

Lay Abstract

The proposed research focuses on an innovative, promising and cost-effective treatment for metastatic breast cancer. Complementary to a current emphasis on cancer immunotherapy, the proposal addresses the role of the neuropeptide MCH in the neuronal system bi-directionally communicating with tumor epithelial cells as well as immune cells and stromal cells and constantly conveying locally derived signals to brain but also to remote parts of the body and vice-versa. Successful proof-of-concept studies here employing mouse models and patient-derived explants (PDE) from cases of metastatic breast cancer would quickly demonstrate that MCH plays a deleterious role in breast cancer metastasis and that MCH antagonists repurposed from other disease therapeutics could have significant therapeutic outcomes.

The main objectives of the project include analysis of samples from breast cancer patients with metastatic disease for expression of MCH and its target receptors and correlation with clinical outcomes; and pharmacological interventions targeting MCH in mice with metastatic breast cancer and treatment of metastatic cancer patient explants with an MCH antagonist versus chemotherapy, immunotherapy and their various combinations to comparatively assess the treatment potential of the proposed pharmacotherapy. The significance of the suggested biological pathway in breast cancer metastases has not been previously appreciated and the successful completion of our studies might offer a paradigm shift in understanding mechanisms that can enhance metastatic tumor potential and facilitate tumor engraftment at distant sites as well as treatments that can effectively inhibit such processes.