Susan G. Komen
Research Grants – Fiscal Year 2014

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Targeted blockade of the inflammatory network in triple-negative breast cancer

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Lead Organization: Duke University Medical Center
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Public Abstract:
While breast cancer is often perceived as a single disease, it can actually be subdivided into several distinct types; these different types are classified by their respective cellular 'engines', molecular known as their 'driver pathways'. While the 'drivers' for several types of breast cancer are known and therapies exist to target them (Estrogen and HER2 receptor positive breast cancers), one type (Triple-Negative) has no known 'drivers' that can be targeted by therapies and, as a result, has a very poor prognosis. This poor survival rate is due to a lack of targeted therapy options and the aggressive nature of these cancers, which have a striking ability to invade and metastasize to other parts of the body. As such, there is a critical need to identify the 'driver' pathways responsible for the aggressive growth, invasion, and metastasis that characterizes Triple-Negative Breast Cancer. Our recent research has indicated that a unique collection of specific inflammatory pathways are actually critical 'drivers' that are required for Triple-Negative Breast Cancer (TNBC) cell growth and survival. While inflammatory pathways are normally activated within the body's specialized defense cells to eliminate invading bacteria and viruses, we have discovered that these inflammatory pathways are actually 'hijacked' in TNBC tumor cells, which use them for their growth and survival. In light of these recent findings, we hypothesize that this combination of specific inflammatory 'driver' pathways are also responsible for the high level of TNBC invasion and metastasis. Our proposal will answer this critical question by determining if this inflammatory network is responsible for the early development of TNBC invasion and later development of TNBC metastasis. Significantly, our project will also determine if TNBC invasion and metastasis can be effectively treated in pre-clinical animal models using existing drugs and strategies that target this collection of pathways. These pathways are critically important for immune responses and thus, multiple drugs have recently been developed to selectively inhibit them. These new drugs are currently in clinical trials for the treatment of different auto-immune diseases, and our proposal would explore the possibility that re-purposing these drugs for cancer would be an effective way to treat early TNBC invasion and late TNBC metastasis. Taking advantage of drugs already under development for other diseases will shorten the time to translate our hypothesis from the bench to clinical application. Thus, if our pre-clinical use of specific anti-inflammatory drugs (or combinations) prove successful, these drugs could be rapidly advanced into clinical trials to treat patients with invasive or metastatic TNBC. Since tumor invasion and metastasis are the critical factors underlying TNBC mortality, we hope that our investigation could make significant progress in extending and enhancing the lives of patients with TNBC.