

# SUPPLEMENTARY INFORMATION

Wang *et al.* 2014

## SUPPLEMENTARY TABLES

### Supplementary Table 1 | Spectral Karyotyping Data for 50 Single SK-BR-3 Cells

This table lists the genomic rearrangements that were detected in each single SK-BR-3 cell by Spectral Karyotyping. Rearrangements that were detected in a single cell are indicated by 1, while blank fields indicate that no rearrangements were detected. The frequencies of each rearrangement across all cells are shown in the bottom row.

### Supplementary Table 2 | Variants Detected in the SK-BR-3 Population Sample After Database Filtering

Table 2.1 - SNVs in Cancer Genes

Table 2.2 - Copy Number Aberrations in Cancer Genes

Table 2.3 - Structural Variations in Cancer Genes

Single nucleotide variants were detected in the SK-BR-3 population sample and filtered using 1000 genomes and dbSNP135 databases. Variants and copy number changes that intersect with regions of cancer genes are reported. Column descriptions are: *REF* (reference allele), *MUT* (mutated allele), *COSMIC* (variant occurs at a mutation site reported in the *COSMIC* database), *CANCER* (mutation occurs in a region of a known cancer gene), *Polyphen* (Polyphen conservation score was annotated), *SIFT* (SIFT conservation score is reported), *Nucleotide* (nucleotide mutation change), *Amino Acid* (amino acid change caused by the mutation), *ORI* (strand orientation) and *SV* (structural variant type: *CTX* – interchromosomal translocation, *ITX* – intrachromosomal translocation, *DEL* – chromosomal deletion).

### Supplementary Table 3 | Somatic Mutations Detected by Sequencing Populations of ER Tumor Cells

Nonsynonymous mutations detected in the ER breast tumor cell population. Column descriptions are: *type* (mutation classification), *COSMIC* (cosmic database), *Cancer* (cancer gene), *TCGA* (frequency in TCGA breast cancer cohort), *Nucleotide* (nucleotide substitution caused by the mutation), *Amino Acid* (amino acid change caused by the mutation).

### Supplementary Table 4 | ER Subclonal Mutations Detected by Whole Genome Single Nuclei Sequencing

Somatic mutations detected in 2 or more single tumor cells and not detected in the population of tumor sample. The column descriptions are: *REF* (reference allele), *VAR* (variant allele), *position* (genomic coordinate).

### **Supplementary Table 5 | Single Nuclei Sequencing Coverage Metrics**

Table 5.1 – ER Single Nuclei Sequencing Coverage Metrics

Table 5.2 – TNBC Single Nuclei Sequencing Metrics

Column descriptions are: *capture* (whole-genome or exome capture experiment), *cov\_depth* (coverage depth); *cov\_breadth* (coverage breadth). Both depth and breadth were calculated using uniquely mapped sequence reads.

### **Supplementary Table 6 | Clonal Nonsynonymous TNBC Mutations Detected by Population Sequencing**

Nonsynonymous point mutations detected by sequencing populations of cells from the triple-negative breast tumor. Mutations were validated by targeted duplex sequencing and the frequencies are reported along with p-values. Column descriptions are: *class* (mutation classification), *chrom* (chromosome), *pos* (nucleotide position), *type* (mutation), *REF* (reference allele), *VAR* (variant allele), *COSMIC* (cosmic database), *CANCER* (cancer gene database), *POLY* (polyphen2 score), *SIFT* (sift prediction score), *Genbank* (genbank identifier), *nucleotide* (mutated nucleotide position within the gene), *amino acid* (mutated amino acid change position within the gene), *duplex\_freq* (mutation frequency determined by targeted duplex sequencing), *duplex\_P\_val* (duplex p-value).

### **Supplementary Table 7 | Subclonal Nonsynonymous TNBC Mutations Detected by Single Nuclei Exome Sequencing**

Subclonal nonsynonymous mutations detected in two or more single cells, but not in the population sample. The subclonal mutations were validated by duplex targeted deep sequencing of the bulk tumor samples and the resulting mutation frequencies are displayed, along with the p-values. Column descriptions: *class* (mutation classification), *cells* (number of single cells with the mutations); *chrom* (chromosome), *pos* (nucleotide position), *REF* (reference allele), *VAR* (variant allele), *zygosity* (heterozygous or homozygous), *COSMIC* (cosmic database), *type* (mutation class), *CANCER* (cancer gene database), *POLY* (polyphen2 score), *SIFT* (sift prediction score), *Genbank* (genbank identifier), *exon* (exon number), *nucleotide* (mutated nucleotide position within the gene), *amino acid* (mutated amino acid change position within the gene), *Duplex\_Freq* (duplex mutation frequency) and *Duplex\_P\_val* (duplex p-value).

