In addition, the CBCRP trains scientific experts from outside California, who review research proposals submitted to the Program for scientific merit, to use criteria that result in funding for promising new research concepts. A new scoring system was developed to help reviewers read proposals with a perspective toward rewarding high-risk research.

## 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, the CBCRP awarded Brunhilde Felding-Habermann, Ph.D., of the Scripps Research Institute in La Jolla, an IDEA grant in 1999. She investigates how breast cancer cells move through the body to form tumors in the brain. Dr. Felding-Habermann's investigations began with basic research on proteins that are critical to the cells' being able to move and spread (metastasize). CBCRP funding has enabled Dr. Felding-Habermann to collaborate with other researchers to translate her basic research into a possible treatment that would deliver cancer-inhibiting protein fragments to the brain through the nose. CBCRP funding is also allowing her to research how stem cells found in tumors are involved in breast cancer metastasis, and to investigate brain stem cells as possible delivery agents of therapy to target breast cancer that has spread to the brain.

The CBCRP also makes it possible for new scientists to begin their careers as specialists in breast cancer research, by making Postdoctoral Fellowship and Dissertation awards. Since the CBCRP's inception, the Program's Postdoctoral and Dissertation awards have launched over 200 new breast cancer research careers.

## Funding by Priority Issue and by Award Type

Every research grant funded under the CBCRP's Core Funding must fit within two separate sets of categories, the Priority Issues (research topic) and the Award Types. The Priority Issues are broad, to allow the Program to have an impact across a wide spectrum of breast cancer research. The Award Types, discussed on previous pages, are narrowly targeted to focus CBCRP funding where it will lead to most rapid progress.

Below, two tables present statistics on 49 of the 53 projects funded during 2006 by Priority Issue and by Award Type.

## Table 5. 2006 Grants Awarded by Priority Issue

| Priority Issue | Number of Grants | Amount | Percentage of Total Funding |
|---|---|---|---|
| Community Impact of Breast Cancer | 18 | $3,172,432 | 32.3% |
| Etiology and Prevention | 3 | $797,337 | 8.1% |
| Biology of the Breast Cell | 15 | $2,331,263 | 23.7% |
| Detection, Prognosis and Treatment | 17 | $3,527,297 | 35.9% |
| Totals | 53 | $9,828,329 | 100% |

## Table 6. 2006 Grants Awarded by Award Type

| Award Type | Number of Grants | Amount | Percentage of Total Funding |
|---|---|---|---|
| Dissertation | 7 | $497,985 | 5.1% |
| Postdoctoral Fellowship | 8 | $945,000 | 9.6% |
| Innovative Developmental and Exploratory (IDEA) | 22 | $5,049,387 | 51.4% |
| IDEA-Competitive Renewal | 1 | $464,750 | 4.7% |
| Community Research Collaboration (CRC) Pilot Award | 8 | $1,459,235 | 14.8% |
| Community Research Collaboration (CRC) Full Award | 2 | $1,347,272 | 13.7% |
| Joining Forces Conference Award | 1 | $24,700 | 0.3% |
| Planning Grants | 4 | $40,000 | 0.4% |
| Totals | 53 | $9,828,329 | 100% |

# Improving the CBCRP through Evaluation

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.

During 2006, the CBCRP conducted a survey of the experts who review grant proposals. The results will be used to make any needed improvements in the review process. The Program also created a framework for evaluating a type of grant the CBCRP will offer for the first time in 2007, the Translational Research award. There are many barriers to conducting translational research, which moves a finding from basic science quickly toward treatment, diagnosis, prevention, public policy or another application that can impact breast cancer. If the CBCRP does not receive enough quality applications to conduct translational research, changes may be needed in outreach, technical assistance, application materials, or review procedures.

## 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 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.
- A three-year priority-setting process led the CBCRP to discontinue award types that were not meeting the program's goals and invest 30 percent of its funds for five years 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.

- 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.

# Research Progress and Results

On the following pages, the results of research funded by the California Breast Cancer Research Program and completed during 2006 are presented. Listings of research in progress and research 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 a blend of diverse communities offering a unique opportunity to investigate disparities and the unequal burden of breast cancer. 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 or diagnosed with breast cancer?*
- *What services are needed to improve access to screening and care, quality of life, and reduce suffering?*

*The CBCRP has been supporting community-based collaborations for 10 years, and we offer pre-application workshops and technical assistance to facilitate new partnerships and successful grant applications. We are encouraged that many CRC grants focus on underserved populations to address the underlying disparities. We feel that an "evidence-based" community project has great potential to lead to a successful intervention.*

*In addition to the CRC awards, the CBCRP supports the Community Impact priority issue with innovative IDEA grants and career development awards.*

*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

**African American Women and Breast Cancer: What Works?**
Although African American women are less likely than white women to be diagnosed with breast cancer, they are more likely to be diagnosed at a later stage and to die of their disease. Regular mammography and prompt follow-up offer the best opportunity for finding and treating breast cancer early. In California, African American women are less likely than women of other racial or ethnic groups to obtain the free mammograms provided for low-income, uninsured, and underinsured women by Cancer Detection Programs: Every Woman Counts (CDP: EWC). **Carol Somkin, Ph.D.,** at the **Kaiser Foundation Research Institute,** and **Priscilla Banks, M.A.,** of the African American Advisory Committee, Oakland, conducted a qualitative study that involved interviews with staff at 56 CDP: EWC sites and African American women who had a mammogram at a CDP:EWC clinic or who called the program's 800 telephone number to ask for a referral but never obtained services. Based on these interviews, Somkin and Banks concluded that establishing new, diverse, and tailored outreach programs, creating a navigator program for women who call the 800 number, and implementing cultural sensitivity training programs for

staff could lead to increased usage of mammography programs at CDP:EWC clinics by African American women.

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

Support groups significantly improve coping and reduce distress for women with breast cancer. However, many women with breast cancer from underserved groups (low-income, little or no formal education, ethnic minority, lesbian, advanced in age, disabled) do not participate in these groups. **Kate Collie, Ph.D.**, at **Stanford University**, Palo Alto, conducted in-depth interviews with fifteen women with breast cancer from underserved groups living in the San Francisco Bay Area. She also interviewed people involved in developing or offering support services that have a focus on creative expression for Bay Area women with breast cancer. The interviews were analyzed using Narrative Analysis, a method that is used to bring forward voices that have been excluded from mainstream discourse and to interpret responses in relation to participants' social and cultural contexts. The analysis of the interviews of the women with breast cancer yielded valuable new insights about their social, cultural, and psychological reactions to support group participation. For example, it became clear that for these women, groups that offered more emotional privacy, were offered in a more familiar format, and emphasized the resources other women in the group could offer, would be most beneficial. Dr. Collie is now conducting a pilot study that will use the recommendations of the participants in this project to create an art-based support group.

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

Clinical trials are necessary to determine if new breast cancer therapies are more effective than those currently available. However, only 3 percent of cancer patients participate in these trials. To make trial enrollment easier, **John Park, M.D.**, and **Morton Lieberman, Ph.D.**, at the **University of California, San Francisco**, along with other researchers at the National Cancer Institute, developed BreastCancerTrials.org, an Internet-based tool for matching breast cancer patients to clinical trials. To use the tool, women complete a detailed online Personal Health Record (PHR). The computer matches the PHR to the eligibility criteria of registered trials. Women are notified that they have matched a trial, and are given the contact information for the clinical investigators. Drs. Park and Lieberman studied the website's practicality and usefulness. They found that among 614 women who started a PHR, 70 percent completed it and that 95 percent of these women matched to at least one trial. They also found that the overwhelming majority of women reported that the site was helpful and easy to use. These findings have allowed the team to prepare for a nationwide launch of BreastCancerTrials.org.

**The Cost of Breast Cancer in California**

Breast cancer is a disease that affects a large number of women of all ages, from young mothers to retired grandmothers. The resulting economic burden of the disease is huge, and includes dollars spent to diagnose and treat women, the value of time lost from productive activities by those living with the disease, and the value of the lives lost prematurely. Estimates of the cost of the illness are valuable for decision makers who need to compare treatments and service delivery systems, determine what groups of people should be targeted to receive improved access to care, and establish program budgets. They also help advocates persuade others to focus on this costly disease. Currently, estimates of the cost of breast cancer in California are unavailable at the state level. **Wendy Max, Ph.D.**, at the **University of California, San Francisco**, developed estimates

of these costs using econometric models and approaches that utilize the best available data. Max found that in 2001, there were 12,934 women hospitalized for a primary diagnosis of breast cancer in California. The total direct cost of providing care to these women was $279 million. Breast cancer claimed the lives of 4,226 California women in 2001. Max found that these deaths represented $1.1 billion in lost productivity and nearly 100,000 years of life. Lastly, Max found that the mean lifetime cancer-attributable Medicare cost for a woman with breast cancer was $31,735. These findings will be useful for policymakers and advocates who want to target prevention, screening, and treatment dollars to the women who bear the greatest economic burden of breast cancer.

**Decision Support in Rural Underserved North Coast Counties**

Women with breast cancer in North Coast counties face many obstacles, including long travel times and cultural or language barriers, in obtaining information from cancer specialists prior to making treatment decisions. In 2001, two North Coast cancer resource centers implemented an in-person Consultation Planning (CP) service to help breast cancer patients prepare questions before physician visits. The resource centers hope to be able is to offer the CP service to all breast cancer patients, including Frontier, Latina and Native American women, by 2010. The centers would like to deliver these CP services via the telephone, instead of in-person. However, it was not known if women would find this acceptable. **Jeffrey Belkora, Ph.D,** at the **University of California, San Francisco**, and **Sara O'Donnell** at the **Mendocino Cancer Resource Center**, conducted interviews about and tested a telephone CP service with an ethnically diverse group of women with breast cancer in Mendocino County. They also interviewed 15 cultural advisors and 12 Latina and Native American breast cancer survivors, along with 10 past recipients of telephone CP services to ensure that the program was as acceptable to these women as it was to white women. Their success in this area led them to receive a new CBCRP award that will allow them to assess the impact of in-person and telephone CP services on cost and quality of life for women in Mendocino. This work will help expand CP services on the North Coast and allow for the development of a model program that resource centers could implement in other areas.

**Determinants of Breast Cancer Treatment in the Underserved**

Low-income women with breast cancer are more likely to be diagnosed with late-stage breast cancer, less likely to get standard treatment, and have lower 5-year survival rates than other women. **Rose Maly, M.D., M.S.P.H**., at the **University of California, Los Angeles**, and colleagues, surveyed 230 low-income, uninsured, newly diagnosed women with breast cancer in Los Angeles County to examine what factors affected their ability to receive appropriate treatment, the type of support services they received, and which patient-physician interaction they found most beneficial. Dr. Maly and her team found that Latinas reported poorer overall health, more difficulties accessing medical care, less physician information giving, less breast cancer knowledge, and more breast cancer-related symptoms. They found that most of the women experienced substantial treatment delays. In addition, the women had higher mastectomy rates than would be expected. These findings suggest that assigning a source of primary care and improving patient-physician communication could improve outcomes in low-income women with breast cancer. The team recently received funding from the National Cancer Institute to study follow-up breast cancer and general medical care, recurrence rates, mortality, and

survivorship in this group of women. Findings from this research were published in *Cancer* 2003; 97(6):1517-27.

**Does a Peer Navigator Improve Quality of Life at Diagnosis**

Women indicate the greatest needs for information at the time of their initial breast cancer diagnosis. However, this is also the time when a woman, overwhelmed by shock and trauma, is least likely to absorb information provided or seek new sources of information. A trained peer counselor, called a peer navigator, can not only provide support but can judge the level of information to disclose and pace that information in a way that can be easily absorbed and understood. **David Spiegel, M.D**., at **Stanford University**, Palo Alto, and **Caroline Bliss-Isberg, Ph.D.**, of WomenCARE, a well-established Santa Cruz agency providing free support services for women with cancer, found in a previous CBCRP-funded pilot study funded that newly diagnosed women with breast cancer, called sojourners, appeared to benefit from being matched with a peer navigator. This new CBCRP grant allowed them to continue to study the impact of peer navigators by randomizing newly diagnosed women to be matched with a navigator or to be put in a control group. (The control group allowed the researchers to assess the impact of a navigator.) The team enrolled 104 newly diagnosed women in their trial; half received a navigator and half received no further intervention. Preliminary findings indicate that the sojourners were more likely than the controls to have less anxiety and distress in addition to having better marital satisfaction. Drs. Spiegel and Bliss-Isberg are now completing the data analysis. These findings will provide additional insights on the extent to which peer navigator programs can improve the quality of life of women with breast cancer.

**Kitchen Divas: Breast Cancer Risk Reduction for Black Women**

African American women are at increased risk for developing pre-menopausal and post-menopausal breast cancer. They also have high rates of obesity. **Janette Robinson Flint** at **Black Women for Wellness,** Los Angeles, and **Kimlin Ashing-Giwa, Ph.D.**, at the **University of California, Los Angeles**, explored the feasibility of initiating a culturally and community-rooted breast cancer risk reduction program, called Kitchen Divas, for African American women. The Kitchen Divas intervention would inform African American women about breast health education and practices and teach them how to modify their dietary behaviors, minimize weight gain, and reduce their risk of obesity-related breast cancer. Ms. Flint and Dr. Ashing-Giwa found that many community members were interested in seeing a program like Kitchen Divas get underway, although a few did express concerns about whether low-income women have the kitchen equipment needed for the recipes that would be disseminated. (Many only have a microwave.) This research led to a revised concept paper that was submitted to the CBCRP for future funding consideration.

