Annual Report

2005

California Breast Cancer Research Program

EXECUTIVE SUMMARY

During 2005, the California Breast Cancer Research Program (CBCRP) awarded $7,740,842 for 53 single- and multiple-year research projects at 24 California institutions. These pages list the studies funded this year, the studies in progress, and summaries of 66 studies funded in previous years that were completed during 2005.

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 a total of $164,631,026 in research funds.

The need is urgent. Every two hours, on average, a California woman dies of breast cancer. More than 200,000 California women are living with the disease, and 25,000 more will be diagnosed this year. Over the past two decades, some progress has been made. The death rate dropped from 32.4 per hundred thousand California women in 1988 to 24.8 in 2001. 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 has climbed 25 percent over the past two decades. 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 breast cancer is on the rise 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. As requested, it includes the following elements:

1. The number and dollar amounts of research grants, including the amount allocated to indirect costs.
2. The subject of research grants.
3. The relationship between federal and state funding for breast cancer research.
4. The relationship between each project and the overall strategy of the research program.
5. A summary of research findings including discussion of promising new areas.
6. The institutions and campuses receiving grant awards.
7. Inclusion of women and minorities in research studies.

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.

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California Breast Cancer Research Program

Annual Report to the State of California Legislature 2005

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 $164,631,026 in research funds since 1993. In 2005, the CBCRP awarded $7,470,842 for 53 single- and multiple-year research projects at 24 California institutions.

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

Pushing the Research Boundaries

During its twelve-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.

During 2005, the CBCRP launched new Special Research Initiatives to investigate the influence of lifestyle and environment on breast cancer and to uncover the reasons why some groups of California women bear more of the burden of the disease. The CBCRP is investing 30 percent of its funds over five years these Initiatives. To assure that the Initiatives have the most impact on breast cancer, the CBCRP is thoroughly reviewing previous research to avoid duplication. During 2005, national and international experts in these areas of research were interviewed. 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 activists 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.cbcrp.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 fifth symposium, "From Research to Action: Seeking Solutions," was held in Sacramento, September 9–11, 2005. In plenary sessions, workshops, and breakout sessions, researchers presented their latest findings, gave overviews of research fields, and predicted coming trends. Keynote speaker, Kenneth Olden, Ph.D., Sc.D., L.H.D., former Director of the National Institute of Environmental Health Sciences and the National Toxiocology Program, predicted that understanding the role of environmental influences on breast cancer will be a key to preventing the disease.

Equally important, women whose lives have been affected by the disease shared 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 were provided for 72 women this year.

Posters illustrating the results of 70 research projects funded by the CBCRP were on display throughout the symposium. Breast cancer advocate volunteers and researchers were on hand at posted times to speak directly with the public, interpret the results, and answer questions.

At a "Meet the Experts" breakfast, the public discussed breast cancer topics in small groups with research scientists and other experts. Topics ranged from alternative medicine to academic careers in breast cancer research to support groups.

"CBCRP Listens," a community town-hall meeting, invited all attendees to give feedback on the research the CBCRP funds, the symposium, and other Program activities. Feedback from these sessions shapes both future activities of the CBCRP and future symposium agendas.

California community organizations sent representatives who provided information on their breast-cancer related programs. The meeting also included an additional day of training for members of community organizations and research scientists interested in teaming up to conduct research with funding from the CBCRP's Community Research Collaboration grants.

This scientific meeting was intertwined with personal stories of women affected by breast cancer and the meeting also showcased the arts. At an evening reception, author and actress Marcia Wallace shared her entertaining story of twenty years as a breast cancer survivor. At a luncheon, the Sacramento-based DIVA Chorus performed three selections from Sing for the Cure, a collaborative collection of breast-cancer themed music and readings.

A curated art exhibition, on display throughout the symposium, used paintings, sculpture, photography and other media to reflect the far-reaching impact of the disease. Also on view was "Expressions: The Art of Science and Healing", the CBCRP's unique collection of wearable breast art

A report, free to the public in booklet form and available on the CBCRP Web site, provides summaries of all presentations made at "From Research to Action: Seeking Solutions."

Web site

The CBCRP Web site (www.cbcrp.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.

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. *Transforming Research: an Evaluation of the Community Research Collaboration Awards* was published in 2005.

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. The CBCRP plans on continuing to exhibit this art collection throughout the state to create an avenue for health education about breast cancer and raise

public awareness about the CBCRP's research. CBCRP publications are available free at these art exhibits. During 2005, portions of *Expressions: the Art of Healing Breast Cancer* were displayed along with the CBCRP's exhibit at scientific meetings. An art catalog of this collection is being published and will be available to the public.

Exhibits at Scientific and Community Meetings: The CBCRP presented an exhibit of the Program's work at a number of scientific meetings during 2005. The meetings included: the Susan Love Foundation Intraductal Approach to Breast Cancer conference in Santa Barbara, the American Association for Cancer Research Annual Meeting in Anaheim, the California Black Health Network Annual Conference in Sacramento, the American Cancer Society Breast Cancer and the Community conference in Oakland, the UC Davis Cancer Center's Health Fair in Sacramento, the UC Office of the President Health Fair in Oakland, the Urban Health Festival in Oakland, the Long Beach Memorial Breast Care Center's Spirit of Survivorship meeting, the Sisters Network's Gift for Life Block Walk and Breast Cancer Health Fair in San Francisco, and Breast Cancer Action's Celebrating Activism conference in San Francisco. The CBCRP also presented its exhibit at Miracles Faith Church in Oakland.

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

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

Collaborating with Breast Cancer Advocates and California Communities

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 twelve-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.

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.

Advocates Doing 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.

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

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.
- 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. The completion of the BHAWD manual will provide a practical resource to disseminate the program's successes, and to replicate it at disability and breast cancer screening programs.

Fostering Community-Based Research

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 $8 million in funding to 39 collaborative projects; however, research on the effectiveness of this type of science-community partnership itself is limited. To fill this gap in scientific knowledge, and to improve the community-based program, the California Breast Cancer Research Program contracted with Leading Spirit Inc. to conduct an evaluation of the CBCRP's Community Research Collaboration awards program.

The evaluation 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. Other findings include:

- Participating in Community Research Collaboration projects provides benefits to community agencies.

- Collaborations between scientists and community members improve the quality of research.
- Collaborative research projects funded by the CBCRP have had an impact on scientific knowledge, community programs, public policy, community agencies, community members, and academic researchers.
- The CBCRP should consider ways to improve the research teams' collaboration on data analysis and publication of scientific articles.

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 have also been 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 Community Research Collaboration awards. As a result of this multi-year process, applications for Community Research Collaboration awards have continued to increase, and the CBCRP has been able to fund more of these grants. During 2005, the CBCRP received a record of 35 concept papers, which are required before application, an increase of almost 400 percent since 2002.

In 2006, the CBCRP is taking on a new challenge: encouraging and supporting the dissemination and implementation of evidence-based interventions and materials proven in Full CRC awards to other community groups and agencies. Collaborations that have successfully completed a full award and have results (i.e., interventions, educational materials) that can be exported to others can receive up to $150,000 in additional funds to apply their research 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. This year, the CBCRP has embarked on a new five-year strategy. The goal is to change the course of breast cancer research and to launch the discoveries that will bring an end to this disease.

New Strategy: Five-Year Special Research Initiatives

Starting in 2005, the CBCRP is launching new Special Research Initiatives with the goal of addressing two overlapping questions:

- The impact of the environment and lifestyle 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 is investing 30 percent of its research funds for the next five years, which will result in at least $17 million for these investigations. With the help of a task force of researchers and advocates from across the nation, the Program is developing a road map to determine how these resources can best be leveraged to make the biggest leaps forward. The CBCRP hopes to engage other partners who will leverage their resources to make more progress possible. The goal is an integrated, coordinated statewide approach to these critical issues 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 two intertwined issues outlined above. 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.

These new Special Research Initiatives are being launched because the CBCRP's previous efforts to increase research addressing these questions have not led to enough progress. It is the result of a long, thoughtful, thorough planning process. Prior to launching our research funding strategy, the CBCRP council and staff collected data and information on breast cancer research nationwide. Ten years of CBCRP research grants were also analyzed. The council used this information—along with feedback from breast cancer advocates, researchers, and the public—to set the CBCRP's plans for the next five to ten years.

New Strategy: Core Funding Efforts are More Focused

After setting aside 30 percent of CBCRP research funds for the new Special Research Initiatives, the remaining 70 percent are being dedicated to challenge

investigators to use the funds to maximum effect. During the past ten years, the CBCRP has developed a number of types of awards designed to stimulate innovative research. After analyzing results from the Program's first ten years, the Program was able to identify the types of research that have the most potential to stimulate rapid progress against breast cancer. The types of awards funded in 2005 include:

- **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 funded up to 18 months and up to $150,000 in direct costs. Full CRC awards 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. This year, the CBCRP introduced the "critical path" requirement. 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 or $150,000 (for studies using animals or humans) in direct costs.
- **IDEA–competitive renewal**: Allows recently-funded recipients of CBCRP IDEA grants to compete for additional funding, if the project has met key milestones and is on a critical path for success. This award was introduced this year and two grants were funded. IDEA-competitive renewal awards were available for up to two years and up to $200,000 or $250,000 (for studies using animals or humans) in direct costs.
- **Postdoctoral Fellowship award**: Funds advanced training under a breast cancer mentor. In 2005 the CBCRP limited the total postdoctoral tenure (prior training plus new CBCRP funding) to five years, and raised the maximum award duration to three years at $45,000 per year.
- **Dissertation award**: Supports the completion of dissertation research by masters or doctoral degree candidates. In 2005, the CBCRP increased the award amount to $38,000 per year for up to two years.
- **Joining Forces Conference award**: To support a conference, symposium, retreat, or other meeting to link breast cancer researchers, non-breast cancer investigators, and community members for the purpose of stimulating new ideas and collaborations.

As part of the CBCRP's refined focus, a number of previous CBCRP award types were eliminated this year. These include awards targeted by topic (RFAs), Translational Research Collaborations, Scientific Perspective Research Collaborations, and New Investigator, Training Program, Career Enrichment, and Mentored Scholar awards.

Focusing CBCRP funding on the Program's most successful award types will lead to further progress in two areas where the CBCRP has previously achieved success. These areas 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 the United States, 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 researchers to specialize in breast cancer research. For example, the CBCRP awarded Benjamin Cravatt, III, Ph.D., of the Scripps Research Institute in La Jolla, an IDEA grant in 2000. Dr. Cravatt's research deals with proteomics, investigations into the status of all of the proteins within a cell to discover which changes are associated with breast cancer. The end goal is to find proteins that could be targets for new therapies and also to better

distinguish which tumors are more likely to spread to other parts of the body. The research team has made rapid progress. CBCRP funding enabled Dr. Cravatt's team to specialize in breast cancer research, to explore a novel approach to research, and to collaborate with other scientists to translate his discoveries from the lab toward use in medical treatment.

The CBCRP also enlarges the pool of breast cancer researchers by making Postdoctoral Fellowship and Dissertation awards, which allow new scientists to begin their careers by specializing in breast cancer research. Since its inception the CBCRP has launched over 150 new breast cancer careers through the postdoctoral and dissertation awards.

Funding by Priority Issue and by Award Type

Every research grant funded under the CBCRP's Core Funding must be responsive in 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 the 53 projects funded during 2005 by Priority Issue and by Award Type.

2005 Grants Awarded by Priority Issue

Priority Issue	Number of Grants	Amount	Percentage of Total Funding
Community Impact of Breast Cancer	**11**	**$1,060,269**	**13.7%**
Etiology and Prevention	**9**	**$1,269,114**	**16.4%**
Biology of the Breast Cell	**24**	**$3,999,131**	**51.7%**
Detection, Prognosis and Treatment	**9**	**$1,412,328**	**18.3%**

2005 Grants Awarded by Award Type

Award Type	Number of Grants	Amount	Percentage of Total Funding
Dissertation	**7**	**$ 512,305**	**6.6%**
Postdoctoral Fellowship	**12**	**$1,359,047**	**17.6%**
Innovative Developmental and Exploratory (IDEA)	**23**	**$4,433,641**	**57.3%**
IDEA-Competitive Renewal	**2**	**$ 696,113**	**9.0%**
Community Research Collaboration (CRC) Pilot Award	**7**	**$ 689,736**	**8.9%**
Joining Forces Conference Award	**2**	**$ 50,000**	**0.6%**

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. The CBCRP's 2005 evaluation of the Community Research Collaboration awards is discussed more fully in this report in the section titled "Collaborating with Breast Cancer Activists and California Communities."

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.
- A three-year priority-setting process led the CBCRP to invest 30 percent of its funds for five years to answer crucial questions about the influence of the environment and lifestyle 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 2005 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
- The Biology of the Breast Cell
- Detection, Prognosis, and Treatment

The Community Impact of Breast Cancer

The CBCRP supports research and formulation of public policies that would contribute to breast cancer prevention, improve the lives of women who have or have had the disease, and lead to fewer deaths. The Program recognizes the need to reduce unequal access to prevention, detection, treatment, and survivorship services. Sociocultural, behavioral, and psychological research projects to reduce the impact of breast cancer on each woman are also encouraged.

Research Conclusions

Breast Cancer Prevention: The Views of Women and Physicians.
Celia Kaplan, Dr.P.H., at ***University of California, San Francisco,*** surveyed 1700 white, Asian Pacific Islander, African American and Latina women who had had mammograms and did not have breast cancer. Almost one-third of the women were at high risk for breast cancer. The goal was to find out whether the women had heard of, talked with their doctors about, or used either of four breast cancer risk-reduction methods: two preventive drugs (tamoxifen and raloxifene), genetic testing with counseling, and preventive surgical removal of breasts or ovaries. Far more women had heard of preventive methods than discussed them with their doctors. Fifty-four percent had heard of tamoxifen and 4% had discussed it with their doctors or used it. The results were similar for raloxifene (27% and 4%), genetic testing (40% and 4%) and preventive surgery (69% and 5%). The researchers also surveyed 822 California physicians specializing in family practice, internal medicine, and obstetrics/gynecology. Eighty-six percent reported initiating counseling about breast cancer prevention, 45% had referred a patient for genetic testing, 31% had prescribed raloxifene, and 11% had prescribed tamoxifen. Forty percent said time was a barrier to counseling about breast cancer prevention, and 19% cited lack of knowledge.

