Supplementary information for:

Discovery and Characterization of Splice-altering Mutations in Inherited Predisposition to Cancer

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This PDF file includes:

Tables S1 to S8

Supplementary references

Table S1. Proportions of pathogenic (P) and likely pathogenic (LP) mutations at intronic splice sites, as reported by ClinVar. Note that mutations at exonic splice sites are defined by ClinVar as missense (if non-synonymous) or silent (if synonymous) so not included below.

Gene	P+LP mutations	At intronic splice site	% splice
BRCA1	3030	170	5.6
BRCA2	3481	160	4.6
PALB2	507	43	8.5
ATM	1008	206	20.4
CHEK2	308	63	20.4
MLH1	917	155	16.9
MSH6	735	48	6.5
APC	861	57	6.6
CDH1	212	36	17.0
TP53	486	56	11.5

Table S2. cBROCA analysis of mutations at canonical splice sites predicted to alter splicing

Gene	Genotype	Position hg19	Exon/ Intron	Distance to splice*	Splice region	NNSPLICE prediction**	MaxEnt prediction**	RT-PCR: intensity of mutant to normal+mutant transcript from diploid RNA test case	RT-PCR: intensity of mutant to normal+mutant transcript from diploid RNA control	TOPO-TA: proportion of mutant clones from diploid RNA test case	TOPO-TA: proportion of mutant clones from diploid RNA control	cBROCA: proportion (PM) of mutant transcripts from mutant allele Z-score	cBROCA: proportion (PM) of mutant transcripts from mutant allele PM	cBROCA result	Family
ATM	c.901G>A; G301S	chr11:108,115,753	exon 7	E|239|1	Donor	0.86 > 0.00	7.08 > -1.69	0.84	0.00	0.83	0.03	>10.00	0.97	skip exon 7, del 239bp, codon 224 stop	CF4576
ATM	c.2250G>A; p.K750K	chr11:108,127,067	exon 14	E|126|1	Donor	0.94 > 0.26	9.45 > 3.63	0.74	0.00	0.72	0.00	>10.00	0.86	skip exon 14, del 126bp (aa 709-750)	CF1019
ATM	c.2638+2T>C	chr11:108,138,071	intron 17	I|2|1066	Donor	1.00 > 0.00	6.62 > -1.13	0.57	0.00	0.64	0.04	>10.00	0.62	skip exon 17, del 172bp, codon 828 stop	CF4449
ATM	c.5497-2A>C	chr11:108,175,400	exon 37	I|1644|2	Acceptor	0.95 > 0.00; 0.04	10.05 > 2.00; 2.59	0.28	0.00	0.33	0.00	>10.00	0.48	cryptic splice, del 61bp, codon 1896 stop	CF1054
ATM	c.6976-2A>C	chr11:108,198,370	intron 47	I|1418|2	Acceptor	0.83 > 0.00	9.04 > 1.00	0.59	0.00	0.48	0.00	>10.00	0.88	skip exon 48, del 114bp (aa 2326-2363) FAT domain	CF4502
ATM	c.7089+1_38del38	chr11:108,198,484	exon 48	I|1|1262	Donor	1.00 > 0.00	10.57 > -15.17	0.72	0.00	0.70	0.00	>10.00	0.94	skip exon 48, del 114bp (aa 2326-2363) FAT domain	CF2327
ATM	c.8418+1delGTGA	chr11:108,214,099	exon 57	I|1|2371	Donor	0.99 > 0.03	10.13 > 0.78	0.72	0.00	0.64	0.00	>10.00	0.86	skip exon 57, del 150bp (aa 2757-2806) kinase domain	CF2091
ATM	c.8988-1G>A	chr11:108,236,051	exon 63	I|106|1	Acceptor	0.87 > 0.00	10.46 > 1.71; 1.06			0.46	0.06	>10.00	0.90	cryptic splice, del 13bp, codon 3002 stop	CF1396
BRCA1	c.5468-1G>A	chr17:41,197,820	exon 24	I|1840|1	Acceptor	0.76 > 0.00	9.53 > 0.78; 3.89			0.48	0.00	>10.00	0.68	cryptic splice, del 11bp, codon 1825 stop	CF3502
BRCA1	c.4484G>T; p.R1495M	chr17:41,228,505	exon 14	E|127|1	Donor	1.00 > 0.90	10.57 > 5.57	0.75	0.00	0.62	0.00	>10.00	1.00	skip exon 14, del 127bp, codon 1462 stop	CF1048
BRCA2	c.517-2A>G	chr13:32,900,634	exon 7	I|215|2	Acceptor	0.98 > 0.00	10.00 > 2.05	0.76	0.00	0.71	0.00	>10.00	0.72	skip exon 7, del 115bp, codon 191 stop	CF1305
BRCA2	c.7618-1G>A	chr13:32,931,878	exon 16	I|1132|1	Acceptor	0.69 > 0.00	7.11 > -1.64; 1.53	0.53	0.00	0.39	0.00	>10.00	0.94	cryptic splice, del 44bp, codon 2550 stop	CF529
BRCA2	c.9117G>A, p.P3039P	chr13:32,954,050	exon 23	E|164|1	Donor	0.57 > 0.00	4.28 > -4.94	0.73	0.00	0.73	0.00	>10.00	0.92	skip exon 23, del 164bp; codon 2988 stop	CF976
BRIP1	c.93+1G>A	chr17:59,938,807	intron 2	I|1|1539	Donor	0.89 > 0.00	7.96 > -0.22	0.72	0.00	0.84	0.00	>10.00	1.00	skip exon 2, loss of first ATG	CF449
CDH1	c.1565+1G>A	chr16:68,849,663	exon 10	I|1|3520	Donor	1.00 > 0.00; 0.18	10.74 > 2.55; 2.87			0.30	0.00	>10.00	0.79	cryptic splice, ins 6bp, codon 523 stop	CF4529
CDH1	c.1711G>A; G571S	chr16:68,853,328	exon 11	E|146|1	Donor	0.99 > 0.77	9.33 > 4.33	0.90	0.31	0.86	0.31	>10.00	1.00	skip exon 11, del 146bp, codon 538 stop	CF1943
CHEK2	c.444+1G>A	chr22:29,121,230	exon 2	I|1|118	Donor	0.99 > 0.00; 0.69	8.10 > -0.08; 7.57			0.34	0.00	>10.00	0.80	cryptic splice, ins 4bp, codon 154 stop	CF653
PALB2	c.2835-1G>C	chr16:23,634,452	exon 9	I|1|877	Acceptor	0.54 > 0.00	8.14 > 0.07	0.77	0.00	0.67	0.00	>10.00	1.00	skip exon 9, del 162bp (aa 946-999)	CF612
PALB2	c.2515-1G>T	chr16:23,640,597	exon 6	I|1|363	Acceptor	0.96 > 0.00	9.47 > 0.87	0.65	0.00	0.60	0.05	>10.00	0.98	skip exon 6, del 72bp (aa 839-869)	CF54
RAD51D	c.904-2A>T	chr17:33,428,057	intron 9	I|163|2	Acceptor	0.95 > 0.00; 0.96	8.16 > -0.20; 11.19			0.45	0.00	>10.00	0.85	cryptic splice, del 7bp, codon 327 stop	CF4623