### **Supplementary Table 8 – Mathematical Modeling of Mutation Rates from Single Cell Mutation Frequency Data**

Table 8.1 – ER single nuclei whole genome data

Table 8.2 – ER single nuclei exome mutation data

Table 8.3 – TNBC single nuclei exome mutation data

These tables show the data from modeling mutation rates using single cell mutation frequency distributions. The simulated distributions for a series of mutation rates (MR) are generated and fit to the empirical datasets (observed). Best fit is determined by calculating the sum of square differences (SSD) and the lowest value is highlighted in yellow.

Supplementary Table 1 - Spectral Karyotype Data for 50 Single SK-BR-3 Cells

cell no.	del 1	der(1)t(1;10)	der(1)t(1;5)	t(2;6)	t(2;6;4)	del (3)	del (5)	t(13;3;8;3;8;13)	t(8;4;6;12)	de(10q)	t(3;12)	t(13;4;17;11;20)	t(9;14)	t(14;22)	t(7;16)	t(17;19;20)	t(19;22)	t(X;8)	t(1;19;11;4;8)	del(18)
1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
17	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
18	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
19	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
20	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
21	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
22	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
23	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
24	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
25	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
26	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
27	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
28	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
29	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
30	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
31	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
32	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
33	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
34	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
35	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
36	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
37	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
38	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
39	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
40	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
41	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
42	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
43	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
44	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
45	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
46	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
47	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
48	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
49	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
50	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
freq	0.9	0.82	0.9	0.88	0.82	0.76	0.74	0.96	0.8	0.98	0.98	0.94	0.82	0.82	0.9	0.9	0.76	0.82	0.8	0.86
mean.freq	0.858																			

Supplementary Table 2 - Variants Detected in the SK-BR-3 Population Sample After Database Filtering

Table 2.1 - SNVs in Cancer Genes

Single Nucleotide Variants															
chrom	start	stop	gene	description	REF	MUT	COSMIC	CANCER	Polyphen	SIFT	Type	Genbank ID	Exon	Nucleotide	Amino Acid
chr1	143642159	143642159	PDE4DIP	phosphodiesterase 4D interacting protein	T	G	NA	PDE4DIP	0.454381	0.53	nonsynonymous SNV	NM_001002811	exon1	c.A907C	p.L303L
chr1	155023172	155023172	PRCC	papillary renal cell carcinoma	C	G	NA	PRCC	0.707	0.06	nonsynonymous SNV	NM_005973	exon3	c.C665G	p.S222C
chr2	131405298	131405298	ARHGEF4	Rho guanine nucleotide exchange factor	A	G	p.K100R	NA	0.015	0	nonsynonymous SNV	NM_032995	exon3	c.A298G	p.K100E
chr2	241726813	241726813	PASK	PAS domain containing serine/threonine k	G	A	p.R224C	NA	0	0.01	nonsynonymous SNV	NM_001252119	exon5	c.C670T	p.R224C
chr7	13994257	13994257	ETV1	ets variant 1	C	A	NA	ETV1	NA	0	nonsynonymous SNV	NM_001163148	exon4	c.G112T	p.D38Y
chr8	23068382	23068382	TNFRSF10D	tumor necrosis factor receptor superfamily A	G	NA	NA	TNFRSF10D	0.005	0.79	nonsynonymous SNV	NM_003840	exon2	c.T206C	p.V69A
chr9	121051197	121051197	DBC1	deleted in breast cancer 1	C	T	NA	DBC1	0.039	0.76	nonsynonymous SNV	NM_014618	exon3	c.G271A	p.V91I
chr11	116595661	116595661	PCSK7	proprotein convertase subtilisin/kexin type C	G	NA	NA	PCSK7	0.989	0.03	nonsynonymous SNV	NM_004716	exon10	c.G1179C	p.Q393H
chr12	55400380	55400380	NACA	nascent polypeptide associated	C	T	NA	NACA	NA	NA	nonsynonymous SNV	NM_001113203	exon3	c.G1201A	p.V401I
chr15	38244647	38244647	BUB1B	budding uninhibited by benzimidazoles	C	G	NA	BUB1B	0.831	0.05	nonsynonymous SNV	NM_003467	exon2	c.C137G	p.A46G
chr16	67413591	67413591	CDH1	ecadherin	G	A	NA	CDH1	0.093	0.58	nonsynonymous SNV	NM_004360	exon12	c.G1898A	p.G633E
chr17	56832330	56832330	TBX2	t-box2	C	T	NA	TBX2	NA	NA	nonsynonymous SNV	NM_005994	exon1	c.C11T	p.P4L
chr17	73006273	73006273	SEPT9	septin9	G	A	NA	41161	NA	NA	nonsynonymous SNV	NM_001113491	exon12	c.G1699A	p.E567K
chr22	21986180	21986180	BCR	breakpoint cluster region	G	C	NA	BCR	0.981	0.12	nonsynonymous SNV	NM_021574	exon20	c.G3351C	p.E1117D

