

Women At Risk-Funded Research

Studies WAR has Funded in its History

Research is at the core of Women At Risk's mission. The largest portion of our funding is allocated to studies on breast cancer and high-risk. WAR's research grants are dedicated to better understanding the complex causes of breast cancer and developing new methods for prevention, early intervention, and effective treatment.

WAR provides seed money to pilot studies, many of which often go on to receive support from the National Institutes of Health and other major granting institutions. In the past 17 years, WAR has funded more than 40 research projects in the areas of surgery, oncology, radiology, laboratory, epidemiology, genetics, complementary and alternative medicine. Many of these studies have been presented at national conferences and published in medical journals.

Below is a list of all the studies WAR has funded in its history. If you would like more information, please contact Jennifer Chun, Research and High-Risk Program Director at 212-305-3238, or jec7001@nyp.org.

2007:

PSYCHOSOCIAL APPROACHES TO PARTICIPATION IN BREAST CANCER GENETIC ASSESSMENT PROGRAMS AMONG AFRICAN AMERICAN WOMEN

***Sherri Sheinfeld Gorin, PhD**, Research Associate Professor of Health Education, Department of Health & Behavior Studies, Columbia University*

There are currently no established psychosocial protocols to address the needs of the African American women in familial risk programs. This study is a two-arm randomized clinical trial, assigning African American women who are first degree relatives of those diagnosed with breast cancer at random to either a 1) Culturally-Tailored Cognitive-Affective-Social Network Intervention (CT-CASN); or 2) a General Health Education Group as a control. The proposed intervention (CT-CASN) is culturally tailored to African American women to systematically counsel individuals about the cognitive, affective, and social network barriers they are likely to experience with regard to breast cancer genetic susceptibility programs.

LONG-TERM NEUROTOXICITY IN BREAST CANCER PATIENTS TREATED WITH TAXANE-BASED CHEMOTHERAPY

***Dawn Hershman, MS, MD**, Florence Irving Assistant Professor of Medicine and Epidemiology, Co-Director, Breast Program, Herbert Irving Cancer Center, Columbia University Medical Center*

The purpose of this study is to evaluate the long-term prevalence, severity, and natural history of neuropathy induced by taxanes in breast cancer patients. A greater understanding of factors which may predispose to the development of taxane-induced peripheral neuropathy may lead to interventions to treat and prevent this therapy-related side effect.

PILOT BIOMARKER MODULATION STUDY OF VITAMIN D IN PREMENOPAUSAL WOMEN AT HIGH RISK FOR BREAST CANCER

Katherine D. Crew, MD, MS, Assistant Professor of Medicine and Epidemiology, Columbia University College of Physicians & Surgeons, Division of Oncology, Columbia University Medical Center

Several studies suggest that vitamin D may influence breast cancer development, which has resulted in increased interest in the use of vitamin D for the treatment and prevention of breast cancer. The purpose of this trial is to determine the biological effects of a one-year intervention of vitamin D on biomarkers of breast cancer risk. The results of this pilot study will be used to implement a larger multicenter trial of vitamin D for breast cancer chemoprevention.

HYBRID BREAST IMPLANTS FROM STEM CELLS AND BIOMATERIALS

Eduardo K. Moiola, PhD, Postdoctoral Research Scientist, College of Dental Medicine, Columbia University Medical Center

Current methods for breast implants rely either on artificial materials such as silicone gel filled and saline filled implants or tissue flaps obtained from other parts of the body such as muscle, fat and skin. All these procedures are associated with certain risks and complications. This study proposes to explore current technologies that have been developed to regenerate fat tissue **from stem cells**, which may be used as a natural implant material for reconstruction of the breast, avoiding the common complications associated with artificial breast implants (allergic and foreign body reactions) and tissue flaps (lack of tissue donor site, donor site scarring, and tissue flap death). Stem cells have the potential to revolutionize medical practice, providing skillful doctors and surgeons with better alternatives for effective treatments. The results obtained here will serve as valuable preliminary data for larger scale grant proposals for the further development of stem cell based breast implants and future transition from the research laboratory to bedside treatments.