*Genomic distance from site of mutation to nearest flanking canonical splice sites

**Strength of splice given wild-type sequence > strength of splice given mutant sequence. NNSPLICE strength predictions are bounded by 0 to +1. MaxEnt strength predictions are unbounded.

Table S3. cBROCA analysis of mutations predicted to have no effect on splicing

Gene	Genotype	Position hg19	Exon|intron	Distance to splice	NNSPLICE prediction	MaxEnt prediction	RESCUE-ESE, HSF	ClinVar	cBROCA result	Family	Foot note
ATM	c.1009C>T, p.R337C	chr11:108,117,798C>T	exon 8	E|108|57	n	n	ESS+	VUS	normal	CF4589	
ATM	c.3963G>A, p.M1321I	chr11:108,155,170G>A	exon 26	E|217|31	n	n	ESE-	LB/VUS	normal	CF4574	
ATM	c.5009C>T, p.A1670V	chr11:108,170,444C>T	exon 34	E|4|169	n	n	ESS+	VUS	normal	CF4471	
ATM	c.5821G>C, p.V1941L	chr11:108,180,945G>C	exon 39	E|59|98	n	n	ESE-	VUS	normal	CF4566	
ATM	c.7181C>T, p.S2394L	chr11:108,199,839C>T	exon 49	E|92|127	n	n	ESE-, ESS+	LP	normal	CF4660	1
ATM	c.8011-6T>G	chr11:108,205,690T>G	exon 55	I|995|6	0.92 > 0.35	7.11 > 6.09	n	LB/VUS	normal	CF3971	
BRCA1	c.5454C>T, p.D1818D	chr17:41,199,673C>T	exon 18	E|48|14	n	n	2ESE+, 2ESS-	VUS	normal	CF4596	
BRCA1	c.5278(-1519)T>C	chr17:41,204,653A>G	intron 20	I|4416|1519	n	-1.69 > 7.05	2ESE+, 2ESS-	B	normal	CF1031	
BRCA1	c.5207T>G, p.V1736G	chr17:41,209,139A>C	exon 20	E|14|71	n	n	3ESE+, 2ESS-	VUS	normal	CF1746	2
BRCA1	c.5097G>A, p.R1699R	chr17:41,215,946C>T	exon 18	E|23|56	n	n	3ESE-	ni	normal	CF4099	
BRCA1	c.5074+1158C>T	chr17:41,218,467G>A	intron 17	I|1158|2699	0.00 > 0.28	n	3ESE+	B	normal	CF1830	
BRCA1	c.4357+518delAAAG	chr17:41,233,900delCTTT	intron 13	I|5272|518	n	0.37 > 1.60	2ESE+	ni	normal	CF1684	
BRCA1	c.4185+37delTG	chr17:41,242,923delCA	intron 12	I|37|8331	n	n	2ESE+, 2ESS-	ni	normal	CF94.02	
BRCA1	c.301+55G>A	chr17:41,256,830C>T	intron 6	I|55|552	n	n	1ESE+, 2ESS-	LB	normal	CF4590	
BRCA1	c.190G>T, p.D67Y	chr17:41,258,486C>A	exon 5	E|65|14	n	n	2ESE-	B/LB/VUS	normal	CF1684	
BRCA1	c.135-20T>G	chr17:41,258,570A>C	exon 5	I|17463|20	0.97 > 0.97	8.19 > 6.96	n	VUS	normal	CF2649	
BRCA1	c.81-6T>C	chr17:41,267,802A>G	intron 2	I|6|8232	0.52 > 0.40	7.05 > 6.16	1ESE-	B/LB/VUS	normal	CF3148	
BRCA1	c.81T>C, p.C27C	chr17:41,2677,96A>G	exon 3	I|8232|6	0.52 > 0.41	7.05 > 6.86	4ESE-	LB/VUS	normal	CF1875	
BRCA1	c.75C>T, p.P25P	chr17:41,276,039G>A	exon 2	E|94|6	n	n	1ESE-, 1ESS+	B/LB	normal	CF729, CF2718	
BRCA2	c.28A>G, p.T10A	chr13:32,890,624A>G	exon 2	E|67|40	n	n	3ESE-	VUS	normal	CF4651	
BRCA2	c.128A>G, p.N43S	chr13:32,893,274A>G	exon 3	E|61|189	0.00 > 0.71	-8.27 > 0.48	4ESE-	ni	normal	CF4568	
BRCA2	c.426(-252)G>A	chr13:32,899,986A>G	intron 4	I|665|252	0.00 > 0.88	-2.20 > 6.65	n	ni	normal	CF4385	
BRCA2	c.750G>A, p.V250V	chr13:32,905,124G>A	exon 9	E|69|44	n	n	4ESE-	B/LB	normal	CF4691	
BRCA2	c.7466A>G, p.D2489G	chr13:32,930,595A>G	exon 15	E|31|152	0.00 > 0.54	-1.54 > 6.64	3ESE+, 2ESS-	VUS	normal	CF943	
BRCA2	c.7559G>C, p.R2520P	chr13:32,930,688G>C	exon 15	E|124|59	n	n	1ESS+	VUS	normal	CF4530	
BRCA2	c.7820C>T, p.T2607I	chr13:32,936,674C>T	exon 17	E|15|157	0.17 > 0.22	5.95 > 7.10	2ESS+	VUS	normal	CF2723	
BRCA2	c.7879A>T, p.I2627F	chr13:32,936,733A>T	exon 17	E|74|98	n	n	3ESE-	P	normal	CF852	3
BRCA2	c.7902G>A, p.M2634I	chr13:32,936,756G>A	exon 17	E|97|75	n	n	4ESE-, 3ESS+	ni	normal	CF4320	
BRCA2	c.8206C>T, p.L2736F	chr13:32,937,545C>T	exon 18	E|230|126	0.73 > 0.81	3.64 > 4.08	1ESE+	VUS	normal	CF4562	
BRCA2	c.8285C>G, p.P2762R	chr13:32,937,624C>G	exon 18	E|309|47	n	n	3ESE-	VUS	normal	CF4520	
BRCA2	c.8350C>T, p.R2784W	chr13:32,944,557C>T	exon 19	E|19|138	0.91 > 0.88	n	4ESE-	VUS/LP	normal	CF4554	
BRCA2	c.8359C>T, p.R2787C	chr13:32,944,566C>T	exon 19	E|28|129	0.30 > 0.39	n	3ESS+	LB/VUS	normal	CF3497	
BRCA2	c.8510G>T, p.G2837V	chr13:32,945,115G>T	exon 20	E|23|123	n	n	5ESE-	VUS	normal	CF4548	
BRCA2	c.9076C>G, p.Q3026E	chr13:32,954,009C>G	exon 23	E|123|42	n	n	1ESE-, 1ESS+	VUS	normal	CF629	
BRCA2	c.9344A>G, p.K3115R	chr13:32,968,913A>G	exon 25	E|88|158	n	n	1ESE-, 1ESS+	VUS	normal	CF4089	
BRCA2	c.9648(+127)G>A	chr13:32,971,308G>A	intron 26	I|127|991	n	-4.40 > 3.55	n	ni	normal	CF4282	
BRIP1	c.2765T>C, p.L922S	chr17:59,763,337A>G	exon 19	E|190|141	n	n	1ESE-	ni	normal	CF4649	
BRIP1	c.2309A>G, p.K797R	chr17:59,793,414T>C	exon 17	E|11|103	n	n	2ESE-, 2ESS+	VUS	normal	CF4607	
BRIP1	c.2372A>T, p.D791V	chr17:59,820,381T>A	exon 16	E|115|8	n	n	6ESE-	VUS	normal	CF4055	
BRIP1	c.297C>T, p.D99D	chr17:59,934,501G>A	exon 4	E|92|83	n	n	5ESE-, 2ESS+	LB	normal	CF4368	

