



BREAST CANCER RESEARCH PROGRAM

Eradicating breast cancer by funding innovative, high-impact research through a partnership of scientists and consumers.

Department of Defense Congressionally Directed Medical Research Programs

CDMRP Summary



Review of proposal submissions is conducted according to the two-tier review model recommended by the National Academy of Sciences Institute of Medicine; this model has received high praise from the scientific community, advocacy groups, and Congress.

The breast cancer advocacy community, led by the National Breast Cancer Coalition, began its grassroots efforts in the early 1990s to increase federal funding for breast cancer research. In fiscal year 1993 (FY93), Congress responded by appropriating \$210 million to the Department of Defense (DOD) to initiate an extramural peer-reviewed research program specifically focused on breast cancer. This launched a unique partnership between the public, Congress, and the military, as the U.S. Army Medical Research and Materiel Command (USAMRMC) was directed to manage the Breast Cancer Research Program (BCRP). The BCRP sought advice from the Institute of Medicine and leaders in the scientific and breast cancer advocate communities, creating a unique and collaborative organization with an emphasis on innovative ideas, high-impact research, and filling gaps in research and practice. This program continues to demonstrate significant responsiveness to the needs of the consumer and scientific community. The BCRP has set a precedent of effective investment and management of public funds for the vision of eradicating breast cancer. The model established by the BCRP led to further congressional appropriations to the DOD for focused biomedical research programs, leading to the creation of the Congressionally Directed Medical Research Programs (CDMRP) within USAMRMC. Funds directed by Congress each year to the BCRP and other CDMRP programs are directly attributed to the ardent lobbying efforts of the individuals affected by the diseases.



BCRP *Vision and goals*

Program VISION

To eradicate breast cancer by funding innovative, high-impact research through a partnership of scientists and consumers.

Investment Goals:

- Encourage innovation and stimulate creativity
- Support research with high-impact potential
- Foster new directions and fill important gaps
- Facilitate synergistic and multidisciplinary collaborations
- Bring new investigators into the breast cancer field
- Train investigators early in their careers
- Encourage research in understudied research areas



find & fund
the **BEST** research

*The BCRP fills important gaps not addressed by other funding agencies in support of breast cancer research. The BCRP funds groundbreaking, high-risk, high-gain research and encourages **out-of-the-box thinking**.*

BCRP Summary

FY <i>Fiscal Year</i>	Funding Level <i>(Millions)</i>
1992–2001	1,218.3
2002	150
2003	150
2004	150
2005	150
2006	127.5
2007	127.5
2008	138
2009	150



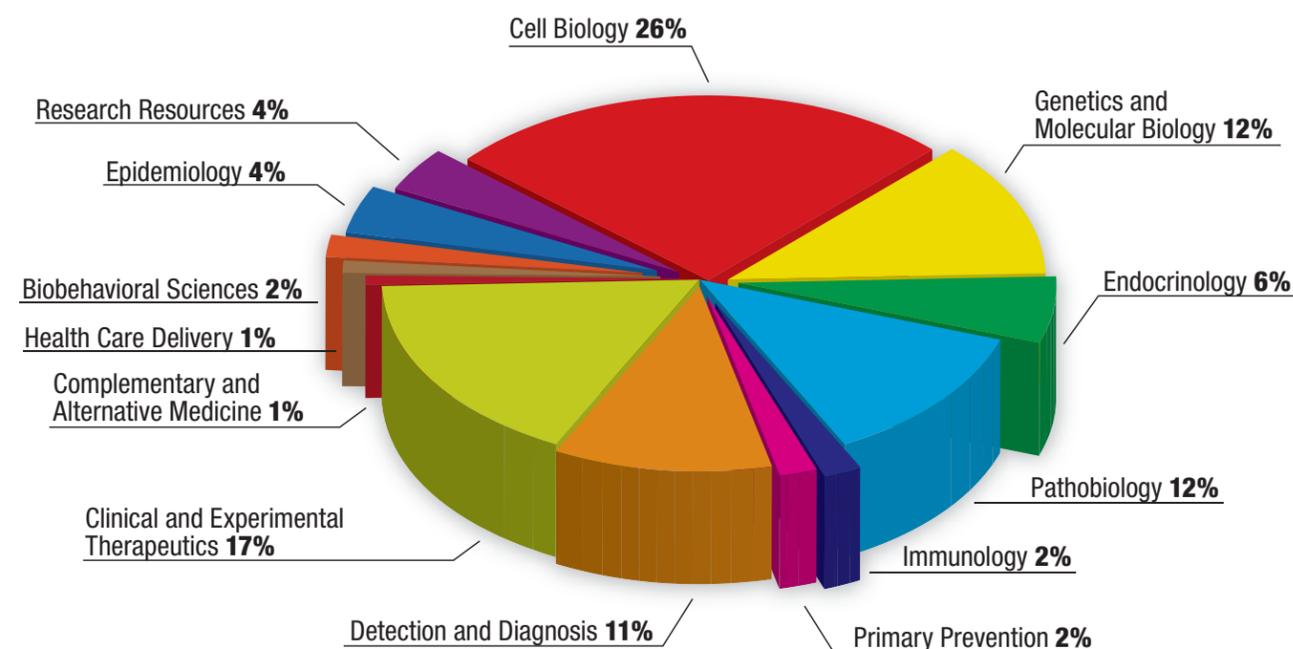
Appropriations for the BCRP from FY92 through FY07 totaled more than \$2 billion (B). The FY08 appropriation was \$138 million (M). To date for FY08, a total of 1,587 proposals have been received and 173 awards have been recommended for funding.

