



Susan G. Komen
Research Grants – Fiscal Year 2014

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Plk2 function in mammary gland development and breast cancer

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Lead Organization: Baylor College of Medicine

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Public Abstract:

Breast cancer is the most common form of cancer found in women. Although mammography screening has decreased the incidence of breast cancer, there are still thousands of women that die every year as a consequence of the disease. One of the most aggressive types of breast cancers is the basal subtype. Within the basal subtype, triple negative cancers are characterized by the absence of steroid hormone receptors such as estrogen and progesterone receptor in addition to having loss of HER2 growth factor receptor. Due to the absence of the hormone receptors, hormone therapy for patients with triple negative breast cancers is not an option. Currently there are no treatments for triple negative breast cancer and patients with this type of breast cancer have a poor prognosis and are associated with poor survival. This lack of treatment strategies is because there is little understanding of the signaling networks regulating triple negative breast cancers. Therefore it is critical to identify drugable pathways and the proteins involved in these pathways to provide new therapeutic targets. Recently we have identified Plk2 as a regulator of normal mammary gland development and a putative tumor suppressor in the basal subtype of breast cancer. Plk2 is involved in the cell cycle and loss of Plk2 leads to an increase in proliferation, misorientation of mitotic spindle and loss of polarity, processes which all have been implicated in tumorigenesis. Moreover we have identified a drugable kinase downstream of Plk2, Plk1. The goal of this proposal is to develop a preclinical model that would allow us to test inhibitors of Plk1 to determine if tumors lacking Plk2 but with increased Plk1 activity are more sensitive to these inhibitors. By identifying a drugable candidate we may be able to rapidly translate our discoveries into a potential therapy for a subset of patients with triple negative breast cancers.