California Breast Cancer Research Program

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BCRP
Cycle VII
2001 Awards
The California Breast Cancer Research Program is proud to announce the initiation of 64 new research projects that will lead to new knowledge about the causes, prevention, detection and treatment of breast cancer. With these new awards, the State of California is investing more than $18 million in the lives of California women. The projects are being performed at 28 institutions across the state, including universities, both public (University of California campuses) and private (e.g., California Institute of Technology); research institutes (e.g., Buck Institute for Age Research), medical centers (e.g., California Pacific Medical Center) and community agencies (e.g., The Wellness Community). Highlights of the 64 new projects that were awarded include:

In summary:

- 6 projects will expand our knowledge of the biology of the normal breast, including searching for and understanding the role of genes and proteins involved in the development of the normal breast, and changes that occur with breast-feeding.

- 6 projects will investigate factors that increase the risk of breast cancer and ways to reduce the risk of breast cancer including exploration of the effects of pesticides on the breast, study of the role of naturally occurring genetic variation on breast cancer risk, and the potential of natural herbs to reduce breast cancer risk.

- 21 projects will further our understanding of how breast cancer develops, including how new blood vessels form to feed tumors, and how this process can be prevented, different pathways by which tumor cells are instructed to grow, how this can be interrupted, and investigation of newly discovered genes involved in breast cancer progression.

- 13 projects will develop new treatments for breast cancer, including exploration of the effectiveness of herbs used in Chinese medicine, new ways to enhance the immune system to fight breast cancer, development of new drugs based on recent discoveries and new technology, and new ways to target drugs selectively to tumors.
• 9 projects are exploring **new ways to detect breast cancer**, including using biomarkers and detection of proteins and tumor cells in the blood, development and refinement of imaging technologies for better detection, and educational interventions for underserved populations.

• 4 projects are exploring **socio-cultural, behavioral, and psychological aspects** of breast cancer, including issues for deaf women, factors affecting quality of life, and innovative ways to provide support to women with breast cancer.

• 5 projects are in the area of **health policy and health services**; examining the impact of the structure of health delivery sites on quality of care, effects of peer navigators on women undergoing breast cancer treatment, and geographic variation in stage at diagnosis within California.

• 4 projects explore **racial/ethnic differences** in breast cancer biology, incidence, morbidity and mortality, or treatment.

• 3 projects are being done by **cross-disciplinary teams of research scientists** collaborating with each other to bring results of scientific research into practical application, including new tools for the detection of breast cancer and measuring the biological effect of preventive compounds.

• 1 award will bring experts from other fields together with breast cancer experts to **generate new ideas**.

• 26 projects are being performed by **new investigators in breast cancer**, which will help them establish careers in areas that will make an impact in breast cancer.

• 8 large projects were awarded in **areas that have been identified as relatively under-funded**, but important to advance our knowledge of breast cancer; namely, health policy and health services, racial/ethnic differences in breast cancer, biology of the normal breast, and socio-cultural, behavioral and psychological issues.

• 21 projects are exploring **new, innovative concepts** that may open up new avenues for breast cancer research and new options for prevention, detection, and treatment of breast cancer.

• 5 projects will be done by **teams of community members/organizations and research scientists** focused on issues identified by, and important to, communities in the state, including measuring the impact of peer navigators on the quality of life for women diagnosed with breast cancer, testing the effectiveness of on-line support groups, and identifying factors that impact women returning to work after breast cancer surgery.

• 5 of the most exciting projects are funded by revenue from the California State Income Tax Check-off.

**More information, including detailed descriptions of these projects, progress reports for completed and on-going research projects, and application materials for the next funding cycle, can be found on the internet at:**

http://www.ucop.edu/srphome/bcrp/

**or can be requested by calling (510) 987-9884 or toll-free (888)313-BCRP**
The biology of the normal breast is a greatly understudied area. That is why the BCRP has continued to support this priority issue. The breast is a complex structure composed of several cell types that function to generate milk or to support the cells that generate milk. We know that the milk forming cells are the ones that are most likely to give rise to tumors, but there are many questions yet to be answered. How do the different types of cells interact in the breast under normal conditions? What normal changes are necessary for the breast to function properly? Without knowing the answers to these questions, it requires a leap of faith to be able to identify the abnormal changes associated with cancer.

