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PRINCIPAL INVESTIGATOR: Susan M. Domchek, M.D.

CONTRACTING ORGANIZATION: University of Pennsylvania
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14. ABSTRACT

Background: Molecular targets to facilitate early detection and preventative therapy for women at high risk for breast cancer have not been characterized. Two recently characterized intracellular enzymes -- human telomerase reverse transcriptase (hTERT) and the cytochrome P450 isoform 1B1 (CYP1B1), each overexpressed in >90% of invasive breast cancers but rarely found in normal tissue -- may fill this gap. Such targets, if found at the earliest time of malignant transformation, may be ideally suited not only for early detection but also cancer prevention by vaccination. A growing clinical experience in advanced cancer patients has underscored the safety and feasibility of vaccination strategies. The universal expression of hTERT and CYP1B1 provide an opportunity for both early detection and cancer vaccination. Objective/Hypothesis: We hypothesize that immunologic responses can be elicited in advanced breast cancer patients using vaccines incorporating hTERT, providing a safety and feasibility platform for ultimately vaccinating women at high risk for breast cancer. Although we have not found ductal lavage a feasible strategy for the detection of tumor antigens, we have made significant progress on vaccination strategies in women with metastatic breast cancer.

15. SUBJECT TERMS
Ductal lavage, breast cancer detection, immunotherapy

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Progress Report
Department of Defense Physician-Scientist Award
Universal Breast Cancer Antigens as Targets Linking Early Detection and Therapeutic Vaccination

Susan M. Domchek, MD
Septebmer 17, 2007

SPECIFIC AIMS OF THE PROJECT

1. Evaluation of molecular markers in ductal lavage fluid from BRCA1 and BRCA2 mutation carriers

2. Determine the safety and feasibility of vaccinating advanced breast cancer patients with hTERT peptide, assessing the generation of hTERT-specific immunity. Explore the role of intravenous cyclophosphamide prior to hTERT vaccination in boosting vaccine response by depleting regulatory T cells.

A. INTRODUCTION

This grant supports studies to understand the potential of universal tumor antigens for cancer immunotherapy, with a particular focus on the characterization of the human telomerase reverse transcriptase (hTERT) as tumor antigen. Telomerase is expressed by >90% of all human breast cancers but absent in most normal cells. Telomerase function has been directly linked to oncogenesis and its inhibition in telomerase-positive human tumors leads to growth arrest.

Dr. Domchek completed the three years of salary support on the DOD grant in 2006. Her ongoing obligations to the Department of Defense at this point are her five years of commitment to clinical breast cancer research. She has fulfilled these obligations. Dr. Domchek has published, or has in press, more than 43 publications since September of 2006. These publications involve work in BRCA1 and BRCA2 mutation carriers and also involve ongoing study of vaccination strategies in women with metastatic breast cancer. Funding has been obtained to continue Dr. Domchek's work beyond the end of the Department of Defense grant. Dr. Domchek is funded by the Cancer Genetics Network of the National Cancer Institute, she is an investigator on RO1 grants held by Dr. Timothy Rebbeck and Dr. Robert Vonderheide at the University of Pennsylvania, and is also a co-Investigator on an Avon Progress for Patients and a Department of Defense grants with Dr. Chanita Hughes Halbert also of the University of Pennsylvania. In addition to all of this, and because of her acknowledged expertise in the field of clinical trials and clinical cancer genetics, Dr. Domchek has been promoted to Associate Professor at the University of Pennsylvania.