Table 2.2 - Copy Number Aberrations in Cancer Genes

COPY NUMBER CHANGES														
chrom	start	stop	gene	description	REF	MUT	COSMIC	CANCER	Polyphen	SIFT	Type	Genbank ID	Exon	CNV Size
chr7	113,553,429	128,201,868	MET	met proto-oncogene (hepatocyte growth f	NA	NA	NA	MET	NA	NA	amplification	NM_001127500	14,648,439	
chr8	80,441,105	82,047,515	TPD52	tumor protein D52	NA	NA	NA	TPD52	NA	NA	amplification	NM_001025252	1,606,410	
chr8	127,944,325	129,238,921	MYC	v-myc myelocytomatosis viral oncogene h	NA	NA	NA	MYC	NA	NA	amplification	NM_002467	1,294,596	
chr17	34,638,124	35,687,866	ERBB2	v-erb-b2 erythroblastic leukemia viral on	NA	NA	NA	ERBB2	NA	NA	amplification	NM_004448	1,049,742	
chr18	47,268,041	49,556,651	DCC	deleted in colorectal carcinoma	NA	NA	NA	DCC	NA	NA	deletion	NM_005215	2,288,610	
chr20	51,237,627	52,752,534	BCAS1	breast carcinoma amplified sequence 1	NA	NA	NA	BCAS1	NA	NA	amplification	NM_003657	1,514,907	

Table 2.3 - Structural Variations in Cancer Genes

chromA	posA	ori	chromB	posB	ori	SV	size	gene1	locA	gene2	locB
chr3	59869602	-	chr4	11848375	-	CTX	na	FHIT	intron	BC042433	intron
chr1	168918112	+	chr5	115026581	-	CTX	na	PRRX1	intron	na	intergenic
chr5	170412592	-	chr4	141158386	+	CTX	na	RANBP17	intron	MAML3	intron
chr7	81839816	-	chr10	72863536	-	CTX	na	CACNA2D1	intron	CDH23	intron
chr7	81839816	-	chr10	123218964	-	CTX	na	CACNA2D1	intron	na	intergenic
chr1	6123615	-	chr12	7724218	-	CTX	na	CHD5	intron	na	intergenic
chr14	68028531	+	chr15	45493129	+	CTX	na	RAD51L1	intron	SEMA6D	intron
chr17	56206424	+	chr1	107732321	+	CTX	na	BCAS3	intron	NTNG1	intron
chr11	84872659	-	chr17	30502226	-	CTX	na	DLG2	intron	UNC45B	intron
chr17	56234250	+	chr3	63679167	-	CTX	na	BCAS3	intron	na	intergenic
chr17	35727911	+	chr8	79637981	-	CTX	na	RARA	intron	PKIA	intron
chr17	56642484	-	chr20	58278795	-	CTX	na	BCAS3	intron	AX747739	intron
chr9	96951143	+	chr11	92515396	-	CTX	na	FANCC	intron	na	intergenic
chr3	25449788	-	chr3	25449791	+	ITX	na	RARB	intron	RARB	intron
chr3	79619024	-	chr3	79619042	+	ITX	na	ROBO1	intron	ROBO1	intron
chr3	189858605	-	chr3	189858642	+	ITX	na	LPP	intron	LAPP	intron
chr5	170759914	-	chr5	170759937	+	ITX	na	NPM1	intron	NPM1	intron
chr10	22066099	-	chr10	22066109	+	ITX	na	MLLT10	intron	MLLT10	intron
chr11	83193271	-	chr11	83193309	+	ITX	na	DLG2	intron	DLG2	intron
chr12	52655935	-	chr12	52655937	+	ITX	na	HOXC11	3'UTR	HOXC11	3'UTR
chr14	80546962	-	chr14	104052296	+	ITX	na	TSHR	intron	na	intergenic
chr17	38477065	-	chr17	38477068	+	ITX	na	BRCA1	intron	BRCA1	intron
chr17	57161153	-	chr17	57161170	+	ITX	na	BRIP1	intron	BRIP1	intron
chr19	59304916	-	chr19	59305075	+	ITX	na	TFPT	intron	TFPT	3'UTR
chr20	9496835	-	chr20	33318447	+	ITX	na	PAK7	intron	MMP24	exon
chr21	35317063	-	chr21	35317089	+	ITX	na	RUNX1	intron	RUNX1	intron
chr21	41764584	-	chr21	41764587	+	ITX	na	TMPPRS2	intron	TMPPRS2	intron
chr9	97080898	-	chr9	97080901	+	ITX	na	FANCC	intron	FANCC	intron
chr7	55107279	+	chr7	55107306	-	DEL	27	EGFR	intron	na	na
chr2	29852732	+	chr2	29852804	-	DEL	72	ALK	intron	na	na
chr21	38785760	+	chr21	38785863	-	DEL	103	ERG	intron	na	na
chr21	35217855	+	chr21	35218063	-	DEL	208	RUNX1	intron	na	na
chr9	138547346	+	chr9	138547617	-	DEL	271	NOTCH1	intron	na	na
chr7	81793863	+	chr7	81794142	-	DEL	279	CACNA2D1	intron	na	na
chr1	114845055	+	chr1	114845352	-	DEL	297	TRIM33	intron	na	na
chr14	80538881	+	chr14	80539181	-	DEL	300	TSHR	intron	na	na
chr3	189787544	+	chr3	189787859	-	DEL	315	LPP	intron	na	na
chr7	81566677	+	chr7	81567001	-	DEL	324	CACNA2D1	intron	na	na
chr8	119049954	+	chr8	119050290	-	DEL	336	EXT1	intron	na	na
chr8	31690798	+	chr8	31691137	-	DEL	339	NRG1	intron	na	na
chr11	128187927	+	chr11	128188621	-	DEL	694	FLJ1	intron	na	na
chr3	61102230	+	chr3	61103231	-	DEL	1001	FHIT	intron	na	na
chr17	53042811	+	chr17	53044914	-	DEL	2103	MSI2	intron	na	na