Women with Breast Cancer: Quality of Life and Diet Adherence.
A diet that includes high amounts of vegetables, fruit, and fiber may protect women from a recurrence of breast cancer. ***Wayne A. Bardwell, Ph.D.,*** at the ***University of California, San Diego,*** studied women in an eight-year (WHEL) trial of the effects of this diet on women who have had the disease. The team observed relationships between quality of life (QOL) and psychological symptoms, obesity, sleep quality, physical activity, stressful life events, pain, and GI symptoms. Thus, better QOL is associated with fewer psychological symptoms, less obesity, better sleep quality, more physical activity, less stressful life events, less pain, and less GI symptoms. Telephone counseling provided during the diet experiment did not result in changes in the women's quality of life or social support. Because the team observed that the WHEL intervention (diet and associated counseling and cooking classes) did not have an effect on QOL, they concluded that any improvement in the WHEL Study intervention is due to changes in the diet, not due to improvements in quality of life (e.g., depression, social functioning). By matching women's self-reports of what they ate with blood analysis, the research team found that women were accurately reporting their dietary intake. Another finding

was that quality of life for early stage breast cancer patients could be improved with interventions targeting psychosocial symptoms, weight reduction, physical activity, sleep quality, and pain. Predictors of depression were the same for breast cancer survivors as for the general population of women, and were not related to cancer. Results from this study were published in *Annals of Behavioral Medicine* 24:S175 (2002).

Breast Cancer Prevention and Control Among Deaf Women.
Breast cancer programs are often inaccessible and inadequate for women who are deaf and hard of hearing. Little research has been done on deaf women and breast cancer. ***Barbara Berman, Ph.D.,*** of the ***University of California, Los Angeles,*** and ***Heidi B. Kleiger,*** of the ***Greater Los Angeles Council on Deafness, Inc.,*** conducted the first-ever exploratory research in this area. Using sign languages, they interviewed 69 deaf women over age 40, seven of whom had had breast cancer. The women interviewed included those deaf from birth and those deafened early or late in life. The research team asked about knowledge, perceptions and practices relevant to breast cancer, and preferences about breast health programs. They also asked about experiences with detection, treatment, and surviving breast cancer. The researchers are analyzing the data from these interviews, and will use it to craft excellent, tailored programs for deaf and hard of hearing women.

Efficacy of a Community Program in Increasing Access to STAR.
African American women have a higher death rate from breast cancer than other groups, and they are under-enrolled in clinical trials (testing on humans) of experimental medications to prevent breast cancer. ***Patricia Ganz, M.D.,*** of the ***University of California, Los Angeles,*** and ***Kathleen Brown, M.D.,*** of the ***Association of Black Women Physicians,*** Los Angeles, collaborated to increase awareness among African American women and African American women physicians of these clinical trials. African American women surveyed by the researchers raised issues that included lack of information about medical trials, the need for African American investigators to be involved in trials, fear of medication and side effects, distrust of research, and time constraints. African American women physicians said barriers to their recommending trials to their patients included the risk of experimental medications, time constraints, and lack of familiarity with available research trials. The researchers used survey results to provide continuing medical education on breast cancer preventive drug trials to members of the Association of Black Women Physicians. They also helped the association present education on this topic to over 150 women at African American churches.

Breast Health Project for Hmong Women and Men.
Marjorie Kagawa-Singer, Ph.D., R.N., M.N., at the ***University of California, Los Angeles, School of Public Health; Mary Anne Foo, M.P.H.,*** at ***Orange County Asian & Pacific Islander Health Alliance;*** and ***Sora Tanjasiri, Dr.P.H.,*** at the ***University of California, Irvine,*** found that culturally-tailored health education motivated Hmong American women to be more aware of breast cancer and obtain mammograms. Breast cancer is the leading causes of cancer death in Asian American and Pacific Islander women. Only about one-quarter of Hmong women have had mammograms. The research team conducted face-to-face interviews with 603 women before and after a breast cancer

education program called Life Is Precious, which was presented to Hmong men and women in their language. The education program was done in Hmong homes, usually with the men and women in different small groups. Enlisting the support of Hmong men was an effort to capitalize on the Hmong cultural strengths of social support, family integrity and on Hmong decision-making styles. After the education, 25% more women in the Hmong communities had a mammogram, compared to only a 5% increase in the Hmong communities where no educational programs were held. There was also a measurable increase in knowledge about causes and prevention of breast cancer among women who received the educational program. This research resulted in a publication in *Journal of Cancer Education* 16(1):50-4 (2001).

A Network-Based Intervention for Chamorros in Southern California.
Chamorros are people indigenous to the Mariana Islands, including Guam and Tonga. ***Sora Park Tanjasiri, Ph.D.,*** of the ***University of California, Irvine,*** collaborated with ***Lola Sablan-Santos,*** of the community organization ***Guam Communications Network, Inc.,*** in Long Beach. The research team surveyed 422 Chamorro women in northern and southern California about their knowledge of and attitudes toward breast cancer, their social networks, and whether they practiced breast self-examination, had clinical breast exams, or had mammograms. The context for this work is that the breast is the most common cancer site for Tongan women. The research team trained Chamorro women to be lay breast educators, using a curriculum developed by the researchers that included a "bingo" card game to educate women in social settings. The team then followed up with a survey of women who had the training to see if it would make them more likely to get appropriate breast cancer screening. The team found low rates for all types of breast cancer screening: only 40% of respondents had ever performed breast self-examinations (BSE), 26% ever received a clinical breast exam (CBE), and 25% ever received a mammogram. Many misperceptions existed about breast cancer causes, signs, and symptoms, as well as the roll of screening in detecting pre-symptomatic cancers. It is clear from this study that much emphasis needs to be placed on improving early breast cancer screenings among Tongan American women, including comprehensive community education, culturally tailored and linguistically appropriate materials, and improved access to low-cost screening sites.

Breast Cancer Screening in Women Surviving Hodgkin's Disease.
Women who had radiation treatment for Hodgkin's disease face a risk for breast cancer 5.66 times that of the general population. Survivors of Hodgkin's disease are also likely to be under age 50 when they are diagnosed with breast cancer. ***Steven L. Hancock, M.D.,*** at ***Stanford University,*** found that telephone counseling about their risk motivated this group of women to have regular mammograms Other factors that led to getting regular mammograms were being married, having a job, being more concerned about breast cancer, and receiving an annual physical exam. The researchers also found that in spite of young women in this study having denser breasts, which make mammograms less effective for detecting cancer, mammograms were effective at pinpointing breast abnormalities for women who survived Hodgkin's disease. This research resulted in a publication in *Journal of Clinical Oncology* 18(4):765-72 (2000).

Geographic Variation in Breast Cancer Stage at Diagnosis.
Women whose breast cancer is diagnosed before it has spread to surrounding tissue or to distant sites in the body have a better chance of surviving. Among California counties, despite a state-funded program that provides screening mammograms to low-income women, the percentage of breast cancer patients who are diagnosed at this early stage ranges from 40% to 71%. ***Pamela Davidson, Ph.D.,*** at the ***University of California, Los Angeles,*** investigated how community-level factors influence the stage at which a woman's breast cancer is diagnosed. She found that compared to white women, African American and Latina women were less likely to be diagnosed at an early stage. In addition women were less likely to be diagnosed at an early stage if they: were under age 65; lived in a neighborhood with low levels of education and high rates of female-headed households, poverty, and recent immigrants; lived in a county where fewer people had health insurance; or used a hospital that served few breast cancer patients. Women were more likely to be diagnosed at an early stage if they: were over age 65; lived in counties where more women had health insurance and had ever had a mammogram; or lived in counties with more primary care physicians and radiologists. This research, which can aid the development of effective community-level interventions, resulted in a publication in *Cancer* 103(5)922-30 (2005).

Effectiveness of Internet vs. Face-to-Face Support Groups.
Previous research has shown that when breast cancer patients suppress negative emotions, they have a worse quality of life and their cancer is more likely to progress. ***Morton A. Lieberman, Ph.D.,*** **of the** ***University of California, San Francisco,*** and ***Mitch Golant, Ph.D.,*** from ***The Wellness Community***, a community organization in Santa Monica, compared Internet and face-to-face support groups led by mental health professionals. The overall findings were that there was no difference in efficacy between the two groups on measures of quality of life, depression, and anxiety. Both groups showed similar improvement. (However, the small sample size precluded the finding reaching statistical significance.) In additional work, the group found women in groups led by professionals expressed more negative emotions than women in groups led by non-professionals. The professional leaders encouraged the expression of anxiety, hostility, and depression because they believe expressing these emotions is therapeutic. The non-professional leaders, on the other hand, offered support and suggested fighting the cause of the negative feelings. When the researchers looked at the issue more closely, they found that women who expressed anger had a higher quality of life and less depression. Those who expressed fear and anxiety had a lower quality of life and more depression. Expressing sadness made no difference to quality of life or depression. These results suggest that expressing some negative emotions benefits breast cancer patients, while expressing other negative emotions does not. This research led to The Wellness Community Virtual Community, an Internet support and educational service for breast cancer and other cancer patients that receives 4,000 visitors per month. It also resulted in publications in *Cancer* 97(4):920-5 (2003) and 97(5) 1164-73 (2003), and *Cancer Nursing* 26(1):37-46 (2003).

Return to Work After Breast Cancer Surgery.
Diane R. Estrin, of the ***Women's Cancer Resource Center,*** a Berkeley community organization, and ***Rani B. Eversley, Ph.D.,*** of the ***University of California, San Francisco***, investigated what helps—and what hinders—women returning to work after breast cancer surgery. The team found that women who had chemotherapy or who had symptoms of depression took longer to return to work. Latina women, low-income women and women with children at home all returned to work more quickly. Latina women had fewer years of education, less income, and were less likely to get paid time off than women from other ethnic groups. They also had more physically demanding work that involved lifting and stooping. Returning to work more quickly may put them at risk for complications such as arm swelling and fatigue that could ultimately affect their long-term ability to work. This research resulted in a publication in *Oncology Nursing Forum* 32(2):250-6 (2003).

Breast Cancer Survivorship: Partner's Role in Recovery.
The transition from being a breast cancer patient on active treatment to being a survivor on long-term follow-up can be upsetting and disruptive. ***Beth E. Meyerowitz, Ph.D.,*** of the ***University of Southern California,*** Los Angeles, investigated how partners' reactions during this transition relate to patients' quality of life, relationship adjustment, personal growth, and coping. Of 384 possible partners in this study, 182 did not take part, either because the breast cancer survivor didn't want them to, or because they refused. The partners who did take part were coupled with breast cancer survivors who were more likely to be white, have higher income, refrain from using avoidance to cope, have more support from their partners, and have better general health. These findings provide evidence of possible biases in recruitment of partners for this type of study. Partners and patients generally reported good quality of life, good marital adjustment, low fear of cancer recurring, low stress, and moderate optimism. Partners of women who had mastectomies or chemotherapy had more difficulties than partners of women who had only part of their breast removed without chemotherapy. Partners perceptions of patients' experience were mostly not accurate. Partners thought the patients' fatigue was worse, and physical symptoms better, than the patients reported. Partners also believed patients were more afraid of recurrence than the patients reported. These results suggest areas where patients may feel misunderstood by their partners, and provide some insight into which partners may have greatest difficulty adjusting.

Assessing the Impact of Shame and Guilt on Recovery.
Shame is a negative evaluation of oneself as a whole person. Guilt is a feeling of having acted in a way that doesn't meet social or moral expectations. Women with breast cancer may experience both, and these emotions could impact their bodies' ability to respond well to stress. ***Janine Giese-Davis***, ***Ph.D.,*** at ***Stanford University***, interviewed ten women with breast cancer using recently-developed methods to measure shame, guilt, embarrassment, and pride. Women spoke most of feelings of pride. They felt pride at accomplishments, such as giving to friends and family, completing a strenuous physical activity while recovering, or for being able to navigate the medical system. Women reported somewhat greater feelings of shame than guilt over the impact of breast cancer on their families. They also expressed shame over bodily appearance, interactions with

physicians, and inability to function completely. When women talked about the impact of cancer on their sexuality, their feelings of guilt were slightly higher than those of shame. Other triggers of guilt included their inability to fulfill their roles with family and others, imposing on others when they were ill, or doing things they thought might have caused their cancer or could worsen their prognosis. Women reported being embarrassed by being seen without clothing in public following surgery, for forgetting things, and for not acting as they did in the past. The long term goal of this research is to understand the role of these emotions in recovery from breast cancer and to train therapists how to best intervene with women feeling shame or guilt.

Child's Stress During Mother's Treatment for Breast Cancer.
Little research has been done on the psychological impact of breast cancer on the patient's children, or how the children's reactions affect their mothers. ***Ellen Levine, Ph.D., M.P.H.,*** and ***Dalia Ducker, Ph.D.,*** at the ***California Pacific Medical Research Institute,*** San Francisco, investigated the reactions of teenagers whose mothers were being treated for breast cancer. Although they recruited for eight months in a wide variety of settings, they had difficulty finding mothers who were willing to participate. The team surveyed 17 women who had breast cancer and 23 teenage children of these mothers. The mother's coping with breast cancer was significantly related to the child's coping, and to the child's depression and anxiety. The teenagers' coping was related to their social adjustment and school performance.

