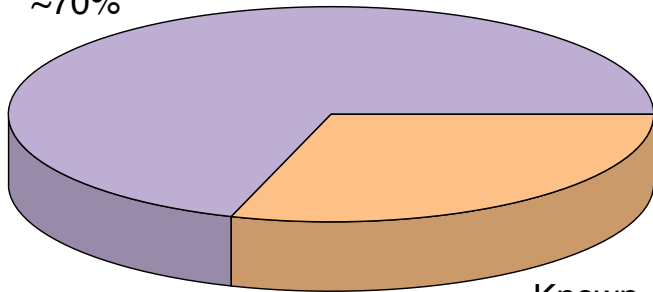


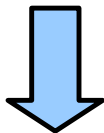
Familial Breast Cancer

No Known
Risk Genes
~70%

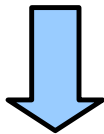


Known
Risk Genes
~30%

Exome-wide
DNA Variation



Impaired
Biological
Processes

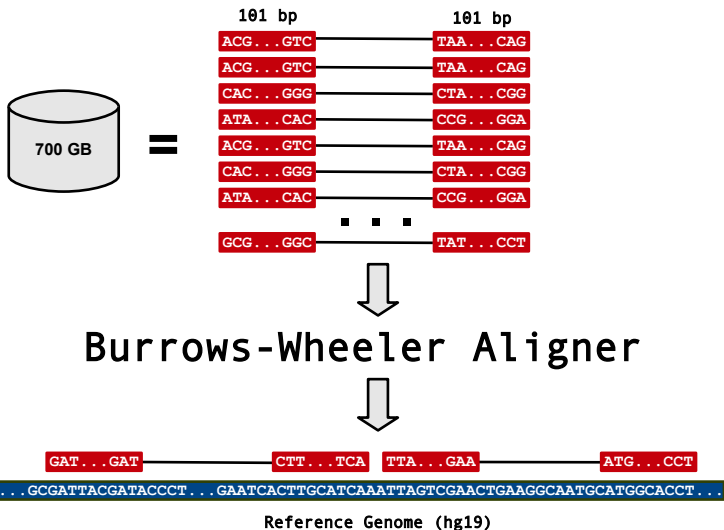


Disease

Next Generation Sequencing



Read Mapping



Variant Calling



Single-Nucleotide Variant (SNV)