Table S3. cBROCA analysis of mutations predicted to have no effect on splicing

Gene	Genotype	Position hg19	Exon|intron	Distance to splice	NNSPLICE prediction	MaxEnt prediction	RESCUE-ESE, HSF	ClinVar	cBROCA result	Family	Foot note
CDH1	c.2296-670T>A	chr16:68,862,887T>A	intron 14	I|680|670	n	n	3ESS+, 1ESS-	ni	normal	CF4316	
CDH1	c.2440-6C>G	chr16:68,867,187C>G	intron 15	I|3487|6	0.98 > 0.94	10.93 > 9.85	2ESS+	B/LB	normal	CF4293	
CHEK2	c.1130A>G, p.E377G	chr22:29,091,827T>C	exon 11	E|35|130	n	n	4ESE-, 3ESS+	VUS	normal	CF4513	
CHEK2	c.246-260del15	chr22:29,130,450-29,130,464de	exon 2	E|252|74	n	n	6ESE-	VUS	normal	CF4493	
GEN1	c.1072-185G>A	chr2:17,955,353G>A	intron 10	I|972|787	n	n	3ESS+	ni	normal	CF94.02	
MLH1	c.678-481C>T	chr3:37,055,442C>T	intron 8	I|2481|481	0.00 > 0.56	-2.19 > 1.56	1ESS+	ni	normal	CF4661	
PALB2	c.2752C>T, p.P918S	chr16:23,635,412G>A	exon 8	E|4|83	n	n	4ESS+	VUS	normal	CF62.08	
PALB2	c.2587-703G>A	chr16:23,638,421C>T	intron 6	I|2104|703	0.62 > 0.64	3.25 > 5.87	1ESE-	ni	normal	CF4673	
PALB2	c.2289G>C, p.L763F	chr16:23,641,186C>G	exon 5	E|605|226	0.00 > 0.17	0.69 > 3.81	1ESS-	LB/VUS	normal	CF4685	
PALB2	c.2204C>T, p.P735L	chr16:23,641,271G>A	exon 5	E|520|311	0.21 > 0.28	-2.64 > 3.49	1ESE+	VUS	normal	CF4500	
PALB2	c.1699C>T, p.H567T	chr16:23,641,776G>A	exon 5	E|15|816	n	n	1ESE-	LB/VUS	normal	CF4462	
PALB2	c.1551A>G, p.K517K	chr16:23,646,316T>C	exon 4	E|1340|134	n	n	5ESE-	ni	normal	CF4667	
PALB2	c.46A>G, p.K16E	chr16:23,652,433T>C	exon 1	E|-|3	0.22 > 0.07	5.74 > 4.05; 2.8	4ESS+	ni	normal	CF4151	
PTEN	c.79+4229A>T	chr10:89,628,534A>T	intron 1	I|4229|25248	n	n	1ESE+, 2ESS-	ni	normal	CF4654	
PTEN	c.79+11548A>G	chr10:89,638,942T>C	intron 1	I|11548|17929	0.00 > 0.89	-3.10 > 5.64	n	LB	normal	CF4361	
PTEN	c.492+7414A>G	chr10:89,700,422A>G	intron 5	I|7414|11453	0.00 > 0.09	-7.00 > 1.18	1ESE+, 1ESS-	ni	normal	CF245	
RAD51D	c.904-3C>T	chr17:33,428,059G>A	intron 9	I|162|3	0.95 > 0.96	8.16 > 7.77	5ESE-, 3ESS+	B/LB/VUS	normal	CF604	
TP53	c.786-60G>A	chr17:7,577,215C>T	intron 7	I|284|60	0.00 > 0.51	-1.08 > 6.87	2ESE+, 3ESS-	LB	normal	CF4431	

Abbreviations: n, no change; ni, no information; ESE, exonic splcing enhancer; ESS, exonic splicing silencer; B, benign; LB, likely benign, VUS, variant of unknown significance; LP likely pathogenic; P, pathogenic; HSF, Human Splicing Finder (see Methods)

Footnotes:

1. Damaging effect of ATM p.S2394L on protein reported by Lin L, et al. (2015) Spontaneous ATM gene reversion in A-T iPSC to produce an isogenic cell line. Stem Cell Reports 5:1097-1108.

2. Damaging effect of BRCA1 p.V1736G on protein function reported by Lee MS et al. (2010) Comprehensive analysis of missense variations in the BRCT domain of BRCA1 by structural and functional assays. Cancer Res. 70:4880-4489, and Findlay GM et al. (2018) Accurate classification of BRCA1 variants with saturation genome editing. Nature 562:217-222.

3. Damaging effect of BRCA2 p.I2627F on protein function reported by Guidugli et al. (2013) A classification model for BRCA2 DNA binding domain missense variants based on homology-directed repair activity. Cancer Res. 73:265-275

Table S4. cBROCA analysis of splice-junction mutations leading to multiple mutant transcripts