The Functional Implications of Taxane-Induced Neuropathy.
Up to 60% of women who take the chemotherapy drugs paclitaxel or docetaxel, also known as taxanes, develop peripheral neuropathy. This condition is a loss of function of the arm and leg nerves. It causes numbness, tingling, pain and muscle weakness. Prior to this research by ***Meredith Edwards Wampler, B.H.S.,*** at the ***University of California, San Francisco,*** it was known that diabetes-induced peripheral neuropathy could impair balance and mobility and also decrease quality of life. However, no research had been done on peripheral neuropathy caused by chemotherapy. Dr. Wampler found that women treated with taxanes for breast cancer, compared to women who hadn't had the disease, had measurable peripheral neuropathy. The best test for this condition is the Total Neuropathy Score, but Dr. Wampler found that a less expensive and less uncomfortable test, the Modified Total Neuropathy Score, was just as valid in measuring the women's impaired balance, impaired mobility and impaired quality of life. Physicians can use this score to identify women who can benefit from physical therapy. Seventy percent of the women with peripheral neuropathy also had pain, but pain was not related to measurements on the Modified Total Neuropathy Score. Therefore, physicians need to assess pain and provide pain relieving treatment separately from chemotherapeutic regimen.

Constructed Meaning and Stress in Breast Cancer Experience.
Jill L. Mitchell, M.A., at the ***University of California, Los Angeles,*** interviewed in depth 23 women whose breast cancer had spread to other parts of their bodies. The goal was to discover the different ways women give meaning to the experience. A number of themes emerged. Breast cancer affected these women's sense of time. Some women perceived

the disease as chronic rather than terminal. Family members, friends, and health care staff can silence women's attempts to find meaning. The fears of women whose tumors have spread are different from those of women who have early stage breast cancer. There is a process of making peace with dying. Women's psychological experience of cancer can change dramatically over the course of a year. In-depth interviews like those used in this study can be therapeutic. Ms. Mitchell also took saliva samples to measure the women's stress levels. In future work, she will investigate whether it lowers a woman's stress levels if she finds positive meaning in the experience of breast cancer that has spread.

Grants in Progress: 2005

Decision Support in Rural Underserved North Coast Counties
Jeff Belkora, Sara O'Donnell and Julie Ohnemus
Mendocino Cancer Resource Center and Humboldt Community Breast Health Project

Socioeconomics and Ethnicity Affect Tumor Endocrine Status
Vinona Bhatia
University of California, San Francisco

Does a Peer Navigator Improve Quality of Life at Diagnosis?
Caroline Bliss-Isberg and David Spiegel
WomenCare and Stanford University

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

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

Reducing Disparities Among Korean American Women
Soo-Young Chin and Annette E. Maxwell
Education, Information & Research Center and University of California, Los Angeles

Weight Loss in Public Hospital Breast Cancer Patients
Roman Chlebowski
Harbor-UCLA Research and Education Institute

Impact of Breast Cancer and Its Therapy on Osteoporosis
Carolyn Crandall
University of California, Los Angeles

Correlates of Lymphedema Severity and Access to Intervention
Diane R. Estrin, Linda Wardlaw, and Rani B. Eversley
Womens Cancer Resource Center, Charlotte Maxwell Complementary Clinic, and University of California, San Francisco

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

The Impact of Structure on Quality of Breast Cancer Care
Katherine Kahn
University of California, Los Angeles

Hormone, Psychologic & Immunologic Factors and Breast Cancer Survivorship
Hillary Klonoff-Cohen
University of California, San Diego

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

Determinants of Receiving Breast Cancer Treatment in the Underserved
Rose Maly
University of California, Los Angeles

The Cost of Breast Cancer in California
Wendy Max
University of California, San Francisco

Peer Mentors Promoting Breast Cancer Clinical Research
Michele Rakoff, John Link and Annette Maxwell
Breast Friends. Long Beach Memorial Medical Center, and University of California, Los Angeles

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

African American Women and Breast Cancer: What Works?
Carol Somkin and Priscilla Banks
Kaiser Foundation Research Institute and African American Committee on Cancer

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

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

Psychobiological Concomitants of Bereaved Women at Risk for Breast Cancer
David Wellisch
University of California, Los Angeles

Research Initiated in 2005

Effect of Bright Light on Fatigue in Breast Cancer
Sonia Ancoli-Israel
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

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

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

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

Cost-Effectiveness of Breast MRI Screening by Cancer Risk
Allison K. Kurian
Stanford University School of Medicine

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

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

Kitchen Divas: Breast Cancer Risk Reduction for Black Women
Janette Robinson-Flint and Kimlin T. Ashing-Giwa
Black Women for Wellness and University of California, Los Angeles

Partnership to Reduce Cancer Disparities in Spanish Speakers
Molly Bergstrom and Rena J. Pasick
Women's Cancer Resource Center and University of California, San Francisco

Etiology and Prevention

What in the environment—interacting with what unique aspects of each woman's body—alters her risk of developing breast cancer? Despite efforts that have identified genes that greatly increase breast cancer risk and many studies on environmental causes, the disease strikes most women seemingly at random. The CBCRP encourages new California-based studies to understand the environmental causes of breast cancer, and how these increase risk and impact different communities of California women.

Research Conclusions

Migration and Breast Cancer Risk in Hispanics.
When women migrate from Latin American countries, where the risk of breast cancer is low, to the U.S., where the risk is higher, they become more likely to get the disease. ***Esther John, Ph.D.,*** of the ***Northern California Cancer Center,*** Union City, investigated why this happens. Her research team compared over 1,100 Hispanic women with breast cancer to over 1,400 Hispanic women who didn't have the disease. They found that a third-generation Hispanic woman was six times more likely to get breast cancer than a Hispanic woman who recently moved to the U.S. Women who still used Spanish as their primary language were less likely to get breast cancer, even if they had been in the U.S. a long time. Changing from Spanish to English is a measure of how much, or little, these women have adopted U.S. culture. U.S.-born Hispanic women were more likely than recent arrivals to use alcohol and hormone replacement therapy. They were less likely to begin menstruation at a higher age, have a baby at a young age, and to breastfeed. These factors explained most of the difference in the breast cancer rates among pre-menopausal, but not post-menopausal, Hispanic women. Their data suggests that changes in hormonal and lifestyle factors associated with living in Western countries like the U.S. have a major influence on the development of breast cancer. Therefore, the identification and communication of risk factors that can be modified (i.e., breast feeding, physical activity, body weight, alcohol consumption, diet) is important in reducing breast cancer risk.

Pesticides and Breast Cancer in Hispanic Women in California.
Paul K. Mills, Ph.D., at the ***Public Health Institute,*** Berkeley, investigated whether exposure to two classes of commonly-used pesticides, organochlorines and triazines increases Hispanic California women's risk for breast cancer. The research team approached the question in two ways. First, they compared the breast cancer rate among Hispanic women with pounds of pesticide used, for each of California's 58 counties during the years 1988–1999. In line with previous research, older and higher-income Hispanic women had higher breast cancer rates, and those with more children had lower rates. The risk of cancer among Hispanic women was also 18% higher in counties with the highest use of the organochlorine insecticide methoxychlor and 16% higher for another organochlorine pesticide, toxaphene. High use of triazine pesticides did not raise the risk for breast cancer. The second approach the researchers used was to evaluate the breast cancer risk among women members of the United Farm Workers of America

union. Their risk of breast cancer was not related to any specific crop, except mushrooms, where a small subgroup faced a risk six times higher than women who didn't work with this crop. Breast cancer risk was also not associated with the women working with specific chemicals. However, the more the women worked with all the pesticides covered in this study combined, the higher their risk, until the women with the most exposure to all pesticides had a risk 41% higher than those with the least. Risk of breast cancer associated with pesticide use was stronger in young women.

4th International Symposium on the Intraductal Approach to the Breast.
The ***Dr. Susan Love Research Foundation,*** Pacific Palisades, held its fourth conference to develop a new model for detecting and preventing breast cancer. Accessing the lining of the milk ducts in the breast, where cancer starts, could be the basis for a test much like the Pap smear for cervical cancer. This conference brought together over 100 researchers, clinicians, and patient advocates from California, the U.S., and the world. The researchers brought a variety of scientific backgrounds, including medical oncology, internal medicine, surgery, radiology, biochemistry, pathology, endocrinology, epidemiology, and biostatistics. Participants shared research findings, developed multi-disciplinary collaborations, and awarded seven pilot grants to stimulate new research. A panel provided the public with an opportunity to learn about the intraductal approach and to ask questions about current breast cancer treatment options.

Breast Cancer Prevention with Phytochemicals in Mushrooms.
Higher levels of the enzyme aromatase in breast tissue raise a woman's risk for breast cancer. Drugs that inhibit aromatase are effective in treating breast cancer that depends on hormones, and may also have the potential to prevent breast cancer in post-menopausal women. ***Shiuan Chen, Ph.D.,*** at the ***Beckman Research Institute, City of Hope,*** Duarte, found that an extract from white mushrooms inhibits aromatase in one type of breast tumor cells growing in culture. These breast tumor cells were dependent on estrogen, high in aromatase, and proliferated when exposed to the hormone testosterone. When fed to animals with tumors that had the same characteristics as the tumor cells in culture, the mushroom extract also slowed down tumor growth. The extract works not by killing cancer cells, but by preventing aromatase from allowing tumor growth. More than one chemical in the mushrooms extract may inhibit aromatase. This study suggests that post-menopausal women can benefit from a diet that includes mushrooms.

Mechanisms of Reduced Metastasis by Conjugated Linoleic Acid.
Conjugated linoleic acid is found in some sources of dietary fat. ***Kent Erickson, Ph.D.,*** at the ***University of California, Davis****,* found prior to this study that conjugated linoleic acid can be a potent protective against mammary tumors in mice, the equivalent of breast cancer in humans. In this study, he found that feeding mice diets that included conjugated linoleic acid lowered the levels of proteins in their tissues that cause tumors to form, compared to mice fed similar diets without conjugated linoleic acid. Tumors took a longer time to establish in mice fed conjugated linoleic acid. When mice fed conjugated linoleic acid had tumor cells injected into their blood, fewer tumors grew. When conjugated linoleic acid is applied directly to tumor cells growing in a lab culture, it kills them. Conjugated linoleic acid also alters the ability of tumor cells to invade and migrate,

and it changes the action of several genes involved in tumor initiation, growth and spread. These findings add to accumulating evidence that conjugated linoleic acid may be an important preventive agent for breast cancer.

Upregulation of BRCA1 as a Cancer Preventive Strategy.
Donna Williams-Hill, Ph.D., and ***Colin K. Hill, Ph.D.,*** at ***University of Southern California,*** Los Angeles, investigated how two genes, BRCA1 and BRCA2, interact with hormones in the breast. The normal versions of these genes suppress tumors by producing proteins, also caused BRCA1 and BRCA2. A small percentage of women have mutated versions of either or both these genes that fail to suppress tumors and make the women more prone to breast cancer. The research team found that in rats, levels of BRCA1 protein rise at puberty. A strain of rats bred to be susceptible to breast cancer had much lower levels of BRCA1 protein than rats bred to be resistant. The team also found strong evidence that fluctuations in hormone levels that occur when the rats go through the estrus cycle control the level of BRCA1 and 2 in cells. Rats exposed to radiation at a time when their levels of BRCA1 protein were high got fewer tumors than rats exposed when their BRCA1 protein levels were low. The team is doing further research to find out whether changing the rats' hormones artificially produces a change in the level of BRCA1 protein.

Genetic and Environmental Modifiers of Breast Cancer Risk.
Women with a family history of breast cancer have a higher than average risk of getting the disease. Only 15–20% of familial breast cancer is accounted for by two breast cancer susceptibility genes, BRCA1 and BRCA2. ***Argyrios Ziogas, Ph.D.,*** at the ***University of California, Irvine***, investigated how several genes that are involved in the metabolism of the hormone estrogen or of cancer-causing substances from the environment may be associated with breast cancer. The research team found that taking the hormone progesterone raises the breast cancer risk of women who have certain variations of two genes, COMT and CYP1A1. Women with a variation of another gene, GSTM, raise their risk for breast cancer if they take oral contraceptives. Lower weight at age 18 raises the risk for breast cancer of women with certain variations of the CYPA1A gene. The MM variation of the GSTT gene raises a woman's risk for breast cancer. None of the genes studied made a woman's breast cancer risk higher if she smoked. The researchers also found that 1.3% of women have the cancer-prone version of the BRCA1 gene, and 1.9% have the cancer-prone version of BRCA2. Results of this study will help improve individualized risk prediction and preventive strategies.

Using Microarrays to Estimate Breast Cancer Risk.
Exposure to X-rays is linked to developing breast cancer. ***Bradley Ekstrand, M.D., Ph.D.,*** at ***Stanford University,*** attempted to find out if the development of breast cancer is related to an abnormal genetic response to X-rays. He obtained blood samples from 41 women who had long ago received radiation to the chest as part of their treatment for Hodgkin's disease. Nineteen of these women had since developed breast cancer. Dr. Ekstrand exposed all the blood samples to radiation. Using microarrays, a technology that allows researchers to search for thousands of genes at a time, Dr. Ekstrand attempted to find genetic differences in the way blood cells from women who'd had breast cancer

handled radiation, compared to blood cells from women who hadn't had the disease. He couldn't find any significant differences, but other researchers at this lab are continuing to pursue this question.

Prolactin and Breast Cancer Risk in a Multiethnic Cohort.
The hormone prolactin circulates in the blood. It is important to breast development during puberty and pregnancy, and to milk production. Women with higher levels of prolactin the their blood may have a higher risk for breast cancer. ***Brian Henderson, M.D.,*** at the ***Keck School of Medicine, University of Southern California,*** investigated whether genes control the levels of prolactin in the blood. He tested blood samples from African American, Hawaiian, Japanese, Latina, and white women who had breast cancer and women from the same ethnic groups who did not. One variation on the prolactin gene (SNP 35 [intron 1] in the region of low linkage disequilibrium) was associated with higher prolactin levels in the blood. However, there was no relationship between breast cancer risk and any variations of the prolactin gene or of the gene that produces a protein that allows cells to take in prolactin.

