

Supplementary Table S3. Putative BRCA1/2 reversion mutations identified in cDNA of ovarian and breast cancer patients using targeted massively parallel sequencing and results of amplicon re-sequencing of putative BRCA2 reversion mutations and other somatic mutations in cDNA and tumor tissue of metastatic breast cancers.

Putative BRCA1/2 reversion mutations identified using a custom targeted massively parallel sequencing panel.

Cancer type	Sample ID	GERMLINE		Chrom	Position	Reference allele	Alternate allele	Mutation type	Coverage	Count	Mutant allele fraction	cDNA change	Wildtype protein length (AA)	Germline mutation protein length (AA)	Reversion mutation protein length (AA)	3' 5 bases microhomology (red)	5' 9 bases microhomology (red)	Exon
		BRCA1 germline mutation protein length (AA) (BRCA1 ENST00000301654.3 (BRCA2 ENST00000301652.3)	BRCA2 germline alternative annotation															
Ovarian	OCT15C	BRCA1 c.68_69delAG	BRCA1 187delAG/185delAG	17	41207768	TG	T	frameshift_variant	2554	1	0.0392%	c.108delC	1863	38	1862	CAGAC	CTTTGT	3
Ovarian	OCT15C	BRCA1 c.68_69delAG	BRCA1 187delAG/185delAG	17	41207763	CT	C	frameshift_variant	2114	1	0.0473%	c.113delAA	1863	38	1862	TTGTC	TCAAC	3
Ovarian	OCT15C	BRCA1 c.68_69delAG	BRCA1 187delAG/185delAG	17	41207791	TC	T	frameshift_variant	2046	1	0.0489%	c.55delG	1863	38	1862	CAGAC	TCAACT	3
Ovarian	OCT10C	BRCA1 c.3908dupT	BRCA1 4027insT	17	41243566	TC	T	frameshift_variant	1214	1	0.0824%	c.3951delG	1863	1328	1863	AAGAA	ACCAAT	10
Ovarian	OCT10C	BRCA1 c.3908dupT	BRCA1 4027insT	17	41243621	AT	A	frameshift_variant	1177	1	0.0850%	c.3926delA	1863	1328	1863	TTGCA	TTTTGA	10
Ovarian	OCT10C	BRCA1 c.4124delC	BRCA1 4843delC	17	41221463	TGA	T	frameshift_variant	2184	1	0.0143%	c.4166_4181delTC	1863	1599	1862	AGATGG	SAAGTT	15
Breast	L031_P2	BRCA2 c.4075delA	NA	13	32899297	TTCTAAATCTTG	T	disruptive_inframe_deletion	1761	1	0.0598%	c.402_413delTCTAAATCTTG	3418	150	3414	TCTTA	TCCACT	4
Breast	1109_P1	BRCA2 c.755_758delACAG	NA	13	32905103	TGATAGATTATCGCTTCTGTGACA	T	disruptive_inframe_deletion	1431	2	0.1398%	c.729_754delGATAGATTATCGCTTCTGTGACA	3418	274	3410	GACAG	AAAAAT	9
Breast	1109_P1	BRCA2 c.755_758delACAG	NA	13	32905114	TGCGTCTGTGACAGA	T	inframe_deletion	1383	2	0.1448%	c.740_756delCGCTTCTGTGACAGA	3418	274	3403	CAGTG	ATTAT	9
Breast	1109_P1	BRCA2 c.755_758delACAG	NA	13	32905115	CGCTTCTGTGACAGAGTGAAAACAAATCAAAGA	C	disruptive_inframe_deletion	1385	1	0.0723%	c.741_756delCGCTTCTGTGACAGAGTGAAAACAAATCAAAGA	3418	274	3403	SAGCG	TTTATC	9
Breast	1109_P1	BRCA2 c.755_758delACAG	NA	13	32905137	AAC	A	frameshift_variant	1357	1	0.0737%	c.767_768delCA	3418	274	3416	ACAAA	GTGAAA	9
Breast	1109_P1	BRCA2 c.755_758delACAG	NA	13	32905140	ACAAT	A	frameshift_variant	1369	2	0.1461%	c.771_775delTCAAA	3418	274	3415	CAAGG	AAAACA	9
Breast	1109_P1	BRCA2 c.755_758delACAG	NA	13	32905146	CAA	C	frameshift_variant	1320	3	0.2273%	c.774_775delAA	3418	274	3416	AGAGA	CAATTC	9
Breast	1109_P2	BRCA2 c.755_758delACAG	NA	13	32905163	TGATAGATTATCGCTTCTGTGACA	T	disruptive_inframe_deletion	1814	1	0.0551%	c.729_754delGATAGATTATCGCTTCTGTGACA	3418	274	3410	GACAG	AAAAAT	9
Breast	1109_P2	BRCA2 c.755_758delACAG	NA	13	32905104	GAT	G	frameshift_variant	1822	1	0.0549%	c.732_733delAT	3418	274	3416	AGATT	AAATG	9
Breast	1109_P2	BRCA2 c.755_758delACAG	NA	13	32905137	AAC	A	frameshift_variant	1778	1	0.0562%	c.767_768delCA	3418	274	3416	ACAAA	GTGAAA	9
Breast	1109_P2	BRCA2 c.755_758delACAG	NA	13	32904629	AATTCATT	A	frameshift_variant	2122	2	0.0943%	c.814_823delAATTCATT	3418	274	3414	AAGT	CAGGGA	10
Breast	1109_P2	BRCA2 c.755_758delACAG	NA	13	32904631	TTCAATTA	T	frameshift_variant	2144	2	0.0933%	c.816_825delTTCAATTA	3418	274	3414	AGTA	GGGAAT	10