B. BODY

Aim 1: Evaluation of molecular markers in ductal lavage fluid from BRCA1 and BRCA2 mutation carriers

The last year has been spent studying genetic polymorphisms in BRCA1 and BRCA2 mutation carriers as a marker of cancer risk. One such study was published in Cancer Epidemiology Biomarkers and Prevention and examined AURKA F31I polymorphism and breast cancer risk in BRCA1 and BRCA2 mutation carriers. The AURKA oncogene is associated with abnormal chromosome segregation and aneuploidy and predisposition to cancer. Amplification of AURKA has been detected at higher frequency in tumors from BRCA1 and BRCA2 mutation carriers than in sporadic breast tumors, suggesting that overexpression of AURKA and inactivation of BRCA1 and BRCA2 cooperate during tumor development and progression. The F31I polymorphism in AURKA has been associated with breast cancer risk in the homozygous state in prior studies. We evaluated whether the AURKA F31I polymorphism modifies breast cancer risk in BRCA1 and BRCA2 mutation carriers from the Consortium of Investigators of Modifiers of BRCA1/2. Consortium of Investigators of Modifiers of BRCA1/2 was established to provide sufficient statistical power through increased numbers of mutation carriers to identify polymorphisms that act as modifiers of cancer risk and can refine breast cancer risk estimates in BRCA1 and BRCA2 mutation carriers. A total of 4,935 BRCA1 and 2,241 BRCA2 mutation carriers and 11 individuals carrying both BRCA1 and BRCA2 mutations was genotyped for F31I. Overall, homozygosity for the 31I allele was not significantly associated with breast cancer risk in BRCA1 and BRCA2 carriers combined [hazard ratio (HR), 0.91; 95% confidence interval (95% CI), 0.77-1.06]. Similarly, no significant association was seen in BRCA1 (HR, 0.90; 95% CI, 0.75-1.08) or BRCA2 carriers (HR, 0.93; 95% CI, 0.67-1.29) or when assessing the modifying effects of either bilateral prophylactic oophorectomy or menopausal status of BRCA1 and BRCA2 carriers. In summary, the F31I polymorphism in AURKA is not associated with a modified risk of breast cancer in BRCA1 and BRCA2 carriers.

Aim 2: Determine the safety and feasibility of vaccinating advanced breast cancer patients with hTERT peptide, assessing the generation of hTERT-specific immunity. Explore the role of intravenous cyclophosphamide prior to hTERT vaccination in boosting vaccine response by depleting regulatory T cells.

Our second clinical trial involving telomerase, utilizing the hTERT I540 peptide was published in Cancer Research with data on 19 patients. Further corollary work examining cell lines of hTERT specific lymphocytes was published in Cancer Biology and Therapy, and could have major implication on how researchers very cell lines vs. clones in this type of work..

We have also completed a study examining the utility of using cyclophosphamide prior to vaccination in women with metastatic breast cancer. Data from this study is undergoing analysis, but initial analysis did not reveal a significant effect of this intervention. Finally, we have recently obtained IRB approval (UPCC 08107) for a clinical trial examining daclizumab prior to vaccination with hTERT (both I540 and heteroclytic peptides) as well as survivin peptides. Funding has been sought and obtained from the Breast Cancer Research Foundation to explore telomerase vaccination in women with high risk breast cancer undergoing adjuvant therapy.

We remain enthusiastic about the prospect of using telomerase vaccination in cancer therapy. We are working to enhance the immunogenicity of our vaccine, while at the same time

exploring the utility of vaccination women who do not have metastatic disease. It is these women in whom a vaccine might have its greatest effect. Finally, vaccination in the adjuvant setting is another step toward the ultimate goal of vaccinating patients who are at high risk for, but who have not had, cancer.

KEY RESEARCH ACCOMPLISHMENTS

1. Promotion of Dr. Domchek to Associate Professor of Medicine at the University of Pennsylvania
2. Dr. Domchek was awarded the Alavi Award for Excellence in Clinical Cancer Research at the University of Pennsylvania
3. In the past year, 26 publications related to breast cancer research.

REPORTABLE OUTCOMES:

A. Publications During This Funding Period (9/2006-9/2007)

1. Brewster K, Wileyto EP, Kessler L, Collier A, Weathers B, Stopfer JE, Domchek S, Halbert CH: Sociocultural predictors of breast cancer risk perceptions in African American breast cancer survivors. Cancer Epidemiol Biomarkers Prev 16(2): 244-48, 2007.

