# THE CORRELATION BETWEEN THE MUTATION OF PROTEIN KINASE GENES AND THE CLINICAL CHARACTERISTICS OF BREAST CANCER PROGRESSION

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It is accepted that breast cancer (BC) is a heterogeneous disease. In order to investigate BC as a group of disease sub-types, the varying clinical characteristics of BC patients must be considered. In this project a series of clinical, pathological, genetic and genomic data, retrieved from multiple data repositories, will be reviewed for selection in a large-scale meta-analysis and then categorised into 5 sub-groups (Luminal A, Luminal B, Basal, HER2 and Normal). The meta-analysis is primarily designed to ascertain if a correlation exists between the mutation of protein kinase (PK) genes and BC progression. As PK genes play important roles in regulating most cellular processes (e.g. cell proliferation, differentiation and apoptosis), it is no surprise that deregulated PK activity is a frequent cause of disease, and that PK genes are often oncogenes.

The meta-analysis objectives are two-fold:
1. To conduct an integrative meta-analysis of the differential gene expression of the PK gene family between clinical categories of BC progression (low vs high proliferation; luminal vs basal tissue; and grade 1 vs grade 3 tumours). Results from the meta-analysis will generate a ranked list of PK gene expression profiles observed in BC progression.

2. Through the use of powerful bioinformatics tools and sequence analysis interfaces the ranked PK list will be used to direct investigations into the correlations between: codon usage bias; aberrant epigenetic factors; somatic mutations; and observed structural/functional changes of deregulated PK genes in different BC progression categories.

To address these objectives a series of *in silico* bioinformatics experiments have been designed. A software program (MYGEO) has been specifically written for: multiple dataset download; calculation of p-values between BC progression groups; finding Q-values to control for the false discovery rate over multiple dataset comparisons; and to perform permutation testing on the ranked PK gene list; and 2D/3D sequence analysis functions for the analysis of structure/function relationships in significantly differentiated PK genes in BC progression.

This project will benefit our understanding of the complex system of BC biology by identifying significantly deregulated PK genes in BC progression. The results will identify BC biomarkers and structural/functional locations within PK genes not yet elucidated, thus providing new directions for the development of PK inhibitors and improving the effectiveness of current BC treatment strategies.