Proposal Title: Targeting Metastatic Breast Cancer with Dual Specificity

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Abstract:
Increased awareness and advances in both diagnostic and therapeutic approaches have significantly improved the treatment outcome in breast cancer patients. However, patients who present with metastatic disease have poor prognosis. The objective of the proposed studies is to garner critical preliminary data supporting the development and use of an anticancer treatment designed to significantly reduce the incidence of metastases and improve the treatment outcomes for patients with advanced metastatic breast cancer. We plan to achieve this goal through the following specific aims. (1) We will use powerful yeast surface display and cellular panning technologies to co-discover cellular receptors and ligands that specifically identify tumor cells that have undergone epithelial-to-mesenchymal transition and are enriched for cancer stem cells. Recent evidence shows that these premetastatic cells likely contribute the metastases, and eliminating these cells could potentially inhibit metastases. (2) We will identify therapeutic agents that can efficiently kill premetastatic breast cancer cells. We will develop technologies to encapsulate these therapeutic agents in polymeric nanoparticles that are then conjugated to ligands (Aim 1) targeting the premetastatic cells. This approach provides two layers of specificity: premetastatic cell targeting and pathway-specific cytotoxic agents. (3) We will use cell culture and mouse tumor models to determine the therapeutic efficacy of the targeted nanoparticles. The results will buttress several major grant applications we envision. We have assembled a multidisciplinary research team to achieve this goal. The ultimate goal of this research is to develop a clinically relevant nanoparticle formulation that will positively impact breast cancer therapy.