**Supplementary Table 3 - Somatic Mutations Detected by Sequencing Populations of ER Tumor Cells**

**Nonsynonymous SNVs**

chrom	position	gene	type	region	REF	VAR	BCN	BCT	Exome	COSMIC	CANCER	TCGA	Polyphen	SIFT	GenBank	nucleotide	Amino Acid
chr1	170277897	DNM3	nonsynonymous SNV	exon8	A	C	A	C	C	NA	NA	1%	NA	0.02	NM_015569	c.A1118C	p.E373A
chr1	246105875	TRIM58	nonsynonymous SNV	exon6	G	A	G	A	A	NA	NA	0%	0	0.06	NM_015431	c.G922A	p.A308T
chr3	113672857	BTLA	nonsynonymous SNV	exon3	C	T	C	T	T	NA	NA	0%	0.08	0.27	NM_181780	c.G439A	p.E147K
chr3	127173667	ROPN1B	nonsynonymous SNV	exon2	G	C	G	C	C	NA	NA	0%	0.999	0.01	NM_001012337	c.G80C	p.R27P
chr3	180434779	PIK3CA	nonsynonymous SNV	exon21	A	G	A	G	G	p.H1047Q	PIK3CA	34%	0.995	1	NM_006218	c.A3140G	p.H1047R
chr3	195874086	LSG1	nonsynonymous SNV	exon1	G	A	G	A	A	NA	NA	0%	0.063	0	NM_018385	c.C95T	p.S32F
chr4	185790457	CASP3	nonsynonymous SNV	exon4	T	C	T	C	C	NA	CASP3	1%	0.99	0	NM_032991	c.A266G	p.N89S
chr5	127708012	FBN2	nonsynonymous SNV	exon25	C	T	C	T	T	NA	FBN2	1%	0.998	0.03	NM_001999	c.G3307A	p.G1103S
chr10	3204939	PITRM1	nonsynonymous SNV	exon1	C	T	C	T	T	NA	NA	1%	NA	0	NM_001242307	c.G26A	p.G9D
chr11	72377664	FCHSD2	nonsynonymous SNV	exon6	C	T	C	T	T	NA	NA	0%	0.252	0.01	NM_014824	c.G514A	p.E172K
chr14	62958514	PPP2R5E	nonsynonymous SNV	exon4	C	G	C	G	G	NA	PPP2R5E	1%	0.998	0	NM_006246	c.G406C	p.D136H
chrX	27908828	DCAF8L1	nonsynonymous SNV	exon1	A	G	A	A	G	NA	NA	1%	0.243	0.02	NM_001017930	c.T545C	p.F182S