GATGACCCGGCCTTATGCAACTAGAT
GATGACCCGGCCATATGCAACTAGAT

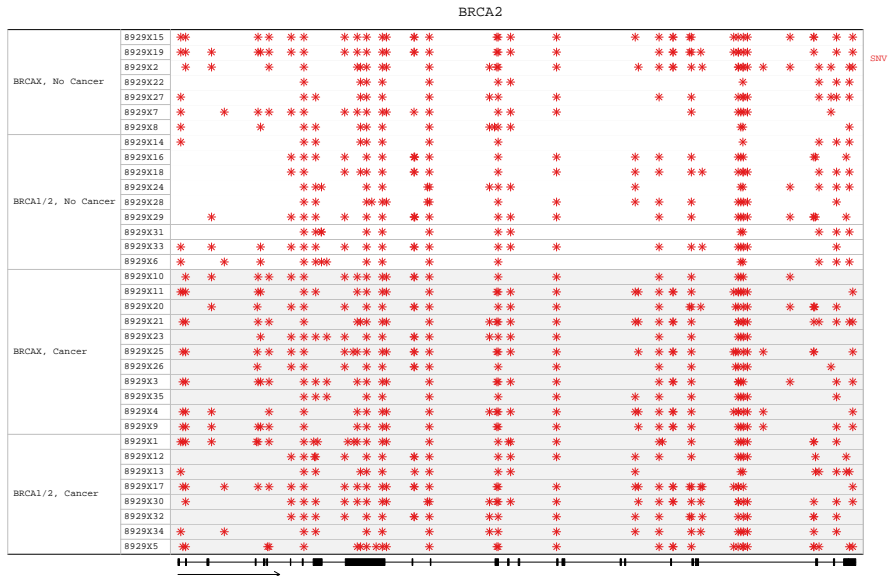
Insertion Variant

TATGACCCGGCCTTATACGCAACTAGAT
TATGACCCGGCCATAT---GCAACTAGAT

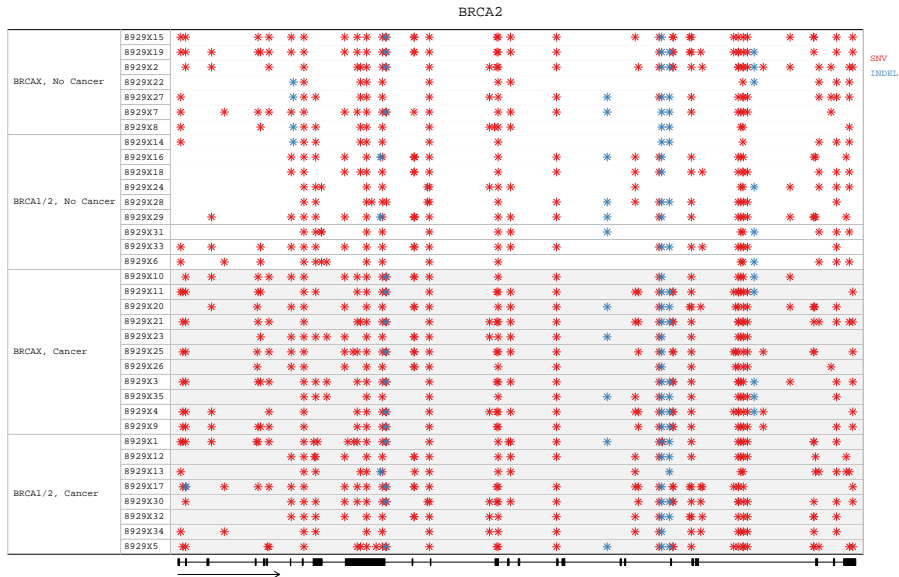
Deletion Variant

GATTAT---ACCCGGCCTTATGCAACTAGAT
GATTATGACCCGGCCATATGCAACTAGAT

Single Nucleotide Variants - Initial Set



SNVs and Indels - Initial Set



Publicly Available Resources

1000 Genomes

A Deep Catalog of Human Genetic Variation

[Home](#)

[About](#)

[Data](#)

[Analysis](#)

[Participants](#)

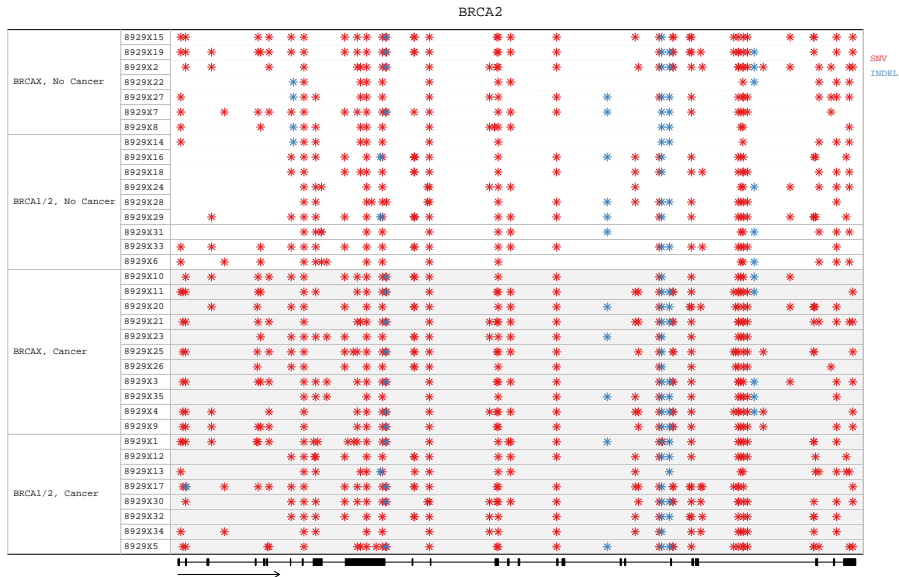
[Contact](#)