							cBROCA read depths				cBROCA interpretation			
				Exon /	Distance		Case		Controls (N=374)		Case vs Control			S4
Event	Transcript	Trap	Genomic position (hg19)	Intron	to splice	ClinVar	Reads	Fraction	mean	s.d.	Z score	PM	Result of cBROCA analysis	Ref
BRCA1	c.212+1G>A (CF98)	0.886	chr17:41,258,472C>T	intron 5	I|1|1499	P								1
	Cryptic donor exon 5 at c.191						516	0.50	0.12	0.02	>10.00	0.88	del 22bp, 64 stop	
	Skip exon 5						108	0.10	0.02	0.01	6.08	0.18	del 54bp, RING domain	
	Full length						406	0.39	0.85	0.03	>10.00			
BRCA1	c.594-2A>C (CF3867, CF3869)	0.517	chr17:41,247,941T>G	intron 10	I|1320|2	B/LB/VUS								2
	Skip exon 10						294; 271	0.37; 0.35	0.01	0.01	>10.00	0.74	del 77bp, 201 stop	
	Skip exons 9+10						225; 253	0.25; 0.28	0.24	0.06	0.21		ns	
	Full length						295; 293	0.38	0.75	0.06	6.31			
BRCA1	c.4185+1insAdel21 (CF831)	ni	chr17:41,242,939	intron 12	I|1|8368	LP/P								3
	Retained intron 11						332	0.41	0.02	0.02	>10.00	0.80	ins 402bp, multiple stops	
	Skip exon 12						25	0.03	0.00	0.00	>10.00	0.06	del 89bp, 1373 stop	
	Skip exon 11q						122	0.15	0.09	0.03	2.04		ns	
	Full length						335	0.41	0.88	0.02	>10.00			
BRCA1	c.4485-1G>A (CF4665)	0.480	chr17:41,226,539C>T	intron 14	I|1966|1	LP/P								
	Cryptic acceptor exon 15 at c.4513						517	0.26	0.00	0.00	>10.00	0.52	del 29bp, 1496 stop	
	Skip exon 15						283	0.14	0.00	0.01	>10.00	0.28	del 191bp, 1059 stop	
	Full length						1177	0.60	1.00	0.01	>10.00			
BRCA1	c.5277+1G>A (CF1012)	0.959	chr17:41,209,068C>T	intron 20	I|1|5934	P								4
	Cryptic splice at c.5277+88						380	0.24	0.00	0.02	9.54	0.48	run-on from exon 20, 1767 stop	
	Skip exon 20						114	0.07	0.00	0.01	9.40	0.14	del 84bp, BRCT domain	
	Full length						1100	0.69	1.00	0.03	9.53			
BRCA2	c.7007G>C, p.R2336P (CF498)	0.960	chr13:32,921,033G>C	exon 13	E|70|1	P								5
	Skip exons 12-13						380	0.19	0.00	0.00	>10.00	0.38	del 166bp, 2311 stop	
	Skip exon 13						222	0.11	0.00	0.00	>10.00	0.22	del 70bp, 2343 stop	
	Full length						1414	0.70	1.00	0.00	>10.00			
BRCA2	c.7007+1G>C (CF4704)	0.940	chr13:32,921,034G>C	intron 13	I|1|7965	P								
	Skip exons 12-13						318	0.25	0.00	0.00	>10.00	0.50	del 166bp, 2311 stop	
	Skip exon 13						139	0.11	0.00	0.00	>10.00	0.22	del 70bp, 2343 stop	
	Full length						829	0.64	1.00	0.00	>10.00			
BRCA2	c.7976G>A, p.R2659K (CF691)	0.997	chr13:32,936,830G>A	exon 17	E|171|1	P								6
	Skip exon 17						889	0.42	0.00	0.00	>10.00	0.84	del 171bp, DNA binding domain	
	Skip exons 17+18						223	0.11	0.02	0.01	>10.00	0.20	del 526bp, 2645 stop	
	Full length						996	0.47	0.98	0.01	>10.00			
BRCA2	c.7976+2C>G (CF4126)	0.953	chr13:32,936,832C>G	intron 17	I|2|484	LP/P								
	Skip exon 17						467	0.32	0.00	0.00	>10.00	0.64	del 171bp, DNA binding domain	
	Skip exons 17+18						196	0.14	0.02	0.01	>10.00	0.26	del 526bp, 2645 stop	
	Full length						781	0.54	0.98	0.01	>10.00			
ATM	c.-30-1G>T (CF3950)		chr11:108,098,321G>T	intron 2	I|4408|1	LP								7
	Cryptic acceptor exon 2 at c.-27						450	0.30	0.00	0.00	>10.00	0.60	del 4bp in 5'UTR	
	Skip exon 2						146	0.10	0.00	0.00	>10.00	0.20	del aa 1-93, including start ATG	
	Full length						880	0.60	1.00	0.00	>10.00			

Table S4. cBROCA analysis of splice-junction mutations leading to multiple mutant transcripts

