



**Susan G. Komen
Research Grants – Fiscal Year 2014**

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Breast cancer risk assessment using copy number variation

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Lead Organization: Baylor College of Medicine

Grant Mechanism: KS

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Public Abstract:

Estrogen receptor-negative (ER-), early stage breast cancer (ESBC) patients show marked clinical heterogeneity with regard to outcomes. Further, there have been no major advances in improving prognostication or prediction over the last decade. The primary goal of this project is to validate, and if necessary, refine our prognostic CNI model for ER-/ESBC. The overarching hypothesis of our study is that inclusion of information tumor genetics will improve risk prediction model for individual ER-, LN +, or high grade patients for recurrence, distant metastasis, treatment response, and overall survival. Secondly, we hypothesize that the pattern of genetic mutations will differ by epidemiological factors (race/ethnicity, age of onset, screening behaviors) providing important public health information. Three specific aims encompass the validation and refinement of prognostic/predictive models based on somatic events for ER- or LN + or high grade disease considering population structure. In aim 1, we will validate our current model as a fixed model in three independent sample sets for prognostication. In aim 2, we will take advantage of advanced methods for variable selection to evaluate whether or not we can improve model accuracy by considering interactions between somatic events and clinical factors. In aim 3, we will conduct comparative analyses of the models to assess overlap in information content, prognostic accuracy. We will explore the models for the ability to predict response to contemporary treatment with and without inclusion of HER2+ cancers including taxanes and HER2-targeted therapy. We will also partner with Dr. Fraser Symmans to incorporate the RCB score into our analysis to determine if the RCB score improves our risk prediction model.

The primary translational goal of this project is to validate and refine our prognostic CNI model for ER-/ESBC to reflect current therapeutic protocols. A second translational goal is to assess the performance of our CNI prognostic model(s) in predicting treatment response. Importantly, we propose novel methods for variable selection that allow consideration of the joint effects of somatic events, epidemiologic factors, and treatment on patient outcomes that can be generalized to other marker discovery efforts.

This project will address an important unmet clinical need to further improve the accuracy of relapse.