The BCRP vision is adapted yearly to facilitate rapid change and to invest funds in the most critical research areas thus ensuring that the program remains responsive to current needs and future opportunities.

The BCRP challenges the scientific community to design innovative research that will foster new directions for, address neglected issues in, and bring new investigators to the field of breast cancer research. The BCRP focuses its funding on innovative projects that have the potential to make a significant impact on breast cancer, particularly those involving multidisciplinary and/or multi-institutional collaborations and alliances. The BCRP encourages risk-taking research; however, all projects must demonstrate solid judgment and scientific rationale.

Funding mechanisms reflect the philosophy of the BCRP to promote novel research that will make revolutionary leaps forward in the field of breast cancer. Many of the mechanisms focus on novel ideas over preliminary data, while other mechanisms look to support researchers very early in their promising careers. The BCRP funding mechanisms also provide opportunities for collaborations that expand research across disciplinary lines and institutes.

BCRP FY92-FY07 Categorized Using the Scientific Classification System



Consumer Advocate Participation

Providing focus, perspective, and unique expertise

The unique two-tier review process established by the BCRP integrates the perspectives and experiences of the breast cancer survivor with the knowledge of the scientific community. This innovative approach, which has been adapted by several other funding organizations, blends the best expertise to evaluate research proposals for their potential to meet the program's goals.

More than 629 consumer advocates have served on review panels for the BCRP.

Did you know?

- Since FY93, consumer advocates have participated in designing the BCRP's priorities and funding opportunities.
- Since FY93, consumer advocates have participated as equal voting members in making funding recommendations during programmatic review.
- Since FY95, consumer advocates have participated as equal voting members in scientific peer review panels.



“I believe the DOD BCRP is our best hope for eradicating breast cancer. The BCRP is innovative, scientifically sound, and adaptable to the needs of the scientific and breast cancer advocate communities. As a breast cancer survivor/peer reviewer I have participated in and observed the rigor and integrity of the program. The DOD BCRP is a critical component in our fight to eradicate breast cancer.”

Christine Carpenter
Cedar Valley Cancer Committee
Iowa Breast Cancer Edu-action
15-year survivor



“Being diagnosed with aggressive breast cancer at age 30 was devastating. The resources available for young women, particularly African American young women were limited. So... I conducted extensive research to educate myself about the disease and treatment options. As a consumer peer reviewer for the DOD BCRP, I serve as a voice for survivors, many of whom are underserved.”

Claudine James
Sisters Network, Inc.
8-year survivor



“I chose to participate in the BCRP peer review process because I am interested in the science of breast cancer. I greatly enjoyed working with the scientists and sharing the perspective of someone struggling with metastatic disease as a way to provide real-life context for scientific review.”

Jhumki Basu
SHARE
7-year survivor



“After telling my story while introducing myself to my panel, one of the scientists later told me that now that he had heard my story, he feels like he needs to do more to get to the cure. It made it worthwhile for me to participate. I realized how powerful it was to share my story in these settings. More than ever, I want to go back to talk to more scientists.”

Olga Ogoussan
Bosom Buddies
7-year survivor



“Being part of the DOD BCRP peer review process is very important to me because research funded by this program produced an important targeted therapy, Herceptin, which has allowed me to live and thrive 5 years (and still going strong) after being diagnosed with advanced breast cancer. I want to give back to the talented, hard-working doctors and scientists whose funded research will produce additional treatments for breast cancer patients and hopefully, one day, a cure.”