## Supplementary Table 4

ER Subclonal Mutations Detected by Whole Genome Single-Cell Sequencing

chrom	position	cells	REF	VAR	location	gene
4 cells						
chr3	117559827	4	C	T	intron	LSAMP
chr10	60254617	4	G	A	intergenic	BICC1
chr15	19306543	4	G	A	intron	POTEB
chr20	5961340	4	C	T	intron	CRLS1
chr11	315910	4	G	A	intergenic	na
3 cells						
chr8	37251228	3	C	T	intergenic	
chr14	87750052	3	T	C	intron	KCNK10
chr21	29751265	3	G	A	intergenic	na
chr19	10056229	3	A	T	intergenic	na
chr1	246588486	3	G	A	intergenic	na
chr5	90529295	3	T	G	intergenic	na
chr1	195812959	3	G	C	intron	C1orf218
chr21	45206308	3	A	G	intron	C21orf70
chr5	16144080	3	G	A	exonic	MARCH11
2 cells						
chr4	190862494	2	G	A	intergenic	na
chr8	96280719	2	C	A	intergenic	na
chr2	1948165	2	C	T	intron	MYT1L
chr5	24884256	2	G	C	intergenic	na
chrX	49747437	2	A	G	3_UTR	CLCN5
chrX	149390723	2	C	T	intron	MAMLD1
chr7	131332648	2	T	C	intergenic	na
chr5	73784959	2	A	T	intergenic	na
chr20	21832958	2	T	C	intergenic	na
chr20	21812989	2	G	A	intergenic	na
chr19	13167561	2	C	G	intergenic	na
chr15	73101337	2	G	A	intergenic	na
chr14	41732753	2	G	T	intergenic	na
chr11	67043877	2	G	A	exonic	CABP2
chr11	50390924	2	G	T	intergenic	na
chr10	13911703	2	G	A	intron	FRMD4A
chr8	52223003	2	C	T	intergenic	na
chrX	30425887	2	C	T	intergenic	na

**Supplementary Table 5.1 - ER Single Nuclei Sequencing Coverage Metrics**

Sample Origin	Sample ID	Type	capture	cov_depth	cov_breadth
tumor	cell1	single cell	whole-genome	43	73.37%
tumor	cell2	single cell	whole-genome	35	78.31%
tumor	cell3	single cell	whole-genome	49	88.98%
tumor	cell4	single cell	whole-genome	60	82.48%
			mean	46.75	80.79%
tumor	c1	single cell	exome	49	96.68%
tumor	c2	single cell	exome	56	96.82%
tumor	c3	single cell	exome	59	96.40%
tumor	c4	single cell	exome	46	96.41%
tumor	c5	single cell	exome	41	96.04%
tumor	c6	single cell	exome	39	96.23%
tumor	c7	single cell	exome	53	96.84%
tumor	c8	single cell	exome	86	97.76%
tumor	c9	single cell	exome	63	97.24%
tumor	c10	single cell	exome	57	97.07%
tumor	c11	single cell	exome	42	96.32%
tumor	c12	single cell	exome	110	96.26%
tumor	c13	single cell	exome	82	95.25%
tumor	c14	single cell	exome	92	93.76%
tumor	c15	single cell	exome	162	96.42%
tumor	c16	single cell	exome	50	92.35%
tumor	c17	single cell	exome	80	92.29%
tumor	c18	single cell	exome	31	88.17%
tumor	c19	single cell	exome	28	88.04%
tumor	c20	single cell	exome	24	86.62%
tumor	c21	single cell	exome	25	85.88%
tumor	c22	single cell	exome	44	94.95%
tumor	c23	single cell	exome	46	92.91%
tumor	c24	single cell	exome	53	96.68%
tumor	c25	single cell	exome	47	92.73%
tumor	c26	single cell	exome	34	94.04%
tumor	c27	single cell	exome	35	94.19%
tumor	c28	single cell	exome	36	93.76%
tumor	c29	single cell	exome	39	94.84%
tumor	c30	single cell	exome	38	94.36%
tumor	c31	single cell	exome	36	93.77%
tumor	c32	single cell	exome	44	94.69%
tumor	c33	single cell	exome	42	94.19%
tumor	c34	single cell	exome	38	94.03%
tumor	c35	single cell	exome	46	94.08%
tumor	c36	single cell	exome	33	90.96%
tumor	c37	single cell	exome	39	95.75%
tumor	c38	single cell	exome	43	96.08%
tumor	c39	single cell	exome	33	91.78%
tumor	c40	single cell	exome	40	95.63%
tumor	c41	single cell	exome	30	94.19%
tumor	c42	single cell	exome	32	95.13%
tumor	c43	single cell	exome	32	95.06%
tumor	c44	single cell	exome	46	93.78%
tumor	c45	single cell	exome	30	91.79%
tumor	c46	single cell	exome	35	89.05%
tumor	c47	single cell	exome	27	90.45%
normal	n1	single cell	exome	50	86.53%
normal	n2	single cell	exome	46	85.84%
normal	n3	single cell	exome	51	88.74%
normal	n4	single cell	exome	48	81.95%
normal	n5	single cell	exome	55	78.92%
normal	n6	single cell	exome	26	85.31%
normal	n7	single cell	exome	30	89.05%
normal	n8	single cell	exome	22	83.51%
normal	n9	single cell	exome	46	94.42%
normal	n10	single cell	exome	34	93.75%
normal	n11	single cell	exome	40	93.32%
normal	n12	single cell	exome	39	94.65%
			mean	46.78	93%

