Susan G. Komen
Research Grants – Fiscal Year 2014

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Epigenetic memory of breast cancer treatment-induced inflammation and fatigue

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Lead Organization: Emory University
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Public Abstract:
During treatment for breast cancer, as many as 70% of women suffer from cancer related fatigue (CRF) and up to 30% note moderate to severe CRF several months to years after completing treatment. The treatments for CRF have not been effective primarily due to a poor understanding of the biology, psychology, and social causes underlying this complex symptom. Increasing data suggest that CRF is associated with inflammation, the biological response to agents like chemotherapy which can injure normal tissues. We have demonstrated that high levels of inflammatory proteins circulating through the body can enter the brain and alter neural circuits leading to symptoms of fatigue. Both breast cancer patients who develop CRF during treatment and survivors of breast cancer with persistent CRF exhibit elevated inflammatory proteins including soluble TNF receptor 2 and interleukin-6 compared to non-fatigued patients. Recently, we have shown that breast cancer patients treated with chemotherapy experience significantly more inflammation and CRF than non-chemotherapy-treated subjects, suggesting that inflammation caused by chemotherapy may play an important role in CRF. Nevertheless, a crucial unanswered question is how does inflammation persist into survivorship and influence fatigue symptoms months to years after treatment? Our preliminary data from a cross-sectional study indicate that one possible mechanism may involve epigenetic changes, which are DNA changes that alter the activity of genes but do not involve a change in the DNA sequence itself. The epigenetic changes we found within circulating non-cancerous immune cells appear to regulate the inflammatory response as a consequence of chemotherapy and potentially other treatments [e.g. surgery, radiotherapy and endocrine therapy]. We propose to conduct a prospective, longitudinal study to determine how specific treatments lead to persistent inflammation and ultimately to CRF in breast cancer patients tracked from diagnosis through chemotherapy, surgery, and up to one year following radiation with or without endocrine therapy. In Aim 1, we will identify breast cancer treatment-related epigenetic changes. In Aim 2, we will evaluate the relationship among specific breast cancer treatments, epigenetic changes, inflammation and fatigue taking into account treatment, tumor and patient characteristics that may contribute to persistent inflammation and CRF. We hypothesize that there is a genetic 'memory' of prior chemotherapy that persists long after initial exposure that contributes to a chronic inflammatory state that is associated with CRF. The results gained from the proposed study will serve as the basis for future therapeutic trials aimed at preventing or reversing cancer treatment-induced epigenetic changes that have the potential to permanently activate inflammatory pathways relevant to both acute and long-term, persistent CRF.