[Browser](#)

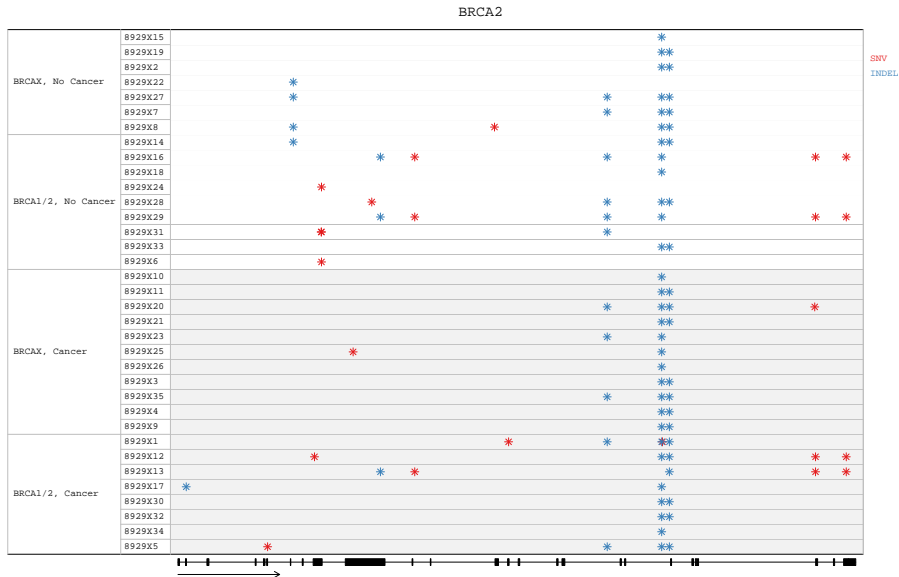


**NHLBI Grand Opportunity Exome Sequencing
Project (ESP)**


SNVs and Indels - Initial Set




Minus 1000 Genomes and ESP Common Variants



The Cancer Genome Atlas (TCGA)

 National Cancer Institute

National Human Genome Research Institute 

The Cancer Genome Atlas Data Portal

Understanding genomics
to improve cancer care

TCGA Home | Contact Us | For the Media

Home | Query the Data | **Download Data** | Tools | About the Data | Publication Guidelines

Home > Download Data > Data Matrix

Data Matrix

Select initial matrix filter settings. To view all data, click [here](#) or click "Apply" without choosing any settings. (Note: unfiltered matrix is large and can take some time to load.)

Filter Settings

Select a disease: BRCA – Breast invasive carcinoma

Data Type:

All
Clinical
DNA Methylation
Expression–Genes

Batch Number:

All
Batch 0
Batch 47
Batch 56

Data Level:

☐ Level 1
☐ Level 2
☐ Level 3

Center/Platform:

All
BCGSC (IlluminaGA_miRNASeq)
BCGSC (IlluminaHiSeq_miRNASeq)
BI (Genome_Wide_SNP_6)

Sample:
ID Matches:

TCGA- --

--

[Remove](#)
[Add Row](#)


Access Tier:

☒ All
☐ Protected
☐ Public


Tumor/Normal:

☐ Tumor - matched
☐ Tumor - unmatched
☐ Normal - matched
☐ Normal - unmatched

Submitted Since (Date):