2. Tchou J, Ward MR, Volpe P, Palma MD, Medina CA, Sargen M, Sonnad SS, Gowdin AK, Daly M, Winchester DJ, Garber J, Weber BL, Domchek S, Nathanson KL: Large genomic rearrangements in BRCA1 and BRCA2 and clinical characteristics of men with breast cancer in the United States. Clin Breast Cancer 7(8): 627-33, 2007.

3. Kotsopoulos J, Lubinski J, Lynch HT, Klijn J, Ghadirian P, Neuhausen SL, Kim-Sing C, Foulkers WD, Moller P, Isaacs C, Domchek S, Randall S, Offit K, Tung N, Ainsworth P, Gershoni-Baruch R, Eisen A, Daly M, Karlan B, Saal HM, Couch F, Pasini B, Wagner T, Friedman E, Rennert G, Eng C, Weitzel J, Sun P, Narod SA: Age at first birth and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers Breast Cancer Res Treat 2007.

4. Kotsopoulos J, Ghadirian P, El-Sohemy A, Lynch HT, Snyder C, Daly M, Domchek S, Randall S, Karlan B, Zhang, P, Zhang S, Sun P, Narod SA: The CYP1A2 genotype modifies the association between coffee consumption and breast cancer risk among BRCA1 mutation carriers. Cancer Epidemiol Biomarkers Prev Vol. 16: 912-6, 2007.

5. Friebel TM, Domchek SM, Neuhausen SL, Wagner T, Evans DG, Isaacs C, Garber JE, Daly MB, Eeles R, Matloff E, Tomlinson G, Lynch HT, Tung N, Blum JL, Weitzel J, Rubinstein WS, Ganz PA, Couch F, Rebbeck TR: Utilization of Bilateral Prophylactic Oophorectomy and Bilateral Prophylactic Mastectomy in a Prospective Cohort of Unaffected BRCA1 and BRCA2 Mutation Carriers. Clnical Breast Cancer Vol. 7: 875-882, 2007.

6. Domchek SM, Recio A, Mick R, Clark CE, Carpenter EL, Fox KR, DeMichele A, Schuchter LM, Leibowitz MS, Wexler MH, Vance BA, Beatty GL, Veloso E, Feldman MD, Vonderheide RH: Telomerase-Specific T-Cell Immunity in Breast Cancer: Effect of Vaccination on Tumor Immunosurveillance. Cancer Res Vol. 67: 10546-10555., 2007.

7. Tai YC, Domchek S , Parmigiani G, Chen S: Breast cancer risk among male BRCA1 and BRCA2 mutation carriers. Journal of the National Cancer Institute Vol. 99: 1811-1814, 2007.

8. Chen D, Leibowitz ML, Recio A, Domchek SM, Vonderheide RH: Differential lysis of tumors by polyclonal T cell lines and T cell clones specific for hTERT. Cancer Biology & Therapy, 2007.

9. Antoniou AC, Sinilnikova OM, … Domchek SM, Nathanson KL, . Couch FJ, Easton DE, Chenevix-Trench G, RAD51 135G-->C modifies breast cancer risk among BRCA2 mutation carriers: results from a combined analysis of 19 studies, Am J Hum Genet Vol. 81: 1186-1200, 2007.

10. Antoniou AC, Spurdle AB, Sinilnikova OM, ... Domchek SM, … Stoppa-Lyonnet D, Chenevix-Trench G, Easton DF, Common breast cancer-predisposition alleles are associated with breast cancer risk in BRCA1 and BRCA2 mutation carriers, Am J Hum Genet Vol. 82: 937-948, 2008.

11. Finlay E, Stopfer J, Burlingame E, Raginwal L, Goldfeder K, Davidson R, Nathanson K, Rebbeck T, Weber B, Domchek SM: Factors Determining Dissemination of Results and Uptake of Genetic Testing in Families with Known BRCA1/2 Mutations. Genetic Testing Vol. 12: 81-91, 2008.

