

## **PUBLIC/LAY ABSTRACT**

Patients diagnosed with stage IV breast cancer are much more difficult to treat when compared to those with localized disease. This concerning discrepancy suggests that specific types of aggressive metastatic cancer cells may avoid destruction by hiding from oncologists and the drugs that they administer. In order to gain new insights into unrecognized cancer cell types that drive metastasis, we recently paired with clinicians to obtain samples of bone and brain metastatic lesions from breast cancer patients. Having access to this precious material presented us with the rare opportunity to analyze patient metastases on a cell-by-cell basis. Our analysis used cutting-edge technologies and discovered a unique type of cancer cell that may disseminate by resembling human immune cells on its surface. Intriguingly, despite looking like immune cells on the outside, these cells maintain the internal features of breast cancer and show other characteristics that suggest they may initiate metastasis. We have also identified these cells in other metastatic cancers apart from breast cancer, and they have yet to be described in oncology. Our research proposal will lay the essential groundwork to detect and target these “immune-like” cancer cells in patients with stage IV disease.

In the first phase of this project, we will determine methods for detecting these “immune-like” cancer cells reliably in tissue or blood specimens collected from breast cancer patients. By surveying all markers that exist on the surface of these cells, we will develop a strategy to distinguish them from other cancer cells and from normal immune cells. The methodology that we create will be tested in patient samples from human breast tumors and metastases. After linking the presence of “immune-like” cancer cells to breast cancer patient outcomes, we will share our strategy with oncologists to help them detect these cells in the clinic. In the second phase of our research, we will then explore the role of these “immune-like” cancer cells in metastasis. We will inject purified populations of this cell type into mice to determine if they initiate metastasis as our initial analysis predicts. We will also track the status of these cells while treating metastatic disease in mice and identify systemic drugs and immunotherapies that promote their destruction. Our results will be circulated amongst the medical community, to assist with their decision about which therapies to use when targeting aggressive types of cancer cells.

METAvisor funding will expedite our study of “immune-like” breast cancer cells, so that our findings can be applied in the near-future to aid patients living with stage IV disease. Figuring out how to best detect and destroy aggressive types of metastatic breast cancer cells is a necessary precursor to meaningful intervention in the clinic.