

**CDMRP**  
Department of Defense



# Breast Cancer Research Semipostal Program



U.S. Army Medical Research and Materiel Command



# Congressionally Directed Medical Research Programs

## History

The Office of the Congressionally Directed Medical Research Programs (CDMRP) was created in 1992 from a powerful grassroots effort led by the breast cancer advocacy community that resulted in a congressional appropriation of funds for breast cancer research. This initiated a unique partnership among the public, Congress, and the military. Since then, the CDMRP has grown to encompass multiple targeted programs and has received over \$7.5 billion in appropriations from its inception through fiscal year 2013 (FY13). Funds for the CDMRP are added to the Department of Defense (DOD) budget, in which support for individual programs, such as the Breast Cancer Research Program (BCRP), is allocated via specific guidance from Congress.

## Application Review Process

The CDMRP uses a two-tier review process for proposal evaluation, with both tiers involving dynamic interaction among scientists and disease survivors (consumers). The first tier of evaluation is a scientific peer review of applications measured against established criteria for determining scientific merit. The second tier is a programmatic review conducted by the Integration Panel, which is composed of leading scientists, clinicians, and consumers. The Integration Panel compares applications to each other and makes recommendations for funding based on scientific merit, adherence to the intent of the award mechanism, relative impact, portfolio composition, and relevance to program goals.

## Partnerships

Partnerships between consumers and scientists are an integral component of several CDMRP processes. Consumers and scientists participate together on:

- Peer review panels to provide expert advice on the scientific merit and potential impact of the proposed research for breast cancer patients
- The Integration Panel to make programmatic recommendations for the program's vision, investment strategies, and funding selections to reflect the needs of both the consumer and research communities
- Research projects to integrate their expertise in establishing project goals, and designing and implementing research strategies

# Breast Cancer Research Semipostal Program

## About the Program

As a result of the efforts of breast cancer advocates, the Stamp Out Breast Cancer Act (Public Law 105-41) led to the U.S. Postal Service issuing a new first-class stamp, the Breast Cancer Research Semipostal (BCRS) in 1998. The Stamp Out Breast Cancer Act has been extended through 2015. The stamp can be purchased by the public for 55 cents. Net revenues from sales of the BCRS are provided to two designated funding agencies, the DoD BCRP and the National Institutes of Health, to support breast cancer research.



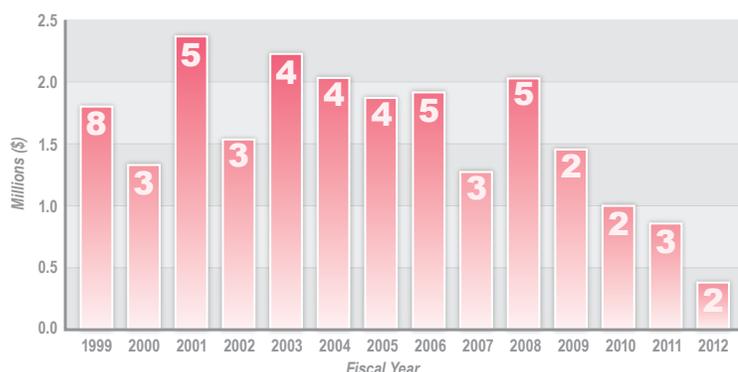
## Research and Management Cost Allocations

Since the BCRS was first issued, the monies received by the BCRP through FY12 have been used to fully or partially fund 53 awards totaling more than \$21 million (**Figures 1A and 1B**). These awards were funded through mechanisms that support highly innovative, high-risk, high-reward research that could lead to critical discoveries in breast cancer. Applications supported with BCRS funds are reviewed according to the two-tier review system.