12. Kauff ND, Domchek SM, Friebel TM, Robson ME, Lee J, Garber JE, Isaacs C, Evans DG, Lynch H, Eeles R, Neuhausen SL, Daly MB, Matloff E, Blum J, Sabbatini P, Barakat RR, Hudis C, Norton L, Offit K, Rebbeck TR: Risk-Reducing Salpingo-Oophorectomy for the Prevention of BRCA1 and BRCA2 Associated Breast and Gynecologic Cancer: A Multi-Center, Prospective Study. Journal of Clinical Oncology Vol. 26:1331-1337., 2008.

13. Halbert CH, Love D, Mayes T, Collier A, Weathers B, Kessler L, Stopfer J, Bowen D, Domchek SM, Retention of African American women in cancer genetics research, Am J Med Genet Vol, A 146: 166-173, 2008.

14. Kessler L, Domchek S, Stopfer J, Halbert CH, BRCA1 and BRCA2 risk perceptions among African American women at increased risk for hereditary breast-ovarian cancer, Community Genet Vol.11: 193-200, 2008.

15. Metcalfe KA, Lubinski J, Ghadirian P, Lynch H, Kim-Sing C, Friedman E, Foulkes WD, Domchek S, Ainsworth P, Isaacs C, Tung N, Gronwald J, Cummings S, Wagner T, Manoukian S, Moller P, Weitzel J, Sun P, Narod SA, Predictors of contralateral prophylactic mastectomy in women with a BRCA1 or BRCA2 mutation: the Hereditary Breast Cancer Clinical Study Group, J Clin Oncol Vol. 26: 1093-1097, 2008.

16. Spurdle AB, Deans AJ, Duffy D, Goldgar DE, Chen X, Beesley J; kConFaB, Easton DF, Antoniou AC, Peock S, Cook M; EMBRACE Study Collaborators, Nathanson KL, Domchek SM, Macarthur GA, Chenevix-Trench G. No evidence that CDKN1B (p27) polymorphisms modify breast cancer risk in BRCA1 and BRCA2 mutation carriers. Breast Cancer Res Treat epub ahead of print, June 2008.

17. Narod SA, Neuhausen S, Vichodez G, Armel S, Lynch HT, Ghadirian P, Cummings S, Olopade O, Stoppa-Lyonnet D, Couch F, Wagner T, Warner E, Foulkes WD, Saal H, Weitzel J, Tulman A, Poll A, Nam R, Sun P; Hereditary Breast Cancer Study Group, Danquah J, Domchek S, Tung N, Ainsworth P, Horsman D, Kim-Sing C, Maugard C, Eisen A, Daly M, McKinnon W, Wood M, Isaacs C, Gilchrist D, Karlan B, Nedelcu R, Meschino W, Garber J, Pasini B, Manoukian S, Bellati C. Rapid progression of prostate cancer in men with a BRCA2 mutation, Br J Cancer Vol 99: 371-4, 2008

18. Gabriel CA, Tigges-Cardwell J, Stopfer J, Erlichman J, K. Nathanson K, Domchek SM; Use of total abdominal hysterectomy and hormone replacement therapy in BRCA1 and BRCA2 mutation carriers undergoing risk-reducing salpingo-oophorectomy, *in press* Familial Cancer, 2008

19. Schwartz GF, Hughes KS, Lynch HT, Fabian CJ, Fentiman IS, Robson ME, Domchek SM, Hartmann LC, Holland R, Winchester DJ, and the Consensus Conference Committee; Proceedings of the International Consensus Conference on
Breast Cancer Risk, Genetics, & Risk Management, April, 2007, *in press*. Cancer, 2008.

20. Dalla Palma M, Domchek SM, Jill Stopfer J, Erlichman J, Siegfried JD, Tigges-Cardwell J, BA, Rebbeck TR, Nathanson KL. The relative contribution of point mutations and genomic rearrangements in *BRCA1* and *BRCA2* in high risk breast cancer families. *In press*. Cancer Research, 2008.