Event	Transcript	Trap	Genomic position (hg19)	Exon / Intron	Distance to splice	ClinVar	cBROCA read depths: Case Reads	Case Fraction	Controls (N=374) mean	Controls (N=374) s.d.	cBROCA interpretation: Case vs Control Z score	PM	Result of cBROCA analysis	S4 Ref
ATM c.3154-1G>A (CF568)			chr11:108,143,448G>A	intron 21	I|114|1	LP								
	Skip exons 21+22						506	0.20	0.00	0.00	>10.00	0.40	del 207bp, 1026 stop	
	Cryptic acceptor at c.3154-15						468	0.18	0.00	0.00	>10.00	0.36	ins 14bp, 1068 stop	
	Skip exon 22						291	0.11	0.00	0.00	>10.00	0.22	del 131bp, 1068 stop	
	Full length						1296	0.51	1.00	0.00	>10.00			
ATM c.5674+1G>T (CF1395)			chr11:108,175,580G>T	intron 37	I|3044|1	new								
	Retained intron 36						1476	0.60	0.04	0.02	>10.00	0.94	degenerate transcript	
	Skip exon 37						57	0.02	0.00	0.00	>10.00	0.04	del 178bp, 1857 stop	
	Skip exons 37+38						14	0.01	0.00	0.00	>10.00	0.02	del 266bp, 1840 stop	
	Full length						913	0.37	0.96	0.02	>10.00			
ATM c.7629+2T>C (CF3442)			chr11:108,202,286T>C	intron 51	I|2|320	LP								
	Skip exon 51						626	0.19	0.00	0.00	>10.00	0.38	del 114bp (aa 2506-2543) FAT domain	
	Cryptic donor at c.7629+5						154	0.05	0.00	0.00	>10.00	0.10	ins 4bp, 2548 stop	
	Full length						2477	0.76	1.00	0.00	>10.00			
BARD1 c.159-1G>T (CF5058)			chr2:215,661,842C>A	intron 2	I|12294|1	LP								
	Skip exon 2						235	0.21	0.00	0.00	>10.00	0.42	del 57bp (aa 53-72) RING domain	
	Skip exons 2+3						201	0.18	0.00	0.01	>10.00	0.36	del 206bp, 53 stop	
	Full length						708	0.62	1.00	0.01	>10.00			
BRIP1 c.93+1G>A (CF449)			chr17:59,938,807C>T	intron 2	I|1|1539	LP								
	Skip exon 2_delATG						1244	0.57	0.01	0.01	>10.00	1.00	loss of first ATG	
	Alternate splice at c.-27						299	0.14	0.33	0.03	6.68			
	Full length						627	0.29	0.66	0.03	>10.00			
CDH1 c.1565+1G>A (CF4529)			chr16:68,849,663G>A	intron 10	I|1|3520	P								
	Cryptic donor at c.1565+7						127	0.30	0.00	0.00	>10.00	0.60	ins 6bp, 523 stop	
	Retained intron 10						40	0.10	0.01	0.01	>10.00	0.19	multiple stops	
	Full length						253	0.60	0.91	0.04	>10.00			
PALB2 c.2835-1G>C (CF612)			chr16:23,634,452C>G	intron 9	I|1|878	P								
	Skip exon 9						1012	0.50	0.00	0.01	>10.00	1.00	del 162bp (aa 945-999) WD domains	
	Cryptic acceptor exon 9 at c.2864						97	0.05	0.00	0.00	>10.00	0.10	del 30bp (aa 945-955) WD domain	
	Full length						897	0.45	1.00	0.01	>10.00			
PALB2 c.3113G>A, p.W1038X (CF1419)			chr16:23,632,683C>T	exon 10	E|117|1	LP/P								8
	Cryptic donor exon 10 at c.3083						402	0.20	0.00	0.00	>10.00	0.40	del 31bp, 1030 stop	
	Skip exon 10						353	0.18	0.00	0.00	>10.00	0.36	del 117bp, WD domain	
	Skip exons 9+10						113	0.06	0.00	0.00	>10.00	0.12		
	Full length						1125	0.56	1.00	0.00	>10.00			