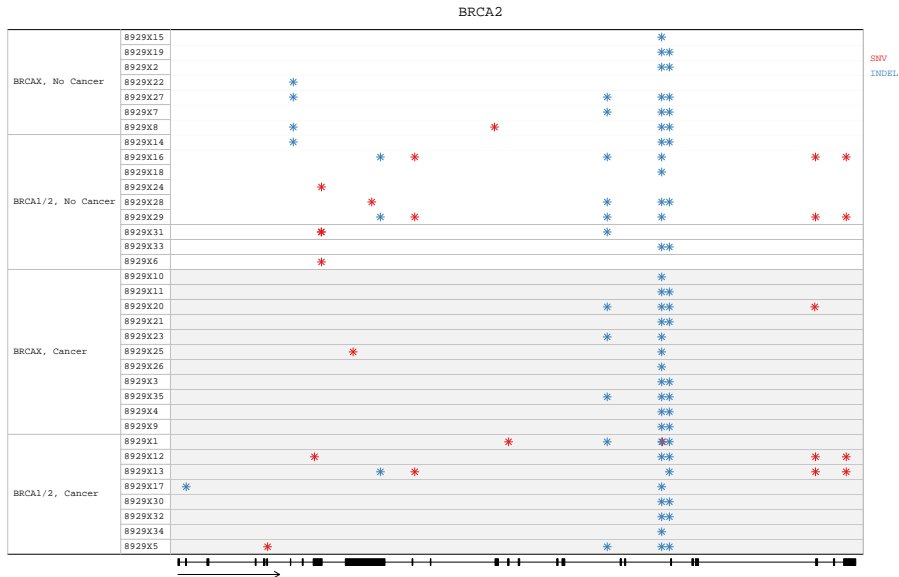


Submitted Up To (Date):