Research Publications, peer-reviewed reviews, editorials and chapters:

1. Rodriguez E, Domchek SM: The Prevention of Hereditary Breast Cancer. Seminars in Oncology Vol. 34: 401-405, 2007.

2. Gulati AP, Domchek SM: The Clinical Management of BRCA Mutation Carriers. Current Oncology Reports Vol. Vol. 10: 47-53, 2008.

3. Rebbeck TR, Domchek SM: Variation of Breast Cancer Risk Among BRCA1/2 Carriers, Breast Cancer Res Treat, *in press* 2008.

4. Domchek SM and Antoniou AC: Cancer risk models: Translating family history into clinical management. Annals of Internal Medicine Vol. 147: 515-517, 2007.

5. Domchek, SM and Weber, BL. Genetic variants of uncertain significance: flies in the ointment, J Clin Oncol Vol. 26: 16-17, 2008.

6. Ashworth A, Weber BL, Domchek SM: Inherited Genetic Factors in Breast Cancer. Diseases of the Breast. Harris J, Lippman M, Morrow M, Osborne CK (eds.). Lippincott Williams and Williams, in press 2008.

C. Funding

Dr. Domchek's work in breast cancer genetics has resulted in a Cancer Genetics Network Contract through the National Cancer Institute as the University of Pennsylvania site PI. She is also co-investigator on several RO1 grants. The first permits the evaluation of I540 peptide as well as surviving peptide vaccination in combination with anti-CD25 mAb in a further attempt to boost immune response by depleting regulatory T cells. The principle investigator on the grant is Dr. Robert Vonderheide, and the grant number is Ro1 CA111377-01A1. Dr. Domchek will be the principle investigator on the clinical trial which will be part of the grant. In addition, Dr. Domchek is the clinical PI of a project entitled, "Telomerase Immunotherapy in Breast Cancer" funded by the Breast Cancer Research Foundation and aiming to move telomerase vaccination into the adjuvant setting. Dr. Domchek is also the lead clinical investigator on two RO1's led by Dr. Timothy Rebbeck (RO1 CA102776 and RO1 CA083855). The first of these grants is examining the impact of prophylactic surgery on *BRCA1/2* mutation carriers, with particular attention to tumor phenotype as well as interaction with hormonal therapy use. The second study is focused on modifier genes in *BRCA1/2* mutation carriers. Dr. Domchek also collaborates closely with Dr. Chanita Hughes Halpert in her work on risk assessment in African American women, which has led to funding from the Department of Defense to examine genetic counseling issue, and from Avon Progress for Patients to examine risk assessment and behavioral interventions.

CONCLUSIONS

Data thus far from our current trials suggest that telomerase peptide vaccination is biologically active and leads to in vivo immune recognition of carcinoma by effector lymphocytes and tumor necrosis. This has great potential for biological therapy of breast cancer and required further exploration. If hTERT expression can be found in women at high risk for breast cancer, this may represent a marker to be used to target candidates for vaccination in the future.

REFERENCES (See "Publications" in "Reportable Outcomes")

APPENDICES

1. Domchek CV

UNIVERSITY OF PENNSYLVANIA - SCHOOL OF MEDICINE
Curriculum Vitae

Date: 8/16/08

Susan M. Domchek

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University of Pennsylvania
3400 Spruce Street

Philadelphia, PA 19104 USA

If you are not a U.S. citizen or holder of a permanent visa, please indicate the type of visa you have:
none (U.S. citizen)

Education:

1990	BA	Dartmouth College, Hanover, NH (Engineering Sciences)
1994		Oxford University, England (English Literature)
1995	MD	Harvard Medical School, Boston, MA

Postgraduate Training and Fellowship Appointments:

1995-1996	Intern, Internal Medicine, Massachusetts General Hospital, Boston, MA
1996-1998	Resident, Internal Medicine, Massachusetts General Hospital, Boston, MA
1998-2001	Clinical Fellow in Hematology and Oncology, Dana-Farber Cancer Institute, Boston, MA
2000	Chief Medical Resident, Massachusetts General Hospital, Boston, MA