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

Breast cancer rates differ among women of different racial and ethnic groups for reasons that remain unclear. **Sally Glaser, Ph.D.,** at the **Northern California Cancer Center** in Fremont, explored whether a genetic risk factor, called HLA gene type, which influences how the immune system functions and is known to differ between racial and ethnic groups, might be responsible in some way for these differences. Dr. Glaser and her colleagues used blood samples that had been provided by white, African American, and Latina pre-menopausal women (206 with breast cancer patients and 269 without) for a Greater Bay Area breast cancer study to determine

specific HLA types for each woman. They found that HLA class I A and B, class II DRB1 and DQB1, and DR-DQ genes were related to breast cancer. Women who had the A-23 gene had a 50 percent lower breast cancer risk, while women with the A-32 or DRB1-12 genes or the DR-DQ 1203 genes had a three times greater risk of developing the disease. The team also found some differences in HLA associations across racial and ethnic groups. If these findings are replicated in other larger studies, this knowledge could lead to new ways of assessing breast cancer risk of women in specific racial or ethnic groups.

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

As breast cancer survival rates continue to improve it becomes increasingly important for breast cancer survivors and their doctors to have more knowledge about how breast cancer and its treatment affect long-term health. This CBCRP grant allowed **Carolyn Crandall, M.D**., at the **University of California, Los Angeles**, to learn how to conduct research on menopause and osteoporosis in breast cancer survivors and to initiate a study on osteoporosis in breast cancer survivors. Dr. Crandall is now exploring whether women with breast cancer start out with better bone health (higher bone density) than women without breast cancer, whether women with breast cancer lose bone at different speeds after menopause compared to women without breast cancer, and whether blood hormone levels can predict the rate at which breast cancer survivors lose bone. Findings from Dr. Crandall's research have been published in *Breast Cancer Research and Treatment* 2004; 88(3):257-61.

**The Impact of Structure on Quality of Breast Cancer Care**

There are three components to quality of health care: structure of care (e.g., setting, financial, and organizational arrangements), process of care (e.g. education, diagnosis, and treatment), and outcomes of care (e.g. survival, recurrence, and quality of life). Understanding the impact structure has on processes and outcomes is vital to improving the quality of breast cancer care. **Katherine Kahn, M.D.**, at the **University of California, Los Angeles**, surveyed 477 medical oncologists, radiation oncologists, and surgeons in Los Angeles County to learn how structure impacts processes and outcomes. Dr. Kahn found, in part, that many specialists report facing financial incentives to provide certain services; that providing routine symptom evaluation to breast cancer patients varies by the physicians' specialty and gender; and that physicians often face barriers in arranging services and referrals. Dr. Kahn and colleagues are now merging these findings with data from surveys completed by breast cancer patients with the goal of identifying which structural change can improve the quality of care breast cancer patients receive.

**Improving Quality of Life in Older Women after Breast Cancer**

A woman's risk of getting breast cancer increases with age, which is why breast cancer is more common in older women. However, studies have found that older women are less likely than younger women to receive appropriate treatment. **Rose Maly, M.D., M.S.P.H.,** at the **University of California, Los Angeles**, studied the differences in the patient-physician relationship between older and younger women and the impact that information support services can have on older women's treatment decisions and quality of life. Dr. Maly and her team found that older breast cancer patients received less informational support at the time of their breast cancer diagnosis than younger women did. In addition, they were more likely to experience treatment delays and to receive a mastectomy rather than a lumpectomy. The team also found that older women believed that informational support services, such as a scheduled follow-up phone call from the

physician after the diagnosis, specific information on support groups, clinical trials, and, most importantly, how to keep functioning normally during treatment, would have improved their quality of life. This research suggests that physicians can play an important role in reducing the health care disparities documented in older women with breast cancer. Findings from this research were published in *Cancer* 2003; 97(6):1517-27, *American Geriatrics Society* 2004; 52(7):1138-45, *Breast Cancer Research and Treatment* 2004; 85(3):201-9, and *Psychooncology* 2005; 14(7):535-45.

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

Overall, more women are choosing to undergo genetic testing to determine if they have an increased risk of developing breast cancer. However, participation rates among minority women remain low. **Beth Glenn, Ph.D.**, at the **University of California, Los Angeles,** studied what role family plays in encouraging or discouraging minority women from being tested. Dr. Glenn interviewed 37 women, including 5 Caucasians, 3 Koreans, 6 Chinese, 2 Filipinos, 7 South Asians, 9 African Americans, and 5 Latinas. Most were breast cancer survivors; others had at least one first-degree relative with breast cancer. Dr. Glenn found that the majority of ethnic minority women who participated in this study had never heard of genetic testing for breast cancer risk. This finding suggests that culturally tailored educational programs need to be developed and implemented in order to increase the number of ethnic minority women who know about and choose to participate in genetic evaluation programs.

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

Although breast cancer patients who receive chemotherapy as part of their treatment frequently complain of memory and concentration problems, even years after completion of therapy, few studies have systematically investigated these changes. **Helen Rebecca Rausch, M.S., Ph.D.,** at the **University of California, Los Angeles**, and colleagues followed a group of breast cancer patients for four years in order to assess what type of long-term impact chemotherapy may have. The team's preliminary analyses suggest that women had problems with their memory for at least 36 months after treatment. Findings from cognitive tests found a subtle decline in attention and concentration in women treated with chemotherapy. However, verbal learning skills, which had declined at 11 months post-treatment, appeared to revert back by 36 months to where women were before they started chemotherapy. This research provides an understanding of the dynamic changes that occur in cognition and memory after adjuvant chemotherapy and provides insight into the overall impact chemotherapy can have on quality of life.

**Reducing Disparities among Korean Women**

Women who receive mammography services at the **Korean Health, Education, Information and Research Center's "**Cancer Detection Programs: Every Woman Counts" program have a low mammography re-screening rate. Lack of re-screening decreases mammography's effectiveness in reducing mortality. **Soo-Young Chin, Ph.D,** at the **Korean Health, Education, Information and Research Center**( KHEIR), Los Angeles, and **Annette Maxwell, Dr.P.H.,** at the **University of California, Los Angeles**, developed a Korean-language brochure designed to increase the low mammography re-screening rate among low-income Korean American women, and pilot tested it at KHEIR and the Koryo Health Foundation. Drs. Chin and Maxell found that the brochure had only a small effect on re-screening rates. This suggests that although a brochure may encourage some women to obtain repeat screening, more intensive efforts are needed, such

as phone calls. This finding helps clarify what is and is not an effective means of improving re-screening and could lead to the development of new types of programs and materials that can educate Korean women about the importance of routine mammography screening.

**Socioeconomics and Ethnicity Affect Tumor Endocrine Status**
Studies have repeatedly found disparities in breast cancer incidence and survival that appear to be linked to race or ethnicity. Researchers believe that these disparities may be, in part, because certain types of breast cancer tumors are more likely to develop in some racial or ethnic groups than they are in others. **Vinona Bhatia, M.D.,** at the **University of California, San Francisco,** and colleagues, explored whether women of different racial and ethnic groups who received breast cancer surgery at San Francisco General Hospital had different types of tumors. They found that African American women were more likely than women of other racial or ethnic groups to have tumors that are estrogen receptor negative, progesterone receptor negative, and HER-2-negative. These so-called triple-negative tumors are the most aggressive and most difficult to treat. The team also initiated a collaboration with breast cancer physicians in Kampala, Uganda, that allowed them to test tumor samples from 12 Ugandan women. They found that the tumors Ugandan women developed were also highly likely to be triple negative. Bhatia and colleagues are continuing to study the frequency of this poor-prognosis breast cancer subtype in African American women. This work could lead to a new understanding of some of the racial disparities seen in breast cancer survival.

**Underserved Women with Breast Cancer at End of Life**
End-of-life care, in general, is poor in the U.S. For low income, underserved women this problem is more acute, since the risk of recurrence and death is higher and their needs are less likely to be met. **Beverly Burns, MS, L.Ac.**, at the **Charlotte Maxwell Complementary Clinic,** Oakland, and **Shelley Adler, Ph.D.**, at the **University of California,** San Francisco, used this grant to address the scientific and collaborative issues raised during the scientific peer review of their pilot Community Research Collaboration application. They established a conceptual framework for end of life issues; determined how they would analyze the data collected from their interviews with women with metastatic breast cancer who are clinic clients and their physicians, complimentary and alternative medicine (CAM) providers, and informal caregivers; reviewed recruitment issues for physician and CAM practitioners; and assessed the patient acceptability of the proposed interview questions. This work led to a revised concept paper and to a CBCRP award that will allow the researchers to study the values and needs of underserved women at end of life.

**Weight Loss in Public Hospital Breast Cancer Patients**
Women who are obese or who gain weight after a breast cancer diagnosis are more likely to have a recurrence or die, compared to lighter women. Obesity results in increases in hormones, like insulin and estrogen, that can stimulate breast cancer growth. Obesity is an even greater problem in ethnic and racial minority women commonly seen in public hospital settings. **Rowan Chlebowski, M.D., Ph.D.**, at **Harbor-UCLA Medical Center,** Torrance, attempted to test the effects of a low-calorie diet and a moderate exercise program on body weight and insulin resistance in overweight postmenopausal women with early stage breast cancer seen in a public hospital. However, it proved impossible to recruit and retain women for this study. This experience, combined with new research that has found that a lifestyle intervention targeting

dietary fat intake (but not weight loss) could reduce the risk of a breast cancer recurrence, helped Dr. Chlebowski develop a dietary study that will use a centralized telephone intervention strategy. This study is being funded by the National Cancer Institute, Canada.

# Grants in Progress: 2006

**Assessing Recurrent Genomic Aberrations Linked to Ethnicity**
Koie Chin
University of California, San Francisco

**A Blueprint for Advancing Quality in Breast Cancer**
Laura Esserman
University of California, San Francisco

**Breast Cancer Risk Profile of Vietnamese Nail Salon Workers**
Kim Nguyen and Peggy Reynolds
Asian Health Services and Northern California Cancer Center

**Consultation Recording for Rural Underserved Breast Cancer Patients**
Sara O'Donnell, Jeff Belkora and Dawn Elsbree
Mendocino Cancer Resource Center, University of California, San Francisco and Humboldt Community Breast Health Project

**Correlates of Lymphedema Severity and Access to Intervention**
Linda Wardlaw, Rani Eversley and Dolores Moorehead
Charlotte Maxwell Complementary Clinic, Woman's Cancer Resource Center and University of California, San Francisco

**Cost-effectiveness of Breast MRI Screening by Cancer Risk**
Allison Kurian
Stanford University

**Effect of Bright Light on Fatigue in Breast Cancer**
Sonia Ancoli-Israel
University of California, San Diego

**Empowering Acupuncturists to Cooperate with Oncologists**
Michael Johnston
University of California, Los Angeles

**Expanding Rural Access: Distance Delivery of Support Groups**
Susan Ferrier, Mary Anne Kreshka and Cheryl Koopman
Northern Sierra Rural Health Network and Stanford University

**Hormone, Psychologic & Immunologic Factors & BC Survivorship**
Hillary Klonoff-Cohen
University of California, San Diego

**Latinas and DCIS: Treatment Decisions and Quality of Life**
Celia Kaplan
University of California, San Francisco

**Lifestyle Factors & Breast Cancer Prognosis in Asian Americans**
Anna H. Wu
University of Southern California

**Living with Advanced Breast Cancer: A Predictive Model**
Annette Stanton
University of California, Los Angeles

**New Breast Cancer Approaches: Integration, Communication**
Leah Karliner
University of California, San Francisco

**Partnership to Reduce Cancer Disparities in Spanish Speakers**
Molly Bergstrom and Rena Pasick
Women's Cancer Resource Center and University of California, Los Angeles

**Peer Mentors Promoting Breast Cancer Clinical Research**
Michele Rakoff, Annette Maxwell and John Link
Breastlink Medical Group, Inc. and University of California, Los Angeles

**Psychobiological concomitants of bereaved women at br ca risk**
David Wellish
University of California, Los Angeles

**Psychosocial Support Services for Latinas with Breast Cancer**
Carmen Ortiz and Anna Nápoles-Springer
Circulo de Vida and University of California, San Francisco

**Racial Disparity in Breast Cancer Mortality**
Rebecca Smith-Bindman
University of California, San Francisco

**South Asian Women with Breast Cancer: What are Their Needs?**
Zul Surani, Roshan Bastani and Beth Glenn
South Asian Cancer Foundation and University of California, Los Angeles

**Treating Insomnia with CBT in Women with Breast Cancer**
Lavinia Fiorentino
University of California, San Diego

**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 2006

**Addressing Cultural & Tribal Issues in Breast Cancer**
Linda Navarro and Marlene von Friedrichs-Fitzwater
Turtle Health Foundation and University of California, Davis