Research Using Data from the Women At Risk (WAR) High-Risk Registry

BREAST CANCER RISK FACTORS IN YOUNG WOMEN

Ben Pocock, MD, Jennifer Chun, MPH, Kathie-Ann Joseph, MD, MPH, Laura Klein, MD, Mahmoud El-Tamer, MD, Freya Schnabel, MD, Department of Surgery, Columbia University Comprehensive Breast Center, Women At Risk, New York Presbyterian Hospital, Columbia University Medical Center

This study queried the Registry for women ≤ 35 years to determine the significance of established risk factors over time in a population of high-risk younger women. High-risk was defined as having one or more of the following: a strong family history of breast cancer (FHBC), a biopsy-proven history of atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), or lobular carcinoma in situ (LCIS). Descriptive analyses were used to look at these factors over time and to compare women with and without breast cancer. Out of 1412 high-risk women, 199 were identified as ≤ 35 years of age with a median follow-up of 4 years. The median age was 32 years (range 15-35 years). 178 (89%) women had a strong FHBC, 21 (11%) had ADH, 5 (3%) had ALH and 12 (6%) had LCIS. Only 3 (1.5%) developed breast cancer during the study period; all of these 3 cases had a strong FHBC and none had a prior high-risk lesion. Patients who had high-risk lesions but no FHBC did not develop breast cancer during this follow-up period. In conclusion, being ≤ 35 years of age and having a strong family history of breast cancer appeared to be associated with the development of breast cancer, while other well-established histologic risk factors were not. Therefore, ADH, ALH, and LCIS may have different prognostic significance in young women. These findings help us to better understand risk factors in this group of younger women and may aid in the evolution of defining age-appropriate risk management and strategies.

Results of the study were presented at the 24th Annual Miami Breast Cancer Conference in Miami, FL.

THE INTERACTION OF INCREASING AGE AND BREAST CANCER RISK FACTORS

Jennifer Chun, MPH, Ben Pocock, MD, Kathie-Ann Joseph, MD, MPH, Laura Klein, MD, Mahmoud El-Tamer, MD, Freya Schnabel, MD, Department of Surgery, Columbia University Comprehensive Breast Center, Women At Risk, New York Presbyterian Hospital, Columbia University Medical Center

Currently, there is no information on how risk factors predict breast cancer incidence in women who are ≥ 70 years of age. This study explored the impact of known risk factors on high-risk women 70 years of age or older. Out of 1412 women in the WAR Registry, 82 women were ≥ 70 years of age (range 70-91). Twenty had a history of ADH (24%), 5 had ALH (6%), 27 had LCIS (33%), and 52 women had FHBC (63%). With a mean follow-up of 4 years, 6 of these women developed breast cancer (7.3%). The mean Gail score for the ≥ 70 age group was 4.3, as compared to 4.7 in the subset with cancer. Of the 6 breast cancer cases, two patients presented with DCIS. The remaining four were stage I at diagnosis. All tumors were low-grade with positive estrogen receptors. The Fisher's exact tests demonstrated that ADH ($p=0.15$), ALH ($p=1.0$), LCIS ($p=0.66$), and FHBC ($p=0.62$) were not statistically significant predictors of breast cancer within this age group of high-risk women. Preliminary data on high-risk women who are ≥ 70 years indicate that having a history of ADH, ALH, LCIS and FHBC were not strong predictors of breast cancer in this population. These findings contribute to a better understanding of the interaction of established risk factors and age. This study also emphasizes the importance of defining age-appropriate recommendations for breast cancer risk management, including surveillance and chemoprevention, for women who are 70 years of age or older. Results of the study were presented at the 31st Annual Symposium of the American Society of Breast Disease in San Francisco, CA.

2006:

IDENTIFICATION OF GENETIC MODIFIERS OF *BRCA1* OR *BRCA2* IN ASHKENAZI MUTATION CARRIERS

Wendy K. Chung, MD, PhD, Herbert Irving Assistant Professor of Pediatrics in Medicine, Columbia University College of Physicians & Surgeons, Director of Clinical Genetics and Clinical Oncogenetics, Division of Molecular Genetics, Columbia University Medical Center

Three common founder mutations in *BRCA1* (185delAG, 5382insC) and *BRCA2* (6174delT) account for over 98% of mutations in *BRCA1* and *BRCA2* in the Ashkenazi population. There are likely genetic variations that modify the risk of cancer in *BRCA1* and *BRCA2* carriers. The purpose of this study is to determine whether these genetic variants (*CHEK2*, *MSH2*, *P53*, *RAD51*, *MTHFR*, and *APC*) are associated with developing breast cancer. This study may improve our ability to stratify cancer risk for *BRCA1* and *BRCA2* mutation carriers and individualize plans for prevention and treatment of breast cancer.

