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.

Diagnostic and therapeutic implications of extracellular HMGA1 in breast cancer

Investigator(s): Josep Villanueva, Ph.D.

Lead Organization: Vall d'Hebron Institute of Oncology

Grant Mechanism: CCR Basic and Translational **Grant ID:** CCR15333737

Public Abstract:

Breast cancer is biologically and clinically diverse. A group of breast tumors, known as basal-like, afflict younger women and is refractory to endocrine and anti-HER2 therapies. These tumors tend to be particularly aggressive and have a higher metastasis incidence than other breast cancer subtypes. Unfortunately, the standard treatment for patients presenting basal-like tumors is limited to generic adjuvant chemotherapy and radiotherapy that has limited success and heterogeneous outcome. Recent research efforts aimed at characterizing the genomic portrait of breast cancer revealed that the somatic mutation catalog for BLBCs do not provide actionable drug targets. The limited results obtained through the genomics approach together with the evidence that BLBC have a strong involvement of its tumor microenvironment show that approaches different from genomics might be necessary to fight against BLBC. A study done in our laboratory and aimed at understanding how basal-like breast cancer cells (BLBC) communicate among them and with its microenvironment during tumor invasion, led us to study a protein called high mobility group A1 (HMGA1). HMGA1 is a protein that controls the transcriptional activity of several genes. HMGA1 has been causally related to tumorigenesis and its overexpression often correlates with the presence of metastasis and reduced patient survival. We discovered using proteomics and invasion-based functional assays that HMGA1 has an alternative extracellular function in tumor invasion and metastasis. Our hypothesis is that HMGA1 plays a key role in tumor invasion and metastasis, and both predicts the development of distant metastasis and is a promising drug target for BLBC. Based on preliminary data, the experimental focus of this proposal is to characterize the potential

of HMGA1 as a biomarker and drug target in BLBC. This research program will lead to a significant advance in the characterization of the potential of HMGA1 as a biomarker and drug target in BLBC, and it will present a basis for new opportunities for cancer diagnostics and therapeutics. We envision that our work will allow stratifying patients who are more likely to develop metastasis to then give them a more aggressive treatment to reduce their metastasis incidence. Furthermore, if we could confirm that a drug against the extracellular form of HMGA1 blocks the establishment of both invasive tumors and metastasis, we would be in a better position to reduce the mortality rate of BLBC patients.