**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

**The Breast Cancer Experience of Slavic Women**
Roman Romaso and Debora Paterniti
Slavic Assistance Center and University of California, San Diego

**Breast Health Literacy and Health Care Decision Making**
Joel San Juan and Suzanne Lindsay
Operation Samahan Health Clinic and San Diego State University Research Foundation

**Dialogue with Breast Cancer Survivors**
Grace Yoo
San Francisco State University

**Filipina Breast Cancer Support: What Model is Meaningful?**
Edwin Jocson and Nancy Burke
West Bay Pilipino Multi-Service Center and University of California, San Francisco

**Fresno Breast Cancer Navigator Pilot Program**
Mary Wallace and John Capitman
San Joaquin Valley Health Consortium and California State University, Fresno

**Increasing Mammography Among Latinas with Disabilities**
Elsa Quezada and H. Stephen Kaye
Central Coast Center for Independent Living and University of California, San Francisco

**Informal and Formal Support and Needs Among Samoan Survivors**
Sala Mataalii and Sora Tanjisiri
Samoan National Nurses Association and CSU Fullerton Auxiliary Services Corporation

**Introducing Acupuncture to Black Survivors for Wellness**
Carolyn Tapp and Michael Johnston
Women of Color Breast Cancer Survivors Support Project and University of California, Los Angeles

**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 Pre-adolescent Girls**
Irene Yen
University of California, San Francisco

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

**Social Support and QOL in Older Minority Women with Breast Cancer**
Yoshiko Umezawa
University of California, Los Angeles

**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

**Special Research Initiatives State of the Science Lit Review**
Peggy Reynolds and Susan Hurley
Northern California Cancer Center

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

# 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.*

*The CBCRP's newly launched Special Research Initiatives seeks to increase knowledge of and create solutions to the environmental causes of breast cancer.*

*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

**Common Genetic Variation & Breast Cancer: A Genomic Approach**
DNA, the long double-stranded molecule found in a cell's nucleus, contains the thousands of genes that store hereditary information and controls how a cell operates. Humans are 99.9% identical to each other at the level of their DNA. The remaining 0.1 percent is responsible for differences in our physical features as well as disparities that may increase breast cancer risk. The majority of these differences are DNA sequence variations called single nucleotide polymorphisms (SNPs, pronounced snips). SNPs occur when a single nucleotide—A, T, C, or G—in the genome is altered; many SNPs are quite common. **Christopher Haiman, Sc.D.,** at the **University of Southern California,** Los Angeles, and colleagues tested a novel genetic (haplotype) approach to identifying genetic markers of non-inherited breast cancer risk. (A haplotype is a combination of genotypes on the same chromosome that tend to be inherited as a group.) Using data from the MultiEthnic Cohort Study, they characterized common SNP patterns in five DNA repair pathways genes: ATM, BRCA1, BRCA2, TP53 and PTEN. Modest evidence of an association between a common haplotype pattern and breast cancer risk was found for the BRCA2 gene. No relationship was seen between SNPs or haplotypes in BRCA1 or PTEN, and no markers were found for TP53 or ATM. These findings advance our understanding of the role that genetic variation plays in breast cancer. Results from this research were published in *Human Molecular Genetics* 2004; 13(20):2431-41.

**Control of Aromatase Expression in Breast Cancer**
Most postmenopausal women with breast cancer have tumors that are hormone-sensitive. These tumors are fueled by the hormone estrogen. A class of drugs called aromatase inhibitors is now widely used to treat hormone-sensitive breast cancer in postmenopausal women. These drugs work by blocking the aromatase enzyme and keeping it from converting androgens into estrogen. However, because aromatase inhibitors block the complete production of estrogen, their use can

lead to side effects associated with estrogen deficiency, such as bone loss. **Ikuko Kijima, M.S.**, at the **Beckman Research Institute of the City of Hope,** Duarte, and colleagues studied regions in the human aromatase gene called promoters I.3 and II. These regions regulate aromatase expression in breast cancer. The team identified several protein binding sites in these promoters. They found that one of these proteins, called CCAAT/enhancer binding protein delta (C/EBPD), increased aromatase activity. The team intends to continue to study how promoters I.3 and II regulate aromatase expression. This work could lead to the development of hormone therapies that suppress estrogen production in breast tissue without decreasing estrogen where it is needed. Results from this research appeared in the *Journal of Steroid Biochemistry and Molecular Biology* 2005; 95(1-5):17-23, and *Cancer Research* 2006; 66(11):5960-7.

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

Obesity appears to decrease breast cancer risk in premenopausal women but increase risk in postmenopausal women. Obesity occurs for complex reasons. **Catherine Carpenter, M.P.H., Ph.D.**, at the **University of California, Los Angeles**, and colleagues explored whether three genes that appear linked to obesity, LEP-R, beta3AR, and PPARgamma2, also increase breast cancer risk. The team observed a sizeable association between waist-to-hip ratio and the LEP-R variant, K109R, among white pre- and postmenopausal women that confirmed an association between K109R and percent body fat observed in their previously funded CBCRP study. They found associations between measured waist, waist-to-hip ratio, and the Pro12Ala PPAR-gamma variant among African American premenopausal women. They also observed associations between Body Mass Index (BMI) and measured waist and the Pro12Ala PPAR-gamma variant among Hispanic premenopausal women. These findings could help to identify groups of women who are susceptible to obesity and an increased risk of breast cancer.

**Preventing Breast Cancer with Ginseng**

Ginseng has been used in traditional Chinese medicine for several thousand years to treat numerous ailments. Some scientists have suggested that it may have a role in breast cancer chemoprevention. **Michael DeGregorio, Pharm.D**., at the **University of California, Davis**, explored whether ginseng is capable of preventing the development of chemically-induced breast cancer in mice. Dr. DeGregorio divided the mice into four groups: a control group that received no treatment; a group that received ginseng; a group that received the breast cancer drug tamoxifen; and a group that received an investigational breast cancer drug called ospemifene. The mice were treated daily for one year. Dr. DeGregorio found that the number of mice that developed breast cancer in the ginseng group was the same as that in the control group. This finding does not support a role for ginseng in breast cancer chemoprevention. However, other studies have suggested that purified components of crude ginseng, known as ginsenosides, may be useful in cancer prevention. Future studies of these purified active components of ginseng will provide more information as to whether ginseng has any value in breast cancer prevention.

**Surrogate Markers for Green Tea**

Chemoprevention is the use of drugs, vitamins, or other agents to prevent cancer occurrence. Epidemiologic and laboratory data suggest that green tea may prevent breast cancer by suppressing the growth of tumor cells and their blood supply. Because chemoprevention clinical trials require thousands of patients and decades of follow up, researchers are looking for surrogate markers that can be used to assess in months, rather than years, whether an agent is

having an impact. To test four potential biomarkers, **Mai Brooks, M.D., and Jian Rao, M.D.,** at the **University of California, Los Angeles**, randomized 72 high-risk women to either a daily dose of 800 mg green tea tablets or placebo tablets for three months. Ductal lavage was performed on all of the women before and after they began using the green tea or the placebo. Drs. Brook and Rao will now analyze the fluid obtained through ductal lavage to see whether the green tea had an affect on the four candidate surrogate biomarkers: nipple fluid basic fibroblast growth factor (bFGF), cellular proliferation marker Ki67, and DNA S-phase values. This work will advance our understanding of the role green tea may play in breast cancer prevention and could lead to new ways of assessing the effectiveness of chemopreventive agents in clinical trials.

**Studying the Interaction of an Essiac Tea and Food Mutagen**
Women who are diagnosed with breast cancer often choose to use complementary and alternative medicines (CAMs) as treatments to supplement conventional therapies or as prevention against another cancer diagnosis. Essiac herbal extract formulations are one of the most commonly used products. **Kristen Kulp, Ph.D.,** at the **Lawrence Livermore National Laboratory**, and colleagues explored whether Essiac could have a protective effect on breast tumor formation by evaluating the ability of the tonic to prevent tumors caused by PhIP, a dietary carcinogen that is formed in well-cooked meats. The team found that Essiac did not increase or decrease PhIP-induced DNA damage in breast cancer cells. They also found that Essiac had no statistically significant effect on PhIP-induced tumor formation in rats. Overall, the results of this project suggest that Essiac does not protect breast cells from DNA damage or subsequent tumor formation from exposure to the breast carcinogen PhIP. However, the affects of Essiac may be different in humans. Findings from this research were published in *Breast Cancer Research and Treatment* 2006; 98(3):249-59.

# Grants in Progress: 2006

**Androgen Receptor Gene and p21 Gene in Breast Cancer**
Wei Wang
University of Southern California

**Birth Characteristics and Breast Cancer in Young Women**
Peggy Reynolds
Northern California Cancer Center

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

**Breast Cancer Breast Cancer Chemoprevention with Dietary Herbal Estrogens**
Dale Leitman
University of California, San Francisco

**Breast Cancer Prevention with Estrogen**
Satyabrata Nandi
University of California, Berkeley

**Breast Cancer Prevention with Phytochemicals in Mushrooms**
Shiuan Chen
Beckman Research Institute of the City of Hope

**Breast Cancer Risk Associated with High Mammographic Density**
Thea Tlsty
University of California, San Francisco

**Estrogen Receptor Beta Agonists to Prevent Breast Cancer**
Peter Kushner
University of California, San Francisco

**Epstein-Barr Virus in Breast Cancer Tissues**
Sally Glaser
Northern California Cancer Center

**Grape Seed as a Natural Breast Cancer Chemopreventive Agent**
Melanie Ruth Palomares
Beckman Research Institute of the City of Hope

**HER-2/neu Gene Variations and Breast Cancer Risk**
Michael Press
University of Southern California

**The Hygiene Hypothesis and Breast Cancer Risk**
Christina Clarke Dur
Northern California Cancer Center

**The IGF Pathway & Breast Cancer Risk in African Americans**
Susan Neuhausen
University of California, Irvine

**PBDEs In Tissues of Women with and Without Breast Cancer**
Myrto Petreas
California Department of Health Services

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

**Targeted Chemoprevention in a Mouse Model for DCIS**
Jeffrey Gregg
University of California, Davis

**Tea, genes and their interactions on breast cancer**
Anna H. Wu
University of Southern California

**USC/NCCC Breast Cancer Research Training Program**
Ronald Ross
University of Southern California

# Research Initiated in 2006

**Breast Cancer Metastasis: a Heritable Trait?**
Alice Whittemore
Stanford University

**Hereditary Breast Cancer and Novel Hispanic BRCA Mutations**
Jeffrey Weitzel
Beckman Research Institute of the City of Hope

**A Novel Biological Framework for the Role of Xenoestrogens**
Shanaz Dairkee
California Pacific Medical Center Research Institute

# Detection, Prognosis, and Treatment

*The detection, prognosis, and treatment topics funded by the CBCRP continue to change as novel technologies and approaches come under investigation. CT (computerized tomography) scanning is emerging with new instruments being designed that are dedicated to breast imaging. Also digital tomosynthesis (a new type of mammography), ultrasound and PET technologies are being used to better image the breast and to allow more accurate excision of tumors. For better disease prognosis, several gene expression profiling tests are coming into both commercial use and clinical testing. The expected benefits of genetic testing performed on tumor samples are to allow individualized therapy to spare women the unnecessary side-effects of treatments with no potential benefit—a common outcome with most non-targeted chemotherapeutics. Cancer therapeutic development continues to evolve with a focus on (i) the validation of novel cell targets and an improved understanding of the disease at the genetic and molecular levels, and (ii) an enhanced ability to match patient subgroups with individual drugs or drug combinations to assess efficacy earlier in pre-clinical testing. Alternative therapies and drugs, especially those derived from plants, engender intriguing areas of investigation.*

*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 Stromal Genes Act as Early Markers of Malignancy**
The earlier that a breast cancer is found, the better the prognosis. Yet with mammography and breast exam, our two current screening techniques, by the time a cancer is found it has probably already been present for about five to eight years. This is why new methods of early detection are needed. **Stefanie Jeffrey, M.D. ,** and **Thea Tlsty, Ph.D.,** at the **University of California, San Francisco**, investigated whether there were changes that occurred in the stroma–the connective tissue and supporting cells in the breast—that could be used to identify an early cancer. (Stromal cells do not actually become cancerous themselves.) Drs. Jeffrey and Tlsty found that there are cancer-associated cells in the stroma of cancer breast tissue that can stimulate the growth of normal breast cells. They are now going to study precancerous tissue, such as hyperplasia and DCIS, to determine when the cells in the stroma begin to act in this fashion. This work could lead to the identification of a molecular "signature" in the stroma and a new method for detecting breast cancer at an earlier stage.