THE ROLE OF NOTCH IN THE PHENOTYPIC SWITCH FROM DUCTAL CARCINOMA IN SITU (DCIS) TO INVASIVE CARCINOMA OF THE BREAST

Nikki M. Feirt, MD, Assistant Professor of Clinical Pathology, Columbia University College of Physicians & Surgeons

Research has shown that the Notch gene plays an important role in cell survival, cellular proliferation, and differentiation. The purpose of this study is to determine whether Notch plays a direct role in regulating the switch from in situ to invasive carcinoma. The findings of this study will increase our knowledge of tumor progression, invasive and subsequent metastatic disease, and may define new targets for cancer therapeutics.

QUANTITATIVE ASSESSMENT OF TISSUE TOXICITY IN ULTRASONIC TISSUE CHARACTERIZATION IMAGING

Tian Liu, PhD, Assistant Professor of Medical Physics, Department of Radiation Oncology, Columbia University College of Physicians & Surgeons

For women with early stage breast cancer, breast-conservation surgery in combination with radiation therapy is an effective treatment. However, there is currently no objective means of measuring breast tissue injury or toxicity of radiation therapy in a clinical setting. This proposed study is the first

application of a novel, non-invasive and quantitative ultrasound-based technique to examine acute and late radiation toxicity in the breast. Recent studies suggest that African-American patients have a higher likelihood of developing radiation toxicity in comparison to Caucasian patients. In this pilot study, we will also investigate the relationship between toxicity and race.

EFFECTS OF PHYSICAL ACTIVITY AND DIETARY CHANGE IN MINORITY BREAST CANCER SURVIVORS

Heather Greenlee, ND, MPH, Postdoctoral Research Scientist, Department of Epidemiology, Columbia University Mailman School of Public Health

Hispanic and African-American breast cancer survivors are more likely to be obese and sedentary compared to non-Hispanic white women, yet there are few studies on obesity, exercise, dietary change, and cancer risk among these high-risk ethnic groups. This pilot study proposes to examine the effects of an exercise and dietary change program (at neighborhood Curves locations) on weight reduction and biological markers associated with breast cancer risk in breast cancer survivors from an ethnic minority urban population.

TELOMERE SHORTENING, OXIDATIVE DAMAGE AND BREAST CANCER RISK

Jing Shen, PhD, Associate Research Scientist, Department of Environmental Health Sciences, Columbia University Mailman School of Public Health

Telomeres are specialized DNA-protein structures that consist of a large number of repeat sequences at the ends of chromosomes. Telomere shortening can lead to genomic instability that in turn drives the tumor formation process in pre-malignant breast lesions and normal breast tissues. The goal of this study is to look at the potential modifying effects of oxidative damage and antioxidant capacity on telomere shortening and breast cancer risk. The findings of this study can have important implications for improved preventive, diagnostic and treatment strategies for breast cancer.

VISUALIZING THE INFLUENCE OF BRCA2 ON THE ASSEMBLY OF RAD51 NUCLEOPROTEIN FILAMENTS DURING DNA REPAIR

Eric C. Greene, PhD, Assistant Professor of Biochemistry & Molecular Biophysics, Columbia University College of Physicians & Surgeons

This research study will focus on understanding the molecular nature of DNA repair mechanisms that are involved in critical cellular processes including the behavior of BRCA2 and Rad51 as they interact with individual DNA molecules. The investigators of this study will employ a novel approach with fluorescence, using an ultra-sensitive optical microscope that can potentially monitor the progress of a single DNA repair reaction in vitro with sub-second temporal resolution. The findings of this research will contribute to our knowledge of aberrant DNA repair systems, molecules of DNA, and determine whether BRCA2 can directly assemble to correct sites on the individual DNA molecules.

