Breast Cancer Subtype-Specific Therapeutic Targets Identified by Anoikis Screen

Investigator(s): Hanna Irie, M.D., Ph.D.
Mount Sinai School of Medicine, NY

Awarded: $450,000.00

Grant Mechanism: Career Catalyst Research

Public Abstract:
Although great strides have been made in advancing the detection and treatment of breast cancer, specific breast tumor subtypes still pose a significant clinical challenge, with higher recurrence risks due to a combination of intrinsic aggressive biology and lack of effective targeted therapies. We utilized a screen approach to identify novel regulators of breast tumor cell survival, with a particular focus on those genes that regulate the ability of breast cancer cells to survive in altered microenvironments, such as those they encounter at distant organ sites where they may eventually form metastases. The screen was designed to identify candidates that regulate tumor cell survival, but do not affect normal breast epithelial cells with the goal of identifying targets that allow for a therapeutic window. Using this approach, we identified several novel candidates that regulate survival and metastatic potential of specific breast cancer subtypes. These candidates could serve as direct therapeutic targets for these subtypes and their inhibition may prevent recurrence in conjunction with current subtype-specific target therapies, such as Lapatinib or Tamoxifen. This proposal focuses on two promising candidate survival regulators, PTK6 and PRKCQ, and aims to critically and thoroughly evaluate the therapeutic potential of inhibiting these molecules to prevent metastases. We will examine the effect of inhibiting these genes on metastasis of tumor cells of specific higher-risk breast cancer subtypes in which they are expressed; PTK6 is expressed in Her2+ and ER+ tumors, while PRKCQ is expressed in basal tumors. We will determine whether these strategies synergize with current subtype-specific targeted therapies. Finally, we will develop methods to identify patient tumors in which targeted inhibition of these candidates may have the most clinical impact; these biomarkers which will be critical for future clinical trials of candidate inhibitors.