Physical Activity and Diet in Adolescents with Disabilities.
A number of research studies suggest that physical activity and nutrition may be associated with the risk of breast cancer. However, this research has not been targeted to women with disabilities. ***Carol Koprowski, Ph.D., R.D.,*** and ***Katherine Hall, Ph.D.,*** at ***California State University, Northridge***, attempted to study the feasibility of developing appropriate assessment tools to measure physical activity and dietary intake in teenage girls with disabilities. The researchers held focus groups where teenage girls with disabilities discussed their views on current dietary and physical activity recommendations. However, the research team was not able to get permission from schools and parents to interview enough teenage girls to complete the research.

Grants in Progress: 2005

Serpentinites & the High Incidence of Breast Cancer in Marin
Janice Barlow and Scott Fendoff
Marin Breast Cancer Watch and Stanford University

Surrogate Markers for Green Tea
Mai Brooks and Jian Rao
University of California, Los Angeles

Genetics, Obesity, and Breast Cancer Risk
Catherine Carpenter
University of California, Irvine

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

The Hygiene Hypothesis and Breast Cancer Risk
Christina Clarke

Northern California Cancer Center

Can Placenta Factors Explain Race Patterns in Breast Cancer?
Barbara A. Cohn
Public Health Institute

Preventing Breast Cancer with Ginseng
Michael DeGregorio
University of California, Davis

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

Immune-Function Genes and Race Differences in Breast Cancer
Sally Glaser
Northern California Cancer Center

Common Genetic Variation & Breast Cancer: A Genomic Approach
Christopher Haiman
University of Southern California

Dietary Fat, Fat Metabolizing Genes, and Breast Cancer Risk
Sue Ann Ingles
University of Southern California

Control of Aromatase Expression in Breast Cancer
Ikuku Kijima
Beckman Research Institute of the City of Hope

Studying the Interaction of an Essiac Tea and a Food Mutagen
Kristen Kulp
Lawrence Livermore National Laboratory

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

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

PDDEs in Tissues of Women With and Without Breast Cancer
Myrto Petreas
California Department of Health Services

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

Birth Characteristics and Breast Cancer in Young Women
Peggy Reynolds
California Department of Health Services

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

Estrogen Metabolizing Genes, Soy and Breast Cancer in Asians
Anna Wu
University of Southern California

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

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

Research Initiated in 2005

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

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

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

Breast Cancer Risk Profile of Vietnamese Nail Salon Workers
Kim D. Nguyen and Peggy Reynolds
Asian Health Services and Impact Assessment, Inc.

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

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

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

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

The Biology of the Breast Cell

The CBCRP encourages new research to understand the pre-cancerous events in the breast that lead to cancer at the tissue, cell, molecular, and gene level. The Program also funds all aspects of basic research on tumors as they progress from DCIS to invasive breast cancer. These studies represent the groundwork for envisioning new biomarkers for disease prognosis, therapies, and detection strategies.

Research Conclusions

Steroid Receptor Coactivators in Mammary Gland Development.
Cells in normal breast tissue and in estrogen receptor (ER)-positive breast cancers need estrogen to grow. Breast cells that do not get estrogen stop proliferating and die. This is why ER-positive breast cancers are treated with drugs that block estrogen activity. ***Shi Huang, Ph.D.,*** at ***The Burnham Institute,*** La Jolla, and colleagues discovered and then investigated a new tumor suppressor gene, RIZ1, and the protein it produces. The RIZ1 gene and its protein are frequently missing in human cancers, particularly in breast cancers. The team found laboratory evidence that suggests that the breast needs RIZ1 to respond to the hormones estrogen and progesterone. They also found that the RIZ1 enzyme appears to affect other proteins in the cell's nucleus. As a result, some genes may be more likely to respond to the commands of the estrogen receptor. For example, they found that reducing RIZ1 levels decreased production of a breast cancer-associated gene called pS2. This new understanding of estrogen receptor function may lead to the development of new ways to prevent and treat breast cancer.

Genetic Aspects of Physiological Response During Lactation.
When a clump of tumor cells grows too large, the level of oxygen in the tissue decreases (i.e., hypoxia). In response, a protein, HIF-1, increases and activates genes that control new blood vessel growth. Recent studies have shown that high levels of HIF-1 are present in a variety of tumors, including breast tumors. ***Randall S. Johnson, Ph.D.,*** at the ***University of California, San Diego***, investigated whether the HIF-1 response to lowered oxygen levels contributes to mammary gland development and the production of milk in mice. They found that mice that lack HIF-1 function do not develop sufficient numbers of alveoli, the small glands that produce milk, and fail to properly nourish their young. They also found that when mice lack a protein called von Hippel-Lindau (VHL), HIF-1 is overproduced. This, in turn, increases vascular endothelial growth factor (VEGF), which regulates the new blood vessels tumors need to grow. These findings could lead to new ways to block blood vessel growth in breast tumors and to new breast cancer treatments. Results from this research were published in *Development* 130:1713-24 (2003).

Effect of Breast Cell Environment on Repair of DNA Damage.
Breast cancer occurs mostly in the epithelial cells—the cells that line the breast duct. These cells are in contact with a basement membrane, a thin layer of connective tissue.

Aylin Rizki, Ph.D., at the ***Lawrence Berkeley National Laboratory,*** investigated how communication between cells and the basement membrane affects a cell's ability to repair damage to its DNA. When the DNA is not repaired properly it can accumulate genetic changes, which sets the stage for cancer to occur. Dr. Rizki and her colleagues focused on a mechanism called the double-strand break repair pathway that prevents mutations. Double strand breaks can be caused by the radiation therapy used to treat breast cancer. Dr. Rizki's findings suggest that basement membrane signaling is important in regulating double-strand break repair and in controlling how DNA responds to radiation. Her team is continuing to explore the effects of this signaling on DNA. They are also looking for the molecules that relay the signals from the basement membrane to the repair mechanism. Results from this research were published in *Nature* 411:713-16 (2001), *Differentiation* 70:537-46 (2002), and *Signal Processing* 5:147-53 (2003) and 83:729-743 (2003).

The Importance of Growth Inhibitory Signals in Normal Breast Cells.
HER-2 is a protein found in larger than normal amounts in about 30% of breast cancer cases. Scientists do not yet fully understand how having too much HER-2 promotes breast cancer. ***Cindy Wilson, Ph.D.,*** at the ***University of California, Los Angeles***, is testing the hypothesis that HER-2 promotes breast cancer by inhibiting the action of proteins in the breast that are the body's first line of defense against the disease. Dr. Wilson and her colleagues studied both normal breast cells and breast cancer cells. They found that higher than normal levels of HER-2 can make some cells less sensitive to a protein called transforming growth factor beta (TGF-ß), which may control the growth of breast epithelial cells. They also found that higher than normal levels of HER-2 can make aggressive breast cancer cells more sensitive to TGF-ß. This research could lead to the development of new treatments for women with HER2-positive breast cancer that combine the anti-HER2 drug Herceptin with drugs that stimulate TGF-ß.

Identification of BRCA1 Ubiquitylation Targets.
Women who have inherited a mutation in a gene called BRCA1 are at higher risk for developing breast and ovarian cancer. How the normal version of BRCA1 functions at the molecular level to suppress tumor development is still not known. ***Peter Kaiser, Ph.D.,*** of the ***University of California, Irvine***, explored the genetic regulation of the BRCA1 gene through a process of protein degradation, called ubiquitylation. Dr. Kaiser compared differences in protein degradation between cells with a BRCA1 gene that worked properly and cells with a BRCA1 gene that did not. He and his colleagues went on to develop a novel approach, called SILAC (stable isotope labeling by amino acids in cell culture), which will allow them to complete their protein analysis. Dr. Kaiser received a second grant from the CBCRP in 2005 to continue this project. This research has the potential to advance our understanding of how the BRCA1 gene keeps tumors from developing, which could lead to new ways to treat women with BRCA1 gene mutations.

Understanding Telomere Dynamics in the Breast.
Telomeres, which cap the ends of chromosomes, shorten as we age, and when they get too short, a cell can no longer divide. Telomeres are made by a special enzyme called

telomerase. Cancer cells learn how to reactivate telomerase. This keeps the telomeres from getting too short, allowing the cell to divide indefinitely. ***Steven Artandi, Ph.D.,*** at ***Stanford University,*** used mice to study how normal breast cells respond to telomere shortening as they age and how breast cancer develops. Dr. Artandi and his team found that when the telomerase enzyme is turned off, the mice have short telomeres, which affects how stem cells in the breast function. Dr. Artandi received CBCRP funding in 2005 to further investigate the role of telomerase in stem cell function. This research on how breast cancer evolves could lead to new methods of prevention and treatment.

Analysis of Genes Predictive of Breast Cancer Metastasis.
Women who have cancer that has metastasized (spread to other parts of the body) have a poor prognosis. ***Jeffrey Gregg, M.D.,*** from the ***University of California, Davis,*** and colleagues examined the action of an enzyme called phosphoinositol kinase 3 (PI-3 kinase) in two lines of mouse mammary tumor cells (mammary tumors in mice are the equivalent of breast tumors in humans). The goal was to learn more about metastasis. They found that when PI-3 kinase is turned on, the tumors were more likely to spread to the lung than to other parts of the body. They also found that tumors that metastasize quickly were more likely to have more copies of the gene osteopontin (OPN) and more of its proteins than tumors that were less likely to spread. These findings led Dr. Gregg and his colleagues to conclude that there is a link between cancers that metastasize, PI-3 kinase, and OPN. His group is continuing to study the relationship between PI-3 kinase and genes like OPN. This research could lead to new way of determining which breast tumors are most likely to spread to other parts of the body.

The Role of Matrix Metalloproteinase 13 in Breast Cancer.
The normal breast contains many cell types, including milk-producing (epithelial) cells and stromal (supporting) cells. Most research on breast cancer focuses on the genetic changes in the epithelial cells, which is where breast cancer begins. However, the stromal cells also undergo changes as breast cancer evolves. ***Mikala Egeblad, Ph.D.,*** at the ***University of California, San Francisco,*** studied an enzyme called matrix metalloproteinase 13 (MMP-13) that is secreted by the supporting stromal cells and that appears to play a role in breast cancer. Dr. Egeblad and her colleagues found that there was an overabundance of MMP-13 in breast tumors in several different mouse models of breast cancer. They also studied the relationship between MMP-13 and a molecule, called type I collagen, that activate MMP-13 and has been linked to the initiation and spread of breast cancer. Their findings suggest that interactions between type I collagen and MMP is necessary for normal breast development. They also found that MMP-14, not MMP-13, was the enzyme that played a role in this process. Dr. Egeblad intends to continue to study type I collagen and the MMP enzymes to determine if the molecule could be used to help doctors assess whether breast cancer is present or is likely to spread. Results from this research were published in *Molecular and Cellular Biology* 23:8614-25 (2003).

A Novel Predictive Test for HER-2/EGFR Ab-based Therapeutics.
About 30 percent of breast tumors have larger than normal amounts of a protein called HER-2. This protein, which plays a crucial role in cell differentiation, can make cancers more aggressive. Trastuzumab (brand name Herceptin) is used to treat breast cancers that make too much HER-2

protein. It is believed that trastuzumab works by attaching itself to the HER-2 proteins on the surface of the tumor cells and then pushing these proteins back into the cell, which keeps the tumor from growing. This process is called internalization. ***Verena Kallab, M.D.,*** at the ***University of California, San Francisco,*** developed a new technique using circulating tumor cells (CTCs) in mouse models of human breast cancer to quickly evaluate whether and to what extent a cancer treatment (trastuzumab) that targets the HER-2 protein is promoting internalization of the receptor. The new technique could help assess the potential effectiveness of new cancer treatments that target breast tumors that overproduce the HER-2 protein.

Hox Transcriptional Regulation of Breast Tumor Angiogenesis.
For a tumor to be able to grow and spread throughout the body it must make its own blood vessels, a process called angiogenesis. Abnormal expression of many HOX genes indicates an involvement of these transcriptional (gene) regulators in cancer progression and metastasis. ***Lucy East, Ph.D.,*** at the ***University of California, San Francisco,*** and colleagues studied a protein called homeobox transcription factor D10 (HoxD10). Previous studies had found that Hox factors control how the endothelial cells—the cells support and feed breast cancer cells—move and grow. Using mice, Dr. East found that HoxD10 did not appear to affect an enzyme that is needed for cancer cells to grow and spread (metastasize). Dr. East is continuing to explore how HoxD10 is able to keep angiogenesis from occurring by acting on a major signaling protein, called Akt. Learning how HoxD10 functions could lead to the development of new breast cancer treatments that can stop cancer cells from metastasizing.

Cell-Killing Effect of Orphan Receptor TR3 in Breast Cancer.
Vitamin A compounds, called retinoids, are being studied for their ability to prevent or treat cancer. Research has shown that one of these compounds, called AHPN, can cause breast cancer cells to die, and that a protein called TR3 (a critical modulator of cancer cell death by its ability to migrate from the nucleus to mitochondria) plays an important role in this process. ***Nathalie Bruey-Sedano, Ph.D.,*** at ***The Burnham Institute,*** La Jolla, found that combining vitamin A compounds with chemotherapy drugs used to treat breast cancer made the chemotherapy drugs more effective at killing breast cancer cells. Dr. Bruey-Sedano and her colleagues found this occurred in both hormone-sensitive and hormone-independent breast cancer cells. The team also was able to identify several genes related to cell death that were altered when the combination therapy was used. These findings could lead to a new approach for treating breast cancer.

