

Public Abstract for the METAvivor Research Award entitled “Assays to determine optimal dosing and therapeutic effects of localized immunotherapy for established metastatic breast cancer to the pleura.”

Rationale. There is an unmet need for treatment for patients with Stage IV breast cancer metastatic to the pleura, the space between the ribs and the lungs. Pleural metastases are a common and devastating complication of breast cancer and most breast cancer patients will develop pleural metastases (10-50%). Today there are no effective treatments for this condition; average survival is 3-12 months. Treatment is only palliative, and patients receive indwelling (long term) catheters to drain tumor and fluid as they accumulate.

Goals. Our ultimate goal is to administer immunotherapy directly to the pleural space, where the tumor has metastasized. The pleural space is a highly protected area which is difficult for the new immunotherapeutic drugs to reach when given by the usual intravenous route. The pleural space of these patients also contains many immune cells in addition to tumor, but these immune cells are controlled by the tumor. Rather than attack, these immune cells have been reprogrammed to help the tumor grow and spread. The fact that potent antibody immunotherapeutic drugs, such as anti-PD-1 can be administered to pleural space, where they can potentially reverse the tumor-mediated control of immune cells and unleash an anti-tumor response, provides a sound rationale for giving immunotherapy directly to the pleura through their drainage catheters. In order to best apply this strategy in patients, we need to develop two new tests. One measures the dose of drug that actually reaches its target in the pleura and determine when the optimal dose has been reached. The second determines whether immune cells in the pleura that have been reprogrammed by immunotherapy leave the pleural space and circulate throughout the body, where they can attack tumor at other sites. When we complete these studies we anticipate that we will have developed two well-validated tests that can be used in the clinic. These tests will be used on patient samples obtained when their catheters are routinely drained.

Potential Impact of the Research Plan to Advance Stage IV Metastatic Breast Cancer Therapy. The studies proposed here are highly translational with a potential immediate impact on metastatic breast cancer. We focus on readily available immunotherapies that are either FDA approved or investigational drugs. We are deeply committed to the use of patient materials to generate compelling preclinical data to support rapid clinical translation addressing an urgent clinical need. This need is best exemplified by the case of a recent patient who presented with a malignant pleural effusion, but who was otherwise in good health. Despite an exemplary attitude and strong support from family, she failed all surgical and oncological interventions, including systemic targeted therapy. The hallmark of this patient’s disease was an extreme pleural immune environment with voluminous secretions that lasted from presentation until her death. We believe that any treatment that would alleviate the symptoms of MPE and meaningfully prolong life would be of great impact on our field. We have confidence that the tests developed in the 2-year funding period will provide convincing evidence that this novel therapeutic approach is worthy of support and clinical implementation.