

## **Public/Lay Abstract**

Today, 70% of US adults are overweight or obese, with the highest prevalence amongst socioeconomically disadvantaged groups. Obese patients with breast cancer have higher rates of metastasis to internal organs such as the lung and liver, decreased response to chemotherapy and worse outcomes. Given the increase in the prevalence of obesity with our society, there is a critical need to better understand how obesity impacts metastatic growth and response to chemotherapy.

Breast cancer cells do not metastasize randomly in the human body, but instead prefer to go specific organs which provide a host environment that is favorable to their survival. One major component of a tissue's host environment is the extracellular matrix, a mesh of proteins that provide structure and support to all our tissues. Work from our lab and others has shown that the matrix promotes cancer cell growth and migration, features that support metastasis formation and survival. It can also impact response to chemotherapy. In addition, obesity is known to affect the matrix of various organs in the body, such as the lung and liver, organs that host metastases from breast cancer cells, particularly in obese patients. Our research seeks to gain an in-depth understanding what impact obesity has on the local environment of metastatic sites and how these changes contribute to poor drug response in obese patients. We will use mouse models of obesity and breast cancer metastasis to first evaluate the composition of the matrix of livers from lean and obese mice and understand how they impact metastatic growth. We will then evaluate how these changes in matrix proteins impact response to chemotherapy drugs used in the clinic to treat metastatic breast cancer.

Our results will help identify mechanisms by which secondary lung and liver metastases grow in obese patients and shed light on new strategies for treating metastases in obese patients. This will lead to the development of tools to visualize growing metastatic lesions and help develop drugs that can be targeted to the changing matrix and help deliver drugs locally to the metastases. It will also reveal which chemotherapeutic drugs are more likely to kill metastases in obese patients, allowing clinicians to adapt treatments to make them more effective for the obese metastatic breast cancer patient.