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.