Shirley Mertz
Breast Cancer
Network of Strength
17-year survivor

Era of Hope

June 25–28, 2008 • Baltimore, Maryland



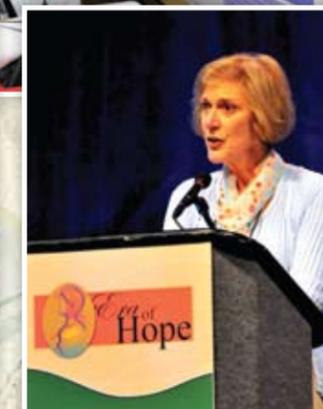
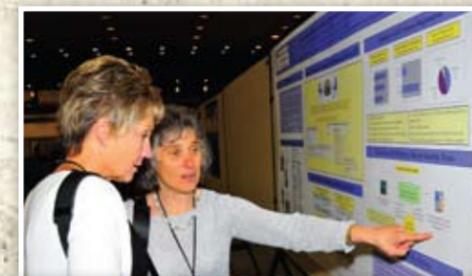
The **Era of Hope** Meeting is an international forum for presenting research studies funded by the CDMRP BCRP. It is a unique opportunity for experts in different fields and research areas to gather, share ideas, identify promising directions in breast cancer research, and develop collaborative relationships.



Three major themes:

- 1 Risk and Prevention
Across the Spectrum of Breast Cancer
- 2 Breast Cancer Diagnosis –
What's on the Horizon?
- 3 Managing Breast Cancer
Across the Spectrum of Disease

- * Plenary sessions focused on emerging issues in breast cancer;
- * Symposia sessions spotlighted the research of more than 216 BCRP-funded investigators; and
- * Poster sessions highlighted more than 1,200 BCRP-funded research projects.



THE SUN
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Lobby led Survivors keep program scientists grounded
to billions in cancer research

Era of Hope

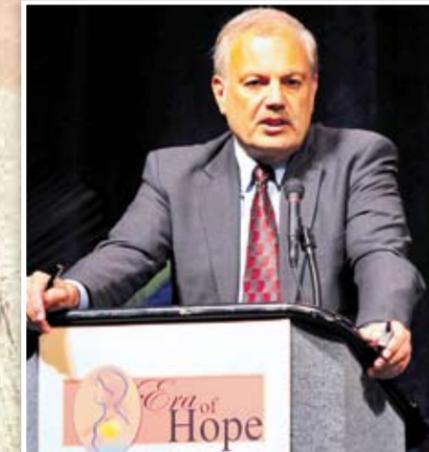
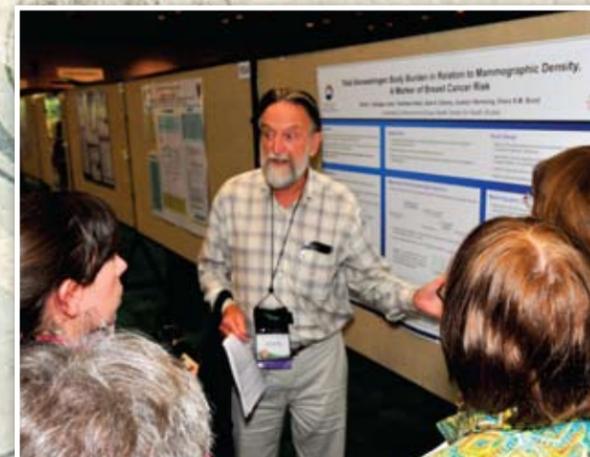
June 25–28, 2008 • Baltimore, Maryland



More than **1,550** scientists, clinicians, breast cancer survivors and advocates, policy makers, and the general public from more than **530** organizations came together to learn about advancements made since the BCRP's inception.



Breast cancer survivor participation, a hallmark of the BCRP and the ***Era of Hope Meeting***, was tremendous: more than **200** breast cancer survivors from **124** organizations attended; **56** survivors were speakers, co-chairs, or session moderators; and **15** survivors presented abstracts.



Innovation



FY05 Concept Awardee **Yayun Liang** of the University of Missouri, Columbia investigated the anti-tumor effects of PRIMA-1, a small molecule that restores the transcriptional function of mutated p53, and monoclonal antibody 2aG4, which binds to anionic phospholipids on the surface of tumor blood vessels. This combination treatment demonstrated efficacy in suppressing tumor growth, inhibiting lymph node metastasis, and shrinking tumors in mouse models of advanced breast cancer.

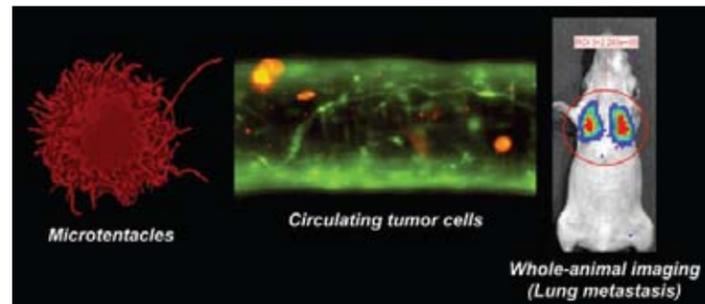


Dr. Alana Welm, recipient of an FY07 Era of Hope Scholar award, is working to elucidate mechanisms of the macrophage stimulating protein (MSP) pathway, which likely plays a role in promoting breast cancer metastasis. Dr. Welm's award builds on her prior studies that established that the MSP pathway is a significant, independent prognostic factor for metastasis and mortality in human breast cancer. Dr. Welm, along with collaborators, will use three-dimensional culture models, mouse xenograft models, and primary human breast tumors to develop a greater understanding of the MSP pathway and to determine if this pathway can be targeted therapeutically in breast cancer.