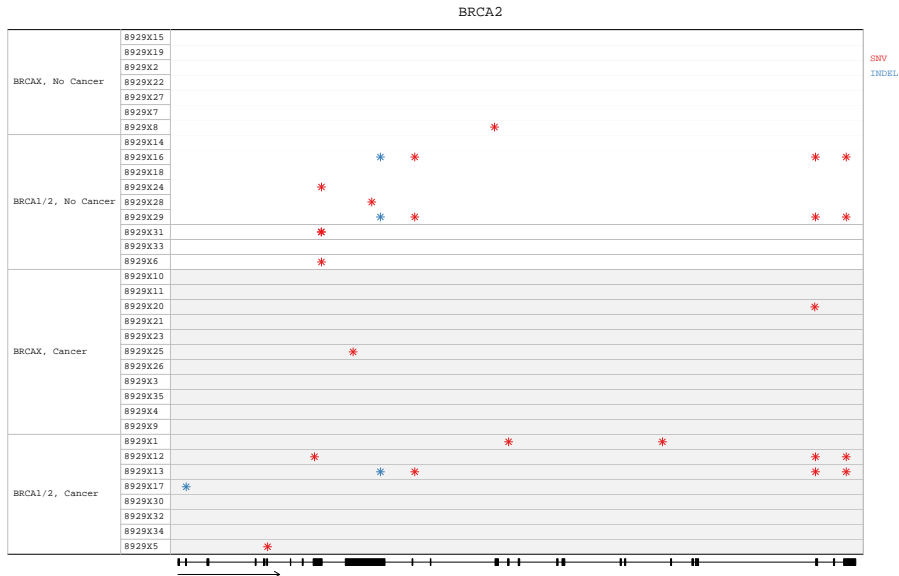


1 / 1024

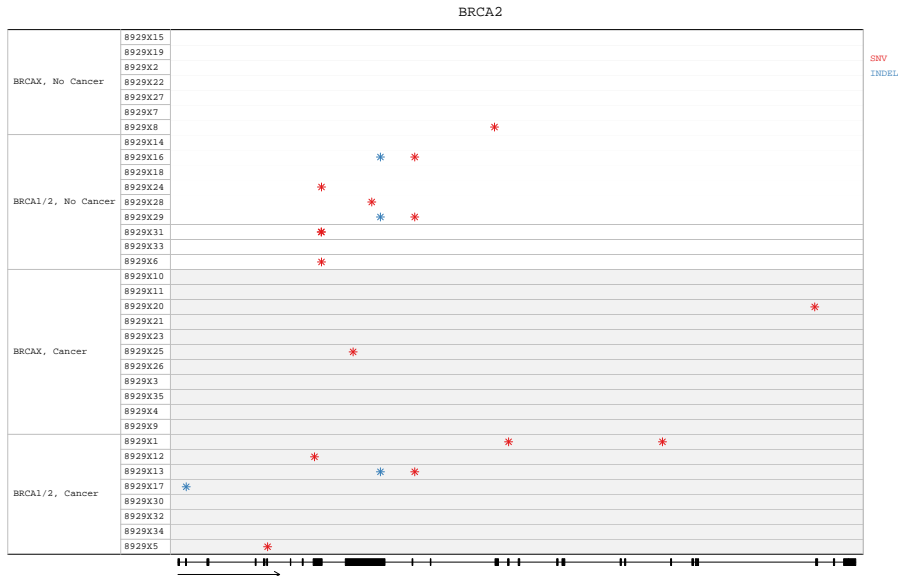
Before



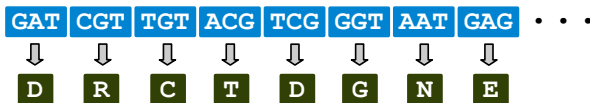
Minus TCGA Common Variants



Minus “Internal” Common Variants



Reference



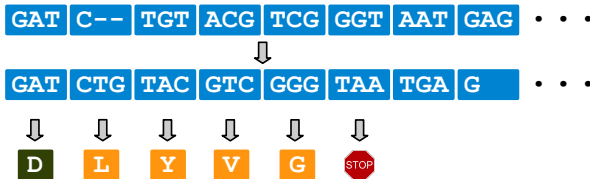
Non-Synonymous
Variant



Stop Gained



Frameshift





PolyPhen-2 prediction of functional effects of human nsSNPs

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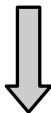
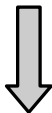
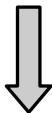
Downloads

Batch query



mutationassessor.org

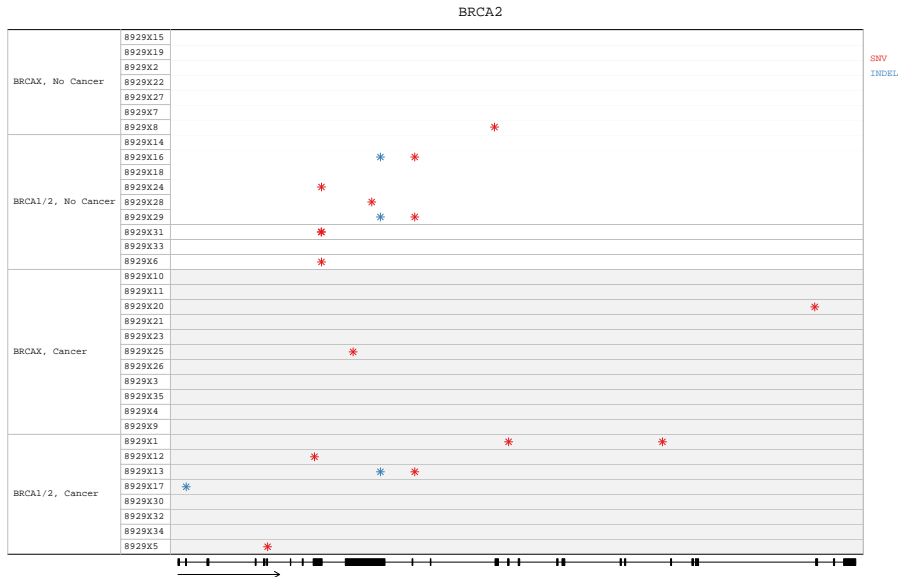
functional impact of protein mutations
release **2**