What we do know about the breast is that it is an organ in constant flux. Researchers are finding that how the breast remodels itself under the influence of internal and external factors dictates how it functions. The production of milk depends on the maturity (differentiation) of the breast cells, which in turn is controlled by hormones and growth factors and the immediate environment of the cells, as well as the internal and external physical structure of the cells. The six newly funded grants in the biology of the normal breast priority area investigate various pathways that contribute to breast cell growth maturation, and death.

- **Influence of breast structure on growth, maturation and milk production** – These grants examine the components responsible for maintaining the shape of the breast cell and identify the factors that regulate these components.

- **Influence of DNA structure on growth and cell growth and maturation** – These grants investigate how the physical structure of DNA can determine whether breast cells divide or die.

- **Role of non-milk producing cells in the breast** – These grants examine the role of cell types that are non-milk producing cells in the breast in regulating breast cell division, maturation and milk production.

- **Mechanisms of action of hormones and internal factors in breast cells** – These explore how cells are cued to divide and behave like breast cells.

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**Role of Chromatin Regulator in Breast Cell Growth**
Chen, Hongwu  
University of California, Davis  
3 years, $286,151

**Genetic Aspects of Physiological Response During Lactation**
Johnson, Randall  
University of California, San Diego  
3 years, $593,997

**Telomere Clustering is Lost in Mammary Epithelial Tumors**
Kaminker, Patrick  
Lawrence Berkeley National Laboratory  
2 years, $80,000

**Role of IKKa in Mammary Gland Development**
Karin, Michael  
University of California, San Diego  
3 years, $563,696
Coactivators in Mammary Gland Development and Tumorigenesis
Wang, Zhiyong
The Salk Institute
2 years, $80,000

Analysis of a Protease Involved in Mammary Development
Zahedi, Rana
Lawrence Berkeley National Laboratory
2 years, $80,000
Earlier Detection

The BCRP continues to support this research topic, because of the close link between earlier detection and increased survival rates. Breast cancers can be present for up to 10 years or longer before becoming large enough to be seen on a mammogram. If smaller tumors could be ‘seen’, then more breast cancers would be caught at the critical point before they spread to other parts of the body. In addition, we need to be able to analyze breast cancers for different characteristics associated with malignancy (e.g., angiogenesis), so that treatment strategies can be individualized for each woman. Finally, external monitoring could determine whether drugs actually find the tumor and have the desired effect of killing malignant cancer cells.

The eight newly funded BCRP research projects for earlier detection in 2001 include these aims:

- **Optical detection.** Can the properties of polarized light be used to detect breast tumors?
- **Computerized tomography.** Developing a pilot system optimized for breast cancer.
- **Magnetic resonance spectroscopy.** Detecting the biochemical signatures of breast cancer without biopsy using a special two-dimensional method.
- **Biomarkers.** Discovery of proteins and genes that indicate the presence of breast cancer, and development of non-invasive blood tests.

These projects respond to the needs expressed by breast cancer advocates and their physicians. Younger women need better and more sensitive detection methods that can find breast cancer hidden in ‘dense’ tissue and find smaller, often more aggressive, tumors. Women would like to avoid any exposure to the ionizing radiation needed to perform mammography. Women want convenience and comfort improvements over mammography. However, if cancer is suspected, then detection techniques should quickly determine whether it is benign or malignant. Waiting for biopsy results causes great psychological stress.

The challenge for research on earlier detection is not just to develop an improved ‘microscope’ for breast cancer, but also to be more disease-informative and cost effective.
Breast CT for Much Earlier Detection of Breast Cancer
Boone, John
Lindfors, Karen
University of California, Davis
3 years, $500,000

LPC as a Potential Tumor Marker for Recurrent Breast Cancer
Chew, Helen
University of California, Davis
1.5 years, $100,000

Optical Spectroscopic Detection and Imaging of Breast Cancer
Demos, Stavros
Lawrence Livermore National Laboratory
Ramsamoju, Rajen
University of California, Davis
1.5 years, $149,667

Targeting of Tumor-Promoting Galectins in Breast Cancer
Huflejt, Margaret
Sidney Kimmel Cancer Center
1 year, $182,500

