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**Project Title:** Targeting Sialic Acid Metabolism to Stop Metastatic Breast Cancer

### **Public/Lay Abstract**

Breast cancer metastasis is accompanied by changes in metabolism – the biochemical processes that convert nutrients into energy and building blocks of life within the cell. Metabolic pathways are specific processes that convert one biochemical, known as a ‘metabolite’, into another over a series of reactions. These metabolic pathways generate energy to fuel cellular processes, provide building blocks for cell growth and division, and produce signaling molecules that direct cell behavior. In order to metastasize, cancer cells need to adapt to new environments, such as the blood, lymph, or lung, which contain different nutrients and conditions. Metastatic cancer cells are therefore dependent on certain metabolic pathways that allow them to survive in new environments. By blocking these specific metabolic pathways, cancer cells could be deprived of the fuel and signals required for metastatic spread and survival. However, a major knowledge gap exists: while metabolic pathways supporting primary breast cancer cells are relatively well-characterized, pathways supporting metastasized breast cancer cells are largely unknown. Our research addresses this gap by specifically studying the metabolism in lung metastases and comparing them to primary tumors, to uncover metabolic pathways that support metastasized breast cancer cells. Preliminary work in our laboratory has identified a key metabolic change associated with metastasis: heightened production of sialic acid, a sugar-like molecule that promotes metastasis in breast cancer cells. High expression of major genes in the sialic acid pathway are also associated with decreased patient survival. Importantly, metastasis is significantly decreased when the sialic acid pathway is targeted. In the proposed work, we will investigate how changes in metabolism drive sialic acid production in metastatic breast cancer cells. Based on these metabolic changes, we will identify therapeutic targets and work towards new therapies for stage IV metastatic breast cancer patients.