



**Application number/Title:** 42130- Genetic determinants of breast cancer prognosis and aggressivity - a phenome-wide association study

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**Keywords provided by the Applicant PI to describe the research project:**

Breast cancer, GWAS, aggressivity, heritability, pleiotropy, prognosis

**Application Lay Summary:**

**Background & Scientific Rationale:** Breast cancer is the most commonly diagnosed cancer in women and the second leading cause of cancer death in women. Although mortality of breast cancer in Western countries is low compared to other types of cancer, understanding the processes that govern survival and disease aggressivity is important to identify patients at risk of dying and to identify novel treatment options. Among the established factors that govern survival are age at diagnosis, type of breast cancer (histological classification based on proteins present on the tumor cells), grade of the cancer (i.e. the extend and spread of cancer cells) and treatment. However, little is known if inherited genetic factors can influence disease prognosis. Recent large association studies have reported conflicting results on the contribution of common variants to survival and aggressivity, although a genetic effect has been implicated by previous familial studies. In order to further our understanding of the genetics of breast cancer prognosis, additional studies are necessary to identify potential confounding factors that might impede assessment of the genetic factors involved.

**Aims:** This proposal has three main aims. First, the total measurable genetic contribution to breast cancer prognosis and aggressivity will be computed. By adjusting the analysis for known and novel confounding factors, we can identify variables that might have prevented previous studies from detecting significant associations. Second, the role of common genetic variants on multiple traits will be investigated in order to identify unique as well as shared genetic factors involved in breast cancer prognosis and aggressivity. Finally, the overall genetic overlap between different measures of breast cancer prognosis and aggressivity will be elucidated to shed light on the genetic architecture of breast cancer.

Project Duration: Around 2 years from the time we have received the data.

Public Health Impact: The identification of genetic markers that correlate with breast cancer prognosis, survival and aggressivity potentially has direct implications for future studies. For instance, the genetic markers can prove useful to identify patients at risk for early death after breast cancer diagnosis. Furthermore, the identified genetic variants point towards genes and pathways involved in breast cancer prognosis, which are potential candidates for novel treatment options. Understanding the genetic architecture of breast cancer prognosis is therefore important to reduce the individual as well as socio-economic burden of breast cancer.