Early Detection of Breast Cancer and its Recurrence
Imam, Syed Ashraf
Huntington Medical Research Institute
2 years, $365,446

Breast Cancer Imaging by 2-D Magnetic Resonance Spectroscopy
Thomas, M. Albert
University of California, Los Angeles
2 years, $249,137

2-D Magnetic Resonance Spectroscopy of Breast Tumors
Wyckoff, Nathaniel
University of California, Los Angeles
2 years, $80,000

Clinical Utility of Breast Cancer DNA Markers in Serum
Hoon, Dave
John Wayne Cancer Institute
2 years, $472,000

Tax Check-off Grant
Finding the cause(s) of breast cancer is the Holy Grail for overcoming the breast cancer epidemic. Identifying the elements that cause breast cancer and developing ways to mitigate or eliminate them will provide the ultimate victory in combating the disease. Unfortunately, the only clearly demonstrable risk factor for developing breast cancer is exposure of breast cells to the female hormone, estrogen. And even this risk factor does not give a clear picture of what is actually causing breast cancer because, although most women are exposed to estrogen, only a portion for them actually develop breast cancer. In order to identify the missing pieces of the puzzle, researchers are looking for explanations in special populations. They are investigating groups of people with similar genetic backgrounds and analyzing how their risks change as they change their environment or lifestyles, or they are trying to determine which genetic variations predispose people to developing breast cancer. BCRP has funded five applications that use these approaches.

- **Changes in breast cancer risk with exposure to environmental factors** - These grants will explore the role of pesticides and herbicides in breast cancer risk.

- **Influence of lifestyle factors on breast cancer risk** - These grants will explore the role of elements such as diet and acculturation on breast cancer risk.

- **Influence of genetic factors on breast cancer risk** - These grants investigate the contribution of genetic differences to breast cancer risk.

Once the causes of breast cancer have been identified, prevention methods can be developed. For now, the most demonstrably successful risk reduction methods have centered on chemoprevention; however the drugs currently available have unwanted side effects. The BCRP grant funded in the prevention priority area is exploring the chemopreventive properties of essiac tea, which can hopefully be developed as an alternative to the drugs that are on the market.

### Evaluation of Essiac Tea to Prevent Mammary Tumors
Bennett, Michelle  
Lawrence Livermore National Laboratory  
1.5 years, $185,642

### Dietary Fat, Fat Metabolizing Genes and Breast Cancer Risk
Ingles, Sue Ann  
University of Southern California  
2 years, $399,285

### Migration and Breast Cancer Risk in Hispanics
John, Esther  
Northern California Cancer Center  
3 years, $997,926

### Pesticides and Breast Cancer in Hispanic Women
Mills, Paul  
Public Health Institute  
3 years, $310,388

### HER-2/neu Gene Variations and Breast Cancer Risk
Press, Michael  
University of Southern California  
3 years, $1,147,535

### Role of Vitamin D Receptor and PI3k Genes in Breast Cancer
Ylstra, Bauke  
University of California, San Francisco  
3 years, $300,000
The health care system in the United States is a bewildering mosaic of organizations, methods of delivery, payment and eligibility for health care coverage, unlike that of any other industrialized nation. The most expensive of “systems”, it is able to provide the highest quality care at the frontiers of medical knowledge, while, by some estimates, nearly half its population is non- or underinsured for medical care, and health care outcomes are still influenced by race and socio-economic status, aside from underlying medical conditions.

The need to better understand medical care organization, service delivery and policies that effect breast cancer prevention, diagnosis, treatment, outcome, and related quality of life has been a major priority of the BCRP for several years, although we have only been able to attract and fund relatively few applications during this time.

This year for the first time, we are funding a significant amount of health policy and services related research. The BCRP awarded five major grants in this area totaling $3.18 million dollars, 17% of its total awarded this year, including two Community Collaborations Research (CRC) Awards.

This research will look at:

- **Quality of care**: understanding how inter-personal, personal and health care system factors interact to impact the quality of breast cancer care.

- **Regional variations**: What is the relationship between community-level health care variables and the stage at which breast cancer is diagnosed?

- **Employment Issues**: What impact does breast cancer surgery have on returning to work?