**Supplementary Table 5.2 - TNBC Single Cell Sequencing Coverage Metrics**

Sample Origin	Identifier	Sample	Capture	cov_depth	cov_breadth
tumor	a1	single cell	exome	56	92.7%
tumor	a2	single cell	exome	61	93.8%
tumor	a3	single cell	exome	56	93.0%
tumor	a4	single cell	exome	52	92.2%
tumor	a5	single cell	exome	42	91.4%
tumor	a6	single cell	exome	50	91.8%
tumor	a7	single cell	exome	48	92.2%
tumor	a8	single cell	exome	46	91.6%
tumor	h1	single cell	exome	43	78.8%
tumor	h2	single cell	exome	55	90.3%
tumor	h3	single cell	exome	58	90.3%
tumor	h4	single cell	exome	47	84.8%
tumor	h5	single cell	exome	50	87.1%
tumor	h6	single cell	exome	47	86.8%
tumor	h7	single cell	exome	41	84.7%
tumor	h8	single cell	exome	57	89.7%
normal	n1	single cell	exome	49	92.4%
normal	n2	single cell	exome	33	88.0%
normal	n3	single cell	exome	52	91.9%
normal	n4	single cell	exome	97	93.5%
normal	n5	single cell	exome	53	91.7%
normal	n6	single cell	exome	56	90.6%
normal	n7	single cell	exome	52	92.3%
normal	n8	single cell	exome	47	91.4%
normal	n9	single cell	exome	52	90.7%
normal	n10	single cell	exome	61	89.2%
normal	n11	single cell	exome	63	87.5%
normal	n12	single cell	exome	43	94.0%
normal	n13	single cell	exome	58	90.7%
normal	n14	single cell	exome	20	89.5%
normal	n15	single cell	exome	55	94.5%
normal	n16	single cell	exome	31	92.8%
mean				50.97	90.4%













