CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120727

Project Title:
Development of a targeted therapy: a treatment that is able to suppress breast cancer initiating cells

Award Mechanism:
Bridging the Gap: Early Translational Research Awards

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Tumor initiation cells (TICs, also known as cancer stems cells) are a small subpopulation of cells within the tumor that are highly aggressive and are suggested to be responsible for initiation of cancer and resistance to traditional cancer therapy. It has been reported that with conventional treatments, such as chemotherapy and radiotherapy, the percent of BTICs in the tumors increases from 9% to 74% after treatment, even though the overall tumor mass is reduced, making resistance to cancer treatment a major obstacle for breast cancer therapies. To our knowledge, there are no drugs that can effectively reduce breast tumor initiation cells (BTICs) in the clinic, although the EGFR/HER2 tyrosine kinase inhibitor, lapatinib, has been shown to stabilize BTICs (i.e. the percent of BTICs remain the same during treatment). Thus, there is an urgent need for the development of novel therapeutics that target BTICs. We have recently developed a breast cancer-specific expression system, VISA-Claudin4, which can drive a gene of interest to selectively express in breast cancer cells, both in cell culture and animal models. Using this expression system, we incorporated a therapeutic gene, BikDD (named VISA-Claudin4-BIKDD), and showed high therapeutic efficacy with virtually no toxicity compared to the commonly used CMV vector due to its nature of breast cancer specific expression. Encouragingly, VISA-Claudin4-BIKDD also demonstrated activity toward suppressing BTICs. Thus, the newly developed targeted therapy may provide an effective treatment that can suppress BTICs, which, if successful, will meet the unmet medical need to suppress BTICs during treatment for breast cancer patients. We will also develop biomarkers to identify the subpopulation of breast cancer cells that will be sensitive to VISA-Claudin4-BIKDD treatment. This will be critical to identify a specific subset of patients that will respond to the treatment in future clinical trials.