Appendix C: Breast Cancer Research Stamp

The Breast Cancer Research Stamp and the Involvement of the Department of Defense Breast Cancer Research Program

The Stamp Out Breast Cancer Act (Public Law 105-41) resulted from the work of breast cancer research advocates. This legislation led to the issuance of a new, first-class semipostal stamp, the Breast Cancer Research Semipostal (BCRS), by the U.S. Postal Service. Net revenues from the BCRS are used to support breast cancer research at the National Institutes of Health (NIH) and the Department of Defense (DOD). The DOD Breast Cancer Research Program (BCRP) receives 30 percent of the monies raised from the sale of this stamp. Thus far, the BCRP has received 18 installments totaling $16,387,657.27. Table C-1 provides the research and management cost allocation of the funds received by the DOD.

Table C-1. BCRS Research and Management Cost Allocations

Total Proceeds from BCRS	$16,387,657.27
Research	$15,779,696.11
Management Costs	$607,958.16

Monies received by the DOD from the BCRS through fiscal year (FY06) have been used to fully fund 34 BCRP Idea Award proposals and partially fund 2 additional Idea Awards. In FY07, the stamp funds began supporting Synergistic Idea Awards. In 2007, the BCRS revenues were able to fully fund 1 Synergistic Idea Award and partially fund 2 others. BCRP Idea Awards are intended to encourage innovative approaches to breast cancer research and are a well-recognized backbone of the BCRP's portfolio of awards. As with all BCRP awards, submissions funded through the BCRS are reviewed according to the two-tiered review system originally recommended by the Institute of Medicine. Highlights of research supported by the BCRS follow on the next two pages. Table C-2 provides details on the installments received and the number of awards funded by fiscal year.

Kermit Carraway, Ph.D.
University of California, Davis

Identification of a Functional Human Homolog of *Drosophila* Kek1, an Inhibitor of Breast Tumor Cell Growth

This FY01 Breast Cancer Stamp Idea Award was designed to evaluate the possibility that a cell surface leucine rich repeat (LRR) protein can act as a growth suppressor of cultured breast tumor cells. The LRR protein from the fruit fly (*Drosophila melanogaster*), Kek1, inhibits mammalian ErbB receptor tyrosine kinases and suppresses the growth of human mammary tumor cells. Kek1 has been found to interact with DER (*Drosophila* EGFR) to prevent ligand binding, thus inhibiting receptor activation. Dr. Kermit Carraway's laboratory revealed that the extracellular domain of Kek1 is sufficient to suppress EGFR signaling and breast tumor cell growth. Dr. Carraway's work allowed him to identify human LRR proteins that were candidate functional homologs of Kek1. The first characterization has been termed LRIG1. His observations indicated that LRIG1 expression lowers the levels of ErbB receptors in cells. The conclusion of this study indicated that LRIG1 acts as a negative regulator of ErbB signaling and suppresses the growth properties of tumor cells. This exciting finding may show that LRIG1's extracellular domain could be exploited for therapeutic benefit.

Todd Giorgio, Ph.D.
Vanderbilt University

Surface Functionalized Nanoparticles and Nanocrystals for Proximity-Modulated, Early Neoplasia Detection, Imaging, and Treatment of Breast Cancer

"The development of quick and reliable means of targeting specific types of malignant cells will be an important step to personalized cancer treatment," writes Dr. Todd Giorgio. One of the hallmark characteristics of invasive breast cancer is the cancer cells' ability to break down surrounding tissue through proteolysis. This process is one of the first steps toward metastasis. Using this cancer-specific characteristic, Dr. Giorgio, a recipient of an FY04 Breast Cancer Stamp Idea Award, is making great strides in synthesizing different types of proximity-activated targeting nanoparticles. These specialized nanoparticles are synthesized with a proteolytically sensitive outer coating and are molecularly designed to target breast cancer cells. The proteolytically sensitive coating shields normal cells from the nanoparticle while the breast cancer cells digest the coating, thus revealing an imaging and treatment package. This study suggests that nanoparticles and nanocrystals could be utilized in a future inexpensive method of screening for breast cancer activity, as well as a mechanism to improve breast cancer imaging and treatment delivery.

Christina Clarke, Ph.D.
Northern California Cancer Center

The Hygiene Hypothesis and Breast Cancer: A Novel Application of an Etiologic Theory for Allergies, Asthma, and Other Immune Disorders

Dr. Christina Clarke received an FY04 Breast Cancer Stamp Idea Award. Her concept revolved around the idea that microbial "germ" exposures might be involved in the development of breast cancer. The hygiene hypothesis implies that reduced exposures to microbes, or living in a mostly disease-free, sanitized environment, hinders the development of a healthy immune response. Dr. Clarke hypothesizes that an underdeveloped immune response subsequently could influence breast cancer development. At present, Dr. Clarke and her team are conducting telephone interviews with women ages 50–79 living in Northern California; half of these women have been recently diagnosed with breast cancer while the remaining have not. To date, over 300 participants have answered a series of questions about childhood and adulthood exposures relevant to their microbial exposures. If microbial exposures are determined to be involved in breast cancer development, this work could lead to new prevention efforts to strengthen immune responses that discourage breast cancers from developing.

Andrew Godwin, Ph.D.
Fox Chase Cancer Center

hTREX84, a Candidate Breast Cancer Susceptibility Gene

Dr. Andrew Godwin and his team are focused on breast cancer genetic risks in this FY02 Breast Cancer Stamp Idea Award. Over the course of the study, Dr. Godwin and his team identified the human TREX complex, a group of proteins that work together to accurately process and transport messenger RNAs from the nucleus to the cytoplasm in a cell. A member of this complex, referred to as hTREX84, was found to be a culprit of aggressive human breast cancers. hTREX84 is expressed at very low levels in normal breast epithelial cells but is highly expressed in breast tumors. hTREX84 expression correlates with tumor size and the metastatic state of the tumor progression. Inhibition of hTREX84 levels blocks breast tumor cell growth and causes the cells to die. Thus, hTREX84 may be a prognostic marker for determining the aggressiveness of breast cancer. It may also be an ideal target for therapeutic drugs against breast cancer.

Table C-2. BCRS Installments and Number of Awards Funded by Fiscal Year

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[a]	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	$312,434	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

Table C-2. BCRS Installments and Number of Awards Funded by Fiscal Year (cont.)

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
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
FY05	Chaudhuri	$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[b]	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 Nonanticoagulant Heparins
	Rastinejad	$454,500	University of Virginia	Structural Characterization of the Interdomain Features of the Estrogen Receptor

Table C-2. BCRS Installments and Number of Awards Funded by Fiscal Year (cont.)

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY07 Synergistic Idea Awards	Kuperwasser	$817,500	Tufts University	Mechanisms of Breast Cancer Associated with Obesity
	Kelly	$244,450[c]	Massachusetts General Hospital	Genetically Encoded Targeted, Amplifiable, Imaging Agents for Early Detection of Breast Cancer
	Gerbi	$155,550[d]	Brown University	Hormonal Involvement in Breast Cancer Gene Amplification

[a] Award was only partially funded by Breast Cancer Stamp Funds; total funding amount for the award was $404,176. The DOD BCRP supplied the majority of the funds for the award.
[b] Remaining monies for Devi were from the BCRP FY06 funds for a total amount awarded of $461,933.
[c] Award was partially funded with $244,450 of the BCRS funds, the remaining monies are from the FY06 BCRP funds. Total award amount is $687,397.
[d] Award was partially funded with $155,550 of the BCRS funds, the remaining monies are from FY06 and FY07 BCRP funds. Total award amount is $787,325.