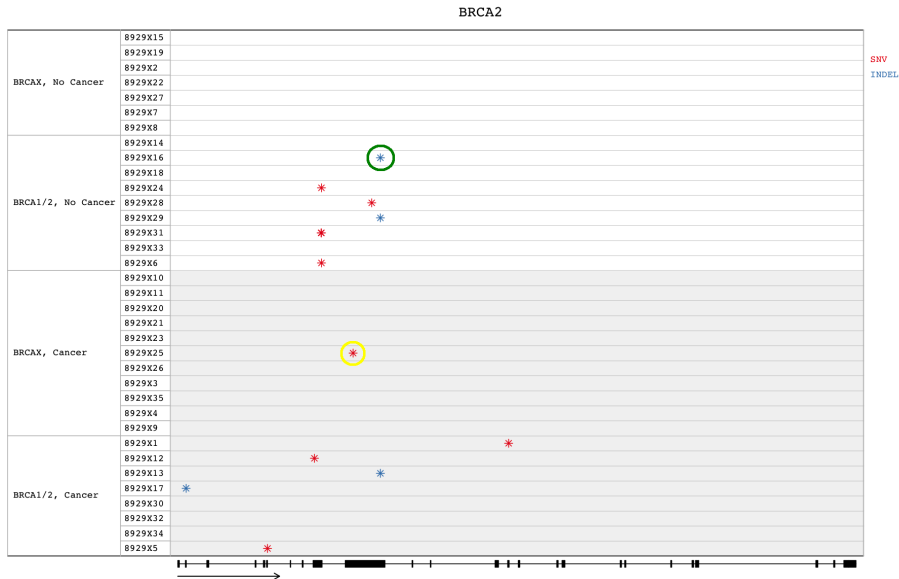
Condel

CONsensus DELeteriousness score of missense SNVs

Before



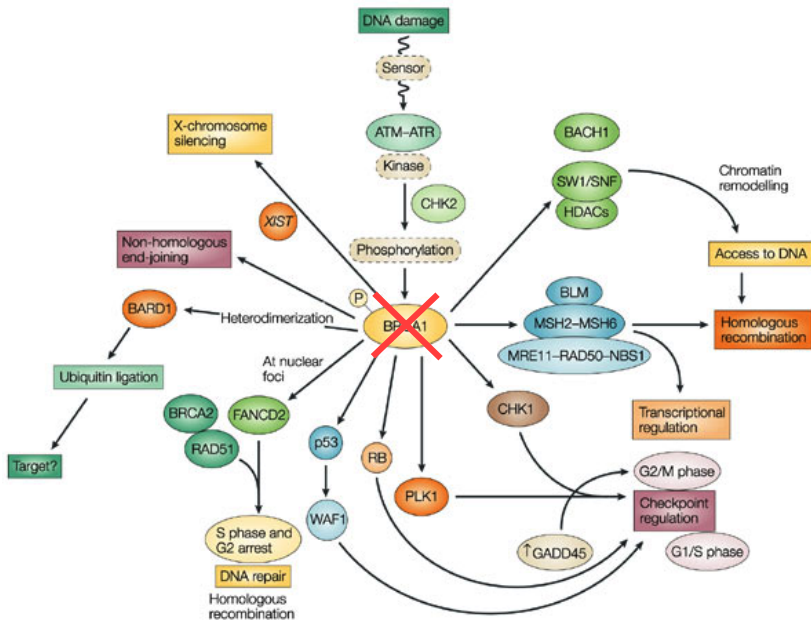
Final Variants