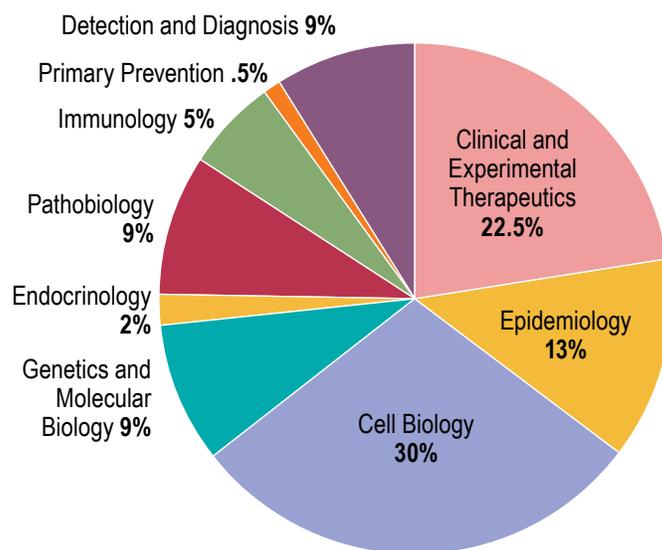
An evaluation of the awards funded through the BCRS Program shows that the projects encompass a diverse range of research areas (**Figure 2**).

Total Proceeds from BCRS	\$22,505,376
Research	\$21,451,770
Management Costs	\$1,053,606

**Figure 1A. BCRS Research and Management Cost Allocation for FY99–FY12**

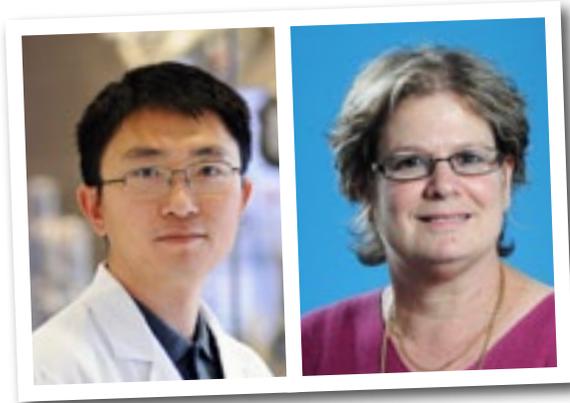


**Figure 1B. BCRS Funding and Number of Awards Made by Fiscal Year**



**Figure 2. BCRS Award Portfolio Composition**

# Research Highlights



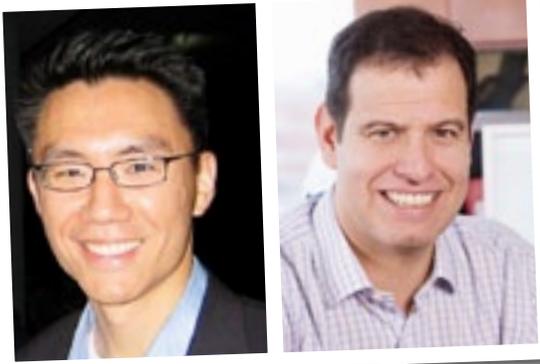
## **Copy Number Signature of Recurrent Gene Fusions Reveals Potential Drug Targets in Invasive Breast Cancer**

**Xiaosong Wang and Rachel Schiff,  
Baylor College of Medicine**

Gene fusions are genetic abnormalities resulting from chromosome translocations in which pieces of two unrelated genes are fused together. Gene fusions have an important role in tumor initiation in many types of cancer and provide specific targets for therapeutic design.

Drs. Wang and Schiff received an Idea Award to identify and investigate new therapeutic targets revealed by a novel bioinformatics analysis called “fusion copy number signature analysis.” Using this integrative bioinformatics strategy, the investigators linked several publically available genomic, molecular, and pharmacologic datasets and nominated Nemo-like kinase (NLK) as a candidate target. They found that NLK promotes endocrine resistance in a subset of breast tumors and may be a new drug target in tumors with deregulation of this pathway by either overexpression or gene fusion. About half of breast cancer patients treated with targeted endocrine therapy will eventually relapse with therapy-resistant disease; therefore, new drugs to overcome endocrine resistance are urgently needed.

