

2021 ACG-IRG Pilot Grant

The Role of Immune Regulation in Metastatic Tumor Dormancy



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Abstract:

The proposed research addresses a major and challenging public health problem of metastatic recurrence in breast cancer. Approximately 15,000 patients per year with a history of early-stage breast cancer will die of breast cancer due to metastases from dormant tumor cells years, and sometimes decades, after primary breast cancer surgery, radiation, and systemic treatment. This protracted latency, or metastatic tumor dormancy, stems from dormant quiescent micrometastases, which can suddenly emerge and proliferate into incurable metastatic breast cancer.

Immunotherapy, such as immune checkpoint inhibitors, has dramatically improved clinical outcomes in melanoma and non-small cell lung cancer and poses as a great promise in improving breast cancer mortality. However, clinical trials using immune checkpoint inhibitors have not significantly benefited most patients with breast cancer. In order to develop effective immunotherapies that increase breast cancer cure rates, a better understanding of the role of immune regulation of breast cancer metastasis and metastatic tumor dormancy is needed.

The main barriers in understanding metastatic tumor dormancy are the paucity of suitable human samples and model systems. This proposal aims to overcome these challenges by leveraging an innovative, immunocompetent, breast cancer metastatic dormancy mouse model that allows well controlled synchronized dissemination and dormancy, to elucidate immune drivers of breast cancer metastatic tumor dormancy.

The research goals of this proposal are to: 1) To define the roles of CD8+ T-cells and tumor infiltrating myeloid cells in metastatic dissemination and dormancy, and 2) To characterize the role of the tumor-immune microenvironment in metastatic tumor dormancy. This research award will build upon Dr. Yeung's background as a breast oncologist and a basic-translational scientist by providing the following training objectives: 1) to gain expertise needed to become an independent investigator; and 2) to master cancer immunology techniques and data analysis through the guidance from collaborations with internationally recognized experts in breast cancer metastasis (Dr. Jing Yang) and immunology (Dr. Judith Varner). By the end of this award period, she expects to not only have gained invaluable insight into the mechanisms underlying metastatic tumor dormancy, but also acquired expertise and preliminary data needed to compete for R01 equivalent funding and to translate this knowledge into new medical therapies to improve long term outcomes and survivals in patients with early breast cancer.