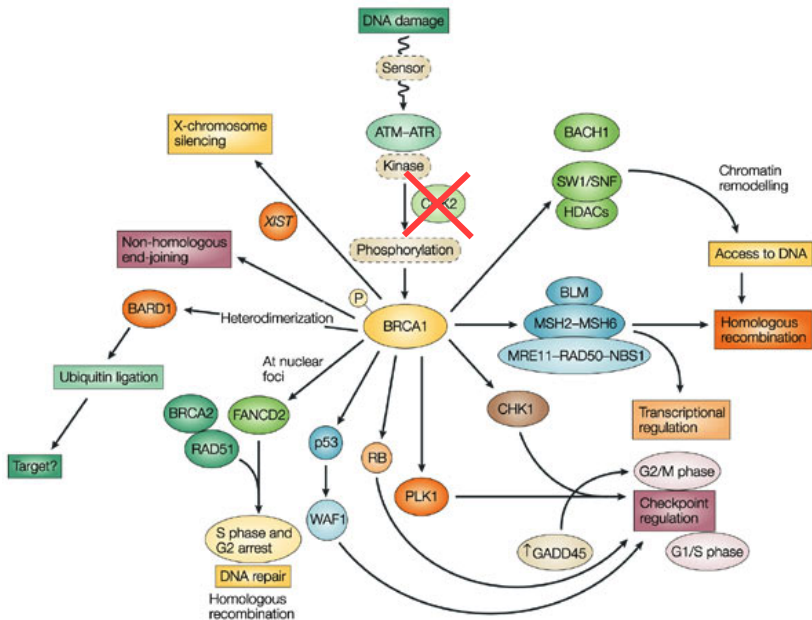


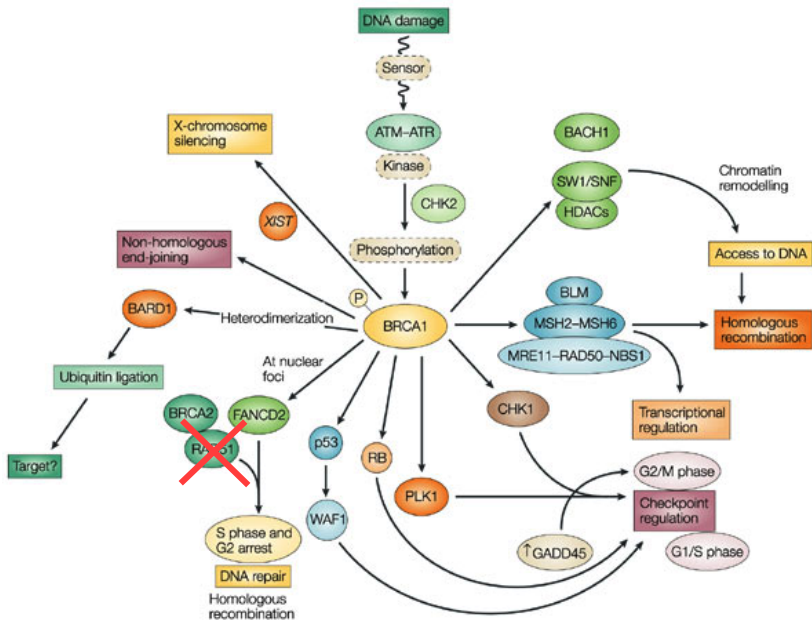
Final Variant Count

2822 variants (80.6 per sample)

2089 genes (1.35 variants per gene)