2005:

THE ROLE OF HINT1 AS A NOVEL TUMOR SUPPRESSOR IN HUMAN BREAST CANCER

Bernard Weinstein, MD, Frode Jensen Professor of Medicine, Professor of Genetics and Development, Professor of Public Health, Director Emeritus, Herbert Irving Comprehensive Cancer Center, Columbia University Medical Center

Dr. Weinstein recently discovered a new gene called *Hint1* and found that mice that are deficient in expression of this gene are highly susceptible to developing both breast and ovarian cancer. The goal of this project is to determine if loss of this gene may also play a role in the causation of breast cancer. This study can lead to new strategies for breast cancer prevention and therapy.

BIOLOGICAL MARKERS IN AFRICAN-AMERICAN WOMEN WITH DCIS

Kathie-Ann Joseph, MD, Assistant Professor of Surgery, Columbia University College of Physicians & Surgeons

The purpose of this study is to determine whether there is a difference in hormone receptor status between African American and Caucasian women diagnosed with ductal carcinoma in situ (DCIS) and whether this difference has an impact on recurrence rates and survival. In addition, by developing a tumor bank, other biological markers that would be predictive of recurrence and survival can also be examined.

PILOT STUDY ON THE EFFECT OF ACUPUNCTURE ON JOINT PAIN INDUCED BY AROMATASE INHIBITORS IN BREAST CANCER PATIENTS

Dawn Hershman, MS, MD, Assistant Professor of Medicine and Epidemiology, Columbia University College of Physicians & Surgeons, Director of the Clinical Breast Oncology Program, Columbia University Medical Center

Musculoskeletal pain can occur in up to 50% of women treated with aromatase inhibitors. The purpose of this study is to evaluate the efficacy of acupuncture in reducing pain, the need for pain medication requirements, and improving quality of life in breast cancer survivors.

EFFECTS OF PHYSICAL ACTIVITY AND DIETARY CHANGE IN MINORITY BREAST CANCER SURVIVORS

Heather Greenlee, ND, MPH, Postdoctoral Research Fellow, Department of Epidemiology, Columbia University Mailman School of Public Health

This study will investigate whether young African American women have increased levels of estrogen metabolites which may increase their risk of developing breast cancer at an earlier age compared to Caucasian women.

DOES BRCA2 ORCHESTRATE ASSEMBLY OF DNA REPAIR PROTEINS?

Eric C. Greene, PhD, Assistant Professor of Biochemistry & Molecular Biophysics, Columbia University College of Physicians & Surgeons

Defects in the human DNA repair proteins BRCA2 and Rad51 lead to the onset of breast cancer. This study will attempt to monitor and understand how these two proteins interact with one another during the repairing of damaged DNA.

DNA DAMAGE RESPONSE IN BREAST CANCER

Rodney Rothstein, PhD, Professor of Genetics & Development, Columbia University College of Physicians & Surgeons

A key underlying cause of breast cancer can be found in failure to repair DNA. The purpose of this study is to screen for alterations in several DNA repair genes and to test whether variations in the function of these genes are important in triggering breast cancer.

DEVELOPMENT OF AN ASSAY FOR OXIDATIVE DNA DAMAGE REPAIR

Regina M. Santella, PhD, Professor of Public Health, Director NIEHS Center for Environmental Health in Northern Manhattan, Department of Environmental Health Sciences, Columbia University Mailman School of Public Health

A previous study funded by WAR demonstrated that poor repair of bulky DNA damage resulting from exposure to environmental chemicals is a risk factor for breast cancer. The study aims to set up a new assay for measuring the capacity of blood cells from women with and without breast cancer to repair another type of DNA damage resulting from oxidative stress.

1998-2004

DUCTAL LAVAGE AND HORMONE REPLACEMENT THERAPY

Beth Ann Ditkoff, MD, Assistant Professor of Surgery, Columbia University College of Physicians & Surgeons

NOVEL THERAPEUTIC APPROACH TO DCIS II

Robert L. Fine, MD, Director of the Experimental Therapeutics Program, Irving Associate Professor of Medicine

NOTCH AND ANGIOGENIC FACTOR INTERACTION IN BREAST CANCER

Nikki M. Feirt, MD, Assistant Professor of Clinical Pathology, Columbia University College of Physicians & Surgeons