Role of Pak Kinase in Breast Cancer Cell Cycle Progression.
Pak kinase is a type of protein that is believed to play a role in how cells transform from normal to cancerous. ***Beatriz Maroto, Ph.D.,*** at the ***Scripps Research Institute,*** La Jolla, studied the role of Pak kinase in breast cancer cells during cell division, a process called mitosis. Dr. Maroto and her colleagues found that Pak activity is required for cells to grow and divide. They also identified a previously unknown way in which Pak operates through a second family of protein kinases (Polo-like kinases) at the time the nucleus divides into two new cells. This research could lead to the development of new breast cancer treatments that keep breast cancer cells from growing and dividing by inhibiting Pak kinase.

Regulation of Estrogen Response by Corepressors.
Breast development is regulated by interactions between hormones and proteins called growth factors. The hormone estrogen is one of the most important in this process. It binds to the estrogen receptor, which is regulated by proteins called corepressors. ***Martin Privalsky, Ph.D.,*** at the ***University of California, Davis,*** investigated chemical interactions between corepressors and other proteins called kinases, and how this affects the estrogen receptor. Dr. Privalsky found that messages sent by growth factors such as epidermal growth factor are able to activate some corepressors 9SMRT), but do not activate other closely related corepressors (N-CoR). This research could lead to the development of new therapies for women whose breast tumors acquire resistance to anti-estrogen chemotherapy.

The Functions of BRCA2 in Repairing DNA Damage.
Women with an abnormal version of the BRCA2 gene are more likely to get breast cancer. The protein produced by the normal BRCA2 gene interacts chemically with a protein complex in cells, Rad51. Rad51 is involved in a part of the process of DNA repair called homologous recombination repair. ***Yi-Ching Lio, Ph.D.,*** at the ***Lawrence Berkeley National Laboratory,*** used molecular biology methods to investigate the normal BRCA2 protein. Dr. Lio found cellular and biochemical evidence that the interaction between BRCA2 and Rad51 is necessary for homologous recombination repair. Dr. Lio and his colleagues also performed studies on the Rad51 family of proteins. Their research produced the first in vivo evidence of how Rad51C works in homologous recombination repair. This research could shed light on why a mutated BRCA2 gene leads to a high number of mutations in tumor genes, and also help scientists understand why cancer cells can repair their DNA, even after being treated with DNA-damaging chemotherapy. Results from this research were published in the *Journal of Biological Chemistry* 279: 42313-20 (2004).

The Detailed Structure of a Model Breast Cancer Genome.
The chromosomes and the genes they carry that are found inside breast cancer cells often look very different from the chromosomes found in normal breast cells. ***Colin Collins, Ph.D.,*** at the ***University of California, San Francisco,*** used a new technique called End Sequence Profiling to identify all the genetic differences between breast cancer cells and normal cells. End Sequence Profiling uses some of the same methods that were used to map the human genome. Dr. Collins began by creating a bacterial artificial chromosome (BAC) library for the tumor being studied. He then compared the BAC with a reference library of chromosomes, which allowed him to quickly see if there were extra genes or missing ones. To date, Dr. Collins and his team have demonstrated the ability of End Sequence Profiling to identify genetic differences in tumors in the brain, breast, ovary, and prostate. This approach could help lead to the development of new breast cancer treatments. Results were published in the *Proceedings of the National Academy of Sciences USA* 100:7696-7701 (2003) and *Bioinformatics* 1:1-12 (2003).

Molecular Analysis of BRCA1 Function.
Women who have inherited a mutation in a gene called BRCA1 are at higher risk for developing breast and ovarian cancer. BRCA1 is hard to study in animal models because mice that lack the BRCA1 gene do not live very long. ***Quan Zhu, Ph.D.,*** at the ***Salk Institute for Biological Studies,*** La Jolla, attempted to develop a mouse that would be a better model for breast cancer using a new gene expression vector. Although Dr. Zhu made progress toward this goal, his efforts did not result in the creation of any mice that carried a human BRCA1 gene.

Locating Novel Breast Cancer Genes Using DNA Microarrays.
Breast cancer occurs when genes that control normal cells go awry. Tumor suppressor genes, which put the brakes on cell growth, are frequently missing in breast cancer. ***Jonathon Pollack, M.D., Ph.D.,*** at ***Stanford University School of Medicine,*** used DNA microarrays (gene-chips) that can look simultaneously at more than 26,000 genes from human tumor samples. The goal was to identify novel tumor suppressor genes in breast cancer by focusing on sites where DNA was missing. Dr. Pollack and his team were able to characterize DNA deletions in 50 different breast cancer cell lines and 144 primary breast tumors. Now they will focus their research efforts on the tumor suppressor genes where DNA is missing. This research could lead to new genetic tools that will help oncologists assess how aggressive a cancer is and to the development of new treatment options.

Genes That Modulate Dioxin-Induced Breast Cancer.
Dioxins are widespread environmental toxins known to cause cancer. Several studies suggest dioxin may be responsible for some breast cancer cases. ***Quan Lu, Ph.D.,*** of ***Stanford University,*** searched for genes that make breast cells more likely to become cancerous if exposed to dioxin. The research team used two techniques. The first, RHKO, has been used to discover genes that inhibit tumor growth. The second, microarrays, is a technology that allows a researcher to study thousands of genes simultaneously. These techniques allowed Dr. Lu to identify several previously unknown genes that are involved in breast cancers caused by dioxins. This work could lead to new ways to prevent, diagnose and treat cancers caused by dioxins and to identify individuals who are most likely to develop dioxin-induced cancers. Results from this research were published by Dr. Lu and his mentor Dr. Stanley Cohen in the *Proceedings of the National Academy Sciences USA* 100:7626-31 (2003).

Tumor Suppression by Dystroglan in Breast Epithelial Cells.
Normal breast epithelial cells (the cells where most cancers arise) are organized in a single layer, with one side of each cell attached to another type of cell, collectively called the basement membrane. Proteins attach the cells together. The cell-basement membrane interaction helps prevent uncontrolled cell growth. There is considerable evidence that restoring critical attachment functions in the very early stages of breast cancer will reverse the disease. ***John L. Muschler, Ph.D.,*** of the ***Lawrence Berkeley National Laboratory,*** studied a basement membrane protein, called laminin, which interacts with a protein present on the surface of breast cells called dystroglycan (DG). In addition to interacting with laminin, DG tells the cell to stop growing. DG appears to be absent or

nonfunctional in breast cancer. Dr. Muschler created breast epithelial cells in which the DG gene can be selectively deleted using a technology called "cre-lox recombination." This allowed him to compare how cells with and without DG function and to learn more about what DG does. Dr. Muschler also explored what causes DG to stop functioning in breast cancer cells. He found that the sugar molecules that are on DG and are necessary for it to function have been altered on invasive cancer cells. This research could lead to the development of new breast cancer treatments that work by restoring DG functioning.

Role of PTEN/Akt Pathway in Progression of Ductal Carcinoma *in Situ*.
Ductal carcinoma in situ (DCIS) is considered a pre-cancer and not true cancer because the altered cells are confined to the breast duct. It is known that about 25–30 percent of DCIS lesions will eventually progress to become invasive cancer, but it is not known how to predict which cases have the potential to become invasive. ***Shikha Bose, M.D.,*** at ***Cedars-Sinai Medical Center*** in Los Angeles, explored how DCIS progresses to invasive breast cancer by studying PTEN, a recently-identified tumor suppressor gene that is missing in invasive breast cancer. Dr. Bose and her team compared genetic changes in tissue from women with DCIS to that of women who had invasive breast cancer. They were able to identify certain pathways (series of chemical reactions within cells) activated early in breast cancer. They also found proteins that were present at higher levels in invasive cancers. This research could lead to the development of genetic markers that physicians could use to identify which cases of DCIS are most likely to become invasive. These genetic markers might also provide insight into which proteins and genes could be investigated for new drug development.

Infinite Expansion of Breast Tumor Samples in Culture.
Research on breast cancer cells growing in lab cultures is limited to about eight types of cells. These cells came decades ago from aggressive tumors that had spread to other parts of the body. This makes it hard to investigate genes and proteins present at earlier stages of the disease. Drugs tested against the currently available cells may not work the same way against tumors caught in early stages of breast cancer. Previous attempts to grow more kinds of breast cancer cells in lab cultures have failed. ***Shanaz Dairkee, Ph.D.,*** at the ***California Pacific Medical Center Research Institute,*** San Francisco, developed a new method that would allow scientists to grow cells in lab cultures from the majority of breast cancer cases. Dr. Dairkee and colleagues showed that this new method produced permanent breast cancer cell lines directly from a variety of human tumors and that these cancer cells retained the same genetic profile as the original tumor, differed from existing tumor lines, and were capable of forming tumors in mice. Dr. Dairkee has received additional funding from the National Institutes of Health to pursue the goal of making these new cells lines available to other investigators. Research using these cells lines could lead to the discovery of new molecules involved at all stages of the disease, and possibly drugs to target these molecules. It could also lead to individualized therapy, where drugs could be tested against a woman's tumor cells before treatment. Results from this research were published in *BMC Genomics* 5:47-56 (2004).

Does the BLM Gene Co-Regulate BRCA1 in DNA Damage Response?
The normal form of the BRCA1 gene prevents uncontrolled cell growth. Women who inherit a mutation in this gene are more likely to get breast cancer. ***Albert Davalos, Ph.D.,*** at ***Lawrence Berkeley National Laboratory***, investigated whether another gene called BLM and the protein it produces interacts with the normal BRCA1 gene to prevent uncontrolled cell growth. Dr. Davalos and his colleagues found that the tumor suppressor protein p53 works with the BLM protein to protect breast epithelial cells when they grow and divide. They also found that two signaling proteins, ATM and ATR, are necessary for BLM to operate properly. Next, they will study breast epithelial cells in a 3-D cell culture system that is similar to normal tissue. This research has the potential to uncover biological markers that could provide a new method for detecting breast cancer early before it has spread. Findings from this research were published in the *Journal of Biological Chemistry* 162:1197-1209 (2003); *Cell Cycle* 3:1579-86 (2004); and *Experimental Cell Research* 298:17-27 (2004). Dr. Davalos received additional funding from the CBCRP through an IDEA grant to continue this line of research.

Molecular Pathogenesis of Metastatic Breast Cancer.
Despite all currently available treatments, the majority of women who develop advanced, metastatic breast cancer will eventually die. ***Robert Debs, M.D.***, at ***California Pacific Medical Center Research Institute,*** San Francisco, used a new technology called cDNA microarray analysis to search for combinations of genes that all work together to allow breast cancer cells to spread to other body parts, a process known as metastasis. They found that FKBPr38, a gene with no previously identified function, helped breast cancers to metastasize. They also identified a network of related genes—FKBP12, MMP-9, and syndecan-1—that together play an important role in causing breast cancers to spread. Knowing which genes play a role in metastases will allow researchers to better understand what causes breast cancer to spread to other areas of the body and could lead to new breast cancer treatments that target these genes. Findings from this research were published in the *Proceedings of the National Academy of Sciences* USA 100:13543-38 (2003) and 100:14253-58 (2003); and *Molecular Therapy* 10:706-718 (2004).

Identification and Prognostic Value of ERß in Breast Cancer.
Estrogens promote breast cancer by binding to the estrogen receptor (ER) molecules in breast epithelial cells. Hormone treatments, such as tamoxifen and a class of drugs called aromatase inhibitors, treat breast cancer by blocking estrogen. However, many tumors eventually become resistant to these drugs. There are two distinct estrogen receptors, ER alpha and ER beta (ERß). ER alpha is currently used to classify tumors as hormone sensitive. The significance of ERß is not known. ***Dale Leitman, M.D., Ph.D.,*** at the ***University of California, San Francisco,*** attempted to develop an accurate test to measure the level of ERß in tumors and to assess whether the presence of ERß makes tumors more aggressive. Dr. Leitman found that ERß was present in about one-third of the tumors he evaluated. However, ERß did not appear to be related to the likelihood that a tumor was more or less likely to spread to other parts of the body. These findings have advanced our understanding of ERß and lay the groundwork for future research on the estrogen receptor molecules.

Three-Dimensional Modeling of Breast Cancer Progression.
Breast cells must respond to many different types of external chemical signals transmitted through hormones and proteins called growth factors. It is possible that cells in certain locations in the breast and at certain stages in their abnormal development may be most likely to become cancerous. ***Carlos Ortiz de Solorzano, Ph.D.,*** at the ***Lawrence Berkeley National Laboratory,*** used mice that have been genetically engineered to develop tumors that mimic a deadly type of breast cancer, erbB2-positive. The goal was to study where in the mouse mammary gland (the mouse equivalent of the breast) the tumors arise, and to plot the cell-by-cell presence of key proteins. To date, the research team has partially constructed 21 mammary glands, 10 from normal mice and 11 from genetically engineered mice, at six-week intervals. When their work is complete, they will have produced a progressive "atlas" to visualize the development of breast cancer. This model of cancer progression could lead to new treatments that target or repair the molecular mechanisms that play a role in the initiation and growth of breast cancer. Findings from this research were published in the *Journal of Biomedical Optics* 9:444-53 (2004).

Mechanism of Estrogen Receptor Loss in Breast Cancer.
Between 30 and 50 percent of human breast cancers have a mutant tumor suppressor gene, p53. Using mice, ***Keon Wook Kang, Ph.D.,*** at the ***University of California, Irvine,*** examined the role of the p53 gene on estrogen signaling in the growth of mammary epithelial cells—the cells where breast cancer begins. Dr. Kang and his mentor, Dr. Eva Lee, found that mammary epithelial cells with a mutant p53 gene responded differently to estrogen than did cells with normal p53 genes. These findings support the notion that p53 affects the role estrogen has on mammary epithelial cells and could lead to new ways to treat breast cancer.