Faculty Appointments:

2000-2001	Instructor in Medicine, Harvard University
2001-2007	Assistant Professor of Medicine at the Hospital of the University of Pennsylvania, University of Pennsylvania School of Medicine
2007-present	Associate Professor of Medicine at the Hospital of the University of Pennsylvania, University of Pennsylvania School of Medicine

Hospital and/or Administrative Appointments:

2005-present	Director, Cancer Risk Evaluation Program, Abramson Cancer Center, University of Pennsylvania

Specialty Certification:

1998	American Board of Internal Medicine
2001	American Board of Internal Medicine: Medical Oncology

Licensure:

1998	Massachusetts
2001	Pennsylvania

Awards, Honors and Membership in Honorary Societies:

1989	Choate Scholar, Dartmouth College
1989	Phi Beta Kappa, Dartmouth College
1990	Summa cum laude, Dartmouth College
1993	Marshall Scholar, Oxford University
1995	Magna cum laude, Harvard Medical School
2000	Chief Medical Resident, Massachusetts General Hospital
2001	Landenberger Scholar, University of Pennsylvania

2002-2007	Ann B. Young Assistant Professor in Cancer Research, University of Pennsylvania
2002-2005	Tracey Starr Award
2003-2006	Department of Defense, Physician Scientist Award
2007	Alavi Award for Excellence in Cancer Research

Memberships in Professional and Scientific Societies and Other Professional Activities:

National:

American Society of Clinical Oncology (Member, 1999-present)

Editorial Positions:

2000-present	Ad Hoc reviewer, Cancer
2001-present	Ad Hoc reviewer, Journal of Clinical Oncology
2002-present	Ad Hoc reviewer, Journal of Medical Genetics
2002-present	Ad Hoc reviewer, New England Journal of Medicine
2002-present	Ad Hoc reviewer, Clinical Cancer Research
2003-present	Ah Hoc reviewer, Journal of General Internal Medicine
2005-present	Ad Hoc reviewer, Cancer Research

Academic and Institutional Committees:

2003	Member, Educational Taskforce for Department of Medicine Strategic Planning Initiative, University of Pennsylvania
2006-present	Member, GEC Executive Committee, School of Medicine, University of Pennsylvania
2006	Member, Obstetrics and Gynecology Strategic Planning Committee, University of Pennsylvania
2008	Member, Search Committee, Division of Rheumatology, University of Pennsylvania

Major Academic and Clinical Teaching Responsibilities:

2000	Chief Medical Resident, Massachusetts General Hospital
2001-present	Associate Professor of Medicine, University of Pennsylvania •Serve as inpatient attending for six weeks a year, supervising team of fellows, residents, interns and medical students •Preceptor to medical students and residents in outpatient clinic •Preceptor to residents in the Women's Health Elective
2002-present	"Cancer screening trials", Educational series for medical oncology fellows. Yearly lecture.
2003-present	"Breast cancer genetics", Medical student, endocrinology course. Yearly lecture
2006-present	"Breast cancer genetics" Yearly lecture for Oncology Fellows
2008	“Cancer Genetics” Lecture series for nurse practitioner students

Lectures by Invitation:

Sep, 2002	"Ductal lavage for the detection of breast cancer: how it works and what's the evidence?", Changing Concepts in Breast Cancer 2002 Conference, University of Pennsylvania, Philadelphia, PA
Oct, 2002	"Ductal lavage", Life After Breast Cancer, University of Pennsylvania, Philadelphia, PA
Oct, 2002	"What is a clinical trial?", Pennsylvania Breast Cancer Coalition, Harrisburg, PA
Oct, 2002	"Breast cancer genetics: who to test and how to manage", Moravian College, Bethlehem, PA
Oct, 2002	"Breast cancer: risk, screening, prevention and management", Moravian College, Bethlehem, PA

