Susan G. Komen

Research Grants – Fiscal Year 2015

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Mammary stem cells and breast cancer

Investigator(s): Geoffrey Wahl, Ph.D.

Lead Organization: The Salk Institute for Biological Studies

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Public Abstract:

Breast cancer comprises a heterogeneous collection of diseases. Work by basic researchers and clinicians has produced drugs targeting specific types of breast cancers based on particular proteins that they require for their growth and survival. Herceptin is one such drug that has proven very valuable for treating only those breast cancers that express its target, the Her2 protein. Drugs that inhibit the estrogen receptor, which is expressed in about 2/3 of breast cancers, have also proven to be effective. Unfortunately, many women are diagnosed with cancers that do not have significant levels of the estrogen receptor, the related progesterone receptor and the Her2 protein. These so-called “triple negative” cancers are often very aggressive and, thus far, have no “targeted” therapies. While initially sensitive to chemotherapy, these “triple negative” cancers often relapse with a vengeance. Thus, an important goal for researchers is to find therapies that are effective in eradicating such tumors. Also, better ways of evaluating the diversity of cell types that characterize almost all cancers and the cellular mechanisms that lead to their ability to adapt to drugs and other challenges could lead to better prognostic and treatment strategies. Attacking both of these problems is at the root of the work we are doing. Over the past several years we have identified when mouse mammary gland stem cells first start to form at the earliest times of development. We isolated these rare cells and analyzed them and found that the genes they express are also expressed by the triple negative cancers referred to above. Thus, it seems that either the triple negative cancers contain cells that have the molecular characteristics of very primitive mammary stem cells OR the tumor cells have reprogrammed themselves to behave like these

primitive cells to gain some of the growth and survival advantages they may have over their mature counterparts. The work we now propose is geared to better understand the cell signaling pathways that are essential to the growth and survival of the nascent normal mammary stem cells and to determine whether the same pathways are important in triple negative breast cancers. We also want to develop very sensitive, rapid and inexpensive methods to find cells with mammary stem cell characteristics even within the complex cellular makeup of a human cancer. Finally, we want to apply our detection methods to see if we can find evidence of these stem-like cancer cells in the blood stream as “circulating tumor cells”. If we can, we will then be able to determine whether the presence of these cells correlates with patient prognosis or if the cells are sensitive or resistant to various therapies used to treat triple negative breast cancers. Our hope is that these studies will lead to a better understanding of the types of cells that make these cancers so dangerous, and to better methods for eliminating them.