



**Susan G. Komen**

**Research Grants – Fiscal Year 2015**

This research grant was approved for FY2015 Research Programs funding. This grant will be funded upon the execution of grant agreements between Komen and the grantee institutions.

**Delineation and mutational analysis of open chromatin regions in breast cancer**

**Investigator(s):** Trevor Pugh, Ph.D.

**Lead Organization:** University Health Network - Toronto

**Grant Mechanism:** CCR Basic and Translational

**Grant ID:** CCR15332792

---

**Public Abstract:**

The most common subtypes of breast cancer, estrogen receptor positive luminal A & B, are often treated with chemotherapy and few personalized treatments are available for these tumors. Expanded whole genome sequencing has yielded thousands of additional mutation cells in breast cancer, creating a major interpretive challenge as the relevance of mutations outside of well-studied protein coding genes remains unknown. We seek to build our knowledge of understudied mutations that dysregulate gene expression and may drive luminal subtype breast cancers. We will do this by examining what portion of the breast cancer genome is actively participating in gene regulation in 30 tumors, and then screening these regulatory regions for abnormal mutations in 150 breast tumors. We expect that these mutations will cluster in common regions across the tumors and that they will implicate specific genes not before implicated in luminal breast cancers. To test whether these mutations truly change gene regulation, we will then assess gene expression profiles across a subset of 120 tumors and look for altered expression levels between tumors that have functional mutations versus those that do not. This research will not only improve our understanding of genetic alterations underlying breast cancer but will also help scientists interpret similar regulatory mutations in other tumor types.

