

Treatment of triple negative breast cancer using a tumor membrane based immunotherapy

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Triple negative breast cancer (TNBC), which includes tumors lacking estrogen receptor, progesterone receptor, and HER-2 proteins, represents one of the most challenging cancers for developing an effective therapy due to lack of a therapeutic target. Here, we tested an immunotherapy approach that is personalized, easy to accomplish, and not requiring establishment of cell lines or gene transfer to treat metastatic TNBC. The defining principle of this cancer immunotherapy technology is the incorporation of glycolipid-anchored forms of immunostimulatory molecules (GPI-ISMs) onto tumor membrane vesicles (TMV) derived from TNBC mice model. We tested our immunotherapy approach in both therapeutic and prophylactic vaccinations. Therapeutic vaccination of mice after tumor resections increased overall survival in mice receiving TNBC tumor membrane-based immunotherapy. Also, prophylactic vaccination of mice with immunotherapy and antibody based combination therapy showed a reduction in lung metastasis by 90% relative to untreated groups in clonogenic assays. To test whether the observed decrease in metastasis in our combination therapy is due to enhanced CD4 or CD8 T cell specific immune response, we depleted CD4 and CD8 T cells separately using their specific antibodies and performed clonogenic assay. Depletion of CD8 (but not CD4) T cells prior to challenge recapitulated full metastasis, suggesting that immunotherapy induced CD8 T cells specific responses. In summary, we have demonstrated the feasibility of this novel immunotherapy in the triple negative breast cancer model when used in combination with antibody therapy. A reduction in metastasis to the lung, prolonged overall survival, and enhanced CD8 T cell responses were observed.