Table S5. cBROCA analysis of intronic mutations

										cBROCA read depths				cBROCA interpretation			
										Case		Controls (N=374)					
Event	Transcript	Genomic position (hg19)	intron	Distance to splice	Splice region	NNSPLICE prediction	MaxEnt prediction	HSF prediction	ClinVar prediction	Reads	Fraction	mean	s.d.	Z score	PM	Result	S5 Ref
BRCA1	c.4986+3G>C CF4616	chr17:41,222,942C>G	16	I|3|3230	Donor	0.66 > 0.00; 0.35	5.91 > -2.37; 2.16	-	LP/P								1
	Cryptic acceptor at c.4986+66									742	0.22	0.00	0.00	>10.00	0.44	ins 65bp, 1676 stop	
	Skip exon 17									187	0.05	0.02	0.03	ns	0.08	del 88bp, 1672 stop; not significant	
	Full length									2486	0.73	0.97	0.03	>10.00			
BRCA1	c.5194-12G>A CF3308	chr17:41,209,164C>T	19	I|6186|12	Acceptor	0.73 > 0.67	9.36 > 4.34	-	P								2
	Retain intron 19									86	0.15	0.03	0.02	5.33	0.27	degenerate transcript, multiple stops	
	Skip exon 20									6	0.01	0.00	0.00	ns	0.02	del 84bp, BRCT domain; not significant	
	Full length									480	0.84	0.97	0.02	5.81			
BRCA1	c.5406+4delAGTA CF4672	chr17:41,201,131del4	22	I|4|1411	Donor	0.98 > 0.00	9.49 > -5.81	-	new								
	Skip exon 22									24	0.53	0.01	0.00	>10.00	1.00	del 74bp, 1804 stop	
	Full length									21	0.47	0.99	0.00	>10.00			
BRCA2	c.7007+5G>A CF4629	chr13:32,921,038G>A	13	I|5|7961	Donor	0.99 > 0.51	10.53 > 5.48	-	VUS								
	Skip exons 12-13									558	0.23	0.00	0.00	>10.00	0.46	del 166bp, 2311 stop	
	Skip exon 13									238	0.10	0.00	0.00	>10.00	0.20	del 70bp, 2343 stop	
	Full length									1580	0.66	1.00	0.00	>10.00			
BRCA2	c.8331+3A>C CF4463	chr13:32,937,673A>C	18	I|3|6866	Donor	0.96 > 0.07	8.88 > 3.77	-	VUS								
	Retain intron 18									776	0.19	0.02	0.02	>10.00	0.36	degenerate transcript, multiple stops	
	Skip exon 18									359	0.09	0.01	0.01	>10.00	0.17	del 355bp, 2702 stop	
	Full length									2921	0.72	0.97	0.02	>10.00			
APC	c.532-1000delGT CF4118	chr5:112,115,487delGT	5	I|4053|1000	Intronic silencer	-	-	2ESE+, 3ESS-	new								
	Exonification of chr5:112,115,381-112,115,547									127	0.44	0.00	0.00	>10.00	0.88	new exon, ins 165bp, 199 stop	
	Normal length									159	0.56	1.00	0.00	>10.00			
ATM	c.5007-3T>A CF4620	chr11:108,170,438T>A	33	I|2329|3	Acceptor	-	2.46 > 0.87	-	VUS								
	Retained intron 33									422	0.36	0.05	0.01	>10.00	0.67	degenerate transcript, multiple stops	
	Cryptic acceptor at c.5006-16									94	0.08	0.00	0.00	>10.00	0.16	ins 15bp	
	Full length									657	0.56	1.00	0.00	>10.00			
ATM	c.8787-13G>T CF4705	chr11:108,225,525T>G	61	I|918|13	Acceptor	0.81 > 0.36; 1.00	8.29 > 6.10; 10.87	-	new								
	Skip exon 61									507	0.17	0.00	0.00	>10.00	0.34	del 64bp, 2941 stop	
	Exonification of chr11:108,225,645-108,225,825									314	0.11	0.00	0.00	>10.00	0.22	new exon, ins 181bp, 2969 stop	
	Full length									2155	0.72	1.00	0.00	>10.00			
BARD1	c.1569-12T>G CF4718	chr2:215,617,291A>C	6	I|14915|12	Acceptor	0.40 > 0.08; 0.22	5.42 > 3.62; 4.55	-	VUS								
	Skip exon 7									506	0.10	0.01	0.01	8.68	0.19	del 109bp, 524 stop	
	Cryptic acceptor exon 7 at c.1603									342	0.07	0.01	0.01	5.58	0.13	del 35bp, 524 stop	
	Full length									4024	0.83	0.98	0.01	>10.00			
