Identification of Candidate Target Genes for Metastasis and Cancer Cell Dormancy in a Novel Triple-Negative Breast Cancer Model

Lay Description of Outcomes: Using genome-wide gene expression analyses (RNA Sequencing) on paired tissue samples of primary and metastatic mammary tumors in novel triple-negative breast cancer models, the collective results obtained from this project established that molecular pathways controlling Integrin cell surface interactions and adhesion molecules may play a role in the metastatic progression. More importantly, metastatic cancer cells exhibited a significantly deregulated expression of numerous genes that have pivotal roles in the JAK/STAT signaling cascade that mediates the intracellular action of inflammatory cytokines. Experimental evidence was provided that the Janus kinase 1 (JAK1), and not JAK2 as commonly believed, is the key signaling node for the inflammatory cytokine-mediated activation of oncogenic STAT3 and metastatic progression. The outcomes of our studies have provided a solid scientific rationale for testing JAK1 tyrosine kinase inhibitors in preclinical models for cancer therapy to prevent the metastatic dissemination of malignant cells (i.e., from primary or secondary sites).