**Chemotherapy-Induced Ovarian Damage: Prevention and Impact**
For many young women with breast cancer, learning that chemotherapy may result in premature menopause and limit their childbearing potential is devastating. Early menopause is also associated with rapid bone loss, increased risk of cardiovascular disease, low libido, and vaginal atrophy. **Hope S. Rugo, M.D.**, at the **University of California, San Francisco**, **Lynn Westphal, M.D.**, at **Stanford University**, Palo Alto, and **Lucy Berlin, M.S.,** of **Young Moms**

**with Breast Cancer**, Palo Alto, enrolled 12 women between the ages of 35 and 44 with early stage breast cancer in a phase II clinical trial to investigate whether giving the drug triptorelin, which suppresses ovarian functioning, along with chemotherapy could prevent chemotherapy-induced premature menopause from occurring. The team also conducted a qualitative study in which they interviewed 24 women about the impact premature menopause had on their quality of life. This work raised awareness of fertility and menopause concerns within the patient and oncology communities, established relationships between breast oncology and the fertility specialists at UCSF and Stanford, and began to explore one option for reducing chemotherapy-induced premature menopause.

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

Traditional Chinese Medicine (TCM), which has been used for centuries to treat cancer, is widely used among breast cancer patients in California today. Yet there have been few controlled clinical trials that have looked at what occurs when the herbs used in TCM are combined with chemotherapy. **Michael Campbell, Ph.D.,** at the **University of California, San Francisco**, and colleagues used breast cancer cells that had been taken from mice to study how the chemotherapy drug doxorubicin (brand name Adriamycin) interacts with some of the different herbs used in TCM. All of the herbs the team investigated had previously been found in laboratory studies to inhibit cancer cell growth. The team found that most of the Chinese herbs added to the effectiveness of doxorubicin when they were administered simultaneously. However, some of the herbs reduced the effectiveness of chemotherapy when administered simultaneously but increased effectiveness when used before or after drug treatment. Additional research by the team suggested that the Chinese herbs impacted effectiveness by increasing or decreasing how much doxorubicin was taken up by the cancer cells. This work expands our understanding of TCM, could lead to the development of new breast cancer treatments, and may result in new recommendations about which Chinese herbs should not be used by women while undergoing chemotherapy.

**Compositional Breast Density as a Risk Factor**

Breast density as viewed on mammography is one of the strongest indicators of breast cancer risk. However, the current methods used to measure mammographic breast density are neither precise nor accurate enough to classify risk status or to follow changes in density over time. **Steven Cummings , M.D., Karla Kerlikowske**, **M.D**., and **John Shepherd, Ph.D.**, at the **University of California, San Francisco**, investigated whether x-ray techniques developed to measure bone density, called dual and single x-ray absorptiometry (DXA & SXA), could precisely quantify breast density. In a study of 36 women (18 with breast cancer, 18 without) they found that all three measures—DXA, SXA, and mammographic density—found higher breast density in the women with cancer. The team also found that SXA breast density measurements were associated with other characteristics known to be related to mammographic breast density and breast cancer risk, such as current use of postmenopausal hormone therapy, menopause, and body mass index. In addition, DXA and SXA appeared to have good potential for monitoring changes in breast density. This work could lead to the development of new methods of assessing breast density during routine risk assessment. Findings from this study were published in *Radiology* 2002; 223(2):554-7.

**Cryptic Peptides-Based Vaccines for Breast Tumor Treatment**
**Her-2/Neu Crossreactive Analogs as Targets for Breast Cancer**
About twenty five percent of all women with breast cancer have tumors that are Her-2/neu positive. These tumors have extra copies of the Her-2/neu gene, which results in too many Her-2/neu receptors on the cell's surface and an overabundance of Her-2/neu protein. This extra protein causes the cell to replicate more than it should. Because Her-2/neu is normally found in the body, it is referred to as a self-protein. The immune system normally does not attack the body's own proteins, which has made it difficult to develop a vaccine that targets Her-2/neu. **Joseph Lustgarten, Ph.D.**, and colleagues at the **Sidney Kimmel Cancer Center,** San Diego**,** identified and then studied a series of small molecules, called cryptic peptides, that mimic or resemble Her-2/neu to see if they could be used as the basis for a cancer vaccine that targets Her-2/neu-positive tumors. After finding that these peptides were not as effective as expected, the team turned its attention to a different small molecule, called a cross-reactive peptide, which appears more promising. They are able to trigger an immune response because they are not normally found in the body. The team received another CBCRP grant that will allow them to continue to study these cross-reactive peptides. This grant allowed them to investigate whether and in what way these cross-reactive peptides can induce an immune response. The goal was to develop a vaccine that could be used to control and eliminate all types of Her-2/neu-positive tumors. They were able to develop a protocol that made the vaccines effective in protecting transgenic mice with a variety of different HER-2/neu mutations from developing tumors. This work could lead to the development of a vaccine that could be used to treat women with tumors that are Her-2/neu positive.

**FKBP Proteins as Molecular Targets in Breast Cancer Therapy**
The spread of breast cancer cells from the primary tumor to other parts of the body, which is called metastasis, is the major cause of death in cancer patients. To date, there are no drug treatments that are able to successfully target and stop metastases. **Sylvia Fong, Ph.D.**, at the **California Pacific Medical Center Research Institute**, San Francisco, and colleagues had previously identified a family of proteins, called FKBPs, that can help keep breast cancer from metastasizing in mice, presumably by reducing the invasive ability of the tumor cells. This current project allowed them to conduct the research necessary to demonstrate that FKBP proteins really are functionally involved in breast cancer progression. The team intends to continue to characterize a novel gene that they found to be part of the network regulated by FKBPs and to explore the possibility of using it as a target for a new breast cancer treatment that can inhibit metastases.

**Inhibitors of Myc: Novel Drugs for Breast Cancer**
If you look inside breast cancer cells, you will see changes in the levels and activities of many proteins that regulate cell growth. One of these proteins, called Myc, can encourage cells to grow faster and make them resistant to anti-cancer drugs. Breast cancers in which Myc is working overtime have been found to be more aggressive—they invade neighboring tissues and grow very rapidly. For Myc to become active, it must first bind to another protein called Max. **Peter Vogt, Ph.D,** at the **Scripps Research Institute,** La Jolla**,** and colleagues screened newly synthesized chemical library that contain tens of thousands of individual drug-like compounds to look for small molecules that could keep Myc from binding to Max. They were able to identify two new types of Myc inhibitors. One class works by getting between Myc and Max, and then

prying them apart. The other works by stabilizing Max, which keeps it from responding to Myc. They are now testing these small molecules to see if they inhibit the growth of breast cancer cells in the lab. They are also exploring whether these Myc inhibitors affect the growth of normal cells. This work could lead to the development of new breast cancer treatments. Findings from this research were published in *Bioorganic Medical Chemistry* 2006;14(8):2660-73.

**Novel I3C Regulated Cell Factor in Breast Cancer Cells**
Relatively little research has been directed at identifying active ingredients in vegetables that might be effective in breast cancer prevention and treatment. Indole-3-carbinol (I3C), a substance found in cruciferous vegetables, such as cabbage, broccoli, and Brussels sprouts, has been found to inhibit cancer cell growth in tumors that are not hormone sensitive. **Gary L. Firestone, Ph.D**., at the **University of California, Berkeley,** and colleagues studied a novel I3C regulated protein to determine what role it plays in I3C's ability to inhibit tumor growth. They discovered that I3C regulates a larger size form of a protein, called cyclin E, which controls the cell cycle. They also found that breast cancer cells not treated with I3C produce smaller forms of cyclin E, while the larger form is detected after I3C treatment. The identification of this relationship between cyclin E and I3C could lead to the development of new breast cancer treatments for tumors that are not hormone sensitive.

# Grants in Progress: 2006

**Apogossypol Derivatives for Breast Cancer Therapy**
Maurizio Pellechia
The Burnham Institute of Medical Research

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

**Breast Cancer Functional Imaging with Optics and MRI**
Bruce Tromberg, Nola Hylton and John Butler
University of California, Irvine and University of California, San Francisco

**cAMP Antagonists of Protein Kinase as Breast Cancer Drugs**
Sanjay Saldahna
Scripps Research Institute

**Dietary Indole Analogs Inhibit Breast Cancer Cell Invasion**
Ling Jong
SRI International

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

**Early Breast Cancer Detection Using 3D Ultrasound Tomography**
Edward Nelson
University of California, Irvine

**HER3 Infidelity and Resistance to Tyrosine Kinase Inhibitors**
Mark Moasser
University of California, San Francisco

**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

**Inhibition of the BRCA2-RAD51 Interaction in Breast Cancer**
Jiewen Zhu
University of California, Irvine

**Molecular Imaging of Breast Cancer Using Breast PET/CT**
Ramsey Badawi
University of California, Davis

**Removing Respiratory Artifacts in Nuclide Breast Imaging**
Brian Thorndyke
Stanford University

# Research Initiated in 2006

**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

**Multilingual Access to Breast Cancer Early Detection**
Susan Stewart and Emily Engelstad
University of California, San Francisco and Alameda County Medical Center

**In Vivo MRS for Cancer Diagnosis and Treatment Monitoring**
Hyeon-Man Baek
University of California, Irvine

**Combined Imaging Modalities for Breast Cancer**
Gultekin Gulsen
University of California, Irvine

**New Technology to Enhance PET Imaging of Breast Cancer**
Craig Levin
Stanford University

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

**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

**A Targeted Therapy for Wound-like Breast Cancers**
Howard Chang
Stanford University

**Artemisinin Disrupts Estrogen Receptor-Alpha and Cell Growth**
Gary Firestone
University of California, Berkeley

**Breast Tumor Inhibition by Vitamin D in a Mouse Model**
David Feldman
Stanford University

**Inhibition of Breast Cancer Aggressiveness by Cannabidiol**
Sean McAllister
California Pacific Medical Center Research Institute

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

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

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

**rADDs: Novel Disintegrins Targeting Breast Cancer**
Stephen Swenson
University of Southern California

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

**Vascular Targeting Therapy for Breast Cancer**
Albert Deisseroth
Sidney Kimmel Cancer Center

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

# Biology of the Breast Cell

*To understand the origin of breast cancers, more research is needed on the pre-cancerous, causative events in the normal breast. In breast development, cell populations must co-ordinate migration, proliferation, and apoptosis (cell death) over space and time. In cancer progression these same processes become dysregulated, initially at the genetic level, it leads to the physiological changes associated with malignancy. To better mimic breast and tumor architecture, 3-D cell culture models provide a means to explore potential underlying mechanisms and show the structure of the breast and interaction of its different cell types lead to the development of a tumor. An emerging paradigm identifies "stem cells" as the key to the origin of tumors. Stem cell populations reside in body organs to provide the raw material for tissue regeneration, repair, and for the cyclic proliferation responses to hormones and pregnancy in the breast. If this theory proves correct, then only a small fraction (1- 2 percent) of cells in a tumor mass retain stem cell properties, and these "cancer stem cells" must be selectively targeted to achieve an effective eradication of the disease.*

*Tumor biology, which the CBCRP refers to as pathogenesis, typically involves basic science cell-based studies. In the past, researchers approached tumor biology from the reductionist level (i.e., studying the contributions of individual genes and proteins to the development of disease). However, over the past decade researchers have realized that the underlying mechanistic driving forces of tumor biology operate though complex, concurrent genetic changes in numerous molecular pathways. Still, it remains the metastatic process that presents the greatest hurdle in our efforts to contain and destroy cancer as it too often presents itself at the time of diagnosis. Breast cancer can spread to almost any region of the body, although metastases are most common to the bone, lung and liver. Understanding the gene and physiological regulatory mechanisms for this cancer cell diaspora is crucial for the design of therapeutic strategies. Other important basic science topics represented in CBCRP's portfolio include: (1) cell proliferation control mechanisms through the estrogen receptor and growth factor receptors (e.g., Her-2), (2) alterations in DNA repair process that permit genetic damage to accumulate in cancer cells, (3) cell cycle changes that permit division under conditions where normal cells would undergo programmed cell death (apoptosis), and (4) novel biomarkers to distinguish pre-cancerous and cancerous cells from normal breast epithelium and their validation as potential new detection and therapy targets.*

*Two research topics are presented in this section.*

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

# Research Conclusions

**Alternative pre-mRNA Splicing in Mammary Epithelial Cells**
Normal breast development requires cells to turn individual genes on and off at the appropriate times. In many cases, a single gene can make multiple products that may exhibit different functions by splicing in (retaining) or splicing out (removing) an internal part(s) of the gene's

coding sequence known as "exons." Exon splicing can be regulated to allow the cell to make predominantly one spliced product at one stage of development, and an alternate spliced product at another stage. This splicing is essential to keep cancer from occurring, yet little is known about how splicing is regulated in normal mammary epithelial cells or how aberrations in this process develop. **John G. Conboy, Ph.D.,** at the **Lawrence Berkeley National Laboratory,** and colleagues studied a gene called protein 4.1 to assess how this splicing process works in specialized breast epithelial cells. They already knew that this gene makes one version of its protein in one type of epithelial cell, and a different version, containing an extra spliced exon "17B", in another. This research allowed the team to identify three potential regulatory elements that stimulate or inhibit splicing. They are now studying the sequences of exon 17B and its adjacent regions and investigating whether changes in splicing occur in other genes as well. This research on the normal breast could lead to a new understanding of how breast cancer develops and new targets for cancer treatment.