Targeted therapies are designed to attack tumors based on the molecular characteristics of the cancerous cells. The long-term goal of Drs. Wang and Schiff is to move their laboratory discoveries to the bedside and, ultimately, contribute to the goal of ending breast cancer. A potent inhibitor of NLK is currently in clinical trials for treating other diseases. If targeting NLK is validated in Dr. Schiff’s breast cancer therapeutic models, then this type of treatment could be tested for its ability to prevent or overcome endocrine resistance. Breast tumor types exhibiting hyperactive NLK signaling could benefit from NLK-targeted adjuvant therapy.



## Regulation of Metastasis and DNA Damage Resistance Pathways by Transposable Elements

**Andy Minn and Roger Greenberg,  
University of Pennsylvania**

Molecular features of breast cancer are paramount to directing and predicting response to therapy. Transposable elements (TEs) are small pieces of DNA that have the ability to move within the genome and are often referred to as “jumping genes.” Although TEs

are normally repressed and silenced, recent sequencing of cancer genomes has revealed aberrant expression of TEs, suggesting that failure to properly silence TEs may be an important property that drives cancer-associated pathways. Drs. Minn and Greenberg are studying how the inappropriate transcription of TEs might influence responsiveness to chemotherapy and radiation, and how this may lead to breast cancer progression. They are exploring how nontraditional genes may be the basis for predicting response to therapeutics.

In the short term, this research may lead to the identification of novel pathways that regulate breast cancer metastasis and response to therapy. In the long term, such pathways may reveal new biomarkers and therapeutic targets that are based on the biology of largely underexplored parts of the human genome.

The partnership between Drs. Minn and Greenberg arose as a result of basic findings from each of their laboratories. The Minn group had been characterizing gene signatures for metastasis and treatment resistance with an emphasis on the signaling events in the cell cytoplasm that can regulate these genes. The Greenberg laboratory had identified novel events that involve silencing of repetitive DNA regions after the DNA damage response. These complementary interests naturally led to a synergistic collaboration exploring novel mechanisms of breast cancer metastasis and response to DNA damaging agents.

Of this research, Drs. Minn and Greenberg have noted, “An important strength of collaborative science is that it brings together seemingly unrelated research interests to explore novel connections. However, exploring these types of ideas is often deemed high-risk, and they prove difficult to get funded. BCRP funding has enabled us to take this higher risk approach with the hope of accelerating breakthroughs.”

