BRCA1 Study

Cohort 1- WBC

30 BRCA1 mutant
with cancer (n=15)
no cancer (n=15)

30 BRCA1 wild type
with cancer (n=15)
no cancer (n=15)

Cohort 2- WBC

42 BRCA1 mutant
with cancer (n=35)
no cancer (n=7)

42 BRCA1 wild type
with cancer (n=0)
no cancer (n=42)

Multivariate Regression
Adjusted for cancer presence, age and cohort

2514 CpG probes (fdr ≤ 0.3) differentially methylated between BRCA1 mutants and BRCA1 wild types

Ensemble Signature Identification Using Elastic Net

100 training and test set partitions of 72 BRCA1 mutants and 72 BRCA1 wild types

Stacked Generalization

Identified a single signature comprising of 1829 CpGs

Tested in

NSHD

Buccal

Inv. BC¹ (n=19)
Inv. other cancers¹ (n=27)
Healthy controls (n=77)

WBC

Inv. BC¹ (n=19)
Inv. other cancers¹ (n=27)
Healthy controls (n=77)

UKCTOCS

Serum DNA

Inv. ER+ BC² (n=119)
Healthy controls (n=122)

¹ samples collected, on average 4.75 years, prior to cancer diagnosis

² samples collected, on average 2 years, prior to cancer diagnosis