Nov, 2002	"Hormone replacement therapy and breast cancer risk", FOCUS panel discussion, University of Pennsylvania, Philadelphia, PA
Jan, 2003	"Management of BRCA1 and BRCA2 mutation carriers", San Antonio Update, Sponsored by Baylor College of Medicine, Washington D.C.
Jun, 2003	"Update on breast cancer susceptibility genes". Medical Grand Rounds, Chester County Hospital, West Chester, PA.
Aug, 2003	"Breast, ovarian and colon cancer genetics", Medical Grand Rounds, Pocono Medical Center, East Stroudsburg, PA
Sep, 2003	"Breast cancer genetics: Who to test and how to manage", Medical Grand Rounds, Lancaster General Hospital, Lancaster, PA
Sep, 2003	"Breast cancer genetics", Life After Breast Cancer Conference, University of Pennsylvania, Philadelphia, PA
Jan, 2004	"Breast cancer genetics", Medical Grand Rounds, St. Joseph's Hospital, Reading, PA
May, 2004	"Risk models in clinical practice", National Cancer Institute Risk Modeling Meeting, Washington, D.C.
May, 2004	"Update in adjuvant therapy for breast cancer", Teich Lecture, Beth-Israel Medical Center, New York, NY
Jun, 2004	"ASCO update: Breast cancer prevention, detection and genetics", University of Pennsylvania, Philadelphia, PA
Sep, 2004	"Breast cancer genetics update", Life After Breast Cancer Conference, Philadelphia, PA
Oct, 2004	"Breast cancer overview", Moravian College, Bethlehem, PA
Jan, 2005	"Telomerase immunotherapy of breast cancer", Breast Cancer Think Tank 15, Cuacao, Dutch Antilles
Apr, 2005	"An update on breast cancer genetics", Changing Concepts in Breast Cancer Conference, University of Pennsylvania CME Symposium, Philadelphia, PA
Apr, 2005	"Genetics and women at high risk for breast cancer", at the 1st Annual Women's Health Summit sponsored by the Cleveland Clinical Foundation Women's Health Center
Apr, 2005	"Genetic Susceptibility and breast cancer", New Strategies in Breast Cancer Conference 2005, Center for Biomedical Continuing Education, Philadelphia, PA
Apr, 2005	"Hereditary breast and ovarian cancer syndroms" at the 1st Annual Women's Health Summit, sponsored by the Cleveland Clinic Foundation Women's Health Center, Cleveland, OH
May, 2005	"How to write a clinical trial", Educational Session at the American Society of Clinical Oncology Annual Meeting, Orlando, FL
Oct, 2005	"Clinical management of BRCA1 and BRCA2 mutation carriers", OB/GYN Grand Rounds, University of Pennsylvania, Philadelphia, PA
Oct, 2005	"Genetics Update", Breast Cancer: Early Detection is the Key Conference, Pennsylvania Hospital, Philadelphia, PA
Apr, 2006	"Genetic susceptibility to breast cancer", Continuing Medical Education Course. Philadelphia, PA
Apr, 2006	"Breast Cancer Genetics", The Second Annual Helene Madeira Breast Cancer Symposium. Lankenau Hospital, Wynnewood, PA
Apr, 2006	"History of Breast Cancer", Pennsylvania Hospital, Philadelphia, PA
Jun, 2006	"ASCO Update: Screening, Prevention and Genetics", Philadelphia, PA
Jun, 2006	"Low penetrance genes and breast cancer: a clinical perspective", American Society of Clinical Oncology Education Session, Altanta GA
Jul, 2006	"Genetic Susceptibility to Breast Cancer", Oncology Seminar, Virginia Commonwealth University, Richmond, VA
Apr, 2007	"Genetic susceptibility to breast cancer", Seventh Annual New Strategies in Breast Cancer, Center for Biomedical Continuing Education, Philadelphia, PA
Apr, 2007	"Hereditary Cancer Syndromes", American College of Physicians Annual Meeting, San Diego, CA