# BCRS Program Funded Awards

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY99	Daly	\$283,649	Garvan Institute	Identification of Novel Prognostic Indicators for Breast Cancer Through Analysis of the EMS1/Cortactin Signaling Pathway
	Deuel	\$5,000 <sup>1</sup>	Scripps Institute	Novel Angiogenic Domains: Use in Identifying Unique Transforming and Tumor-Promoting Pathways in Human Breast Cancer
	Heyer	\$111,444	University of California, Davis	In Vitro Recombination Activities of the Breast Cancer Predisposition Protein BRCA2
	Musgrove	\$222,652	Garvan Institute	Role of Cyclin D1 and p27 in Steroidal Control of Cell Cycle Progression in the Mammary Gland in Vivo
	Shah	\$279,000	University of Arkansas	Role of a Novel Matrix-Degrading Metalloproteinase in Breast Cancer Invasion
	Wang	\$317,510	Texas A&M University	Scanning Microwave-Induced Acoustic Tomography
	White	\$334,094	University of Texas Southwest Medical Center	Isolation of Factors That Disrupt Critical Protein/Protein Interactions Within the Telomerase Holoenzyme for Use in Breast Cancer Therapeutics
	Wreschner	\$225,000	Tel Aviv University	Analysis of the Secreted Novel Breast Cancer-Associated MUC1/Zs Cytokine
FY00	Adamson	\$578,183	Burnham Institute	Cripto: A Target for Breast Cancer Treatment
	Akporiaye	\$454,500	University of Arizona	Tumor-Mediated Suppression of Dendritic Cell Vaccines
	Penn	\$296,142	University of Toronto	Exploiting the Novel Repressed Transactivator Assay to Identify Protein Interactors and Peptide Inhibitors of the Myc Oncoprotein
FY01	Cai	\$560,144	Vanderbilt University	Genetic Polymorphisms, Mitochondrial DNA Damage, and Breast Cancer Risk
	Carraway	\$427,225	University of California, Davis	Identification of a Functional Human Homolog of Drosophila Kek1, an Inhibitor of Breast Tumor Cell Growth
	Chaudhary	\$312,000	University of Texas Southwest Medical Center	The Role of Ectodysplasin A (EDA) and Its Receptors in the Pathogenesis of Breast Cancer
	Geahlen	\$425,425	Purdue University	Characterization of Syk in Breast Carcinoma Cells
	Rosner	\$454,181	St. Luke's-Roosevelt Hospital Center	Autocrine and Paracrine Control of Breast Cancer Growth by Sex Hormone-Binding Globulin
FY02	Dou	\$491,999	University of South Florida	Synthetic Beta-Lactam Antibiotics as a Selective Breast Cancer Cell Apoptosis Inducer: Significance in Breast Cancer Prevention and Treatment
	Godwin	\$504,000	Fox Chase Cancer Center	The Nuclear Death Domain Protein p84N5, a Candidate Breast Cancer Susceptibility Gene
	Perkins	\$490,500	Yale University	Rapid Genomic Approach to Cancer Gene Discovery in Breast Cancer
FY03	Chung	\$490,447	Yale University	Quantitative in Situ Assessment of the Somatostatin Receptor in Breast Cancer to Assess Response to Targeted Therapy with 111-in-Pentetreotide
	Kaaks	\$367,639	International Agency for Cancer Research	Fatty Acid Synthesis Gene Variants and Breast Cancer Risk: A Study Within the European Prospective Investigation into Cancer and Nutrition (EPIC)
	Yaswen	\$508,790	Lawrence Berkeley National Laboratory	Functional Analysis of BORIS, a Novel DNA-Binding Protein
	Ziv	\$767,171	University of California, San Francisco	Admixture and Breast Cancer Risk Among Latinas
FY04	Bissell	\$386,569	Lawrence Berkeley National Laboratory	Use of HA-Metal Nanoparticles to Identify and Characterize Tumorigenic Progenitor Cell Subsets in Breast Tumors
	Clarke	\$588,738	Northern California Cancer Center	The Hygiene Hypothesis and Breast Cancer: A Novel Application of an Etiologic Theory for Allergies, Asthma, and Other Immune Disorders
	Giorgio	\$453,000	Vanderbilt University	Surface Functionalized Nanoparticles and Nanocrystals for Proximity-Modulated, Early Neoplasia Detection, Imaging, and Treatment of Breast Cancer
	Lemmon	\$475,500	University of Pennsylvania	Harnessing Novel Secreted Inhibitors of EGF Receptor Signaling for Breast Cancer Treatment

<sup>1</sup> Total award amount was \$404,176; remaining funds were from the FY99 BCRP.

<sup>2</sup> The original Principal Investigator, Dr. Tandra Chaudhuri, is deceased.

<sup>3</sup> Total award amount was \$461,933; remaining funds were from the FY06 BCRP.

<sup>4</sup> Total award amount was \$687,397; remaining funds were from the FY06 BCRP.

<sup>5</sup> Total award amount was \$787,325; remaining funds were from the FY06 and FY07 BCRP.

<sup>6</sup> Total award amount was \$554,987; remaining funds were from the FY08 BCRP.