- **New Models of Care**: What is the impact of breast cancer care peer-navigators on breast cancer care, and what impact does the process of “navigating” have on both the patients and the navigators themselves?

### Geographic Variation in Breast Cancer Stage at Diagnosis
Maly, Rose
University of California, Los Angeles
3 years, $425,497

### Determinants of Breast Cancer Treatment in the Underserved
Kahn, Katherine
University of California, Los Angeles
3 years, $851,916

### Return to Work after Breast Cancer Surgery
Estrin, Diane
Women’s Cancer Resource Center
Eversley, Rani
University of California, San Francisco
3 years, $625,000

### Does a Peer Navigator Improve Quality of Life at Diagnosis?
Bliss-Isberg, Caroline
Central Coast Women’s Cancer Consortium
Spiegel, David
Stanford University
3 years, $500,000

### The Impact of Structure on Quality of Breast Cancer Care
Kahn, Katherine
University of California, Los Angeles
3 years, $851,916

### Geographic Variation in Breast Cancer Stage at Diagnosis
Davidson, Pamela
University of California, Los Angeles
3 years, $425,497

### Tax Check-off Grant
The development of a new drug to the market can require spending hundreds of millions of dollars. So, how can the BCRP expect to accomplish very much by spending tens or hundreds of thousands of dollars on an innovative treatment research grant? The lesson with Herceptin is that small groups of researchers can provide both the key information and the incentive to develop a new drug. This might not happen in an environment dominated by ‘the bottom line.’ We know that individuals and small groups of creative researchers are still willing to tackle the immense hurdles of treating breast cancer. These researchers are in touch with the latest knowledge of the disease, and they are impacted by the human needs expressed by breast cancer advocates and activists.

The BCRP supports innovative treatments research for multi-disciplinary, exploratory, and innovative research projects. Some representative topics in 2001 include:

- **Immunotherapy.** New ways the immune system can be triggered to fight breast cancer more effectively.
- **Drug delivery.** Formulating breast cancer drugs to go directly to tumors and spare women the harmful side-effects.
- **New drugs.** Novel technologies and the latest information on breast cancer are being put to work to find new therapeutics.
- **Alternative therapies.** Herbs and other alternative approaches will be studied in a context outside the strict parameters of how drugs are tested in Western medicine.
Targeting the EphB4 Receptor to Inhibit Breast Tumor Growth
Pasquale, Elena
The Burnham Institute
1.5 years, $188,442

Blood Vessel Markers in Breast Cancer
Ruoslahti, Erkki
The Burnham Institute
2 years, $389,120

Novel Technologies to Identify Tissue-Selective Estrogens
Schaufele, Fred
University of California, San Francisco
1 year, $75,000

Patient-Individualized Chemotherapy in Breast Cancer
Silverman, Daniel
University of California, Los Angeles
3 years, $296,994

Engineering Antibodies Specific for Breast Cancer Proteases
Sun, Jeonghoon
University of California, San Francisco
2 years, $80,000

Herba Scutellaria Barbatae for Metastatic Breast Cancer
Tripathy, Debasish
University of California, San Francisco
2 years, $232,364

Selective Targeting of Breast Cancer with Radioiodide
Wapnir, Irene
Stanford University
2 years, $315,200
The underlying cellular, genetic, and biological processes of breast cancer continue to be major topics of research interest and BCRP funding for 2001. There remains much we do not know about the development, progression, and spread of breast cancer. Why do cancer cells have the ability to divide beyond the point when normal breast cells become limited? What is the underlying biology that explains why drugs used for treatment don’t work very well or stop working after initial success in a patient? What is the total number of critical breast cancer genes, and what can this tell us about the best clinical treatment options? Basic researchers are working with an increased appreciation of the complexity of the actual disease, and they are more aware of the concerns of women being diagnosed with breast cancer.

Some of the topics in this area the BCRP funded in 2001 include:

- **Apoptosis.** The process of programmed cell death that often becomes defective in breast cancer and allows tumors to survive drug treatment and the immune response.

- **Angiogenesis and the tumor microenvironment.** How breast cancers differ from normal breast cells in stimulating blood vessel growth, attachment events, cell movement, and invasion properties.

- **Cell growth.** Why breast cancer cells divide in an uncontrolled manner, especially through the Her-2 (ErbB2) oncogene and estrogen receptors.