The primary cause of patient death from breast cancer is the bloodborne spread of transformed mammary epithelial cells. When these large epithelial cells enter the narrow capillaries of organs such as the lung, they can be destroyed by physical fragmentation due to the hydrostatic pressure of blood flow and size restriction within the capillary. Therapies that inhibit the exit of tumor cells from the vasculature (extravasation) would thus effectively "trap" tumor cells in the capillaries, increasing the likelihood of their fragmentation and destruction. Since this therapeutic strategy does not require cell division, it provides a novel mechanistic alternative to

traditional chemotherapies that target dividing cells. **Dr. Stuart Martin**, recipient of an FY06 Idea Award, has found that detached breast tumor cells produce unique tubulin-based cytoskeletal protrusions, dubbed microtentacles, which are distinct from the actin-based protrusions that are well studied in adherent tumor cells. Microtentacles are required for the attachment of circulating tumor cells to surfaces, such as the interior of blood vessels. Using advanced imaging of tumor cells circulating in the bloodstream of living mice, Dr. Martin is investigating the molecular mechanisms that underlie microtentacle formation and further characterizing their role in vessel wall attachment. Elucidation of the molecular components and their role in microtentacle formation could provide novel targets for the design of therapies that would inhibit extravasation, ameliorating the threat of metastasis for breast cancer and other types of epithelial carcinomas.

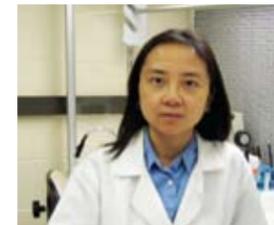


Imaging circulating tumor cells

Exploring new ideas and encouraging creativity



Dr. Stephen Doxsey, FY07 Idea Awardee from the University of Massachusetts, is investigating the role of the midbody, a cellular structure previously thought to be discarded from the cell, in breast cancer development and progression. Evidence to date shows that midbody derivatives preferentially accumulate in putative breast cancer stem cell populations. Dr. Doxsey hypothesizes that midbody derivatives may serve as markers for breast cancer stem cells and that targeted disruption of midbody derivatives may be a useful therapeutic strategy for preventing breast cancer development.



Despite its efficacy as a chemotherapeutic agent against breast cancer, doxorubicin has been linked to life-threatening, dose-dependent cardiotoxicity. As a recipient of an FY05 Concept Award and an FY06 Idea Award, **Dr. Yi Lisa Lyu** of the University of Medicine and Dentistry of New Jersey Robert Wood Johnson Medical Center has been investigating the possible link between the DNA topoisomerase II beta (Top2b) isozyme, which is highly expressed in terminally differentiated tissues such as the heart, and doxorubicin cardiotoxicity. Dr. Lyu's findings have shown that the cardioprotective agent dexrazoxane inhibits doxorubicin-induced DNA damage in cardiomyocytes by

antagonizing Top2b cleavage complex formation. In addition, dexrazoxane also can induce rapid proteasome-mediated degradation of Top2b in parallel with the reduction of doxorubicin-induced DNA damage. These results suggest a link between cardiotoxicity and Top2b targeting by doxorubicin.



FY07 Idea Awardee **Dr. Patricia Keely** is working to advance state-of-the-art microscopic imaging techniques to better understand how breast cancer cells interact with collagen fibers found in the stromal environment. Specifically, she is looking at key signaling pathway changes in three-dimensional collagen matrices and in mouse

mammary glands that are related to increased collagen formation and breast density. This work is significant because of the elevated risk of breast cancer that is associated with mammographically dense breasts.

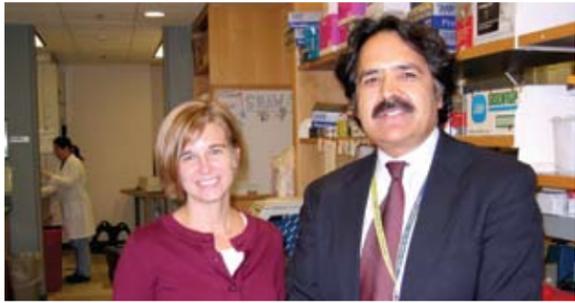


Electron micrograph of mouse mammary gland, demonstrating mammary cells in intimate contact with collagen fibers. Note that collagen fibers have physical and biochemical effects on cells.