Molecular Analysis of DCIS Progression in a Mouse Model.
Breast cancer development is a multi-step process. DCIS (ductal carcinoma in situ) is a type of pre-malignant breast cancer that can transform into invasive cancer. To learn more about this progression, better mouse models for DCIS are needed. ***Ruria Namba, Ph.D.,*** at the ***University of California, Davis,*** developed a mouse cell line in which mammary cancer (the mouse equivalent of the breast cancer) progresses from DCIS to invasive cancer. Dr. Namba's research confirmed that the model reflects the biology of DCIS that occurs in humans and that the cell line can be transplanted into other mice. This mouse model could be used to develop new ways to prevent and treat breast cancer. Findings from this research were published in *Clinical & Experimental Metastasis* 22:47-58 (2005); *Molecular Cancer Research* 2:453-463 (2004); and *Breast Cancer Research* 5:S7 (2003).

Grants in Progress: 2005

Role of Bl-1 Protein in Breast Cancer Apoptosis
Beatrice Bailly-Maitre
The Burnham Institute

Role of FGF10 in Early Mouse Mammary Gland Development
Saverio Bellusci
Childrens Hospital Los Angeles

Prognostic Value of Ras Activation in Breast Cancer
Gerry Boss and Anne Wallace
University of California, San Diego

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

Proteomic Profiling of Adhesive Structures in Breast Cancer
Jason Bush
The Burnham Institute

Characterizing Breast Cancer Cells in Blood and Bone Marrow
Robert Carlson
Stanford University

Role of Chromatin Regulator in Breast Cell Growth
Hongwu Chen
University of California, San Francisco

Alternative pre-mRNA Splicing in Mammary Epithelial Cells
John Conboy
Lawrence Berkeley National Laboratory

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

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

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

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

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

Protective Role of Estrogen Receptor Beta in Mammary Gland
Leslie Hodges
University of California, San Francisco

Translational Proteomics of Normal to Benign Breast Disease
Dave Hoon, Armando Giuliano and Lori Wilson
John Wayne Cancer Institute

Study of the Apoptotic Phenotype as a Hallmark of Malignancy
Nola Hylton
University of California, San Francisco

Role of IKKα in Mammary Gland Development
Michael Karin
University of California, San Diego

Dissection of Signaling Events in the Mammary Gland in Vivo
Yuehai Ke
The Burnham Institute

In Vivo Gene Expression Profiling of Developing Mammary Gland
Hosein Kouros-Mehr
University of California, San Francisco

Understanding Aging Effects in the Breast
Ana Krtolica
Lawrence Berkeley National Laboratory

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

Targeting of DNA Methylation in Mammary Epithelial Cells
David Liston
Salk Institute

Cloning of Putative Tumor Suppressor Gene on the X Chromosome
Sergei Malkhosayan
The Burnham Institute

Does Disregulaton of Centrosomes Cause Breast Cancer?
Kimberly M. McDermott
University of California, San Francisco

Statistical Techniques for Breast Biology and Cancer Research
Saira Mian
Lawrence Berkeley National Laboratory

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

Targeting Estrogen Receptors to Mammary Epithelial Cells
Richard H. Price, Jr.
University of California, San Francisco

Novel Genes in Mammary Gland Development and Cancer
Euan Slorach
University of California, San Francisco

The Breast Cancer Suppressor Maspin: A Proteasome Inhibitor?
Jeffrey Smith
The Burnham Institute

A Novel Approach to Inactivate the Estrogen Receptor
Alex So
University of California, San Francisco

Angiogenesis in Hyperplasia to In-Situ Breast Cancers
Min-Ying (Lydia) Su
University of California, Irvine

Early Transitions in Breast Cancer
Thea Tisty
University of California, San Francisco

The Role of Gli3 in Mouse Embryonic Mammary Gland Formation
Jacqueline Veltmaat
Children's Hospital, Los Angeles

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

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

Research Initiated in 2005

Breast Cancer Studies in a 3-D Cell Culture System
Robert T. Abraham, Ph.D.
The Burnham Institute

Reactivation of the Inactive X Chromosome and Breast Cancer
Angela Andersen, Ph.D.
University of California, San Francisco

Role of Telomerase in Mammary Stem Cell Function
Steven Artandi, Ph.D.
Stanford University

Defining Mammary Cancer Origins in a Mouse Model of DCIS
Alexander Borowsky, M.D.
University of California, Davis

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

The Role of the ECM in Breast Cancer DNA Damage Repair
Albert R. Davalos, Ph.D.
Lawrence Berkeley National Laboratory

Novel Approach to Analyze Estrogen Action in Breast Cancer
Brian P. Eliceiri, Ph.D.
La Jolla Institute for Molecular Medicine

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

Survivin: Target for Breast Cancer Brain Metastases
Florence M. Hofman, Ph.D.
University of Southern California

Stem Cells of Molecularly Diverse ER Negative Breast Cancers
Stephanie Jeffrey, M.D.
Stanford University

Identification of BRCA1 Ubiquitylation Targets
Peter Kaiser, Ph.D.
University of California, Irvine

Apaf-1 is a Transcriptional Target for the ZNF217 Oncogene
Sheryl R. Krig, Ph.D.
University of California, Davis

Identifying Metastatic Breast Cells from Peripheral Blood
Kristen S. Kulp, Ph.D.
Lawrence Livermore National Laboratory

The Role of B-Myb in Human Breast Cancer Progression
Joseph Lipsick, M.D.,Ph.D.
Stanford University

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

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

A Novel Epithelial-Stromal Model of Metastatic Breast Cancer
Richard M. Neve, Ph.D.
Lawrence Berkeley National Laboratory

Histone Methylation as a Marker of Breast Cancer Progression
Judd C. Rice, Ph.D.
University of Southern California

Structural Analysis of Cancer-Relevant BCRA2 Mutations
Henning Stahlberg, Ph.D.
University of California, Davis

Imaging RhoC-induced Breast Cancer Invasion and Angiogenesis
Konstantin V. Stoletov, Ph.D.
The Scripps Research Institute

Role of Integrins in Lymphangiogenesis During Breast Cancer
Barbara Susini, Ph.D.
University of California, San Diego

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

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

The Role of LMO4 in Breast Cancer
Zhengquan Yu, Ph.D.
University of California, Irvine

Detection, Prognosis, and Treatment

Although early detection of breast cancer does not guarantee a cure, it provides both the patient and the clinician with a wider array of treatment options. Improved imaging technologies may someday replace mammography, which misses many cancers and requires women to undergo unnecessary biopsies and emotional strain. Replacing toxic chemotherapy with targeted therapies that match the specific tumor subtype is emerging as the first step towards individualized therapy. The CBCRP also supports investigations into novel, alternative therapies.

Research Conclusions

Breast CT for Much Earlier Detection of Breast Cancer.
John Boone, Ph.D., and ***Karen Lindfors, M.D.,*** at ***University of California, Davis***, built the first dedicated breast computerized tomography (CT) scanner. CT scanners are a special kind of X-ray machine producing thin image "slices" that can be reconstructed into three-dimensional pictures. In contrast, a mammogram is a two-dimensional X-ray taken through the entire breast at once, so the resulting image may not detect a tumor obscured by other tissues within the breast. Prior to this research, CT scanning was not considered feasible for breast cancer screening due to unacceptably high radiation doses. The research team was able to show that the radiation dose for breast imaging could be lower and make annual scanning by CT a reality. They also developed a special table for breast imaging that keeps other parts of the body from being exposed to radiation and eliminates breast compression, a major discomfort with mammograms. These solutions make the breast CT scanner a practical alternative to mammograms. The researchers predict this technology will allow radiologists to detect breast cancers the size of a small pea. Mammograms currently detect cancers the size of a garbanzo bean. The new CT breast scanner is now being tested on women with funding from the National Institutes of Health. It will be five years before it is commercially available. Results of the research were published in *Medical Physics* 31(2):226-35 (2004) and 29(5):869-75 (2002); and *Molecular Imaging* 3:149-58 (2004).

MRI for High Risk Breast Cancer Screening and Surveillance.
Nola Hylton, Ph.D., John Zeigler, M.D., M.Sc., and ***Shelley Hwang, M.D.,*** at ***University of California, San Francisco,*** worked to evaluate the benefit of magnetic resonance imaging (MRI) screening for women at higher than average risk for breast cancer. MRI can easily detect small cancers and it is more effective than mammograms in the dense breasts of younger women. However, MRI frequently flags tissue as cancerous that turns out to be normal. The technology has also lacked standards and guidelines for equipment, imaging techniques and interpretation. The research team developed several imaging methods to use MRI to characterize breast tissue, along with a breast tissue index that can be used to predict risk for developing breast cancer. The CBCRP has funded Dr. Hylton and another CBCRP-funded researcher, ***Bruce Tromberg, Ph.D.,*** at ***University of California, Irvine,*** to continue research into the combination of MRI and

light-based detection. Results from this research were published in *Breast Cancer Research and Treatment* 88(1)S163 (2004).

Combined Optical and MRI Imaging for Breast Cancer.
Sean Merritt, at ***University of California, Irvine,*** changed the aims of this study, with CBCRP approval, to include magnetic resonance imaging (MRI), rather than ultrasound. Using MRI as the standard, he provided validation measurements for a hand-held laser breast scanner that uses infrared light to detect tumors. The scanner was developed at UC Irvine, with CBCRP funding, by ***Bruce Tromberg, Ph.D.,*** and colleagues. Mr. Merritt developed mathematical formulas for use with the laser scanner's measurements of bound water in the breast. Differences in water content can be used to distinguish normal breast tissue from cancer. He measured lower bound water in tumor tissue than was expected from MRI measurements. He also validated the scanner's measurements of deep breast tissue temperature, which can be useful in some breast cancer treatments. Results from this study were published in *Technology in Cancer Research and Treatment* 2(6):563-9 (2003).

Clinical Utility of Breast Cancer DNA Markers in Serum.
David Hoon, M.Sc, Ph.D., at ***John Wayne Cancer Institute,*** Santa Monica, made significant progress toward a blood test to detect breast cancer and to predict how a tumor will progress in the near future. Normal DNA and DNA from tumors both circulate in the blood. The research team developed the first blood test to detect multiple DNA markers, which are patterns in the structure of DNA. The team found that as tumors grow and acquire the ability to spread to other parts of the body, their DNA contains more and more markers that indicate cancer. The presence of some of these markers can be used to get information about a tumor similar to that obtained from examining tumor tissue taken in a biopsy. The team is testing this blood test further, at multiple sites, to see if it can predict or reveal a recurrence of breast cancer in women who have already had the disease, and to validate the usefulness of the test to diagnose and predict the outcome of breast tumors. This research resulted in publications: *Annals of the New York Academy of Sciences* 945:22-30 (2001), *Cancer Research* 63(8):1884-7 (2003), and *Proceedings of the American Association for Cancer Research* 44:563 (2003).

Early Detection of Breast Cancer and its Recurrence.
Cancer treatment specialists need reliable tests that can be done on tumor cells to predict whether the tumor is likely to recur. ***Syed Ashrat Imam, M.S., Ph.D.,*** at ***Huntington Medical Research Institute***, Pasadena, investigated LEA-135, a protein found on the surface of some breast cancer cells. The research team examined frozen tissue samples from 367 women who had breast cancer that had spread to nearby lymph nodes. The team found that tumors with a high or moderate number of tumor cells containing LEA-135 had a 46% lower probability of the tumor recurring within ten years. The presence of LEA-135 on tumor cells was not related to whether the tumor depended on the hormones estrogen or progesterone to survive, or to the patient's age, tumor size, or how far the tumor had progressed at diagnosis. Women whose tumors contained high or moderate levels of LEA-135 had less chance of recurrence regardless of whether they had a lumpectomy or mastectomy, and regardless of whether they had chemotherapy or

radiation treatment. This research could lead to a test that could identify women at high risk for a recurrence of breast cancer who could benefit from more aggressive treatment. Results from this research were published in *Anticancer Research* 22(5):2933-7 (2002).

Patient-Individualized Chemotherapy in Breast Cancer.
The effectiveness of chemotherapy for breast cancer varies highly from patient to patient. As a result, a substantial proportion of patients either receive toxic drugs that do not help target the tumor, or they are not treated with the most effective chemotherapy for their type of breast cancer. ***Daniel Silverman, M.D., Ph.D.,*** at ***University of California, Los Angeles***, is developing a method to use positron emission tomography (PET) imaging while chemotherapy is being administered to see if the drug is entering a tumor and acting against it. For PET imaging to detect the drug, the drug must be combined chemically (labeled) with radioactive fluorine. The research team succeeded in labeling two commonly used chemotherapy drugs, paclitaxel and cyclophosphamide. The team found both labeled drugs distribute themselves in the blood and organs of mice in the same ways as the drugs without radioactive fluorine. The team uses a micro PET scanner on mice with human breast tumors grafted in them. The micro PET scanner provided information on chemotherapy concentration in tumor and normal tissues. The measurements could be used to forecast whether paclitaxel would be effective against the tumors. Future directions for this research include expanding the number of chemotherapy drugs that can be measured with PET scanning and testing the technology on women with breast cancer. After CBCRP funding ended, Dr. Silverman published this promising PET-based approach for individualized therapy in *Molecular Imaging and Biology* 14:1-7 (2005).

Herba Scutellaria Barbatae for Metastatic Breast Cancer.
Metastatic breast cancer, cancer that has spread to other parts of the body, is incurable. Most medications used to treat it have toxic side effects and eventually stop working. New, less toxic treatments are needed. ***Hope Rugo, M.D.,*** at the ***University of California, San Francisco***, investigated an herb traditionally used in Chinese medicine to treat cancer, *Scutellaria Barbatae*, or skullcap. (It was also at one time considered to be a remedy for rabies, thus its name, “mad dog weed.”) Her research team had previously showed that a liquid form of this herb could kill cancer cells in cultures and in animals. This study was a Phase 1 clinical trial, testing the therapy in 21 women who had already had an average of three treatments for metastatic breast cancer. The initial dose was 350 ml per day of extract in tea form. During the study, the women did not receive any other chemotherapy, hormone therapy, or herbal medicine. Sixteen women could be evaluated for their response to the treatment. The main side effects were mild nausea, diarrhea, headache, vomiting, constipation, and fatigue. The women also complained of the bitter taste of the tea. Four of the sixteen women had stable disease for longer than three months, three for longer than six months, and the treatment shrank five of the women’s tumors. This herbal treatment is safe and tolerable. The tea has been reformulated to taste better and a larger trial is planned. This study has important implications for research into herbal extracts that may have significant anti-tumor effects.

