



## **BREAST CANCER VACCINES OFFER HOPE FOR HIGH-RISK PATIENTS AS PROMISING DATA ARE PRESENTED AT 2008 ERA OF HOPE MEETING**

*Phase 2 Trial Initiated for Vaccine Combination Therapy Targeting HER2 Breast Cancer*

*Scientists Explore New Prophylactic Breast Cancer Vaccine Based on "Foreign" Peptides Generated by Different Breast Tumors*

Baltimore, Md. – June 26, 2008 – New research into the development of breast cancer vaccines is being unveiled this week at the 5th Era of Hope meeting sponsored by the Department of Defense Breast Cancer Research Program (BCRP). During the 4-day meeting being held June 25–28 at the Baltimore Convention Center, breast cancer survivors and researchers are exploring the latest progress and opportunities for breast cancer vaccines as well as reflecting on the BCRP's achievements toward its vision of eradicating breast cancer, the most commonly diagnosed cancer among women in the United States (excluding skin cancer).

Vaccines have demonstrated success in fighting traditional infections. However, due to the way cancer progresses, researchers have found it difficult to bring effective breast cancer vaccines to the market. However, the tide may be turning. New vaccine research is being presented at the Era of Hope meeting, including the development of a prophylactic vaccine, as well as a new therapy involving a vaccine containing HER2 intercellular domain peptide in combination with trastuzumab, which showed early positive results in its Phase 2 trial.

"While the manipulation of a patient's immune system to identify and eliminate breast cancer tumor cells is becoming an increasingly more common approach in breast cancer research, traditional breast cancer disease management strategies are having to be reconsidered," said Dr. Kim Lyerly of Duke Comprehensive Cancer Center. "New treatment strategies, some of which integrate investigational vaccines with novel therapeutics, are being explored and hold great promise for future generations of breast cancer patients."

The BCRP will showcase its progress in research surrounding breast cancer vaccines at a symposium session entitled "Harnessing the Immune System: Therapeutic Vaccines" scheduled to be held on Thursday, June 26 at 10:30 a.m. Some of the latest research on cancer vaccines will be presented within the context of the following abstracts:

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### **Telomerase-Specific T-Cell Immunity in Breast Cancer: Effect on Vaccination of Tumor Immunosurveillance – Susan Domchek, University of Pennsylvania**

The human telomerase reverse transcriptase (hTERT) protein is overexpressed in nearly all human cancer cells, contributes critically to oncogenesis, and is recognized by cytotoxic T cells that lyse tumors. CD8+ T cells specific for hTERT naturally occur in certain populations of cancer patients in remission, but it remains poorly understood whether such T cells could contribute to tumor immunosurveillance. To address this issue, researchers performed several studies investigating approaches to hTERT vaccination in 19 patients with metastatic breast cancer who had no measurable T-cell response to hTERT at baseline. An exploratory landmark analysis revealed that median overall survival was significantly longer in those patients who achieved an immune response to hTERT peptide (32 months) compared with patients who did not (17.5 months). This result suggests that hTERT-specific T cells could contribute to the immunosurveillance of breast cancer and points to novel opportunities for both therapeutic and prophylactic vaccine strategies for cells.

### **Phase 2 Study of a HER-2 Neu Peptide-Based Vaccine Plus Concurrent Trastuzumab for Prevention of Breast Cancer Relapse – Lupe Salazar, University of Washington**

Breast cancer relapse after optimal therapy is common in patients with HER-2/neu positive (HER2+) tumors and is likely due to residual microscopic disease. One approach to the eradication of residual subclinical disease is tumor vaccines that generate tumor-specific T cell immunity, specifically, memory T cells capable of eradicating tumor antigen-bearing cells over an extended period of time. Immunity against the intracellular domain (ICD) of the HER2 protein correlates with antitumor responses in animal models. Patients with HER2+ cancers can be immunized to the HER2 ICD using peptide-based vaccines. Moreover, trastuzumab, a standard therapy for HER2+ patients, increases the activity of HER2-specific T cells in vitro. Thus, concurrent administration of trastuzumab with HER2 vaccines may enhance the generation of HER2-specific CD4+ and CD8+ T cell responses and potentially translate into improved overall survival (OS) for patients with advanced-stage disease. To examine this hypothesis, researchers initiated a Phase 2 study to examine the OS, safety, and immunogenicity of a HER2 ICD peptide-based vaccine when administered concurrently with trastuzumab to patients with stage IIIB or stage IV breast cancer. Early data suggest that subjects with HER2+ stage IIIB and stage IV cancer can be safely immunized with an HER2 peptide vaccine while receiving concurrent trastuzumab. Additionally, the approach is immunogenic, generating significant levels of HER2-specific T cell immunity. Accrual for this trial continues, and long-term follow-up is ongoing for survival benefit analysis.