Putative BRCA2 reversion mutations in serial plasma samples of case L031 (amplicon-resequencing)

	RUN 1		RUN 2	
	BRCA2 reversion 1 c.403_413delTCTAAATCTT TTG	BRCA2 reversion 2 c.389_406delTTTCTGCTCCACT TCTAA	BRCA2 reversion 1 c.403_413delTCTAAATCTT G	BRCA2 reversion 2 c.389_406delTTTCTGCTCCACTTCTAA G
	Variant Allele Frequency			
Plasma 1	0.003682	0	0.002080	0.000067
Plasma 2	0.000604	0	0.000862	0
Plasma 3	0.013141	0.004984	0.005768	0.003093
Mean Depth				
	RUN1 9308 X	RUN2 564259 X		

Putative BRCA2 reversion mutations in plasma sample of case 1109 (amplicon re-sequencing)

Putative BRCA2 reversion mutations	RUN 1	RUN 2
	Variant Allele Frequency	Variant Allele Frequency
c.728_738delATGATAGATT	0.001137	0.000082
c.728_738delATGATAGATTATCGCTTCTGTGACA	0.000296	0.000211
c.731_732delAT	0.001147	0.000296
c.735insT	0.000237	0.000739
c.728_738delATCGCTTCTGTGACAGAGTGAA	0.001609	0.000063
c.763insC	0.000534	-
c.764_765delAC	0.001084	0.001108
c.766insC	0.000531	-
c.773_774delAA	0.000547	-
Mean Depth		
	RUN1 3651 X	RUN2 147132 X

Variant allele fractions of somatic mutations in the pre-treatment tumor and post-treatment plasma sample from patient 1109 (amplicon re-sequencing)

	Plasma (post-treatment)	Tumor (pre-treatment)
	Variant Allele Frequency	
FAT3 c.13447 A>T	0.110357	0.160037
ERCC4 c.749 A>G	0.382705	0.518661
RDWBC c.2321 A>G	0.328663	0.555681
Mean Depth		
	219132 X	

Percentages of cDNA and variant allele fractions of somatic mutations and reversion mutations in cDNA in the samples from the four ovarian cancer patients harboring putative BRCA1 reversion mutations.

Tumor sample	Fraction cDNA in cDNA (%)	Variant allele fractions in cDNA		Putative BRCA1 reversion mutations variant allele fractions in cDNA (Reversion mut. %)
		Mutation type (gene - mutation)	(%)	
OCT1	NA	NF111145Y	0.0263	Rev1 - 0.0314
OCT5	NA	FAT3-D2598Y	0.0749	Rev1 - 0.0362
OCT10	0.26	TP93 E339*	0.1312	Rev1 - 0.0850
OCT15	0.31	PRKDC-Q3083*	0.0484	Rev1 - 0.0824
		TP53-T211fs	0.3096	Rev2 - 0.0473