CYSTOSARCOMA PHYLLODES, ANALYSIS BY COMPARATIVE GENOMIC HYBRIDIZATION, EXPRESSION MICROARRAY AND IMMUNOHISTOCHEMISTRY; CORRELATION WITH HISTOPATHOLOGICAL GRADING AND CLINICAL OUTCOME

Hanina Hibshoosh, MD, Associate Professor of Clinical Pathology, Columbia University College of Physicians & Surgeons

SCREENING OF A NOVEL CHEMO-ATTRACTANT SECRETED BY BREAST CANCER CELLS TOWARD THE NOVEL THERAPEUTIC INTERVENTION TO INHIBIT METASTASIS OF BREAST CANCER TO BONE

Hahn-Jun Lee, PhD, Assistant Professor of Orthopaedic Surgery, Center for Orthopaedic Research, Department of Orthopaedic Surgery, Columbia University College of Physicians & Surgeons

Francis Y. Lee, MD, Assistant Professor of Orthopaedic Surgery, Director of Center for Orthopaedic Research, Department of Orthopaedic Surgery, Department of Orthopaedic Surgery, Columbia University College of Physicians & Surgeons

BREAST CANCER SURVIVAL IN RELATION TO BRCA1 AND BRCA2 GENE STATUS

Donna Russo, MS, Coordinator, Cancer Genetics Program; **Mahmoud El-Tamer, MD**, Assistant Professor of Surgery, Columbia University College of Physicians & Surgeons

PILOT STUDY OF DNA DAMAGE IN WOMEN AT RISK FOR BREAST CANCER

LaVerne Mooney, DrPH, Assistant Clinical Professor of Public Health, Columbia University

Mailman School of Public Health; **Elizabeth Hovey, MD**, Medical Oncologist, Columbia University College of Physicians & Surgeons

A NOVEL VACCINE OR IMMUNOTHERAPY FOR PATIENTS WITH METASTATIC AND HIGH-RISK BREAST CANCER

Charles S. Hesdorffer, MD, Director of the Bone Marrow and Stem Cell Transplant Program and the DiBella Cellular Immunotherapy Laboratory, Associate Professor of Clinical Medicine, Columbia University College of Physicians & Surgeons

NOVEL APPLICATION OF SODIUM MAGNETIC RESONANCE IMAGING TO BREAST CANCER DIAGNOSIS AND TREATMENT

Richard P. Kline, PhD, Research Scientist, Columbia University

CLINICAL SIGNIFICANCE OF MICRO-METASTASIS DETECTED BY IMMUNO-HISTOCHEMISTRY IN DCIS PATIENTS

Mahmoud El-Tamer, MD, Assistant Professor of Surgery, Columbia University College of Physicians & Surgeons

CYSTOSARCOMA PHYLLODES , GENOMIC ANALYSIS WITH CLINICAL CORRELATION

Hanina Hibshoosh, MD, Associate Professor of Clinical Pathology, Columbia University
College of Physicians & Surgeons

DIET, DNA DAMAGE, AND GENETIC SUSCEPTIBILITY IN WOMEN WITH LOBULAR NEOPLASIA OR
A FAMILY HISTORY OF BREAST CANCER

LaVerne Mooney, DrPH, Assistant Clinical Professor of Public Health, Columbia University
Mailman School of Public Health; **Deliang Tang, DrPH**, Assistant Clinical Professor of Public Health,
Columbia University Mailman School of Public Health

DEVELOPMENT OF METHODS TO USE AFFYMETRIX CHIPS FOR ANALYSIS OF P53 MUTATIONS IN
DNA FROM PARAFFIN SECTIONS OF BREAST TISSUE

Regina M. Santella, PhD, Professor of Public Health, Columbia University Mailman School of Public Health

PREVENTIVE BEHAVIOR AND CHOICES IN A GENETIC COUNSELING COHORT

Victor R. Grann, MD, MPH, Associate Professor of Medicine and Public Health,
Director of Health Outcomes Research at the Herbert Irving Comprehensive Cancer Center, Columbia University; **Judith S.
Jacobson, DrPH**, Assistant Professor of Public Health in Division of Epidemiology,
Columbia University Mailman School of Public Health; **Andrea Troxel, ScD**, Assistant Professor of Public Health,
Department of Biostatistics, Columbia University Mailman School of Public Health

