



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
DP150099

Project Title:
Immunotherapy targeting triple negative breast cancer using NY-ESO-1-specific TCRs and blockade of immune suppression

Award Mechanism:
Bridging the Gap: Early Translational Research Awards

Principal Investigator:
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Entity:
The Methodist Hospital Research Institute

Lay Summary:

Breast cancer is a leading cause of cancer-related deaths of women in the United States and worldwide. Harnessing the immune system to eradicate malignant cells is a promising approach to cancer therapy. Recent FDA approval of sipuleucel-T (Provenge) for the treatment of metastatic prostate cancer and ipilimumab (Yervoy) for the treatment of melanoma represents milestones in the field of cancer immunotherapy. Despite rapid progress of cancer immunotherapy, there is no effective therapy for patients with metastatic triple-negative breast cancer (ER/PR/HER-2-negative, TNBC). We found that NY-ESO-1 is highly expressed in 18-30 % of TNBC samples, thus serving a potential target for immunotherapy of TNBC patients. Importantly, clinical trials using NY-ESO-1 T cell receptor (TCR)-transduced T cells showed 55% of clinical response in metastatic synovial sarcoma without toxicity. However, therapeutic effects of NY-ESO-1 TCRs on TNBC remain unknown. We propose to target NY-ESO-1 for development of immunotherapy of TNBC patients using NY-ESO-1 T cell receptor (TCR). The maximal therapeutic immunity could be achieved by use of TCR-transduced CD4+ T cells, in combination of TCR transduced CD8+ T cells. Furthermore, TCR-induced antitumor immunity could be further expanded in vivo by blockade of immune suppression. The advantages of our proposed studies include available unique resources of many NY-ESO-1-specific T cell lines and clones and expertise of our team and collaborators on TCR technology and blockade of immune suppression. A positive outcome of this project would substantially advance our knowledge and treatment of metastatic TNBC, and a clear path to phase I clinical trials, thus leading to development of new therapeutic treatment of TNBC, perhaps many other types of cancer as well.