Synergy



As recipients of an FY06 Synergistic Idea Award, **Dr. William Lee** of the University of Pennsylvania and **Dr. Badrinath Roysam** of the Rensselaer Polytechnic Institute along with **Ms. Wiem Lassoued** of the University of Pennsylvania are teaming up to unlock the wealth of biological information that is preserved in formalin-fixed paraffin-embedded tumor specimens. A novel cell-based (cytometric) approach is being developed to analyze immunostaining of tumor sections for antigens that reveal cell fate and cell signaling activity. This approach uses multispectral microscopy to image multiple targets (e.g., estrogen receptor, progesterone receptor, and signaling proteins) on a single pathology slide. A software platform is being developed to analyze the multispectral images. Algorithms will identify which cells in the sample contain the different targets and how the levels change in response to treatment. It is anticipated that this system could retrieve the biological information preserved in human tumor tissue and become a valuable tool for breast cancer translational research and patient care.



Dr. Leslie Shaw and **Dr. Ashraf Khan** from the University of Massachusetts Medical School are working together to understand how patients with HER2-positive tumors develop resistance to the drug Herceptin. Through their FY06 Synergistic Idea Award, they are studying human breast tumors to determine if there is a connection between insulin receptor substrate (IRS) proteins and how HER2-positive tumors respond to treatment. IRS proteins play a critical role in cellular responses to insulin growth factor. The investigators found that the amounts and distribution of the IRS-1 and IRS-2 proteins

differ, with IRS-1 predominantly expressed in normal or benign breast disease tissue and IRS-2 expressed primarily in high-grade tumors, including HER2-positive tumors. Drs. Shaw and Khan continue to try to develop cellular and animal models to specifically manipulate the levels of these two intracellular proteins to Herceptin therapy and the aggressiveness of these tumors.



Dr. Katherine Weilbaecher of Washington University and **Dr. Ross Cagan** of Mount Sinai School of Medicine are researching new and innovative approaches to study cancer metastasis. Their FY06 Synergistic Idea Award combines the power of previous findings in the fruitfly *Drosophila* to identify genes that may be important in cancer metastasis and applies these findings to a mouse model of breast cancer. They have demonstrated

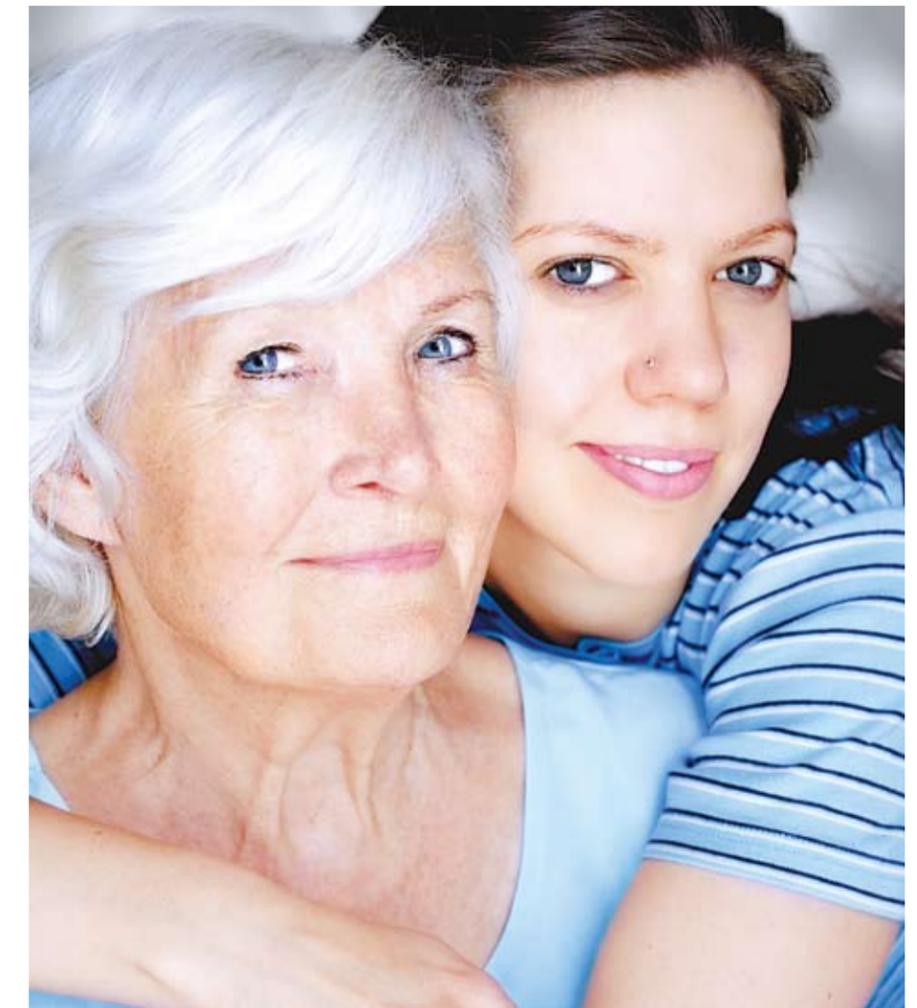
that a compound identified as antimetastatic in *Drosophila* is an efficient inhibitor of breast cancer metastasis to the lung in a mouse xenograft model. Their work could provide a template for how to move candidate therapeutic compounds from the fly to the mouse and eventually to clinical trials and breast cancer patients.