2	subclonal	chr17	65640950	KCNJ16	nonsynonymous SNV	C	T	het	NA	NA	0.303	0.21	NM_001270422	exon6	c.C1127T	p.A376V	0.000000	NA
2	subclonal	chr6	42820873	TBCC	nonsynonymous SNV	G	A	het	NA	NA	1	0.01	NM_003192	exon1	c.C917T	p.S306F	0.000243	NA
2	subclonal	chr15	88411840	ZNF710	nonsynonymous SNV	T	C	het	NA	NA	0.004	0	NM_198526	exon2	c.T467C	p.V156A	0.000000	NA
2	subclonal	chr8	70748004	SLCOSA1	nonsynonymous SNV	A	G	het	NA	NA	0.999	0.16	NM_030958	exon10	c.T2201C	p.F734S	0.000000	NA
2	subclonal	chr7	27823155	TAX1BP1	nonsynonymous SNV	T	A	het	NA	NA	0.99	NA	NM_006024	exon15	c.T2058A	p.D686E	0.000000	NA
2	subclonal	chr6	31887710	HSPAL1	nonsynonymous SNV	T	C	het	NA	NA	0	0	NM_005527	exon2	c.A196G	p.I7V	0.000000	NA
2	subclonal	chr18	6938500	LAMA1	nonsynonymous SNV	A	G	het	NA	NA	0.974	0.16	NM_005559	exon60	c.T8612C	p.L2871P	0.000000	NA
2	subclonal	chr6	28466767	ZSCAN12	nonsynonymous SNV	A	G	het	NA	NA	NA	0.01	NM_001163391	exon4	c.T1279C	p.S427P	0.000000	NA
2	subclonal	chr17	32586770	ACACA	nonsynonymous SNV	T	C	het	NA	NA	0.838	0.33	NM_198834	exon43	c.A5395G	p.S1799G	0.000220	0.043662191
2	subclonal	chr6	99390705	POU3F2	nonsynonymous SNV	T	C	het	NA	NA	0.996	0	NM_005604	exon1	c.T1235C	p.M412T	0.000000	NA
2	subclonal	chr5	145611530	RBM27	nonsynonymous SNV	C	T	het	NA	NA	0.793	0	NM_018989	exon9	c.C1343T	p.P448L	0.000000	NA
2	subclonal	chr14	92755443	UBR7	nonsynonymous SNV	A	G	het	NA	NA	0.73	0.06	NM_175748	exon8	c.A943G	p.T315A	0.000123	0.069184657
2	subclonal	chr3	58495200	ACOX2	nonsynonymous SNV	C	T	het	NA	NA	0	0.33	NM_003500	exon3	c.G250A	p.A84T	0.000190	0.049284686
2	subclonal	chr11	85123211	SYTL2	nonsynonymous SNV	G	A	het	NA	NA	0.535681	0	NM_032943	exon7	c.C806T	p.P269L	0.000271	0.002702989
2	subclonal	chr9	79236100	GNA14	nonsynonymous SNV	C	T	het	NA	GNA14	0.998	0	NM_004297	exon4	c.G550A	p.G184S	0.000269	0.002700196
2	subclonal	chr6	43720925	RSPH9	nonsynonymous SNV	G	A	het	NA	NA	0.009	0.24	NM_001193341	exon1	c.G112A	p.D38N	0.000000	NA
2	subclonal	chr2	134915832	MGAT5	nonsynonymous SNV	C	A	het	NA	NA	0.813	0.29	NM_002410	exon15	c.C1903A	p.L635I	0.000460	2.63E-43
2	subclonal	chr15	32142634	CHRM5	nonsynonymous SNV	C	T	het	p.R142C	CHRM5	1	0	NM_012125	exon3	c.C424T	p.R142C	0.010630	1.63E-167
2	subclonal	chr14	23678497	EMC9	nonsynonymous SNV	T	C	het	NA	NA	0.989	0.25	NM_016049	exon5	c.A352G	p.N118D	0.005144	3.13E-120
2	subclonal	chr5	39170767	FYB	nonsynonymous SNV	C	T	het	NA	NA	NA	NA	NM_199335	exon8	c.G1622A	p.R541H	0.004064	3.79E-72
2	subclonal	chr11	129245178	NFRKB	nonsynonymous SNV	C	A	het	NA	NA	0.991	0.11	NM_001143835	exon24	c.G2952T	p.Q984H	0.003068	4.48E-58
2	subclonal	chr15	43036445	C15orf43	nonsynonymous SNV	G	A	het	NA	NA	0.812	0	NM_152448	exon2	c.G124A	p.A42T	0.000164	0.05563136
2	subclonal	chr3	31596325	ST3B	nonsynonymous SNV	A	G	het	NA	NA	0.009	0.07	NM_178862	exon3	c.A444G	p.I148M	0.000000	NA
2	subclonal	chr3	158245950	LEKR1	nonsynonymous SNV	C	T	het	NA	NA	0.63	0.21	NM_001004316	exon13	c.C1796T	p.P599L	0.003457	7.28E-62
2	subclonal	chr19	7598245	XAB2	nonsynonymous SNV	C	T	het	NA	NA	0.742	0	NM_020196	exon4	c.G406A	p.A136T	0.002758	2.46E-86
2	subclonal	chr11	44245705	ALX4	nonsynonymous SNV	C	T	het	NA	NA	0.999	0	NM_021926	exon3	c.G821A	p.R274H	0.000252	0.003016664
2	subclonal	chr11	7937993	NLRP10	nonsynonymous SNV	A	G	het	NA	NA	0.662	0.03	NM_176821	exon2	c.T1742C	p.M581T	0.000000	NA
2	subclonal	chr11	93446151	HEPH1	nonsynonymous SNV	A	G	het	NA	NA	NA	NA	NM_001098672	exon8	c.A1402G	p.T468A	0.000000	NA
2	subclonal	chr1	168381957	METTL11B	nonsynonymous SNV	A	G	het	NA	NA	NA	0.56	NM_001136107	exon1	c.A85G	p.I29V	0.000000	NA
2	subclonal	chr19	48914954	IRGC	nonsynonymous SNV	A	G	het	NA	NA	0.999	0	NM_019612	exon2	c.A404G	p.D135G	0.000000	NA
2	subclonal	chrX	67854334	STARDB8	nonsynonymous SNV	T	C	het	NA	NA	0	0.12	NM_014725	exon5	c.T613C	p.S205P	0.000000	NA
2	subclonal	chr12	112182630	TPCN1	nonsynonymous SNV	C	A	het	NA	NA	0.067	NA	NM_017901	exon3	c.C187A	p.P63T	0.000000	NA
2	subclonal	chr16	31342719	ITGAD	nonsynonymous SNV	G	A	het	NA	NA	0	1	NM_005353	exon27	c.G3098A	p.S1033N	0.000609	9.80E-07
2	subclonal	chr1	152017273	SLC27A3	nonsynonymous SNV	C	T	het	NA	NA	0.057	0.17	NM_024330	exon5	c.C1315T	p.R439C	0.000295	0.002292157
2	subclonal	chr22	43974435	KIAA0930	nonsynonymous SNV	C	T	het	NA	NA	0.87	0.36	NM_015264	exon8	c.G1013A	p.R338Q	0.000000	NA
2	subclonal	chr3	187782498	DNAJB11	nonsynonymous SNV	C	T	het	NA	NA	0.005	0.16	NM_016306	exon6	c.C620T	p.T207M	0.000093	0.083784775
2	subclonal	chr6	30655688	ABCF1	nonsynonymous SNV	C	T	het	NA	NA	0.471	0.06	NM_001025091	exon7	c.C491T	p.A164V	0.000000	NA
2	subclonal	chr11	6607914	DCHS1	nonsynonymous SNV	C	T	het	NA	NA	0	0.42	NM_003737	exon10	c.G4687A	p.A1563T	0.000000	NA
2	subclonal	chr3	185573071	THPO	nonsynonymous SNV	G	A	het	NA	NA	0.036	0.26	NM_001177597	exon6	c.C974T	p.A325V	0.000000	NA
2	subclonal	chr21	15261541	NRIP1	nonsynonymous SNV	C	T	het	NA	NA	0.98	0.08	NM_003489	exon4	c.G844A	p.E282K	0.000132	0.065547296
2	subclonal	chr5	71792719	ZNF366	nonsynonymous SNV	G	A	het	NA	NA	0.97	0	NM_152625	exon2	c.C361T	p.R121C	0.000373	0.000150196
2	subclonal	chrX	53449158	SMC1A	nonsynonymous SNV	G	A	het	NA	NA	1	0	NM_006306	exon11	c.C1903T	p.R635C	0.000000	NA
2	subclonal	chr19	56274650	KLK14	nonsynonymous SNV	G	A	het	NA	NA	0.197	NA	NM_022046	exon5	c.C382T	p.L128F	0.000000	NA
2	subclonal	chr1	195364270	ASPM	nonsynonymous SNV	A	G	het	NA	NA	0.242	0.01	NM_001206846	exon10	c.T2909C	p.V970A	0.000000	NA
2	subclonal	chr17	36760244	KRT33A	nonsynonymous SNV	G	A	het	NA	NA	0	0.16	NM_004138	exon1	c.C302T	p.A101V	0.000000	NA
2	subclonal	chrX	48724750	GRIPAP1	nonsynonymous SNV	G	A	het	NA	NA	0.017	0.23	NM_020137	exon16	c.C1319T	p.T440M	0.000000	NA
2	subclonal	chr1	247109204	ZNF672	nonsynonymous SNV	C	T	het	NA	NA	0.289	0.89	NM_024836	exon4	c.C1108T	p.P370S	0.000000	NA