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY05	Zinn <sup>2</sup>	\$436,500	University of Alabama at Birmingham	Novel Screening and Precise Localization of Early Stage Breast Cancer in Animal Model
	Huang	\$483,600	Cornell University, Weill Medical College	Migrastatin Analogues as Potent Inhibitors of Breast Cancer Metastasis
	Liu	\$448,500	Ohio State University	Hunting for Novel X-Linked Breast Cancer Suppressor Genes in Mouse and Human
	Rao	\$468,000	Stanford University	Ribozyme-Mediated Imaging of Oncogene Expression in Breast Tumor Cells
FY06	Devi	\$155,085 <sup>3</sup>	Duke University Medical Center	Modulation of Regulatory T Cells as a Novel Adjuvant for Breast Cancer Immunotherapy
	Lee	\$489,000	University of Southern California	A New Mechanism for Estrogen-Starvation Resistance in Breast Cancer
	Li	\$438,455	Baylor College of Medicine	The ER/PR Status of the Originating Cell of ER-Negative Breast Cancer
	Mousa	\$377,620	Albany College of Pharmacy	Enhancing the Efficacy of Chemotherapeutic Breast Cancer Treatment with Non-Anticoagulant Heparins
	Rastinejad	\$454,500	University of Virginia	Structural Characterization of the Interdomain Features of the Estrogen Receptor
FY07	Kuperwasser	\$817,500	Tufts University	Mechanisms of Breast Cancer Associated with Obesity
	Kelly	\$244,450 <sup>4</sup>	University of Virginia	Genetically Encoded Targeted, Amplifiable, Imaging Agents for Early Detection of Breast Cancer
	Gerbi	\$155,550 <sup>5</sup>	Brown University	Hormonal Involvement in Breast Cancer Gene Amplification
FY08	Park	\$111,663	North Dakota State University	In Utero Exposure to Dietary Methyl Nutrients and Breast Cancer Risk in Offspring
	Radosz	\$528,939	University of Wyoming	Breast Cancer-Targeted Nuclear Drug Delivery Overcoming Drug Resistance for Breast Cancer Therapy
	Hill	\$577,500	Oregon Health and Science University	Vaccine Vector for Sustained High-Level Antitumor CTL Response
	You	\$503,666	University of Oklahoma Health Science Center	Targeted Delivery and Remote-Controlled Release of Chemotherapeutic Agents
	Seagroves	\$166,667 <sup>6</sup>	University of Tennessee Health Science Center	The Role of HIF-1 Alpha in Breast Cancer: A Positive Factor in Cancer Stem Cell Expansion via Notch?
FY09	Reynolds	\$730,000 <sup>7</sup>	Cancer Prevention Institute of California	Hazardous Air Pollutants and Breast Cancer: An Unexplored Area of Risk
	Wysolmerski	\$620,626	Yale University	Effects of Nuclear Parathyroid Hormone-Related Protein Signaling in Breast Cancer
FY10	Schedin	\$368,125 <sup>8</sup>	University of Colorado, Denver	The Immune Modulatory Program of Post-Partum Involution Promotes Pregnancy-Associated Breast Cancer
	Leung	\$556,875 <sup>9</sup>	Johns Hopkins University	The Role of Poly(ADP-Ribose) in microRNA Activity in Breast Cancers
FY11	Minn	\$399,942	University of Pennsylvania	Regulation of Metastasis and DNA Damage Resistance Pathways by Transposable Elements
	Wang	\$409,693	Baylor College of Medicine	Copy Number Signature of Recurrent Gene Fusions Reveals Potential Drug Targets in Invasive Breast Cancer
	Gonzalow	\$58,975 <sup>10</sup>	St. Louis University	Stabilization of 53BP1 in Triple-Negative and BRCA-Deficient Breast Tumors: A Novel Therapeutic Strategy
FY12	Yang	\$465,000	University of California, San Diego	Regulation of Breast Cancer Stem Cell by Tissue Rigidity
	Giancotti	\$174,837 <sup>11</sup>	Memorial Sloan-Kettering Cancer Center	Autophagy and TGF-Beta Antagonist Signaling in Breast Cancer Dormancy at Premetastatic Sites

<sup>7</sup> Total award amount was \$860,883; remaining funds were from the FY09 BCRP.

<sup>8</sup> Total award amount was \$556,028; remaining funds were from the FY10 BCRP.

<sup>9</sup> Total award amount was \$585,652; remaining funds were from the FY10 BCRP.

<sup>10</sup> Total award amount was \$744,661; remaining funds were from the FY11 BCRP.

<sup>11</sup> Total award amount was \$331,449; remaining funds were from the FY12 BCRP.



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