Bringing people and ideas together



The “Center of Excellence for Individualization of Therapy for Breast Cancer” is a collaborative research project with Indiana University, the Hoosier Oncology Group LLC, and research centers in the United States, Canada, and Peru. **Dr. George Sledge** is overseeing the project. Combining emerging technologies with existing ones, the investigators are studying how to match the right patient to the right drug for women with advanced breast cancer. According to Dr. Sledge, standard treatments for advanced breast cancer are often plagued by drug failure and toxicity: “The tragedy of modern therapy is not just its toxicity; rather, it is that so many experience so much toxicity for so little benefit.” Through individualized treatment, Dr. Sledge and his colleagues hope to increase effectiveness and lessen toxicity of treatment for women with advanced breast cancer. Samples of each patient’s breast cancer tumor tissue and blood are analyzed using genomics, proteomics, and pharmacogenetics. By combining the predictive powers of these technologies, the team is striving to derive individualized treatments that can be tested in the clinical setting.



Training



Mr. Xinran Xu of Mount Sinai School of Medicine was awarded an FY05 Predoctoral Traineeship Award to examine whether there is an association between breast cancer survival and one-carbon metabolism, which is a key pathway in DNA methylation and synthesis. By utilizing the resources available from the Long Island Breast Cancer Study Project, Mr. Xu found that higher prediagnostic intake of vitamins B1 and B3 was associated with decreased mortality rates. Polymorphisms in two of the one-carbon metabolizing genes, MTHFR C677T and BHMT G742 A, were associated with reduced mortality. The association of the MTHFR C677T polymorphism with survival was modified by estrogen and progesterone receptor status. These findings suggest that the one-carbon metabolism pathway is a potential target for improving breast cancer survival.



New methods of tumor profiling and predicting clinical outcome are needed to ensure that breast cancer patients receive the best individualized treatment. **Mr. Francois Pepin** of McGill University was awarded an FY05 Predoctoral Traineeship Award to obtain training in breast tumor biology, genomics, and bioinformatics. Mr. Pepin is part of a collaborative, multidisciplinary group focusing on the role of tumor stroma in breast cancer. Tissue samples from patients with invasive breast cancer were characterized by the research group using genetic microarray profiling and defined gene expression signatures based on variation between tumor tissue and normal stroma. This led to development of a 26-gene predictor called the stroma-derived prognostic predictor (SDPP), which can forecast disease outcome with greater accuracy than standard clinical prognostic factors and current predictors that are derived from whole tissue. The ability of the SDPP to differentiate tumor response to treatments emphasizes the importance of stromal biology in breast cancer diagnosis.



As a recipient of an FY04 Multidisciplinary Postdoctoral Award, **Dr. Hong Song** of Johns Hopkins University sought to combine targeted alpha-particle radioimmunotherapy and a whole-cell cancer vaccine to treat breast cancer. Specifically, Dr. Song studied the combined efficacy of 213Bi-labeled anti-HER-2/neu antibody Fab' fragment and 3T3 cells that express HER-2/neu and secrete GM-CSF in an immune-tolerant HER-2/neu transgenic mouse model. The combined treatment demonstrated improved efficacy in a mouse model of residual micrometastasis, compared to localized radiation or cancer vaccine alone, by reducing tumor growth and improving survival. The addition of the chemotherapy drug cyclophosphamide, which inhibits the T regulatory cell population, further improved efficacy of the combined treatment. Dr. Song's studies indicate that the combined treatment can specifically deliver radiation to HER-2/neu-positive tumor cells and boost the antitumor immune response, representing a new potential therapeutic approach.

Investing in tomorrow's future in breast cancer research



Following initial diagnosis and treatment, the majority of breast cancer patients face the uncertainty of experiencing a recurrence of the disease. The cellular and molecular mechanisms underlying tumor recurrence are not clearly delineated. **Dr. James Alvarez** of the University of Pennsylvania received an FY06 Era of Hope Postdoctoral Award to focus on the problem of tumor recurrence. He proposed to identify clinically relevant candidate recurrence genes and characterize their functions and molecular mechanisms of regulation. Using mouse models that have inducible expression of the Neu, Myc, or Wnt1 oncogenes and mimic breast cancer recurrence, Dr. Alvarez found that recurrent tumors from all three models have similar gene expression patterns, suggesting a similar route to recurrence. He identified a list of genes that are differentially expressed in recurrent tumors and analyzed the association of these genes with clinical outcome using human breast cancer expression datasets. The function and regulation of these candidate genes will be extensively characterized. Dr. Alvarez's primary goal of identifying genes that play a causal role in recurrence may eventually lead to therapeutic approaches to preventing recurrence.