Lactulosamines: Novel, Non-toxic Therapies for Breast Cancer.
Galectins are proteins found in breast tumors cells that promote tumor growth. One of them, galectin-4, helps turn normal breast cells into cancer cells by allowing aging cells to live longer than normal and to continue to form new cells. ***Margaret Huflejt, Ph.D.,*** at the ***Sidney Kimmel Cancer Center*** in San Diego, created a laboratory culture of normal breast cells with extra galectin-4 that allowed these cells to survive in cancer-like conditions. After testing various compounds on these cells, the research team found that a galectin-4 inhibitor killed off the cells and kept them from dividing to form new cells. This makes the galectin-4 inhibitor, which is not toxic, a potential anti-cancer drug. Dr. Huflejt also found antibodies that target parts of galectin molecules in the blood of breast cancer patients. These antibodies also have potential as breast cancer treatments. This research resulted in publications: *Glycoconjugate Journal* 20(4):247-55 (2004), *Proceedings of the National Academy of Sciences, USA* 101(49):17033-8 (2004).

Novel Retinoids with Enhanced Anti-Breast Tumor Efficacy.
Marcia Dawson, Ph.D., of ***The Burnham Institute*** in La Jolla, had previously identified a compound called APHN that caused the death of breast cancer cells. APHN is a retinoid, a molecule derived from vitamin A. However, the research team discovered that APHN's ability to kill breast cancer cells was not related to the part of the molecule that resembles vitamin A, and, moreover, that this part of the molecule made APHN too toxic to be used as a treatment. The research team therefore modified APHN's molecular structure to create a new compound, 3-Cl-AHPC. 3-Cl-AHPC stops breast cancer cells from dividing and triggers the normal process of cell death. It works by stopping the growth and division of specialized cells that form tumor blood vessels. In mice, 3-Cl-AHPC reduces the volume of mammary tumors—the mouse equivalent of breast cancer—by 70–80%, compared to untreated mice. This research resulted in publications: *Journal of Medicinal Chemistry* 47(14):3518-36 (2004); *Blood* 102(10):3743-53 (2003).

Enhanced HER-2 Directed Liposomal Therapeutics.
Delivering chemotherapy drugs selectively to breast cancer cells, and leaving normal cells alone, would greatly reduce chemotherapy side effects. ***Daryl Drummond, Ph.D.,*** of ***Hermes BioSciences, Inc.*** in South San Francisco, focused on putting chemotherapy drugs inside microscopic fat particles called liposomes. The liposomes have an antibody fragment attached to them that binds to a protein, the HER2/neu receptor, found on the surface of cells of one type of breast cancer. In addition, Dr. Drummond's research team developed highly stable liposomes that significantly delay the release of the chemotherapy drug until the liposomes have accumulated in the tumor. This makes it possible to deliver vinca alkaloids, a type of chemotherapy drug that liposomes haven't effectively delivered in the past and that are too toxic to be delivered systemically. The research team also modified liposomes in a way that improves the action of another chemotherapy drug, doxarabicin. This research provides hope for new, less toxic treatment methods. It was published in *Clinical Cancer Research* 11(9):3392-401 (2005).

Drug Dose Tailoring Based on Patient-Specific Factors
Women who have advanced breast cancer receive chemotherapy that can be just as toxic to their bodies as it is to their tumor cells. Chemotherapy doses are now set according to a

woman's height and weight. Individual doses based on the way a woman's body processes and eliminates the drug would maximize effectiveness and minimize toxicity. ***Christine Case Lo,*** of the ***University of California, San Francisco***, found that immune system molecules called cytokines are associated with drug metabolism and elimination from the body. This makes cytokines, which are also involved in inflammation, promising candidates for further research into tailing chemotherapy dosage.

Chinese Herbal Therapy for Symptom Management.
Chinese herbal medicine has been used to treat a variety of diseases for more than a thousand years. It has been suggested that some Chinese herbal combinations may improve immune function. Women with breast cancer sometimes use Chinese herbs to counteract the nausea caused by chemotherapy, but no research had been done, prior to this study by ***Hope S. Rugo, M.D.,*** at the ***University of California, San Francisco***, as to whether the herbal treatment was safe or effective. The research team conducted a study on women who were treated with nausea-causing chemotherapy for early stage breast cancer. Half of the women received a commonly used Chinese herbal formula called CT101; half received a placebo. Twenty-six women completed the study. The Chinese herbal treatment caused no toxicities and appeared to be safe. However, there were no differences in nausea reduction or immune function between the women who took the Chinese herbs and those who took the placebo. The women in this study were also taking many other necessary medications, which may have affected the results that point to the Chinese herbal treatment being ineffective.

Potential New Drug Therapy for Breast Cancer.
The insulin-like growth factor receptor (IGF-IR) is a protein located on the surface of almost all cells. Activation of this protein contributes to the development of breast cancer cells, stimulates their growth and promotes their survival. The action of this protein limits the effectiveness of several breast cancer treatments. ***Jack F. Youngren, Ph.D.,*** at the ***University of California, San Francisco***, developed small molecules that inhibit the activity of IGF-IR. The research team synthesized and screened over 200 compounds. Two compounds with slightly different chemical structures, PQ401 and NDGA, showed the most promise. Both of these are a type of compound called diaryl urea. PQ401 was 5 times stronger than NDGA at inhibiting the growth breast cells in lab cultures. This appears to be because PQ401 blocks the series of chemical reactions through which IGF-IR promotes cell survival, and triggers the normal process of cell death that cancer cells have to evade to survive. Both PQ401 and NDGA significantly reduced the growth of breast tumors in mice. These results were published in *Breast Cancer Research and Treatment* 94(1):37-46 (2005).

Inhibition of Breast Cancer Cell Invasion by Natural Indoles.
The spread of breast cancer to other parts of the body accounts for the majority of deaths from the disease. The chemical indole-3-carbinol (I3C), found in vegetables like broccoli and Brussels sprouts, reduces the spread of breast cancer by decreasing the cells' ability to move. ***Christine Brew, Ph.D.,*** at ***University of California, Berkeley,*** investigated how I3C works on a molecular level using breast cancer cells growing in a lab culture. She found that I3C dramatically alters two components of cell structure, actin and vinculin.

Breast cancer cells have tiny actin filaments that propel them forward. Breast cancer cells treated with I3C don't have them. Breast cancer cells also have temporary fibers containing vinculin that anchor only the forward part of the cell. Treating these cells with I3C causes them to form fibers that anchor the entire outer surface of the cell. I3C causes these changes by activating a series of chemical reactions in the cells called the RhoA/Rho pathway. Moving is crucial to breast cancer cells being to spread. Using I3C to stop cells from moving should limit their ability to invade other body parts. Additional work supported by the CBCRP involved the ability of I3C to block key elements of the cell cycle in breast cancer cell lines. This research was published in the *International Journal of Cancer*, 118(4):857-68 (2006)

Retinoids in Combination Therapies Against Breast Cancer.
Retinoids are compounds derived from Vitamin A, with a slightly different chemical structure. Some retinoids kill off cancer cells and, in experiments with animals, have stopped the growth of breast tumors. Angiostatic therapy prevents the formation of blood vessels tumors need to survive, but the treatment doesn't eliminate the tumor. ***F. Javier Piedrafita, Ph.D.,*** at the ***Sidney Kimmel Cancer Center,*** San Diego, investigated combining these therapies, to enhance their anti-tumor activity and minimize the risk of undesirable side effects, but the attempt did not work.

Grants in Progress: 2005

Chinese Herb/Chemotherapy Interactions in Breast Cancer
Michael Campbell
University of California, San Francisco

Novel I3C Regulated Cell Cycle Factor in Breast Cancer Cells
Gary L. Firestone
University of California, Berkeley

FKBP Proteins as Molecular Targets in Breast Cancer Therapy
Sylvia Fong
California Pacific Medical Center Research Institute

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

UCLA Biomedical Physics Graduate Training in Breast Cancer
Carolyn Kimme-Smith
University of California, Los Angeles

Cryptic Peptide-Based Vaccines for Breast Tumor Treatment
Joseph Lustgarten
The Sidney Kimmel Cancer

Her-2/neu-Crosreactive Analogs as Targets for Breast Cancer
Joseph Lustgarten

Sidney Kimmel Cancer Center

Pilot Studies of Breast Cancer Immunophototherapy
Edward Nelson
University of California, Irvine

Novel Agents for Breast Cancer Therapy
Maurizo Pellecchia
The Burnham Institute

Chemotherapy-Induced Ovarian Damage: Prevention and Impact
Hope Rugo, Lynn Westfal, and Lucy Berlin
University of California, San Francisco; Stanford University; and Young Moms with Breast Cancer

Compositional Breast Density as a Risk Factor
John A. Shepherd and Steven R. Cummings
Veterans Affairs Medical Center

Breast Stromal Genes Act as Early Markers of Malignancy
Thea Tisty
University of California, San Francisco

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

Inhibitors of Myc: Novel Drugs for Breast Cancer.
Peter Vogt
Scripps Research Institute

Research Initiated in 2005

Molecular Imaging of Breast Cancer Using Breast PET/CT
John M. Boone, Ph.D.
University of California, Davis

Inhibition of Brain Metastases in Breast Cancer
Brunhilde Felding-Habermann, Ph.D.
The Scripps Research Institute

ID4: A Prognostic Factor of Breast Cancer Metastasis
David S. Hoon, Ph.D.
John Wayne Cancer Institute

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

Early Breast Cancer Detection Using 3-D Ultrasound Tomography
Thomas R. Nelson, Ph.D.
University of California, San Diego

cAMP Antagonists of Protein Kinase as Breast Cancer Drugs
Sanjay Adrian Saldanha, Ph.D.
The Scripps Research Institute

Removing Respiratory Artifacts in Nuclide Breast Imaging
Brian Thorndyke, Ph.D.
Stanford University

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

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

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) 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 Commission on Cancer, Massachusetts Department of Public Health) receive funding from state general funds 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 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.

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

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. Eleven-year-old Sydney Low of Newport Beach reacted to the news that her favorite aunt had breast

cancer by brainstorming with her Girl Scout troop. They decided to make pink ribbons, which they distributed at public events, collecting donations for the CBCRP. Jewelry maker Janet Bocciardi of Soquel teamed up with her breast cancer survivor friend Leann Proud to hold a benefit party where they sold jewelry, with the proceeds going to the CBCRP. Janet Bocciardi's company, Honey from the Bee, also markets jewelry over the Internet, with the CBCRP receiving a portion of the price.

Businesses that made the CBCRP the beneficiary of their community or employee fundraising efforts included Acco Engineered Systems in San Leandro; Costco in Fremont, Livermore, San Bruno, San Leandro, and Redwood City; Farrallon Restaurant in San Francisco; and Wells Fargo Community Support Campaign in Princeton, NJ. Del Mar Middle School in Tiburon also raised funds for the CBCRP.

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

During 2005, the CBCRP continued to do outreach to increase citizen contributions on their state income tax forms. Using the results of a focus group conducted previously, the CBCRP initiated 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.

These efforts resulted in the California Breast Cancer Research Program amassing nearly $650,000 in contributions, the top beneficiary organization receiving donations through the state income tax check-off 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.

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 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.

- **Research Facilitation.** The breast cancer research field is becoming increasingly complex, making liaisons between disparate disciplines all the more critical. An additional staff scientist would enable the CBCRP to increase the potential to 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 2005, the CBCRP turned down 148 grant applications that requested a total of $25,279,448. While some of these applications lacked merit, the majority contained good ideas. With technical assistance from the CBCRP, the majority of these applications could become good, creative projects that could help enlarge the scope of breast cancer research.

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: Research Priorities

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.

In 2005, the CBCRP launched a new five-year program initiative to fill a significant gap in breast cancer research. This initiative will address three 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, and the influence of lifestyle on breast cancer. 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 a scoring system, based on the recommendations of an NIH Advisory Committee, 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 was not 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 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. During 2005, the CBCRP modified the "impact" criterion of the scoring system. Researchers are now 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 has 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 will also aid 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

Forty-five percent (24 of 53) of the grants that the CBCRP awarded in 2005 studied either women or tissues from women, while the remaining 55% were laboratory studies that did not directly involve women or tissues from women.

Of the 24 grants that involved women or tissues from women, 88% (21) had women as participants in the study and 8% (2) used tissues or tumor samples (some grants included both women participants and tissues or tumor samples from women).

One-hundred percent (24) of these studies included minority women in the study.

- Thirty-eight percent (9) are focused on underserved women.
- Thirty percent (7) are focused on minority women.

