Susan G. Komen
Research Grants – Fiscal Year 2014

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Predictive Factors of Recurrences and distant metastases in ER+ Breast Cancer

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Lead Organization: Indiana University
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Public Abstract:
Estrogen receptor positive (ER+) subtype constitutes 65-70% of all breast cancers. Although endocrine therapy is effective in early-stage of ER+ breast cancer, resistance to therapy and development of recurrence/metastasis are the principal cause of morbidity and mortality from breast cancer. The exact process by which this occurs is complex. We have identified novel genes that can regulate the resistance andrecurrence in ER+ breast cancer. In addition, next generation sequencing studies have documented that only 2% of the RNAs (coding RNAs) are converted into proteins. The remainder (non-coding) RNAs contribute significantly to regulation of the coding RNAs. A recent study showed that a long non coding RNA (Transcription regulatory RNA, TreRNA) was elevated in the lymph node metastases when compared to the primary breast cancers. Moreover, modulation of the levels of this RNA in experimental conditions resulted in corresponding alterations in the incidence of lymph node and lung metastases. In this proposal, we will study the mechanistic role of non-coding RNA in the regulation of metastasis suppression as well as novel genes such as ESRPl and ESRP2. The overarching goal of these project is to understand the mechanisms of recurrence and resistance to endocrine therapy, mainly, tamoxifen, and develop novel strategies to prevent recurrence and metastasis in ER+ breast cancer. Completion of these studies will reveal the druggable utility ofthese novel identified targets in an effort to improve the response to endocrine therapy. At the end of study, we further develop new algorithms to identify genes that undergo alternative splicing due to the regulation of the validated splicing factors ESRPl, and ESRP2. Prevention of recurrence/metastasis development should be the primary method of controlling the morbidity and mortality in breast cancer since metastatic breast cancer is incurable. This proposal seeks to identify the root cause of metastasis development by identifying master regulators responsible for the expression of metastatic phenotype.