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

Virtually all breast cancer begins as ductal carcinoma in situ (DCIS), but not all DCIS will go on to become invasive breast cancer. **Min-Ying (Lydia) Su, Ph.D.,** at the **University of California, Irvine**, attempted to use magnetic resonance imaging (MRI) to study whether hyperplasia, DCIS, or invasive cancers contain cells that have the ability to develop new blood vessels, a process known as angiogenesis. However, they were unable to find a reliable way to use MRI to differentiate between the different types of cancers and precancers. The team is now trying to develop a computerized mathematical procedure for characterizing, comparing, and analyzing the different structures of hyperplasia, DCIS, and invasive cancers. This work could lead to the development of a computer-aided diagnostic system for breast MRI that could aid in breast cancer diagnoses and treatment. Results from this research were published in four separate articles, the most recent in *Technology in Cancer Research and Treatment* 2006; 5(4):401-10.

**Characterizing Breast Cancer Cells in Blood and Bone Marrow**

Small numbers of cancer cells are known to circulate in the blood of many women with newly diagnosed or metastatic breast cancer. Cancer cells can also be found in the blood forming parts of bone in women with newly diagnosed breast cancer. Whether the presence of these circulating tumor cells (CTCs) increases a woman's risk for recurrent disease is unclear. **Robert Carlson, M.D.**, at **Stanford University**, and colleagues attempted to isolate CTCs from blood and bone marrow samples taken from women with breast cancer so that they could study the biologic characteristics of these cells. They found that neither of the two commercially available methods for isolating tumor cells was able to obtain sufficient numbers of these cells. Dr. Carlson and his team intend to continue to try to identify methods of isolating CTCs from blood and bone marrow. This work could lead to the development of new methods of assessing which tumors are most likely to recur or spread.

**Dissection of Signaling Events in the Mammary Gland in Vivo**

Changes that occur in the physical and chemical properties of a cell's environment act as cues that control many aspects of how a cell functions, including migration, proliferation, differentiation, and death. If a problem develops in one of the many different pathways that cooperate and participate in these processes, it could set the stage for the cellular disorders that lead to cancer. **Yuehai Ke, Ph.D.,** at the **Burnham Institute for Medical Research,** La Jolla**,**

and colleagues, studied a tyrosine phosphatase, called Shp2, and its associate protein Gab2m in the mammary gland in mice. They learned that Shp2 controls activities inside the cell that regulate the ability of the breast to produce milk, and that when mice are missing Shp2 the mammary gland does not develop properly. They also discovered that Gab2 plays a role in controlling breast cancer growth and metastases. These findings could lead to a better understanding of how breast cancer develops and progresses and to the development of new breast cancer treatments.

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

Cell division is a normal part of the cell cycle. During the cell division process the genetic material is duplicated and the old and new copies are segregated to opposite side of the cell. This procedure prepares the cell to split into two daughter cells that each contains one complete copy of the genetic material. Scientists believe that unequal segregation of the genetic material may be an early step in the formation of breast cancer. **Kimberly McDermott, Ph.D**., at the **University of California, San Francisco**, explored why some breast cells do not separate the genetic material into two equal parts. She and her colleagues found that, unlike normal cells, these variant breast cells have more than the two centrosomes. (The centrosome orchestrates where, when, and how the old and new copies of genetic material are segregated during cell division.) They discovered that a tumor suppressor protein, called p16, is involved in the process that leads a cell to acquire an abnormal number of centrosomes. And they demonstrated, for the first time, that cells that have more than two centrosomes do not divide the genetic material equally. These findings strongly suggest that a cell's loss of the tumor suppressor protein p16 and its acquisition of an abnormal numbers of centrosomes are critical factors in the development of breast cancer. This work could lead to the development of new ways to detect and treat precancerous cells, which could stop breast cancer from occurring. Results of this research were published in *PLoS Biology* 2006; 4(3):e51.

**Early Transitions in Breast Cancer**

To improve cancer treatment and prevention, a greater understanding is needed of the earliest steps in the transition of normal cells to cancerous ones. **Thea Tlsty, Ph.D**., at the **University of California, San Francisco**, and colleagues have identified a rare population of cells, called variant human mammary epithelial cells (vHMEC) that exhibit characteristics similar to those seen in precancerous breast cells. Dr. Tlsty and her team used a powerful new microscope (dual photon confocal microscopy) to study how the vHMEC take on cancer-like characteristics. They found that vHMEC have a nonfunctioning p16 gene, which prevents the telomeres, which sit on the end of the chromosomes, to accurately keep track of how many times a cell has divided. Dr.Tlsty and her colleagues suggested that this may be the genesis of the telomoeric dysfunction that is one of the hallmarks of a cancer cell. The team also determined that nonfunctioning p16 was associated with an increase in the level of a stress activated protein called COX-2, and that increased levels of COX-2 prevent the cell from properly responding to DNA damage. This demonstrates that stress activation precedes the onset of proliferation, and that these two events occur in the premalignancy stage as a cell transitions from normal to cancerous. The team also discovered that cells called cancer-associated fibroblasts (CAF), which are found in the extracellular matrix that surrounds and supports the cells, can stimulate the growth and alter the appearance of premalignant mammary epithelial cells. All of these findings have the potential to lead to new ways of detecting precancerous cells before they have had the opportunity to transition into cancerous ones.

**In Vivo Gene Expression Profiling of Developing Mammary Gland**
At different stages in a woman's life, such as during puberty and during pregnancy, normal breast duct cells receive messages that tell them to start developing the breast ductal tree. Only when the ductal tree is fully formed can the breast produce milk. **Hosein Kouros-Mehr, B.S**., at the **University of California, San Francisco**, and colleagues, used a technique called DNA microarray profiling to identify the genes that appear to control the development of this ductal structure. They also examined the communication that occurs between the non-ductal cells and the developing ductal tree. The team found that the genes that are involved in the development of the ductal system mirror those that are involved in the development of other branching systems, such as the airways in the lungs. Mr. Kouros-Mehr and others in the lab of Dr. Zena Werb are now studying how these genes affect the form and shape of the breast's ductal branches. Learning how normal mammary gland cells communicate with their environment to create the ductal structure may shed light on how this communication goes awry in breast cancer cells. This work could lead to a greater understanding of known breast cancer risk factors, such early menarche and late pregnancy, and the development of breast cancer treatments. A number of publications resulted from this research, including *Cell* 2006; 127(5):1041-55.

**Maspin: Breast Cancer Suppression Through Enzyme Inhibition?**
A tumor suppressor gene called maspin was first identified in human breast cancer tumors in 1994. However, it's still not yet fully understood what maspin is, how it acts biochemically, and whether it works inside or outside the cell. **Jeffrey Smith, Ph.D.,** at the **Burnham Institute of Medical Research,** La Jolla, and colleagues attempted to clarify how maspin works to keep tumors from metastasizing (spreading) by exploring a novel connection between maspin and another protein complex, called the proteasome, that recycles proteins expressed in a cell. Dr. Smith and his team found that cells that express maspin also express a distinct form of proteasome. This suggests that maspin-expressing cells can contain either a "metastatic" proteasome or a "non-metastatic" proteasome. The team went on to find the areas on the maspin gene that give it the ability to slow or stop metastases from occurring and to demonstrate that maspin affects the type of proteasome that develops. This work could lead to an increased understanding of what triggers metastatic disease as well as new treatments that target the metastatic proteasomes. Results from this study were published in the *FASEB Journal* 2005; 19(9):1123-4.

**A Novel Approach to Inactivate the Estrogen Receptor**
Nearly two-thirds of postmenopausal women with breast cancer have tumors that are estrogen receptor (ER)-positive. These tumors are fueled by the hormone estrogen. Hormone therapies, like the selective estrogen receptor modulator (SERM) tamoxifen, are used to treat these tumors. But they are not perfect. Because SERMS are anti-estrogenic in the breast but estrogenic in other tissues, they carry an increased risk for uterine cancer and blood clots. Further, over time, many tumors will stop responding to hormone therapy**. Alex So, B.A.**, at the **University of California, San Francisco**, studied a region of the ER, called the ligand-binding domain (LBD), that keeps the receptor turned off when estrogen is not present. Once estrogen arrives at the receptor, it releases LBD from its duties. Mr. So and his team also explored the role that a nucleosome, called Swi/Snf, which interacts with a number of proteins that have been linked to breast cancer development, plays in transcribing a gene's DNA sequence into messenger RNA. Mr. So and

colleagues are now trying to develop a model of LBD inactivation of ER. They are also continuing to explore the role of Swi/Snf. This work could lead to the new treatments for ER-positive tumors as well as new methods of keeping these tumors from becoming resistant to current treatments.

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

Biomarkers are used in breast cancer to guide the course of treatment. **Gerry Boss, M.D.**, and **Anne Wallace, M.D.**, at the **University of California, San Diego**, used a patented biochemical assay to study a protein called Ras that transmits growth-promoting signals from the cell's surface to the nucleus. Ras can either be "active" or "inactive." Drs. Boss and Wallace found that Ras was abnormally activated in 100 (40 percent) of the breast cancer tumors they studied. They are following the women whose tumor tissue they tested to determine whether Ras activation is evidence of increased risk of recurrence or metastasis. At 18 months of follow up, no correlation between abnormal Ras activation and the risk of recurrence was seen. However, it is possible that an association will be seen after a longer follow-up period. If this occurs, Ras activation may one day be used to predict whether a tumor is more likely to recur or metastasize. It could also lead to use of newly developed Ras inhibitors for cancer treatment.

**Protective Role of Estrogen Receptor Beta in the Mammary Gland**

The hormone estrogen has been found to fuel breast cancer growth. The effects of estrogen are mediated by two similar versions of the estrogen receptor. Estrogen receptor alpha (ERα is known to be the major mediator of growth in the breast. Estrogen receptor beta (ERβ) was only recently identified and its function in the normal breast remains unclear. However, studies have found that ERβ is often missing in breast cancer cells, and that introducing ERβ into breast cancer cells can inhibit cell growth by altering the action of (ERα). **Leslie Hodges Gallagher, Ph.D**., at the **University of California, San Francisco**, studied the role of ERβ by developing breast cancer cells that express ERβ when a certain regulator is not present. Dr. Gallagher and her team found that when ERβ was expressed these cells grew more slowly during two specific phases of the cell cycle. They also found that ERβ enhanced the effects of tamoxifen, increasing the rate of cell death. To investigate how the presence of ERβ may differentially regulate genes, the team studied two known estrogen-regulated genes, cyclin D1 and Bik. They found that Bik, a mediator of cell death, responded early to tamoxifen when ERβ was expressed. The team is now studying how ERβ and tamoxifen regulate Bik. This work could lead to the development new treatments for preventing or treating breast cancer.

**Proteomic Profiling of Adhesive Structures in Breast Cancer**

In order for breast cancer cells to spread (metastasize) to other parts of the body, they must first acquire the ability to change the way they interact with both other cells and their immediate environment. **Jason A. Bush, Ph.D.,** at the **Burnham Institute for Medical Research**, La Jolla, and colleagues in Dr. Kristiina Vuori's lab used a breast cancer model to study a class of proteins, called integrins, that help establish and regulate the cellular interactions that take place between the cell and its environment. This work led them to define and validate a new biochemical relationship between an integrin and a specific protease that is often found in increased levels in breast cancer cells. Dr. Bush and his co-workers are now confirming their observations by studying actual breast cancer cell lines. This work will increase our

understanding of how cancer cells grow and metastasize and has the potential to lead to the development of new breast cancer treatments.

**Role of BI-1 Protein in Breast Cancer Apoptosis**
Defects in apoptosis, or programmed cell death, play an important role in the initiation and progression of breast cancer. However, relatively little is known about which apoptosis-regulating genes are expressed in breast tumors. **Beatrice Bailly-Maitre, Ph.D.,** at the **Burnham Institute for Medical Research**, La Jolla, and colleagues in Dr. John Reed's lab, investigated an anti-apoptotic protein, called BI-1 (Bax Inhibitor-1), that their lab had recently discovered. They also studied the endoplasmic reticulum (ER), which is found inside the cell's cytoplasm. The ER transports substances within the cell; it also regulates calcium levels inside the cell in response to chemotherapy. The team found that BI-1 appears to be an important regulator of cell death pathways linked to ER stress in the breast. This finding could lead to new ways of making tumors more sensitive to chemotherapy and to new methods of monitoring a tumor's response to cancer treatments. Results from this research were published in *Molecular Cell* 2004; 15(3):355-66, the *Journal of Clinical Investigation* 2005; 115(10):2656-64, and the *Proceedings of the National Academy of Sciences of the United States of America* 2006; 103(8):2809-14.

**Role of Chromatin Regulator in Breast Cell Growth**
ACTR/AIB1, a member of the p160/SRC transcriptional coactivator gene family, was recently found to be present at high levels and/or to have multiple copies in over 30 percent of breast tumors. ACTR interacts directly with the estrogen receptor. However, whether elevated levels of ACTR/AIB1 play a causal role in promoting breast cancer development and progression has not been determined. **Hongwu Chen, Ph.D.**, at the **University of California, Davis**, found that the presence of the ACTR gene makes noncancerous breast epithelial cells live longer while the overexpression of ACTR in ER-positive breast cancer cells enhances cell growth. This suggests that the ACTR/AIB1 gene could play important roles both in normal human breast cell growth and in breast cancer. Dr. Chen's team found that elevated levels of ACTR can stimulate the proliferation of breast cancer cells, regardless of whether estrogen or the estrogen receptor are present, as well as overcome the growth inhibitory effect of anti-estrogens. They also noted that ACTR interacts with the cell cycle regulatory protein E2F in cancer cells. The finding that ACTR may interact directly with important cell cycle regulators to promote breast cancer cell growth suggests that learning how to disrupt the interaction between ACTR and E2F could represent a new treatment strategy for women whose tumors have high levels of ACTR.