October, 2007	"Update on breast and ovarian cancer genetics": Gyn Onc Grand Rounds, University of Pennsylvania
June, 2007	"ASCO Update 2007: Prevention, screening and genetics", Philadelphia, PA
January 10, 2008	"Large genomic rearrangement: impact of genetic testing strategies for BRCA1 and BRCA1": Breast Cancer Program Group, University of Pennsylvania
January 30, 2008	"San Antonio Update: Tumor Biology": Fox Chase Cancer Center Continuing Medical Education Course, Philadelphia, PA
January 30, 2008	"Update on genetic testing strategies for BRCA1 and BRCA2", Center for Research on Reproduction and Women's Health, University of Pennsylvania
February 15, 2008	"Large genomic rearrangement: impact of genetic testing strategies for BRCA1 and BRCA1", Fox Chase Cancer Center, Oncology Lecture Series, Philadelphia, PA
March 19, 2008	"Update of breast cancer treatment", Pennsylvania Hospital, Grand Rounds, Philadelphia, PA
June 25, 2008	"ASCO Update 2008: Prevention, screening and genetics", Philadelphia, PA
September 4, 2008	"The Genetics of male breast cancer", National Institutes of Health, Bethesda, MD

Organizing Roles in Scientific Meetings:

May, 2005	Planning Committee Member, Education Committee, Tumor Biology and Genetics, American Society of Clinical Oncology Annual Meeting Orlando, FL
May, 2005	Chairperson, "Risk modifiers in hereditary cancer syndromes", American Society of Clinical Oncology Annual Meeting Orlando, FL
Jun, 2006	Planning Committee Member, Education Committee, Tumor Biology and Genetics, American Society of Clinical Oncology Annual Meeting Atlanta, GA
Jun, 2006	Chairperson, Cancer Genetics Education Committee, American Society of Clinical Oncology Altlanta, GA
Jun, 2007	Chairperson, "What oncologists need to know about hereditary gastric, kidney and thryoid cancers", ASCO 2007 Annual Meeting Chicago, IL
Jun, 2007	Planning Committee Member, Education Committee, Tumor Biology and Genetics, American Society of Clinical Oncology Annual Meeting Chicago, IL
Sept, 2008	Discussant for oral abstract, ASCO Breast Symposium, Washington D.C.

Bibliography:

Research Publications, peer reviewed (print or other media):

1. Domchek SM, Auger KR, Chatterjee S, Burke TR Jr, Shoelson SE: Inhibition of SH2 domain/phosphoprotein association by a nonhydrolyzable phosphonopeptide. Biochemistry Vol. 31: 9865-9870, 1992.

2. Piccione E, Case RD, Domchek SM, Hu P, Chaudhuri M, Backer JM, Schlessinger J, Shoelson SE: Phosphatidylinositol 3-kinase p85 SH2 domain specificity defined by direct phosphopeptide/SH2 domain binding. Biochemistry Vol. 32: 3197-3202, 1993.

3. Domchek SM, Younger J, Finkelstein DM, Seiden MV: Predictors of skeletal complications in metastatic breast cancer. Cancer Vol. 89: 363-368, 2000.

4. Domchek SM, Hecht JL, Fleming MD, Pinkus GS, Canellos GP: Lymphomas of the breast: primary and secondary involvement. Cancer Vol. 94: 6-13, 2002.

5. Bendell JC, Domchek SM, Burstein HJ, Harris LN, Younger J, Kuter I, Bunnell C, Rue M, Gelman R, Winer EP: Central nervous system metastases in women who receive trastuzumab-based therapy for metastatic breast cancer. Cancer Vol. 97: 2972-7, 2003.

6. Domchek SM, Eisen A, Calzone K, Stopfer J, Blackwood A, Weber BL: Application of breast cancer risk prediction models in clinical practice. Journal of Clinical Oncology Vol. 21: 593-601, 2003.

7. Huang J, Domchek SM, Brose MS, Rebbeck TR, Nathanson KL, Weber BL: Germline CHEK2*1100delC mutations in breast cancer patients with multiple primary cancers. Am J Hum Gen Vol. 41: e120, 2004.

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