**Award ID:**
RP170537

**Project Title:**
Identification of novel immune targets and neoantigens for development of immunotherapy for breast cancer

**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 one of the leading causes of death in women worldwide including Texas. During 2008-2012, approximately 14000 women were diagnosed with breast cancer in Texas alone (Source: Texas Cancer Registry). Further studies are warranted to improve with stronger efficacy particularly against metastatic Triple negative breast cancer (TNBC) patients who do not respond to available standard therapy. By and large, the primary weapons in the frontline fight against breast cancer are surgical interventions, chemotherapeutic regimens or radiation therapy. The efforts in identifying immunotherapeutic approaches or regimen to treat breast cancer are emerging. However, immunotherapy now holds a great promise. A patient’s own immune cells can be manipulated to attack tumor cells. Harnessing the immune system to eradicate malignant cells is a powerful novel approach to develop cancer therapy. However, cancer immunotherapy for many types of solid tumors is still lacking, in part, due to limited information on immune targets of many types of cancer and their heterogeneity. Here we plan to identify TNBC patient-specific tumor mutations and novel antigens for TNBC because the information on immune targets in this metastatic cancer is limited. Tumor-derived T cells, in particular CD4+ T cells, play an important role in recognizing neoantigens that drive antitumor immunity.

Our goal is to identify multiple neoantigens from each cancer patient since it is not known which neoantigen is more immunogenetic than others. Due to genetic heterogeneity of cancer cells, it is better to target multiple neoepitopes than single one epitope to cover all cancer cells and prevent immune escape. We will also determine whether potent therapeutic antitumor immunity can be generated by neoantigens loaded nanotechnology-based dendritic cell (Nano-DC) vaccine to regress tumor growth. To summarize, the proposed studies are highly innovative in respect to both conceptual and experimental aspects, because we have pioneered in the identification of neoantigens recognized by patient's own T cells, particularly CD4+ T cells. Thus our studies focused towards the Identification of ideal breast cancer antigens and the improvement of in vivo delivery by Nanotechnology based approach against TNBC are highly significant and of public health significance. Comprehensively, the positive outcome of our proposed studies will shift the paradigm by paving the way for the development of novel immunotherapies to eradicate metastatic breast cancer in Texas and worldwide.