CHEK2	c.320-5T>A CF4428, CF4436	chr22:29,121,360A>T	2	I|9031|5	Acceptor	0.93 > 0.63	7.66 > 5.99	-	B/LB/VUS								3
	Skip exons 3+4									16; 31	0.03	0.00	0.00	>10.00	0.06	del 273bp, 91 aa, FHA domain	
	Skip exons 3+4+5									15; 45	0.03	0.00	0.00	>10.00	0.06	del 364bp, 113 stop	
	Full length									428; 1039	0.93	1.00	0.00	>10.00			
CHEK2	c.592+3A>T CF4447	chr22:29,120,962T>A	4	I|3|5489	Donor	0.78 > 0.26	8.49 > 1.81	-	VUS/LP								3

Table S5. cBROCA analysis of intronic mutations

										cBROCA read depths				cBROCA interpretation			
										Case		Controls (N=374)					
Event	Transcript	Genomic position (hg19)	intron	Distance to splice	Splice region	NNSPLICE prediction	MaxEnt prediction	HSF prediction	ClinVar prediction	Reads	Fraction	mean	s.d.	Z score	PM	Result	S5 Ref
	Skip exon 4									227	0.16	0.00	0.00	>10.00	0.32	del 148bp, 155 stop	
	Skip exons 4+5									206	0.15	0.01	0.02	8.19	0.29	del 239bp, 164 stop	
	Skip exon 5									201	0.14	0.17	0.10	ns		del 91bp, 204 stop, not significant	
	Full length									779	0.55	0.81	0.12	2.23			
CHEK2	c.846+4delAGTA	chr22:29,105,987del4	7	I|4|6436	Donor	0.99 > 0.00	8.31 > 4.42	-	VUS								
	CF3575																
	Skip exons 7+8									2034	0.48	0.00	0.01	>10.00	0.96	del 54bp, 18aa, kinase domain	
	Skip exon 7									387	0.09	0.00	0.00	>10.00	0.18	del 116bp, 272 stop	
	Skip exon 8									756	0.25	0.45	0.17	0.81		ns	
	Full length									526	0.17	0.55	0.17	0.78			
MLH1	c.1732-264A>T	chr3:37,088,746A>T	15	I|4924|264	Cryptic donor	0.00 > 0.99	1.54 > 9.72	-	new								
	CF4679																
	Exonification of chr3:37,088,604-37,088,744									692	0.22	0.00	0.00	>10.00	0.44	new exon, ins 141bp, 587 stop	
	Exonification of chr3:37,088,660-37,088,744									318	0.10	0.00	0.00	>10.00	0.20	new exon, ins 85bp, 581 stop	
	Full length									2085	0.67	1.00	0.00	>10.00			
MSH2	c.2635-24A>G	chr2:47,709,894A>G	15	I|1884|24	Branch point	-	-	BP-; 4ESS+	new								
	CF4659																
	Retained intron 15									811	0.23	0.05	0.04	5.04	0.41	degenerate transcript, multiple stops	
	Alternate 3'UTR at chr2:47,739,442-47,739,573									176	0.05	0.00	0.00	>10.00	0.10	ins 132bp, 922 stop	
	Full length									2539	0.72	0.95	0.04	6.37			
PTEN	c.210-7del5	chr10:89,690,796del5	3	I|5492|7					LB/VUS								6
	CF66.02,.03																
	Skip exon 4									194; 253	1.02; 0.02	0.00	0.00	>10.00	0.04	del 44bp, 76 stop	
	Full length									9951; 13843	1.98; 0.98	1.00	0.00	>10.00			
RAD51C	c.904+5G>T	chr17:56,798,178G>T	6	I|5|3223	Donor	0.91 > 0.02	5.56 > -0.93	-	LP								4
	CF2522																
	Skip exon 6									2271	0.32	0.01	0.00	>10.00	0.63	del 67bp, 291 stop	
	Skip exons 6+7									690	0.10	0.00	0.00	>10.00	0.20	del 128bp, 304 stop	
	Skip exons 6+7+8									363	0.05	0.00	0.00	>10.00	0.10	del 189bp, del aa 280-342 not conserved	
	Full length									3749	0.53	0.99	0.00	>10.00			
RAD51C	c.1026+5delGTA	chr17:56,809,910del3	8	I|5|1569	Donor	0.77 > 0.00	1.98 > -6.29	-	P/LP								5
	CF4694																
	Skip exon 8									3524	0.42	0.00	0.00	>10.00	0.84	del 61bp, 1029 stop	
	Skip exons 7+8									454	0.05	0.02	0.01	>10.00	0.08	del 122bp, 306 stop	
	Full length									4372	0.52	0.98	0.01	>10.00			