- **Genetic defects.** Why gene mutations accumulate during breast cancer progression and are either not repaired or recognized.

- **Model systems and technology.** The use of lower organisms for genetic studies and new technologies, such as DNA array (gene chips), for rapid analysis of multiple genes and proteins of interest for breast cancer.

To study breast cancer, researchers use sophisticated tools to detect previously unknown genes and the factors that cause defects in the regulation of known genes. The intricate protein pathways inside breast cancer cells are dissected, the breast cancer cells are experimentally modified, and breast cancer growth and spread are studied in cell and animal models.

The recent success of the Human Genome Project to identify the 30,000+ human genes has provided us the ‘pieces of the puzzle’, but clinicians and basic researchers must assemble these pieces into a coherent picture of breast cancer. How might this happen? Current thinking is that breast cancer is actually not one disease, but a group of genetically different diseases. Work is in progress to define these distinct clinical subsets based on discrete differences in genes and proteins found in each woman’s breast cancer. This has implications for basic research, too. In the near future, hopefully, we will see a better integration of basic research model systems that more closely replicate the ‘real world’ clinical situation.
Role of PTEN/Akt Pathway in Invasion in Human Breast Cancer
Bose, Shikha
Cedars-Sinai Medical Center
1 year, $100,000

Molecular Study of BAG Domains: A New Motif in Breast Cancer
Briknarova, Klara
The Burnham Institute
2 years, $86,400

Trypsin-like Proteases as Metastatic Agents in Breast Cancer
DeFea, Kathryn
University of California, Riverside
3 years, $295,980

Role of Id-2 in Breast Cancer and its Relationship to Id-1
Desprez, Pierre-Yves
California Pacific Medical Center Research Institute
2 years, $296,541

The Role of BRCA1 in Nucleotide Excision Repair
Hartman, Anne-Renee
Stanford University
2 years, $86,400

The Functions of BRCA2 in Repairing DNA Damage
Lio, Yi-Ching
Lawrence Berkeley National Laboratory
3 years, $495,388

Genes That Modulate Dioxin-Induced Breast Cancer
Lu, Quan
Stanford University
2 years, $86,400

Genetic Analysis of ErbB Signaling in C. Elegans
Moghal, Nadeem
California Institute of Technology
2 years, $86,400

Smoking Effect on Lung Metastasis from Breast Cancer
Murin, Susan
University of California, Davis
1.5 years, $75,000
(Co-funded with the Tobacco-Related Disease Research Program)

Tumor Suppression by Dystroglycan in Breast Epithelial Cells
Muschler, John
Lawrence Berkeley National Laboratory
2 years, $328,214

Rodent Model for Human Ductal Carcinoma in Situ
Nandi, Satyabrata
University of California, Berkeley
1 year, $100,000

Molecular Characterization of ErbB2 Positive Breast Cancers
Neve, Richard
Buck Institute for Age Research
2 years, $86,400

Tax Check-off Grant
SBP-1: A Novel Survivin Binding Protein in Breast Cancer
Okada, Kazuya
The Burnham Institute
2 years, $86,400

P132Cas and Antiestrogen Resistance of Breast Cancer
Rehn, Marko
The Burnham Institute
2 years, $86,400

Novel Enzymes Associated with Breast Cancer Angiogenesis
Rosen, Steven
University of California, San Francisco
1.5 years, $100,000

Are EGF-Receptors Activated by IL-8 in Breast Cancer?
Schraufstatter, Ingrid
La Jolla Institute for Molecular Medicine
1 year, $155,475

Pathway-Specific Gene Expression in Breast Cancer Cells
Sweeney, Colleen
University of California, Davis
3 years, $299,287

Overcoming Drug Resistance in Breast Cancer
Vuori, Kristiina
The Burnham Institute
2 years, $386,457

Regulation of the ATR Checkpoint Response in Breast Cancer
Yean, Dawn
Stanford University
2 years, $86,400
A diagnosis of breast cancer is often the beginning of many serious issues that affect not only a woman’s quality of life, but her treatment experience, and perhaps how long she may live. Because no breast cancer survivor knows whether her treatment has resulted in a cure, there is a lifetime of uncertainty for her, her family and loved ones. This medical and psychological uncertainty is often made worse by the fear of subsequent discrimination in public life such as the workplace, health insurance coverage and so on.