**Supplemental Table 8 - Mathematical Modeling of Mutation Rates**

**Table 8.1 - ER Whole Genome Single-Cell Modeling**

Cells	Observed	MR:0.6	MR:0.7	MR:0.8	MR:0.9	MR:1.0	MR:1.1	MR:1.2	MR:1.3	MR:1.4	MR:1.5	MR:1.6	MR:1.7	MR:1.8	MR:1.9	MR:2.0
2	18	6	8	8	16	10	14	16	12	13	15	20	23	26	30	26
3	9	1	1	1	4	1	2	3	1	1	1	2	3	4	10	4
4	5	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SSD		233	189	189	45	153	90	65	125	114	98	78	86	114	161	114

**Table 8.2 - ER Single Cell Exome Modeling**

Cells	Observed	MR=0.1	MR=0.2	MR=0.3	MR:0.4	MR:0.5	MR:0.6	MR:0.7	MR:0.8	MR:0.9	MR:1.0	MR:1.1	MR:1.2	MR:1.3	MR:1.4
2	16	4	8	7	9	13	14	20	20	19	25	28	28	29	36
3	2	2	3	3	3	4	4	6	6	6	8	9	9	10	11
4	2	1	2	1	1	2	2	4	2	3	3	5	5	4	4
5	1	0	1	0	1	1	1	2	1	2	2	3	3	3	3
6	0	0	1	0	1	1	1	2	1	1	1	2	2	2	1
SSD		123	51	67	40	9	7	51	43	36	140	236	236	273	532

**Table 8.3 - TNBC Single Cell Exome Modeling**

Cells	Observed	MR:4	MR:5	MR:6	MR:7	MR:8	MR:9	MR:10	MR:11	MR:12	MR:13	MR:14	MR:15
2	64	36	43	63	63	72	75	100	107	135	116	140	138
3	57	9	11	17	16	23	18	25	34	43	25	50	50
4	16	4	6	10	5	9	12	13	16	20	7	19	21
5	4	3	3	6	3	7	9	6	8	7	4	6	8
6	4	1	2	6	3	4	6	4	3	5	2	4	3
SSD		3124	2672	2000	2182	1781	2266	3378	3521	6897	5195	7514	7207