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

1. **New Breast Cancer Approaches: Integration, Communication**
    - Leah Karliner, Ph.D. - University of California, San Francisco
2. **Improving Quality of Life at the end of Life for the Underserved Women**
    - Shelley Adler, Ph.D. - University of California, San Francisco
    - Beverly Burns - Charlotte Maxwell Complementary Clinic
3. **Psychosocial Support Services for Latinas with Breast Cancer**
    - Carmen Ortiz, Ph.D. – Circulo de Vida
    - Anna Napoles-Springer, Ph.D. - University of California, San Francisco
4. **Consultation Recording for Rural Underserved Breast Cancer Patients**
    - Sara O'Donnell – Mendocino Cancer Resource Center
    - Jeff Belkora, Ph.D. - University of California, San Francisco
    - Joy Hardin, Ed.D – Humboldt Community Breast Health Project
5. **South Asian Women with Breast Cancer: What are their needs?**
    - Zul Surani - South Asian Cancer Foundation
    - Roshan Bastani, Ph.D. - University of California, Los Angeles
    - Beth Glenn, Ph.D. - University of California, Los Angeles
6. **Breast Cancer Risk Profile of Vietnamese Nail Salon Workers**
    - Kim Nguyen – Asian Health Services
    - Peggy Reynolds, Ph.D. – California Department of Health Services
7. **Partnership to Reduce Cancer Disparities in Spanish Speakers**
    - Rena Pasick, Dr.PH - University of California, San Francisco
    - Molly Bergstrom – Women's Cancer Resource Center
8. **Androgen Receptor Gene and p21 Gene in Breast Cancer**
    - Wei Wang, M.D. – University of Southern California

California Breast Cancer Research Program Staff

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Biomedical Research Administrator

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Program Assistant

California Breast Cancer Research Council

Chairs and Vice Chairs:

Chairs	Vice-Chairs
Debra Oto-Kent (July 1, 2003 – June 30, 2005) Health Education Council	Jacqueline Papkoff (July 1, 2004 – June 30, 2005) diaDexus, Inc.
Christine White, M.D. (July 1, 2005 – June 30, 2006) Biogen IDEC, Inc.	Lisa Wanzor (July 1, 2005 – June 30, 2006) Breast Cancer Action

Ex-Officio Members:

Georjean Stoodt, M.D., M.P.H. (10/25/00 – 2/28/05)
Chief, Cancer Detection Section, State of California Department of Health Services
Kurt Snipes, Ph.D. (3/1/05 – Ongoing)
Acting Chief, Cancer Detection Section, State of California Department of Health Services

Advocates:

Vicki Boriack (7/1/02 – 6/30/05)
WomenCARE

Janet Howard-Espinoza (7/1/02 – 6/30/05)
Women of Color

Angela Padilla (9/1/05 – 8/30/08)
Bay Area Young Survivors

Kim Pierce (7/1/03 – 6/30/06)
National Breast Cancer Coalition

Kathy Walters (7/1/03 – 6/30/06)
Community Breast Health Network

Lisa Wanzor (7/1/04 – 6/30/07)
Breast Cancer Action

Maria Wetzel (9/1/05 – 8/30/08)
Cancer Resource Center of Mendocino County

Industry Representatives:

Jacqueline Papkoff, Ph.D. (7/1/02 – 6/30-05)
diaDexus, Inc.

Christine White, M.D. (7/1/03 – 6/30/06)
Biogen IDEC, Inc.

Scientists/Clinicians:

Dorothy Bainton, M.D. (7/1/02 – 6/30/05)
Vice Chancellor, Academic Affairs, University of California, San Francisco

Moon Chen, Jr., Ph.D., M.P.H. (7/1/04 – 6/30/07)
Professor, University of California, Davis

Carol D'Onofrio, Dr.P.H. (7/1/03 – 6/30/05)
Adjunct Research Scientist, Northern California Cancer Center

James Ford, M.D. (7/1/03 – 6/30/06)
Professor of Medicine/Oncology, Stanford University

Felicia Hodge, Dr.Ph.H. (9/1/05 – 8/30/08)
Director, Center for American Indian Research and Education
Professor, School of Nursing, University of California, Los Angeles

Amy Kyle, Ph.D., M.P.H. (7/1/04 – 6/30/07)
Research Scientist, University of California, Berkeley

Mark Pegram, M.D. (9/1/05 – 8/30/08)
Associate Professor of Medicine, University of California, Los Angeles

Medical Specialist:

Michael Figueroa (7/1/02 – 6/30/05)
Cancer Care Consultants

Nonprofit Health Organizations:

Anuja Mendiratta (9/1/05 – 8/30/08)
Program Officer, The Marin Community Foundation

John Morgan, Dr.P.H. (7/1/03 – 6/30/06)
Cancer Epidemiologist, Desert Sierra Cancer Surveillance Program

Debra Oto-Kent (7/1/02 – 6/30/05)
Director, Health Education Council

Summary of Research Funded in 2005

Institution and Investigator	Yrs	Project Title	Direct	Indirect	Total
Asian Health Services					
Kim Nguyen	1.5	Breast Cancer Risk Profile of Vietnamese Nail Salon Workers	$56,102	$11,220	$67,322
This is a collaborative grant with Peggy Reynolds, Ph.D., with the California Department of Health Services, contracted through Impact Assessment, Inc.					
Beckman Research Institute					
Yanyan Hong	2	Structural Characterization of Aromatase	$68,850	$0	$68,850
Melanie Ruth Palomares	1.5	Grape Seed as a Natural Breast Cancer Chemopreventive Agent	$149,252	$102,984	$252,236
Black Women for Wellness					
JanetteRobinson-Flint	1.5	Sisters in Motion-Breast Cancer Risk Reduction thru Nutrition	$10,000	$0	$10,000
This is a collaborative planning grant with Kimlin Ashing-Giwa, Ph.D., with University of California, Los Angeles.					
California Department of Health Services					
PeggyReynolds	1.5	Breast Cancer Risk Profile of Vietnamese Nail Salon Workers	$43,867	$8,774	$52,641
This is a collaborative grant with Kim Nguyen, with Asian Health Services					
Charlotte Maxwell					
Beverly Burns	1	Underserved Women with Breast Cancer at End of Life	$42,677	$10,669	$53,346
This is a collaborative grant with Shelly Adler, Ph.D., with University of California, San Francisco					
Circulo de Vida					
Carmen Ortiz	1	Psychosocial Support Services for Latinas with Breast Cancer	$0	$0	$0
This is a collaborative grant with Anna Nápoles-Springer, Ph.D., with University of California, San Francisco					
Dr. Susan Love Research Foundation					
Susan Love	1	4th Inter. Symp. on the Intraductal Approach to the Breast	$25,000	0	$25,000
Humboldt Community Breast Health Project					
Dawn Elsbree and Joy Hardin	1	Consultation Support for Diverse Rural Breast Patients	$33,032	$8,258	$41,290
This is a collaborative grant with Sara O'Donnell with the Mendocino Cancer Resource Center and Jeff Belkora, Ph.D., with the University of California, San Francisco					
John Wayne Cancer Institute					
David Hoon	1.5	ID4 A Prognostic Factor of Breast Cancer Metastasis	$150,000	$133,200	$283,200
La Jolla Institute					
Brian Eliceiri	1.5	Novel Approach to Analyze Estrogen Action in Breast Cancer	$150,000	$160,950	$310,950
Lawrence Berkeley National Laboratory					
Albert Davalos	1.5	ECM, Caretaker Proteins Role in Repair of Replication Damage	$150,000	$101,298	$251,298
Richard Neve	1.5	A Pre-clinical Model of Human Metastatic Breast Cancer	$150,000	$65,643	$215,643
Lawrence Livermore National					
Kristen Kulp	2	Identifying Metastatic Breast Cells from Peripheral Blood	$250,000	$246,113	$496,113
Mendocino Cancer Resource Center					
Sara O'Donnell	1	Consultation Support for Diverse Rural Breast Patients	$28,531	$7,133	$35,664
This is a collaborative grant with Dawn Elsbree and Joy Hardin with Humboldt Community Breast Health Project and Jeff Belkora, Ph.D., with the University of California, San Francisco					
Scripps Research Institute					
Kyle Chiang	2	Integrated Proteomic and Metabolic Analysis of Breast Cancer	$76,000	$0	$76,000
Brunhilde Felding-Habermann	1.5	Inhibition of Brain Metastases in Breast Cancer	$150,000	$128,850	$278,850
Ewa Lis	2	Defining Mutagenesis Pathways in Breast Cancer Evolution	$67,120	$0	$67,120
Sanjay Saldanha	2	cAMP Antagonists of Protein Kinase as Breast Cancer Drugs	$90,000	$0	$90,000
Konstantin Stoletov	3	Imaging RhoC-induced Breast Cancer Invasion and Angiogenesis	$135,000	$0	$135,000
South Asian Cancer Foundation					
Zul Surani	1.5	South Asian Women with Breast Cancer: What are Their Needs?	$0	$0	$0
This is a collaborative grant with Roshan Bastani, Ph.D., and Beth Glenn, Ph.D., with University of California, Los Angeles.					
Stanford University					
Steven Artandi	1.5	Role of Telomerase in Mammary Stem Cell Function	$150,000	$86,519	$236,519
Stefanie Jeffrey	1.5	Stem Cells of Molecularly Diverse ER Negative Breast Cancers	$150,000	$84,165	$234,165

Allison Kurian	2	Cost-effectiveness of Breast MRI Screening by Cancer Risk	$90,000	$0	$90,000
Joseph Lipsick	1.5	The Role of B-Myb in Human Breast Cancer Progression	$100,000	$56,106	$156,106
Stanley Rockson	1.5	Breast Cancer Lymphedema: Role of Insulin Resistance/FOXC2	$150,000	$84,178	$234,178
Brian Thorndyke	2	Removing Respiratory Artifacts in Nuclide Breast Imaging	$90,000	$0	$90,000
The Burnham Institute					
Robert Abraham	1	Breast Cancer Research in Three Dimensions	$100,000	$91,000	$191,000
University of California, Davis					
John Boone	1	Molecular Imaging of Breast Cancer Using Breast PET/CT	$100,000	$0	$100,000
Alexander Borowsky	1.5	Mammary Pre-Cancer Origins and Behavior	$150,000	$0	$150,000
Jeffrey Gregg	18	Targeted Chemoprevention in a Mouse Model for DCIS	$135,726	$0	$135,726
Sheryl Krig	2	Apaf-1 is a Transcriptional Target for the ZNF217 Oncogene	$53,649	$0	$53,649
Henning Stahlberg	1	Structural Analysis of Cancer-Relevant BCRA2 Mutations	$100,000	$0	$100,000
University of California, Irvine					
Peter Kaiser	2	Identification of BRCA1 Ubiquitylation Targets	$200,000	$0	$200,000
Lan Truong	2	A Role for p53 and Splicing Factor SAP145 in Breast Cancer	$76,000	$0	$76,000
Xiaoman Xu	2	Modulation of TGF-beta Signaling in Mammary Epithelial Cells	$76,000	$0	$76,000
Zhengquan Yu	3	The Role of LMO4 in Breast Cancer	$135,000	$0	$135,000
Jiewen Zhu	3	Validation of Small Molecules Disrupting BRCA2-RAD51 Interac	$135,400	$0	$135,400
University of California, Los Angeles					
Kimlin Ashing-Giwa	1.5	Sisters in Motion-Breast Cancer Risk Reduction thru Nutrition	$2,000	$0	$2,000
This is a collaborative planning grant with Janette Robinson-Flint with Black Women for Wellness.					
Roshan Bastani and Beth Glenn	1.5	South Asian Women with Breast Cancer: What are Their Needs?	$112,214	$0	$112,214
This is a collaborative grant with Zul Surani with South Asian Cancer Foundation					
Marc Milstein	2	Evaluating the Role of the RIN1 Gene in Breast Cancer	$72,335	$0	$72,335
University of California, San Diego					
Sonia Ancoli-Israel	1.5	Effect of Bright Light on Fatigue in Breast Cancer	$149,496	$0	$149,496
Lavinia Fiorentino	2	Treating Insomnia with CBT in Women with Breast Cancer	$76,000	$0	$76,000
Thomas Nelson	1.5	Early Breast Cancer Detection Using 3D Ultrasound Tomography	$149,878	$0	$149,878
Barbara Susini	3	Role of Integrins in Lymphangiogenesis During Breast Cancer	$135,000	$0	$135,000
Oksana Tyurina	3	An Approach to Antiestrogen Resistance in Breast Cancer	$135,000	$0	$135,000
University of California, San Francisco					
Shelley Adler	1	Underserved Women with Breast Cancer at End of Life	$57,323	$0	$57,323
This is a collaborative grant with Beverly Burns with Charlotte Maxwell Complementary Clinic.					
Angela Andersen	2	Reactivation of the Inactive X Chromosome and Breast Cancer	$90,000	$0	$90,000
Jeff Belkora	1	Consultation Support for Diverse Rural Breast Patients	$38,437	$0	$38,437
This is a collaborative grant with Sara O'Donnell with Mendocino Cancer Resource Center and Joy Hardin and Dawn Elsbree with Humboldt Community Breast Health Project.					
Laura Esserman	1	A Blueprint for Advancing Quality in Breast Cancer	$25,000	0	$25,000
Andrew Ewald	3	Regulation of Mammary Epithelial Invasion by MMPs and FGFs	$135,000	$0	$135,000
Leah Karliner	1.5	New Breast Cancer Approaches: Integration, Communication	$150,000	$0	$150,000
Peter Kushner	1.5	Estrogen Receptor Beta Agonists to Prevent Breast Cancer	$150,000	$0	$150,000
Mark Moasser	1.5	HER3 Infidelity and Resistance to Tyrosine Kinase Inhibitors	$150,000	$0	$150,000
Anna Nápoles-Springer	1	Psychosocial Support Services for Latinas with Breast Cancer	$100,000	$0	$100,000
This is a collaborative grant with Carmen Ortiz, Ph.D., with Circulo de Vida.					
Rena Pasick	1.5	Partnership to Reduce Cancer Disparities in Spanish Speakers	$21,999	$0	$21,999
This is a collaborative grant with Molly Bergstrom, with Women's Cancer Resource Center.					
Thea Tlsty	1.5	Breast Cancer Risk Associated with High Mammographic Density	$148,163	$0	$148,163
University of Southern California					
Florence Hofman	1.5	Survivin: Target for Breast Cancer Brain Metastases	$149,836	$93,897	$243,733
Judd Rice	1	Histone Methylation as a Marker of Breast Cancer Progression	$100,000	$62,500	$162,500
Wei Wang	3	Androgen Receptor Gene and p21 Gene in Breast Cancer	$134,998	$0	$134,998
Women's Cancer Resource Center					
Molly Bergstrom	1.5	Partnership to Reduce Cancer Disparities in Spanish Speakers	$78,000	$19,500	$97,500
This is a collaborative grant with Rena Pasick, Dr.P.H., with University of California, San Francisco					