In this cycle, BCRP funded 5 grants in this area, in addition to two other grants (in the health policy and innovative treatment priority areas) which have significant socio-cultural, behavioral and psychological components. Significantly, four of these seven involve a partnership between community organizations and community researchers through our Community Research Collaboration (CRC) award.

The topics in this area the BCRP funded in 2001 include:

- **Health behaviors:** improving early detection behaviors among underserved populations.
- **Quality of life:** understanding and increasing adherence to a healthy diet among survivors to improve psychological well-being and, perhaps, affect recurrence, and examining how family stress, particularly children’s, affects patients’ well-being and coping.
- **Providing support:** studying the efficacy of an internet support group to improve quality of life for breast cancer survivors.

Of the two grants in other areas, a Health Policy and Services award (Spiegel and Bliss-Isberg) will study how peer navigators affect patients’ care while also studying the effect on the well being of the navigators themselves. The other Health Policy and Services award (Maly) will look at how personal and inter-personal factors (particularly patient-physician interaction affect breast cancer care outcomes), as well as health care system factors affect quality of life.

### Women with Breast Cancer: Quality of Life and Diet Adherence

Bardwell, Wayne  
University of California, San Diego  
3 years, $164,427

### Breast Cancer Prevention and Control Among Deaf Women

Berman, Barbara  
University of California, Los Angeles  
Kleiger, Heidi  
Greater Los Angeles Council on Deafness  
1.5 years, $109,707

### Influence of Child’s Stress on Women with Breast Cancer

Ducker, Dalia  
California School of Professional Psychology  
Levine, Ellen  
California Pacific Medical Center Research Institute  
1.5 years, $129,000

### Effectiveness of Internet vs. Face-to-Face Support Groups

Golant, Mitch  
The Wellness Community-National  
Lieberman, Morton  
University of California, San Francisco  
3 years, $586,593

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

Sablan-Santos, Lola  
Guam Communications Network, Inc.  
Tanjasiri, Sora  
University of California, Irvine  
3 years, $573,010

### Tax Check-off Grant

Levine, Ellen  
California Pacific Medical Center Research Institute  
1.5 years, $129,000
The research grants awarded in 2001 were initially reviewed and scored for scientific merit and other criteria in 6 separate peer Review Committees. The Committees consisted of distinct types of reviewers, and they reviewed grants following established practice at the National Institutes of Health (NIH).

The Chair leads the review process and is a senior researcher in breast cancer areas associated with the Committee’s central topic or priority issue. Committee Members have broad expertise in topics associated with individual applications. Breast cancer Advocate Reviewers are women living with the disease, and they bring their personal experiences to the review process. Often, the Advocates have specialized training in grant review and have served on prior review committees. The California Advocate Observer is not assigned applications for review and does not vote, but represents the California advocacy community to gain insight and provide feedback to the Program. Ad Hoc Members participate by teleconference and bring their specialized expertise to the review of individual applications.

Over the past four years, BCRP has developed, tested and phased in a scoring system that allows our expert reviewers to better differentiate applications that are especially innovative and that have the most potential impact on breast cancer. This has improved our ability to choose the most innovative and creative research for funding.

In the past, the majority of research funding agencies, including the BCRP and the National Institutes of Health, rated proposals with a single score based solely on scientific merit. With this method, an application with an excellent research plan to test an idea that wasn’t particularly novel could receive the same score as an application with a flawed research plan to test a novel idea. BCRP’s new scoring method can distinguish these two applications. Applications are evaluated and voted on by the Committees for the following scientific merit score components:

- **Innovativeness**
- **Impact**
- **Approach**
- **Feasibility**
- **Career Development** (new investigator and postdoctoral fellowships)
All applications are then reviewed by the Breast Cancer Research Council for programmatic issues. The following criteria are used:

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

The Breast Cancer Research Council recommends the grants to be funded, based upon both the scientific merit scores and the programmatic review, to ensure both scientific excellence and relevance of the research to BCRP's mission and goals.

The BCRP wishes to thank the participants in our 2001 Review Committees for their service and dedication to our Program.
BASIC BREAST BIOLOGY REVIEW COMMITTEE

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