**Role of FGF10 in Early Mouse Mammary Gland Development**
Significant breast development takes place before birth in humans and mice. Molecules that control the migration of epithelial cells oversee this early breast development. Studies have suggested that a gene encoding a secreted molecule called Fibroblast Growth factor 10 (FGF10) may control the early steps of breast development. **Saverio Bellusci, Ph.D.**, at **Children's Hospital**, Los Angeles, studied the role of FGF10 and its potential interaction with another important family of growth factors, called WNTs in the process of epithelial cell migration (WNTs are known to be involved in normal breast development as well as in the process of tumor progression). Dr. Bellusci and his colleagues demonstrated that FGF10 controls the expression of WNTs as breast development occurs in the mouse embryo. It is likely that these pathways also play a critical role in breast development during both the embryonic and post-natal

phases. Learning more about cell migration in normal breast development could allow scientists to create new breast cancer treatments that keep breast cancer cells from spreading to other parts of the body. Findings from this research were published in *Developmental Dynamics* 2004; 229(2)349-56.

**Role of IKKa in Mammary Gland Development**

The majority of the cells in the female breast, or the mammary gland as it is called in other mammals, are epithelial cells—the cells that form the milk producing duct where most breast cancers begin. **Michael Karin, Ph.D.,** at the **University of California, San Diego**, and colleagues studied the molecular mechanisms involved in regulating mammary epithelial cell growth during pregnancy, the time at which the mammary gland becomes a milk-producing organ. The team focused its attention on a protein, called NF-κB, that regulates gene expression in both normal cells and in breast cancer. They identified a biochemical pathway involving NF-κB that leads to the division of mammary epithelial cells. And they created a special mouse that would allow them to study this pathway and its involvement in breast cancer. Dr. Karin and his team discovered that when an enzyme called IKKα was inactivated, the mice were less likely to develop breast cancer. The team now intends to investigate whether IKKα plays a different role in a tumor that is HER2-positive than it does in a tumor that is HER2-negative. They are also going to study a related protein called IKKβ. This research could lead to the development of new breast cancer treatments that work by inhibiting IKKα. Findings from this research were published in *Cell* 2001; 107(6):763-75 and *Nature Reviews Cancer* 2002; 2(4):301-10.

**Statistical Techniques for Breast Biology and Cancer Research**

New molecular profiling technologies allow for the rapid and simultaneous measurement of thousands of genes, proteins, and other molecules. The results provide a "fingerprint" of the state of a cell. For researchers, this technology has the potential to be used to assess how networks that regulate cellular growth become defective in breast cancer. For physicians, monitoring tumors before, during and after therapy could provide molecular portraits that could guide cancer treatment. But before this can occur, advanced, statistically sound analytical techniques must be developed and evaluated. **I. Saira Mian, Ph.D.**, at the **Lawrence Berkeley National Laboratory,** developed a variety of statistical techniques to identify subtle, but significant, patterns present in the data derived from molecular profiling technologies. These techniques have the potential to provide more reliable diagnoses, uncover previously unrecognized categories of cancer, yield new discovery and imaging tools, and explain why some people respond to cancer treatments while others do not. Findings from this research were published in *Genome Biology* 2004; (5):R18, *The Lancet* 2003; 362():440, *Journal of Biological Chemistry,* 278(2003)3882, *Molecular and Cellular Biology* 2003; 23():8440, *Current Opinions in Cell Biology* 2003; 15():753, *Mechanisms of Aging and Development* 2003;124():109, *Signal Processing* 2003; (83):729, *Nucleic Acids Research* 2003(31)6392, *Eukaryotic Cell* 2002(1)967, and *Radiation Research* 2002(158)568.

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

Molecular and functional imaging is an important component of the developing field of molecular medicine. For doctors, this imaging may one day make it possible to offer women a non-invasive method of characterizing their tumors and assessing their response to treatment. To

enhance her understanding of techniques in basic science, **Nola Hylton, Ph.D.,** at the **University of California, San Francisco**, studied the p53 regulation of the Myc oncogene in genetically engineered mice. This project was performed in the laboratory of her colleague Dr. Gerard Evan at UCSF. This training will help Dr. Hylton to develop better imaging methods for the detection, prognosis, and treatment of breast cancer in women.

**Targeting of DNA Methylation in Mammary Epithelial Cells**
Many breast cancers have disorders that keep genes that control cell growth from working the way that they should. These abnormalities can be genetic mutations that alter the DNA sequence of a particular gene, or they can be epigenetic alterations that affect the cell without directly altering its DNA. A chemical change to DNA called DNA methylation is one of the best-known epigenetic traits. **David Liston, Ph.D**., at the **Salk Institute**, La Jolla, and colleagues explored the molecular mechanisms by which DNA methylation targets two growth control genes called p16 and p15. (p15 is not silenced in breast cancer cells, but it is very similar to p16, which is.) The team investigated the mechanism by which a protein called TGF-beta induces p15, and identified three proteins, called transcription factors, that bind to the p15 gene and may cooperate with TGF-beta. Since the failure to stop growing in response to TGF-beta is a key abnormality in breast cancer cells, this research on how TGF-beta regulates its target genes could provide important clues as to how DNA methylation occurs and how it affects cancer progression.

**Targeting Estrogen Receptors to Mouse Mammary Epithelium**
The uterus and breasts require estrogen for normal growth. Estrogen also fuels most breast cancers. However, precisely which cells in the normal breast respond to estrogen and become cancerous is not known. **Richard Price, M.D**, at the **University of California, San Francisco**, and colleagues studied excess estrogen signals by adding a super-active estrogen receptor to mouse mammary glands. The experimental mice were followed over time and their mammary glands were sampled for growth abnormalities. Numerous abnormalities were found, which suggested that the super-active estrogen receptor was able to stimulate excessive growth. Dr. Price intends to continue to use these mice to conduct more research on the role of excess estrogen signaling in the development and the treatment of breast cancer.

**Translational Proteomics of Normal to Benign Breast Disease**
How benign breast disease develops is not well understood. Proteins are the functional components of the cell that are directly responsible for disease development. Proteomics—the study of proteins and their functions—has the potential to provide new information about early cellular changes that could lead to better diagnoses of early stages of breast disease. **Dave S.B. Hoon, Ph.D., Armando E. Giuliano, M.D.,** and **Lori L. Wilson, M.D**., at the **John Wayne Cancer Institute,** Santa Monica**,** used ProteinChip array technology to create a proteomic profiling assay that could be used to identify significant proteomic signatures linked with breast disease. The team identified proteins that are present in breast cancer and proteins that could predict which tumors are more likely to have already spread to the lymph nodes. They also developed an algorithm that could be used to identify protein signatures that are linked to breast cancer. The team is now working on further characterizing these specific proteins and on developing detection assays. This work could lead to the development of a proteomic-based tool that could be used to diagnose early breast disease.

**Understanding Aging Effects in the Breast**
Most human cells are programmed to stop growing and dividing after they have produced a certain number of daughter cells. Cells damaged by radiation and other agents may also stop dividing. This permanent arrest in cell growth is called cellular senescence. Studies have found that senescent cells acquire characteristics that enable them to stimulate the growth of nearby cells. **Ana Krtolica, Ph.D.**, at the **Lawrence Berkeley National Laboratory,** and colleagues**,** explored whether the increase in the number of senescent cells that are present in a person's body as they grow older is linked to the increase in breast cancer risk that occurs with age. The team established how changes in the environment induced by aging and/or tissue damage can work together with mutations that can develop inside a breast cell to promote the transformation of a normal cell into a cancer cell. And they identified some of the factors produced by senescent cells that contribute to the changes they observed. The team is continuing to look for the molecules that may be responsible for the effects of aging or damaged tissue on the breast. This work could lead to the identification of molecules that could be the target of new breast cancer treatments. Findings from this research appeared in the *International Journal of Biochemistry and Cell Biology* 2002; 34(11):1401-14, *Cytometry* 2002; 49(2):73-82, *Nature Cell Biology 2003*; 5(8):741-7, *Advances in Gerontology* 2003; 11:109-16, *EMBO Journal* 2003; 22(16):4212-22, *Journal of Cell Science* 2005; 118(Pt. 3):485-96, and *International Journal of Biochemistry and Cell Biology* 2005; 37(5):935-41.

# Grants in Progress: 2006

**A Novel Epithelial-Stromal Model of Metastatic Breast Cancer**
Richard Neve
Lawrence Berkeley National Laboratory

**A Role for p53 and Splicing Factor SAP145 in Breast Cancer**
Lan Truong
University of California, Irvine

**Apaf-1 is a Transcriptional Target for the ZNF217 Oncogene**
Sheryl Krig
University of California, Davis

**Axon Guidance Proteins in Mammary Gland Development**
Lindsay Hinck
University of California, Santa Cruz

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

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

**Defining Mutagenesis Pathways in Breast Cancer Evolution**
Ewa Lis
The Scripps Research Institute

**Discovering Novel Cell-ECM Interactions in Breast Cells**
John Muschler
California Pacific Medical Center Research Institute

**Epithelial Polarity, Organization and the Angiogenic Switch**
Nancy Boudreau
University of California, San Francisco

**Evaluating the Role of RIN1 in Breast Cancer**
Marc Milstein
University of California, Los Angeles

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

**Histone Methylation as a Marker of Breast Cancer Progression**
Judd Rice
University of Southern California

**Identification of BRCA1 Ubiquitylation Targets**
Peter Kaiser
University of California, Irvine

**Identifying Metastatic Breast Cells from Peripheral Blood**
Kristin Kulp
Lawrence Livermore National Laboratory

**Imaging RhoC-induced Breast Cancer Invasion and Angiogenesis**
Konstantin Soletov
University of California, San Diego

**Integrated Proteomic and Metabolic Analysis of Breast Cancer**
Kyle Chiang
The Scripps Research Institute

**Modulation of TGF-beta Signaling in Mammary Epithelial Cells**
Xiaoman Xu
University of California, Irvine

**Normal Mammary Biology of Phosphorylated Prolactin**
Ameae Walker
University of California, Riverside

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

**Oxidative Stress and Estrogen Receptor Structural Changes**
Christopher Benz and Bradford Gibson
Buck Institute for Age Research

**Profiling Enzyme Activities in Human Breast Cancer**
Benjamin Cravatt and Stefanie Jeffrey
Scripps Research Institute and Stanford University

**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 Role of Gli3 in Mouse Embryonic Mammary Gland Formation**
Jacqueline Veltmaat
Childrens Hospital, Los Angeles

**Role of Integrins in Lymphangiogenesis During Breast Cancer**
Barbara Susini
University of California, San Diego

**Role of Oxidative DNA Damage to Breast Tumor Progression**
Paul Henderson
Lawrence Livermore National Laboratory

**Role of Telomerase in Mammary Stem Cell Function**
Steven Artandi
Stanford University

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

**Stem Cells of Molecularly Diverse ER Negative Breast Cancers**
Stefanie Jeffrey
Stanford University

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

**Survivin: Target for Breast Cancer Brain Metastases**
Florence Hofman
University of Southern California

**The Role of B-Myb in Human Breast Cancer Progression**
Joseph Lipsick
Stanford University

**The Role of LMO4 in Breast Cancer**
Zhengquan Yu
University of California, Irvine

**The Role of the ECM in Breast Cancer DNA Damage Repair**
Albert Davalos
Lawrence Berkeley National Laboratory

# Research Initiated in 2006

**A Candidate Marker of Mammary Tumor Initiating Cells**
Alexey Terskikh
The Burnham Institute of Medical Research

**A New Marker for Mammary Epithelial Stem Cells?**
Robert Oshima
The Burnham Institute of Medical Research

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

**Identification of Metastasis Competent Breast Cancer Cells**
Barbara Mueller
La Jolla Institute for Molecular Medicine

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

**Isolation of Cancer Precursors from Normal Human Breasts**
Bob Liu
University of California, San Francisco

**Modeling, Targeting Acetyl-CoA Metabolism in Breast Cancer**
Chen Yang
The Burnham Institute of Medical Research

**MYC and CSN5 in the Breast Cancer "Wound Signature" Profile**
Adam Adler
Stanford University

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

**Role of Cell Division Asymmetry in Breast Cancer Stem Cells**
Claudia Petritsch
University of California, San Francisco

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

**The Role of Estrogen-Related Receptors in Breast Cancer**
Anastasia Kralli
Scripps Research Institute

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

**The Role of Serine and Metallo-Hydrolases in Breast Cancer**
Sherry Niessen
Scripps Research Institute

**Twist Activation in Breast Cancer Metastasis**
Jing Yang
University of California, San Diego

# Relationship between Federal and State Funding for Breast Cancer Research

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

## Sources of Funding

Funding for breast cancer research in the U.S. is available from a variety of sources:

- **Federal Agencies** (National Institutes of Health, Department of Defense) receive funding through Congress from the national budget and from voluntary purchase of more expensive postage stamps.
- **National Voluntary Health Organizations** (such as the American Cancer Society, Komen Foundation, Breast Cancer Research 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) 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 is unique in its funding source. Rather than coming from the state general fund or solely from voluntary donations, almost all of the Program's funds come from a 45 percent share of revenue from a two-cent State tax on cigarettes. This source of funds 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 voluntary donations on individual state income tax returns and from individual contributions. To increase this source of revenue, the CBCRP conducts a public outreach and fundraising effort. the Community Partners Program. A distinguished panel of Californians provides leadership to the Community Partners Program as members of the Community Partners Executive Team. The Executive Team is chaired by Sherry L. Lansing, Founder, Sherry Lansing Foundation, and Regent, University of California.