### **A Novel Breast Cancer Vaccine Using Immunostimulatory Peptides – Davorka Messmer, University of California, San Diego Cancer Center**

Immunotherapies have shown promising results in several cancers. One major challenge for immunotherapies is to break tolerance in order to achieve cytotoxic T lymphocyte-mediated killing of tumor cells. For a successful induction of immune responses, dendritic cells (DCs), which are the most potent antigen-presenting cells, need to encounter both antigen and stimulus. If they take up antigen without receiving a stimulus or this occurs at different times, they can induce tolerance. Therefore, it is critical to avoid this scenario and maximize the number of DCs that encounter both antigen and stimulus at the same time to achieve an effective antitumor immune response. The objective of this study is to test if poly-lactic-glycolic acid nanoparticles (PLGA-NPs), which are loaded with the HER2 peptide and carry the immunostimulatory peptide Hp91 on the outside or inside, will allow antigen-presenting cells like DCs to induce the development of breast cancer-specific immune responses. The study found that PLGA-NPs that carry the immunostimulatory peptide Hp91 on the surface are potent stimulators of mouse DCs and are nontoxic under the conditions tested.

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Also, the study shows that PLGA-NPs that carry the peptide Hp91 inside the particles stimulate DCs. The study is now conducting a comparison between these different modifications to identify which one is more potent in activating DCs to carry it further to the vaccine testing. Thus, PLGA-Hp91 NPs hold promise as carriers for breast cancer-specific peptides and/or proteins since they will deliver the antigen cargo and provide the necessary maturation stimulus needed for proper T cell activation.

### **Toward a Prophylactic Vaccine for Breast Cancer – Stephen Albert Johnston, Arizona State University, Tempe**

The goal of this study is to create a vaccine that can be given to healthy adults to prevent breast cancer. This concept is based on the fact that tumors produce many protein variants that are foreign to the immune system. If some of these variants occur in nascent breast tumors in many individuals, they can be used to vaccinate women to prevent cancer as is done for infectious diseases. Using mouse models, the researchers have shown that this principle works in concept; however, the question now is whether enough of such protein variants are frequent enough in breast tumors to constitute such a vaccine. A primary initial focus of this study has been a thorough search of both the literature and databases for tumor-specific translocations that would create new peptides. Additionally, a database for the predicted potential variant proteins in tumors has been created, serving as the basis for the search for non-normal peptides from the surface of tumor cells. This approach has produced a large number of candidates, the best of which are now being evaluated.

### **About the BCRP and Era of Hope**

The Department of Defense BCRP is a congressionally mandated program managed by the U.S. Army Medical Research and Materiel Command's Congressionally Directed Medical Research Programs (CDMRP). The BCRP seeks to eradicate breast cancer by funding innovative, high-impact research and has integrated the ideas and perspectives of breast cancer survivors into all aspects of the program. As the second largest source of breast cancer research in the United States, the BCRP has received over \$2 billion in congressional appropriations since its inception in 1992, granting over 5,000 unique awards that fulfill unmet needs in breast cancer research. The success of these grants is illustrated in part by the fact that over 10,000 publications have resulted from BCRP-funded research, more than 11,000 abstracts have been published, and over 400 patents and licensures have been issued. In 2008, the program received \$138 million in congressional appropriations to be invested in breast cancer research. For more information about the BCRP, please visit <http://cdmrp.army.mil/bcrp/>.

The BCRP is hosting its fifth international Era of Hope meeting, a unique forum for scientists, clinicians, breast cancer survivors and advocates, policy makers, and the public to come together and discuss the latest findings in breast cancer research and future directions to eradicate this disease. More than 1,600 awardees, researchers, breast cancer survivors, and health advocates will attend this year's Era of Hope, which will feature more than 1,200 abstracts focusing on the program's breakthroughs in the prevention, detection, diagnosis, and treatment of breast cancer as well as quality of life issues. For more information about the Era of Hope meeting, please visit: <https://cdmrpcures.org/>.

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