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Title: Bispecific monoclonal antibodies for treatment of advanced breast cancer

Public/Lay Abstract:

Immunotherapies, including strategies to invigorate immune cells and to engineer tumor-specific immune cells, have had tremendous success against a number of cancer types. However, immunotherapy has demonstrated minimal results in breast cancer patients as of yet. Clinical trial results have observed responses to checkpoint blockade monoclonal antibodies in approximately 20% of triple negative breast cancer (TNBC) patients, and even fewer hormone receptor positive (HR⁺) breast cancer patients. Additionally, current efforts using engineered T cells only promise to benefit small subsets of breast cancer patients whose cancer cells express antigens, such as HER-2/neu or MUC1. *Therefore, there is an urgent need for immunotherapies that offer clinical benefits to both TNBC and HR⁺ metastatic breast cancer patients.* CD8⁺ tumor infiltrating lymphocytes (TILs) have a clear role in anti-tumor immunity and are largely responsible for recent clinical successes with immunotherapy. Recently, we have found that CD8⁺ TILs are present and functional in metastatic tissues of advanced breast cancer patients. Bispecific antibodies are a simple and effective therapeutic tool that can force engagement of two types of cells, such as CD8⁺ T cells and cancer cells. Our preliminary data show that bispecific antibody engagement of these CD8⁺ TILs can lead to effective cytokine production and target cell killing. Excitingly, this 'synthetic immunology' therapeutic can be produced on a large-scale and stably stored until administration of this 'off-the-shelf' drug is required. It is a therapy that requires little personalization and can be adapted to many different types of breast cancer patients. **We hypothesize that harnessing functional T cells found within the tumors of metastatic breast cancer patient tumors via bispecific antibodies will mediate potent killing of patient cancer cells and tumor regression.** This proposal aims to establish the groundwork for using off-the-shelf bispecific antibody therapeutics for the treatment of metastatic breast cancer patients.