

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 ($\text{fdr} \leq 0.3$) 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)

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

UKCTOCS

Serum DNA

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

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