Since 2002, the CBCRP's Community Partners Program has pursued two goals: increasing voluntary donations through the Income Tax Check-Off Program and new sources, and increasing public awareness of the CBCRP.

## Community Partners Program: Increasing Voluntary Donations

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.

This year, the public demonstrated continued enthusiasm for the CBCRP's research. Businesses, community groups, and individuals initiated their own efforts to provide funds for the Program's research, without being solicited to do so. Belmont city hall employee Kirk Buckman, joking with co-workers, agreed to have his head shaved if they raised $500. The co-workers eventually raised $621 and Buckman's 16-year-old son shaved his dad's head in front of the donors at Belmont City Hall. Buckman donated the funds to the CBCRP in honor of a breast cancer survivor friend, Judy Sheldon. The online retailer Wonders of the Wind sold their Pink Easy Flyer kites, with proceeds going to the CBCRP.

Businesses that made the CBCRP the beneficiary of their community or employee fundraising efforts included: Quota International of Gridley; New United Motor Manufacturing, NUMMI Team Member Giving Campaign; and the Wells Fargo Community Support Campaign. Other donations were received from Mayfield Junior School of the Holy Child Jesus, Pasadena, and America's Charities, Chantilly, VA.

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

## Community Partners Program: Increasing Awareness of the CBCRP

During 2006, the CBCRP's outreach campaign focused on raising awareness of both the Program's work and on increasing citizen contributions on their state income tax forms.

This year the CBCRP produced a five-minute video which showcases the Program. This video—narrated by TV host, breast cancer survivor, and former Olympic figure skater Peggy Fleming—is shown at exhibits and outreach events. It can also be viewed over the Program Web site.

With the assistance and participation of Community Partners, individual donors to CBCRP, and breast cancer advocacy organizations, the CBCRP held public exhibits calling attention to the opportunity to donate to the CBCRP on state tax returns. Using the results of a focus group conducted previously, the CBCRP also conducted an advertising campaign targeted to those most likely to make donations in this way. Advertisements with the slogan "Invest in a Cure for Breast Cancer," which encouraged people to use their state income tax forms to make donations, appeared over public radio stations, on Bay Area Rapid Transit (BART), and over the Internet. Targeted advertising was also mailed to CBCRP and University of California contacts.

The CBCRP gained exposure in a wide variety of media over 2006. The Program was profiled on the cable TV program *Inside Health*. CBCRP Director Marion H. E. Kavanaugh-Lynch spoke on KQED radio's *California Report* program in a segment on the problems facing young women with breast cancer. A radio public awareness campaign was also conducted in the San Francisco Bay area. This campaign included the CBCRP being selected as co-sponsor of Alice Radio's Summerthing festival, along with ads and public service announcements on Alice

Radio and also on stations KDFC, KOIT and KMAX, with additional publicity on those stations' Web sites.

In addition, the CBCRP this year prepared a combined outreach effort 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 of the opportunity to make donations on state tax returns. The campaign will launch in January 2007.

## Community Partners Program: Results

These fundraising and outreach efforts resulted in the California Breast Cancer Research Program amassing nearly $600,000 in contributions, the top beneficiary organization receiving donations through the state income tax check-off program.

## Unmet Need

Ensuring the CBCRP's present funding sources and increasing funds from new sources are both necessary. Current funds are not sufficient to do all that needs to be done. The CBCRP is unable to make grants to meet the following needs:

- **Clinical Trials.** In a clinical trial, some patients receive a promising new therapy and the outcome is compared to a group receiving standard therapy. Clinical trials are the way science discovers which treatments work. Currently, almost every child with cancer in the U.S. is treated through a clinical trial, compared to 3 percent of women with breast cancer. With California's diverse population, statewide clinical trials here could lead to the discovery of information that could be discovered nowhere else.

- **Drug Development.** Developing a new drug can take 10–15 years and cost hundreds of millions of dollars. Pharmaceutical companies select potential drugs most likely to be profitable; discoveries that are too risky or only have the potential to help a small population may never become treatments.

- **Long-term Studies.** A 20- or 30-year study of California women and girls could reveal a lot about risk factors that lead to breast cancer and point to ways to prevent the disease.

- **Tissue Banks**. Samples of tumors from California women, along with the women's medical history, could provide answers to research questions now and in the future.

- **Services.** The CBCRP provides funding for community-based organizations to test services for women with cancer, but once those services have been shown to help women with breast cancer cope or survive, the Program is unable to ensure that those services will be provided.

- **Collaborative Consortium with Biotechnology.** One of the most promising areas to support new therapies and drug discovery is the potential collaboration between the CBCRP and

biotechnology leaders in academia, industry, and government. Agenda-setting conferences could propel research into development.

- **Staff Scientist at the CBCRP.** The CBCRP's funding is devoted to research grants. The addition of a staff scientist would enable the CBCRP to significantly increase the potential to efficiently coordinate programs with scientific and medical communities, and to pursue new research opportunities on both a short and long-term basis.

- **National Priority-Setting Conferences.** As the largest state-funded research organization in the nation, the CBCRP carries a leadership role. The Program has the opportunity to attract experts from medicine, research, and science to take part in a series of "think tank" conferences to support new directions in breast cancer research. The conferences would also draw new researchers into this field.

- **Grant Proposals the CBCRP Does Not Fund**. During 2006, the CBCRP turned down grant applications requesting a total of $25,279,448 that were rated by expert reviewers as having sufficient scientific merit for funding.

Since the CBCRP's major source of funding, the state tobacco tax, is decreasing every year, the Program will not be able to meet these critical needs or continue to fund the broad range of projects it has funded in the past.

## Types of Research Funded by the CBCRP: Fulfilling our Mandate

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 identifying gaps in the research funded by the federal government, and providing funding to fill those gaps
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

## Filling Research Gaps

The federal government funds most health-related research through the National Institutes of Health. 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 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 five-year program initiative, begun in 2005, to fill a significant gap in breast cancer research. This initiative addresses two overlapping research questions that California is uniquely positioned to address. They are the relationship between breast cancer and the environment, the reason for the unequal burden of breast cancer among various populations of women. More information on this initiative may be found in a previous section of this report, "The CBCRP Strategy for Funding Research."

## 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 Coordinate Federal, State, and International Funding

The CBCRP is 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 Program pursues these goals is by taking part in 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 CBCRP joined with eight other breast cancer funding organizations in the U.S. and United Kingdom to launch the International Cancer Research Portfolio (ICRP) Web site (www.cancerportfolio.org). This Web site includes research abstracts from more than 14,000 active research projects, and the online database is searchable by a variety of 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 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 the funded research.

# Research on Women and Minorities

Sixty percent (32 of 53) of the grants awarded by the CBCRP in 2006 studied either women or tissues from women, while the remaining 40% were laboratory studies that did not directly involve women or tissues from women.

Of the 32 grants that involved women or tissues from women, all of the grants involved women as participants and four of the grants (13%) also used tissues or tumor samples.

One-hundred percent (32) of these studies included minority women in the study.

- Fifty-three percent (17) are focused on underserved women.
- Fifty-three percent (17) are focused on minority women.

The following are grants with a primary emphasis on minority and/or underserved women:

**Factors Influencing Breast Cancer Screening Among Older Thai**
Mary Jo Clark, Ph.D., R.N., University of San Diego
Bulaporn Natipagon-Shah, Ph.D., R.N., Thai Health and Information Service

**Fresno Breast Cancer Navigator Pilot Program**
Mary Wallace, San Joaquin Valley Health Consortium

**Mammography Screening for Latinas with Diabetes**
Christine Noguera, M.S., Golden Valley Health Centers

**Increasing Mammography Among Latinas with Disabilities**
H. Stephen Kaye, Ph.D., University of California, San Francisco
Elsa Quezada, Central Coast Center for Independent Living

**Addressing Cultural & Tribal Issues in Breast Cancer**
Marlene von Friederichs-Fitzwater, Ph.D., University of California, Davis

**The Breast Cancer Experience of Slavic Women**
Debora Paterniti, Ph.D., University of California, Davis

**Informal and Formal Support and Needs Among Samoan Survivors**
Sora Tanjasiri, Dr.P.H., M.P.H., CSU Fullerton Auxiliary Services Corporation
Sala Mataalii, Samoan National Nurses Association

**Breast Cancer Education for Deaf and Hard-of-Hearing Women**
Barbara Berman, Ph.D., University of California, Los Angeles
Heidi Kleiger, B.S., Greater Los Angeles Council on Deafness, Inc.

**Telephone-Based Decision Support for Rural Patients**
Jeffrey Belkora, Ph.D., University of California, San Francisco
Sara O'Donnell, Mendocino Cancer Resource Center

**Social Support and QOL in Older Minority Women with Breast Cancer**
Yoshiko Umezawa, M.H.S., University of California, Los Angeles

**Neighborhood Environment and Obesity in Pre-adolescent Girls**
Irene Yen, Ph.D., University of California, San Francisco

**Hereditary Breast Cancer and Novel Hispanic BRCA Mutations**
Jeffrey Weitzel, M.D., Beckman Research Institute of the City of Hope

# California Breast Cancer Research Program Staff and Advisory Council

## CBCRP Staff in 2006

**Marion Kavanaugh-Lynch, M.D., M.P.H.**
Director

**Roslyn Roberts**
Assistant to the director

**Joyce Price**
Administrative Assistant
**Maurice Matthews**
Administrative Assistant

***Core Funding***
**Laurence Fitzgerald, Ph.D.**
Manager; Biomedical Research Administrator
**Sharon Cooper, M.A.**
Grants Analyst
**Mary Daughtry**
Administrative Assistant

***Community Research***
**Walter Price, Dr.P.H.**
Manager; Public Health Research Administrator
**Natalie Collins, M.S.W.**
Technical Outreach Coordinator

***Special Research Initiatives***
**Janna Cordeiro, M.P.H.**
Coordinator of Special Projects
**Catherine Thomsen, M.P.H.**
SRI Research Analyst

***External Relations***
**Katherine McKenzie, Ph.D.**
Manager; Biomedical Research Administrator
**DeShawn Boyd**
Administrative Assistant
**Brenda Dixon-Coby**
Community Outreach & Special Events

**Lyn Dunagan**
Communications Project Coordinator
**Eric Noguchi**
Senior Designer

# Advisory Breast Cancer Research Council

**Chairs**
Christine White (2005-2006)
Lisa Wanzor (2006-2007)

**Vice-Chairs**
Lisa Wanzor (2005-2006)
Amy Kyle (2006-2007)

**Advocates**

- **Crystal D. Crawford, Esq.**, serves as CEO of the California Black Women's Health Project, where she performs legislative, educational and policy advocacy to improve the health status of Black women and girls. Throughout her career, she has combined legal and policy approaches to civil rights and social justice issues. Crawford was born in Harlem, New York and graduated from Dartmouth College with a B.A. in history and sociology. She earned her J.D. from New York University Law School where she served as an editor of the Journal of International Law & Politics, a Hays-Weber Civil Rights Fellow and Chairperson of the Black Law Students Association. Crystal gained litigation experience as an associate with premier corporate law firms in Los Angeles, Boston and New York. After spending a few years in the private for-profit sector, she turned her attention to the non-profit sector, serving as Legal Director of the Alliance for Children's Rights. Crawford serves on a variety of boards and councils including Health Access, VIP Mentors and the Women's Health Council for the state of California. She is admitted to the bar in California, New York & New Jersey and serves as an officer of her church in Inglewood, California. (9/1/06 - 7/1/09)
- **Diane Griffiths** currently serves as Chief Counsel to the California State Assembly Rules Committee. In 1995-96, Griffiths served as Chief of Staff to Assemblywoman Barbara Friedman, the author of the legislation that created the California Breast Cancer Research Program. In 2002, she was herself diagnosed with breast cancer and underwent surgery, chemotherapy and radiation therapy to treat the disease. She also has served from 2002-2006 as a Commissioner of the California Medical Assistance Commission, which administers California's selective provider contracting program for hospitals serving Medi-Cal patients. She also previously served in a number of legislative positions affecting a broad range of health policy decisions, including efforts to expand access to health care and to secure funding for California's trauma network. She represented the Assembly on the Managed Health Care Advisory Committee and on the Managed Health Care Improvement Task Force. (9/1/06 - 7/1/09)
- **Angela Lucia Padilla** is the co-founder and leader of Bay Area Young Survivors (BAYS), the only support and activist group for women under 45 affected by breast cancer in the Bay Area. She is currently forming *Mighty Moms*, a support group for

women with young children who are affected by cancer. Last year Angela was nominated by Lifetime Television as a breast cancer hero. (09/01/05 - 08/30/08)

