Susan G. Komen

Research Grants – Fiscal Year 2015

This research grant was approved for FY2015 Research Programs funding. This grant will be funded upon the execution of grant agreements between Komen and the grantee institutions.

Targeting urokinase receptor for diagnosis & therapy of aggressive breast cancers

Investigator(s): Efrat Harel, Ph.D.; Charles Craik, Ph.D. (Mentor); Laura van't Veer, Ph.D. (Co-Mentor)

Lead Organization: University of California, San Francisco

Grant Mechanism: PDF Basic and Translational **Grant ID:** PDF15330246

Public Abstract:

Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer representing 15-20% of the invasive breast cancer cases of women. These women have a high rate of recurrence with a poor prognosis. Cancer cells from the breast can leave the confines of the gland and spread or metastasize to other parts of the body making their new environments cancerous. TNBC most commonly spreads to visceral organs including lung, liver, brain and bone leading to the formation of cancer metastases. Once a primary TNBC tumor has metastasized, death generally occurs within two to three years.

The ability to monitor the disappearance or reappearance of metastases would be beneficial to physicians selecting the best treatment for a specific patient. Accurate and reliable diagnostic methods for TNBC are urgently needed and could be achieved by identifying cellular markers (proteins) that are expressed at higher levels in metastatic cancer. Antibodies (Abs), proteins of the immune system that naturally recognize other proteins with high selectivity and specificity, will be developed to recognize the cancer markers. Abs that recognize the cancer cells marker, uPAR, will serve as a diagnostic tool to stratify breast cancer subpopulations according to their marker's expression levels. That will be done using human breast cancer tissue from biopsies with known outcomes and classification. In addition, we will combine two or more antibodies against uPAR into a modular platform that will result in a specific tool for non-invasive detection of uPAR, predicting early metastases of TNBC. Our preclinical antibody

platform will be evaluated also as a therapeutic monotherapy that could, if successful, be offered to patients at the earliest stage of metastasis, inhibiting tumor aggressiveness and growth, and leading to better patient outcomes.

My academic training has provided me with an excellent background for the project in multiple biological disciplines. The current research plan is designed to develop tools that will provide a better understanding of breast cancer aggressiveness as well as in targeting both primary tumors and their subsequent metastases. This research proposal presents interdisciplinary research and required expertise in antibody engineering, andbreast cancer oncology and immunology which will be supported by the mentor committee that includes a patient advocate and collaborators that are experts in these respective areas and who are committed to providing training for the proposed research.