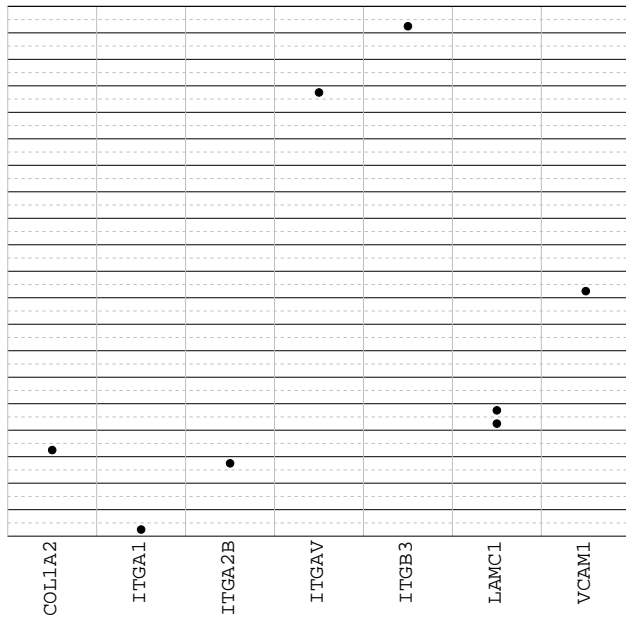




Integrin cell-surface interactions

BRCA1/2 No Cancer	8929X15								
	8929X19								
	8929X2								
	8929X22								
	8929X27								
	8929X7								
	8929X8							*	*
BRCA1/2 No Cancer	8929X14								
	8929X16								
	8929X18								
	8929X24								
	8929X28								
	8929X29								
	8929X31								
	8929X33								
BRCA1/2 Cancer	8929X6						*		
	8929X10								
	8929X11					*			
	8929X20								
	8929X21	*							
	8929X23								
	8929X25								
	8929X26			*					
	8929X3					*			
	8929X35								
	8929X4								
BRCA1/2 Cancer	8929X9								
	8929X1								
	8929X12						*		
	8929X13								
	8929X17								
	8929X30		*						
	8929X32			*	*				
	8929X34								*
	8929X5								
		COL1A1	COL1A2	FGF	ICAM3	ITGA4	ITGA7	APGFF4	TLN1

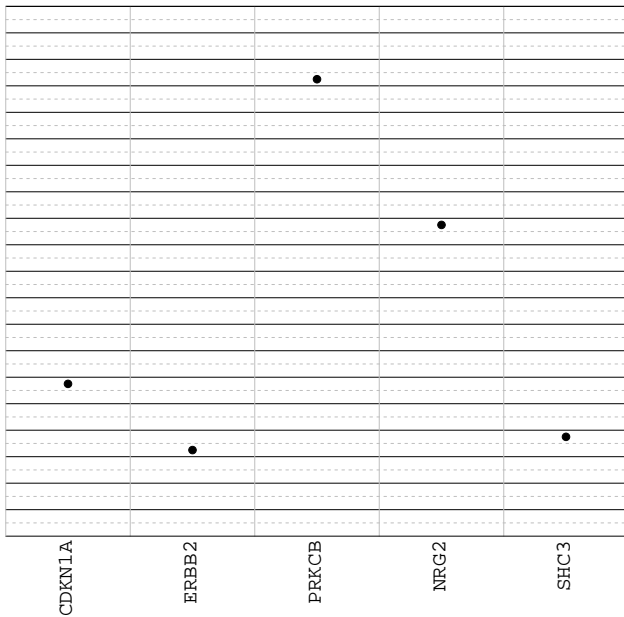
Integrin cell-surface interactions



ERBB Signaling Pathway

BRCA1/2 No Cancer	8929X15								
	8929X19								
	8929X2								
	8929X22								
	8929X27								
	8929X7							*	*
BRCA1/2 No Cancer	8929X8								
	8929X14								
	8929X16								
	8929X18								
	8929X24								
	8929X28								
BRCA1/2 No Cancer	8929X29						*		
	8929X31								
	8929X33								
	8929X6								
BRCA1/2 Cancer	8929X10					*			
	8929X11								
	8929X20						*		
	8929X21								
	8929X23								
	8929X25								
BRCA1/2 Cancer	8929X26								
	8929X3								
	8929X35			*					
	8929X4								
	8929X9					*			
	8929X1				*				
BRCA1/2 Cancer	8929X12								
	8929X13								
	8929X17								
	8929X30								
	8929X32								
	8929X34	*							
BRCA1/2 Cancer	8929X5		*						
		ARAF	ERBB2	NRG2	NRG3	PIK3CA	PIK3R5	SHC3	STAT5A

ERBB Signaling Pathway



Top Pathway Results

Pathway	AUC	Controls Mutated	Cancer Mutated
Integrin cell surface interactions	0.687	3/16	9/19
Cell adhesion molecules	0.682	2/16	8/19
PI3K Signaling System	0.676	4/16	10/19
Citrate/Krebs cycle	0.678	0/16	7/19
Fructose and mannose metabolism	0.668	1/16	7/19
ERBB signaling pathway	0.658	3/16	7/19

Pathways that performed well in both analyses
are known to play a role in tumor development!