Breast cancer survivors who have undergone surgical resection to remove tumors often elect to have breast reconstruction. The inability to produce large volumes of engineered adipose tissue has limited the reconstructive methods for restoring the aesthetic function of the breast. Preadipose and mature adipocytes may potentially be used in breast reconstruction, but a better understanding of the mechanisms of adipogenesis is needed. **Ms. Cheryl Gomillion** of Clemson University, recipient of an FY06 Predoctoral Traineeship Award, is devising new methods to grow adipose cells in vitro under specific conditions that will yield cells that are at the precise differentiation state needed. These systems will allow not only expansion of the adipose cells in culture but also stimulation of cellular differentiation under controlled conditions. The ability to control the differentiation of adipose cells will provide a means to improve tissue engineering strategies for breast reconstruction.



Dr. Julie Ostrander, an FY07 Multidisciplinary Postdoctoral Award recipient from Duke University, is focusing on two emerging technologies to try to improve early detection in asymptomatic women who are at high risk for breast cancer. Optical spectroscopy is a powerful experimental imaging technique that is currently being developed to exploit differences in the vascularity, hemoglobin oxygenation, and proteins in breast tissues from different risk groups. Random periareolar fine needle aspiration (RPFNA) is a research technique designed to sample breast tissue for pre-malignant cytological changes, particularly in asymptomatic high-risk women. Importantly, RPFNA yields sufficient cellular samples to permit simultaneous cytological analysis, biomarker development, and biological profiling. Dr. Ostrander will combine these two technologies to test whether optical spectroscopy can improve the ability of RPFNA to predict short-term breast cancer risk.

Impact



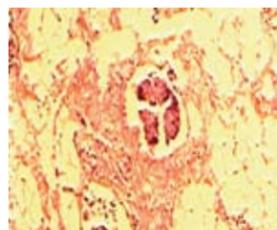
Building Networks Symposium

The Minority and Underserved Populations Program coordinated with the BCRP to host a symposium to bring scientists funded through the HBCU/MI (Historically Black Colleges and Universities/Minority Institutions) Partnership Training Award together for discussion and networking opportunities toward the common goal of addressing disease disparity. The Building Networks Symposium was held June 24–25, 2008, in Baltimore, Maryland (immediately preceding the Era of Hope Meeting).



Latinas face many potential barriers to undergoing breast cancer screening. Financial barriers alone do not explain the limited screening in this population, however. Economist **Dr. José Pagán** of the University of Texas-Pan American, recipient of an FY05 HBCU/MI Partnership Training Award, is establishing a research and training partnership between his institution and the University of Pennsylvania. Through this collaboration, Dr. Pagán is identifying sociodemographic factors that underlie the relative lack of mammography screening among border Latina populations. Identification and correction of

these factors, which may include lack of health literacy skills, knowledge and language, high health system distrust, lack of health insurance coverage, and cultural attitudes about mammography, should increase mammography screening in border-dwelling Latinas, thereby reducing the burden of breast cancer in this population.



Inflammatory breast cancer (IBC) is a relatively rare but highly aggressive form of breast cancer that disproportionately affects younger women and African Americans. To better understand the etiology and biology of IBC, **Dr. Paul H. Levine**, with the support of an FY00 Idea Award, established the IBC Registry and Biospecimen Repository at George Washington University. It is the first national registry of IBC patients and contains standardized clinical, epidemiological, and pathological information, along with recurrence and survival data. Data from the registry and repository have allowed researchers to conduct much-needed studies into the molecular basis

of IBC and also have helped develop better clinical and pathological diagnostic measures for IBC. Several retrospective clinical trials building on the data and samples from this registry are currently being supported by the National Cancer Institute, and although the BCRP-supported work has been completed, the IBC Research Foundation has committed to maintaining and expanding this important resource.

Making a difference



Dr. Andrea Cheville of the Mayo Clinic and recipient of an FY02 Physician-Scientist Training Award has focused her studies on lymphedema, an incurable, debilitating condition that poses a serious quality of life issue after radiation treatment. Dr. Cheville sought to develop a method to determine whether radiation to the lymphatic vessels and nodes essential for arm drainage correlates with increased lymphedema. Fusing SPECT images with CT scans enabled Dr. Cheville to identify the draining lymph nodes in a prospective cohort of breast cancer patients. This fusion technique allowed precise quantification of the lymph nodes' exposure to radiation and paved the way for minimizing incidental, nontherapeutic radiation. This achievement has important implications in radiation treatment and reducing the risk of developing lymphedema.