PILOT STUDY ON USING DUCTAL LAVAGE TECHNIQUE IN WOMEN
WITH LOBULAR NEOPLASIA

Beth Ann Ditkoff, MD, Assistant Professor of Surgery, Columbia University College of Physicians & Surgeons

MOLECULAR REGULATION OF METASTATIC BREAST CANCER TO BONE:
DEVELOPMENT OF NOVEL THERAPEUTIC STRATEGY

Francis Y. Lee, MD, Assistant Professor of Orthopaedic Surgery, Orthopaedic Oncology, Department of
Orthopaedic Surgery, Columbia University College of Physicians & Surgeons

BIOMARKERS OF OXIDATIVE DAMAGE IN BREAST CANCER

Regina M. Santella, PhD, Professor of Public Health, Columbia University Mailman School of Public Health

PHYSICAL ACTIVITY LEVELS AS A PREDICTOR OF BLOOD GLUTATHIONE LEVELS AMONG
WOMEN AT HIGH RISK OF BREAST CANCER

Andrew Rundle, DrPH, Assistant Professor of Clinical Epidemiology, Columbia University Mailman School of
Public Health

INFORMED CONSENT FOR WOMEN AT RISK OF BREAST CANCER: EXPLORING NEW MODELS

Barron H. Lerner, MD, PhD, Angelica Berrie-Gold Foundation Associate Professor of Medicine and Public
Health, Columbia University

GROWTH INHIBITORY ACTIVITY OF EXTRACTS OF BLACK COHOSH ON
HUMAN BREAST CANCER CELLS

Linda Einbond, PhD, *Herbert Irving Comprehensive Cancer Center, Center for Complementary and Alternative Medicine Research in Aging and Women's Health, Columbia University Medical Center;*

Bernard Weinstein, MD, *Frode Jensen Professor of Medicine and Professor of Genetics and Development, and Public Health Director Emeritus, Columbia University Medical Center;*

Fredi Kronenberg, PhD, *Associate Professor of Clinical Physiology, Columbia University College of Physicians and Surgeons;* **Edward Kennelly, PhD**, *Assistant Professor of Biological Sciences, Lehman College*

NOVEL THERAPEUTIC APPROACH TO DCIS I

Robert L. Fine, MD, *Director of the Experimental Therapeutics Program, Irving Associate Professor of Medicine*

ULTRASOUND SCREENING OF HIGH-RISK WOMEN FOR BREAST CANCER

Cecilia L. Mercado, MD, *Assistant Professor of Surgery, Columbia University College of Physicians & Surgeons;* **Shara Millman, MD**, *Assistant Professor of Surgery, Columbia University College of Physicians & Surgeons*

BLOCKADE OF RECEPTOR FOR AGE (RAGE): A NEW STRATEGY FOR THE TREATMENT OF
BREAST CANCER

Kathie-Ann Joseph, MD, *Clinical Fellow of Surgery, Columbia University College of Physicians & Surgeons;* **Ann Marie Schmidt, MD**, *Assistant Professor of Surgery, Columbia University College of Physicians & Surgeons*

BRCA FOUNDER MUTATIONS AMONG JEWISH PARTICIPANTS OF THE LONG ISLAND BREAST CANCER
STUDY PROJECT

Ruby T. Senie, PhD, *Professor of Public Health in the Division of Epidemiology, Columbia University Mailman School of Public Health;* **Wendy Chung, MD, PhD**, *Assistant Professor of Pediatrics and Medicine, Columbia University College of Physicians & Surgeons*

TISSUE ENGINEERED BREAST RECONSTRUCTION USING FAT-DERIVED
STEM CELLS AND GENE THERAPY

Arnold S. Breitbart, MD, *Assistant Professor of Clinical Surgery, Division of Plastic Surgery, Department of Surgery, Columbia University College of Physicians & Surgeons*

FUNCTIONAL SIGNIFICANCE OF AKT SUBSTRATES FOR PREDICTING CLINICAL OUTCOME

Thomas F. Franke, MD, PhD, *Assistant Professor of Pharmacology, Department of Pharmacology, College of Physicians & Surgeons, Columbia University*

To find out more about this study and other research projects that WAR has funded from 1996 to the present, please contact WAR's Research and High-Risk Program Director, Jennifer Chun, at 212-305-3238 or jec7001@nyp.org