- As Executive Administrator for the University of California, Los Angeles, **Kim Pierce** is responsible for all the administrative functions of six campus departments, including four departments within the School of Medicine. In addition, she is the Executive Director for the Academy of Molecular Imaging, a 1500-member nonprofit international professional society for physicians, scientists, technologists, and professionals in the field of molecular medicine; the Chair of the Imaging for Hope Patient Advocacy Committee; and a member of both the National Breast Cancer Coalition and the Los Angeles Breast Cancer Alliance. She has a solid, extensive management experience in research and clinical administration, and her range of accomplishments include developing long range plans for patient care and developing strategies for maintaining high-quality patient care in the UCLA Hospital System. (07/01/03 - 06/30/06)
- **Kathy Walters, J.D.,** has served as Program Manager and Director of Volunteer Services in The Community Breast Health Project, an information and support organization in Palo Alto for people touched by breast cancer. A breast cancer survivor, she is a member of their writing group whose work is recently published in A Healing Journey, Writing Together through Breast Cancer. She also serves as the advocate member of a medical research team investigating breast cancer cells circulating in the blood, and as an advocate on an NCI steering committee. (07/01/03 - 06/30/06)
- **Lisa Wanzor** is the Associate Director of Breast Cancer Action, a nonprofit organization whose mission is to carry the voices of people affected by breast cancer to inspire and compel the changes necessary to end the epidemic. Lisa has worked for various nonprofit organizations since graduating from Princeton University in 1985. Social justice issues have always been Lisa's passion, and she has worked for immigrant rights, economic justice, racial equality as well as women's health. Lisa was a participant on the steering committee for the International Summit on Breast Cancer and the Environment held in 2002, is on the planning consortium for the California Environmental Health Tracking Program, and is a graduate of NBCC's Project Lead. (07/01/04 - 06/30/07)
- **Maria Wetzel** is an eight-year survivor of breast cancer. She has been active on BCList.org—an internet support list—since her diagnosis, a member of NBCC for the past six years, and is a volunteer with the Mendocino Cancer Resource Center, where she serves as a patient navigator, a consultation planner, and an information specialist to women newly diagnosed with breast cancer. (09/01/05 - 08/30/08)

**Ex-officio**

- **Kurt Snipes, M.S., Ph.D.,** Acting Chief, Cancer Control Branch California Department of Health Services. Dr. Snipes currently serves as the Acting Chief of the Cancer Control Branch (CCB) of the California Department of Health Services. Dr. Snipes has been with CCB for the past 13 years, as a Research Scientist with the California Cancer Registry, as Chief of the California Cancer Research Program (a state-funded cancer research program that administered over $100 million in applied, biomedical, and clinical cancer research over 5 years), as Chief of Comprehensive Cancer Control, and as Acting Chief of the Cancer Detection Section. In addition to his duties described above, Dr. Snipes also serves on the California Committee for the Protection for Human Subjects, as Principal Investigator for the Sacramento Region of the Asian American Network for

Cancer Awareness, Research, and Training, as Community Advisory Board Member for both the UC Davis and UCSF Cancer Centers, as Vice-Chair of the California Dialogue on Cancer, and is a faculty member with the UC Davis Cancer Center. (03/2005 - Ongoing)

**Industry**

- **Gordon Parry, Ph.D.**, is currently Head of the Cancer Research Department at Berlex Biosciences in Richmond, California. He has focused his research on utilizing genomics technologies to find new targets for drug development and in discovering small molecule and antibody-based drugs. Prior to joining Berlex, Dr. Parry was head of cancer gene therapy efforts at Somatix Gene Therapy, (now Cell Genesys), where he developed some of the first cytokine based (GM-CSF) tumor cell vaccines. Prior to his work in the biotechnology sector Dr. Parry spent 12 years in academic research, mostly as a Staff Scientist at the University of California's Lawrence Berkeley Laboratory (LBL). At LBL he made significant contributions to research on the regulation of mammary epithelial cell differentiation and to the discovery of antibodies targeting breast tumor cells. Dr. Parry obtained his Ph.D. in Biochemistry from the University of London, and carried out post-doctoral work at the University of California Berkeley. (07/01/05-06/30/08)
- **Christine White, M.D.,** is Sr. Vice President, Global Medical Affairs at Biogen Idec, where she has been employed since 1996. Dr. White is a medical oncologist and hematologist who completed medical school and Internal Medicine residency at the University of Chicago, and Hematology and Oncology fellowship at University of California, San Diego, and the Salk Institute. She served as Director, Clinical Oncology Research 1994-1996 at the Sidney Kimmel Cancer Center in San Diego. From 1984-1994, she cared for cancer patients at Scripps Memorial Hospitals, La Jolla and Encinitas, where she served as Medical Director, Oncology Research from 1989-1994, and Dept of Medicine Chair, in 1994. She was an Assistant Professor at UCSD/VA Hospital from 1983-1984 and a research associate at the Salk Institute from 1982-1992. She has been a member of the Board of Directors of the San Diego Regional Cancer Center (1990-1991) and the Hospice of North Coast, (1984-1988) serving one term as Vice President at the latter; She also served on the North Coast Regional Advisory Board at American Cancer Society in San Diego (1986-1989), the Scientific Advisory Committee to San Diego-Imperial Counties Organization for Cancer Control (1989-1991), was a member of the Medical Ethics Committee at Scripps Member Hospital, Encinitas, (1985-1990) and chaired the Investigational Review Board at San Diego Regional Cancer Center (1990-1996). She serves on numerous medical journal editorial boards. (07/01/03 - 06/30/06)

**Nonprofit health organizations**

- **Anuja Mendiratta** is a Senior Program Officer with the Women's Foundation of California. Prior to joining the Foundation, she managed the San Francisco Foundation's Environmental Health and Justice Initiative for four years and worked as a Program Officer at the Marin Community Foundation. Ms. Mendiratta currently serves on the boards of the La Peña Cultural Center in Berkeley, the Center for Environmental Health, and the Community Toolbox for Children's Environmental Health, and the advisory board of the California Breast Cancer Research Program. She holds an undergraduate

degree from Antioch College in Yellow Springs, Ohio, and a Masters in Environmental Studies from York University in Toronto, Canada. (09/01/05 - 08/30/08)

- **John W. Morgan, Dr.P.H.,** is a Professor of Epidemiology and Biostatistics at Loma Linda University and the Cancer Epidemiologist for Region 5 of the California Cancer Registry. Dr. Morgan is a member of the Board of Professional/Scientific Advisors for the American Council on Science and Health and is a member of the board of directors for the California Division of the American Cancer Society. His interests include epidemiologic research that identifies control and prevention strategies for cancer. (07/01/03 - 06/30/06)
- **Catherine Quinn** is the Executive Director of the California Health Collaborative. She has provided steadfast leadership to community health efforts in the Central Valley and throughout the state for more than 20 years. She directed health services for the Fresno County Economic Opportunities Commission and for Urban Indian Health Services, Inc. She is recognized for her program development skills and credited with the collaborative's transition from a three-program, non-profit affiliate of the Hospital Council with an operating budget of less than $500,000 to an independent, Fresno-based, non-profit public benefit corporation with more than 20 local, regional and statewide programs and an annual operating budget of more than $15 million. (9/1/06 - 7/1/09)

**Medical specialist**

- **Klaus Porzig, M.D.**, received both his undergraduate and Doctor of Medicine degrees at Stanford University, then completed his internship at University of California, San Francisco. He completed his residency in internal medicine and clinical fellowship in medical oncology at Stanford University. He was also a research fellow in the Laboratory of Cellular and Molecular Biology at the National Cancer Institute. For twenty-seven years he was a partner in Southbay Oncology Hematology Partners in Campbell, CA. During the past ten years he has concentrated on the care of patients with breast cancer. He retired from private practice in September 2006 and continues to practice at the Stanford University cancer center in the Breast Oncology Program. He is an active participant in the teaching program of the Department of Medicine and has received the Russell Lee Teaching Award for Excellence in Clinical Teaching several times. (9/1/06 - 7/1/09)

**Scientists/clinicians**

- **Moon S. Chen, Jr., Ph.D., M.P.H.,** is professor and Associate Director for Cancer Prevention and Control (Population Sciences) at University of California Davis Cancer Center in Sacramento, which is the scientific headquarters for the NCI-funded Asian American Network for Cancer Awareness Research and Training (AANCART). AANCART links eight universities and NCI-designated cancer centers from the East Coast (Harvard, Columbia) with those of the South (University of Texas MD Anderson) and the West (University of Washington; University of California, San Francisco; University of California, Los Angeles; University of Hawaii) to reach approximately 50% of Asian Americans residing in the US. He previously served as Chair, Division of Health Behavior and Health Promotion, School of Public Health at The Ohio State University's College of Medicine and Public Health. He is known as a pre-eminent scholar/researcher

in public health issues affecting Asian Americans. He has authored or co-authored over 90 refereed articles or abstracts that have appeared in top journals such as the American Journal of Preventive Medicine, American Journal of Public Health, Cancer, Ethnicity & Health, Health Education Quarterly, and Preventive Medicine. Dr. Chen's public health expertise has led to several consultancies, including the Ministry of Public Health of the People's Republic of China, the US Centers for Disease Control, the National Institutes of Health, and several universities and state public health departments throughout the country. In 2002 he joined the National Cancer Advisory Board, and in 2003 became one of two non-federal co-chairs of the Trans-HHS (US Health and Human Services) Cancer Health Disparities Progress Review Group, charged with overseeing and leading a national effort to reduce cancer health disparities. Dr. Chen received the 2003 American Cancer Society's Humanitarian Award for his "unfailing commitment and considerable contributions to the field of public health…," his "dedication to addressing and improving the health of Asian Americans and Pacific Islanders…," and his "leadership in investigating and securing funds for continued research on the health disparities within minority populations." (07/01/04 - 06/30/07)

- **James Ford, M.D.,** is Assistant Professor of Medicine (Oncology Division), Genetics, and Pediatrics (Medical Genetics Division) at Stanford University School of Medicine; Director of the Stanford Program for Applied Cancer Genetics and the Breast Cancer Genetics Clinic; and Director of Stanford's Oncology Fellowship Training Program. He graduated in 1984 magna cum laude from Yale University where he later received his M.D. from the School of Medicine. He performed a residency in Internal Medicine and clinical fellowships in Medical Oncology at Stanford University Medical Center, and was a research fellow in Biological Sciences at Stanford from 1993-1997. Dr. Ford is an internationally recognized expert in the fields of DNA repair and the genetics of solid tumors. His laboratory and clinical research programs focus on the genetics and genomics of familial breast and GI cancers, and the use of new technologies for cancer diagnosis, prevention, and treatment. He is a member of numerous professional societies, is currently the chairman of the Human Genetics and Tumor Biology section of the American Society of Clinical Oncology and is an associate editor for Cancer Research. (07/01/03 - 06/30/06)
- **Felicia S. Hodge** is a professor of Primary Care Nursing and director of the Center for American Indian Research and Education at the University of California, Los Angeles. She is a health policy researcher and a Native American who has been involved in a large number of research projects on breast cancer and other health issues among ethnic populations. Her current research focuses on chronic health conditions and health beliefs and behaviors among American Indians and Alaska Natives. (07/01/05 - 11/30/06)
- **Amy Kyle, Ph.D., M.P.H.,** works on issues at the intersection of science and public policy and to further the links between the realms of "environment" and those of "health." Her goal is to move the practice of policy for health and environment further toward the current state of knowledge about how health is affected by the environment. She holds research and teaching appointments at the School of Public Health, University of California, Berkeley. There, her work focuses on children's environmental health, policy for persistent pollutants, methods to measure net population burdens of pollution and to address cumulative risk and environmental justice, and environmental public health tracking. She is a co-investigator at the Berkeley Center for Environmental Public Health

Tracking. She an author of the first national assessment that integrates environmental and health data and presents measures relevant to children's environmental health. She has a background in public policy and public service at the state level, having served for five years as deputy commissioner for the Alaska Department of Environmental Conservation and in a variety of other positions. She is currently serving on the Committee on Emerging Contaminants of the National Academy of Sciences. She works with a variety of governmental and non-governmental agencies on science translation and policy issues. Recently, she worked with state health and environment agencies to develop a national strategy to address environmental factors that contribute to asthma in children, a ground-breaking project sponsored by the Environmental Council of the States and the Association of State and Territorial Health Officials, and with the National Drinking Water Advisory Committee to identify better means to identify "new" contaminants of concern in drinking water. (07/01/04 - 06/30/07)

- **Mark Pegram** is an oncologist and researcher at the University of California, Los Angeles's Jonsson Cancer Center, assistant professor at the UCLA School of Medicine, and Director of the Women's Cancer Program. He was a co-investigator on Dennis Slamon's research that led to the development of Herceptin. His career is devoted to clinical translational research with a strong focus on breast and ovarian cancer. He has worked extensively with advocates and has been a contributor to the Susan Love MD website. (09/01/05 - 08/30/08)