Clinical trials provide data about the benefits of a particular therapy for a whole population. To achieve the best clinical outcome, however, oncologists must match the right therapeutic regimen with the right patient. **Dr. Kelly Marcom** of Duke University Medical Center, an FY06 Clinical Translational Research Award recipient, is identifying genomic signatures that will predict the sensitivity of individual patients to common chemotherapeutic drugs. Through a prospective clinical trial that incorporates individualized gene expression profiling, Dr. Marcom hopes to distinguish between chemotherapy-sensitive and -resistant early-stage breast cancers and to establish the differential sensitivities of tumors to specific cytotoxic chemotherapies in individual patients.



Dr. Roger Tsien of the University of California, San Diego, recipient of an FY04 Innovator Award, was awarded the 2008 Nobel Prize in Chemistry. Dr. Tsien has pioneered the transformation of green fluorescent protein (GFP) and its spectral variants into the powerful molecular biology tools that are now routinely used by scientists in biomedical research.

Dr. Tsien is developing a technology that uses activatable cell-penetrating peptides (ACPPs) to image and destroy tumor cells specifically. ACPPs are peptides that can import covalently attached payloads into cells. These payloads may consist of both fluorescent markers for cell labeling and chemotherapeutic agents to kill cells. Dr. Tsien is targeting tumor cells specifically by incorporating into ACPPs a linker region that is cleaved by specific extracellular proteases that are concentrated in the tumor microenvironment. This technology will enable preoperative delineation of tumor margins by MRI, more complete tumor removal by fluorescence-guided surgery, and postoperative review by MRI. ACPPs can image primary tumors and lung metastases in transgenic models of breast cancer, as well as in malignant regions in human breast cancer tissue samples. Dr. Tsien is currently maximizing the contrast between tumors and normal tissue, making ACPPs synergistic with other established targeting mechanisms, improving the delivery of chemotherapeutic agents, and advancing this technology into clinical trials. The research supported by Dr. Tsien's Innovator Award may lead to new and powerful treatment regimens that combine diagnosis, imaging, and therapy into a single modality.

Selected Award Outcomes

HERCEPTIN

Dr. Dennis Slamon

Provided the early funding for research leading to the development of monoclonal antibodies against the HER2/neu receptor.

SENTINEL LYMPH NODE BIOPSY

Dr. Lorraine Tafra and Dr. Kathryn Verbanac

Supported a clinical trial testing the validity and accuracy of sentinel lymph node biopsy, the current standard of care for disease staging.

ATLAS TRIAL

Dr. Richard Peto

Supported initiation of the Phase III clinical trial, Adjuvant Tamoxifen Longer Against Shorter, the largest breast cancer treatment trial ever undertaken that is examining the optimal duration of adjuvant tamoxifen in early breast cancer.

DUCTAL LAVAGE

Dr. Susan Love

Supported the development of a minimally invasive diagnostic procedure for detecting precancerous and cancerous breast cells in fluid from the breast ducts.

MARGARET DYSON

FAMILY RISK ASSESSMENT PROGRAM

Dr. Mary Daly

Evolved from BCRP funding for establishment of the Fox Chase Network Breast Cancer Risk Registry, this program serves a large urban area with a range of risk assessment, screening, and preventive services for high-risk patients and families.

CAROLINA MAMMOGRAPHY REGISTRY

Dr. Bonnie Yankaskas

Funded the infrastructure for a population-based mammography registry as a resource for studying community-based screening; now a member site for the NCI Breast Cancer Surveillance Consortium.

3D CELL CULTURE SYSTEM AND ASSAY

Dr. Mina Bissell

Supported the development of a 3D culture system and assay to study breast cancer heterogeneity and the role of the tissue microenvironment in breast cancer development.

shRNA LIBRARIES

Dr. Gregory Hannon and Dr. Stephen Elledge

Supported the development of gene silencing strategies and genetic screening strategies to identify new potential therapeutic targets.

MOLECULAR BREAST IMAGING

Dr. Carrie Hruska

Supported studies showing that molecular breast imaging has comparable sensitivity and specificity to magnetic resonance imaging and may be a more cost-effective alternative for women who have increased risk and dense breast tissue.

DISPARITY IN MINORITY POPULATIONS

Dr. Funmi Olopade

Supported early studies examining how genetic risk factors contribute to the high incidence and mortality from breast cancer in young African American women.

HOMING PEPTIDES

Dr. Erkki Ruoslahti

Funded the identification of homing peptides that specifically home to breast tumors and have the potential to deliver drugs or treatments to tumors with higher efficacy and reduced side effects.

HER2/neu VACCINE

Dr. Constantin Ioannides

Funded the characterization of immunodominant epitopes in breast cancer; led to development of E75 peptide vaccine, which is now entering Phase III clinical trials.



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