Table S6. cBROCA analysis of exonic mutations

Event	Transcript	Genomic position (hg19)	exon	Distance to splice	ClinVar	cBROCA read depths: Case Reads	Case Fraction	Controls (N=374) mean fraction	Controls (N=374) s.d. fraction	cBROCA interpretation: Case vs Control Z score	PM	Result	S6 Ref
BRCA1 c.5072C>T, p.T1691I	CF1380.01,02; CF1555.01,02	chr17:41,219,627G>A	17	E|85|3	LP								1
	Skip exon 17					1409±70	0.31±0.01	0.04	0.02	>10.00	0.60	del 88bp, 1672 stop	
	Full length					3029±347	0.69±0.01	0.96	0.02	>10.00			
BRCA1 c.5022C>T, p.I1674I	CF4469	chr17:41,219,677G>A	17	E|36|52	LB								
	Skip exon 17					371	0.18	0.04	0.02	6.73	0.32	del 88bp, 1672 stop	
	Full length					1677	0.82	0.96	0.02	6.73			
BRCA1 c.4992C>T, p.L1664L	CF832.01,.02	chr17:41,219,707G>A	17	E|5|83	B/LB	420±47	0.14±0.01	0.04	0.02	5.00	0.26	del 88bp, 1672 stop	
	Skip exon 17					2594±44	0.86±0.01	0.96	0.02				
	Full length												
BRCA2 c.7992T>A, p.I2664I	CF4561	chr13:32,937,331T>A	18	E|16|340	LB/VUS								
	Skip exon 18					1220	0.22	0.01	0.01	>10.00	0.43	del 355bp, 2702 stop	
	Skip exons 17+18					223	0.04	0.02	0.01	3.15	0.06	del 526bp, 2645 stop	
	Full length					4160	0.74	0.97	0.01	>10.00			
BRCA2 c.8009C>T, p.S2670L	CF1106	chr13:32,937,348C>T	18	E|33|323	VUS/LP/P								
	Skip exon 18					759	0.26	0.01	0.01	>10.00	0.51	del 355bp, 2702 stop	
	Skip exons 17+18					139	0.05	0.02	0.01	4.25	0.08	del 526bp, 2645 stop	
	Full length					2029	0.69	0.97	0.01	>10.00			
BRCA2 c.7802A>G, p.Y2601C	CF4683	chr13:32,932,063A>G	16	E|185|4	VUS								3
	Cryptic splice at c.7802					641	0.25	0.00	0.00	>10.00	0.50	del 4 bp, 2646 stop	
	Full length					1905	0.75	1.00	0.00	>10.00			
BRIP1 c.82A>G, p.M28V	CF4211	chr17:59,938,819T>C	2	E|112|12	VUS/LP								
	Skip exon 2					111	0.22	0.01	0.01	>10.00	0.43	loss of first ATG	
	Alternate splice 5' UTR					129	0.26	0.33	0.03	2.28		ns	
	Full length					258	0.52	0.66	0.03	4.59			
PALB2 c.2559C>T, p.G853G	CF1534	chr16:23,640,552G>A	6	E|45|28	VUS								2
	Cryptic donor exon 6 at c.2558					1077	0.49	0.00	0.00	>10.00	0.98	del 29bp, 873 stop	
	Full length					1130	0.51	1.00	0.00	>10.00			

Table S7. Transcriptional effects of genomic copy number mutations

Event	Transcript	genomic coordinates (hg19)	cBROCA result
BRCA2 exons 14-24 triplicated		chr13:32,927,735-32,958,445	
	CF1815, CF4541, CF4748, CF4755		
	3 tandem repeats of exons 14-24		ins 4498bp, 3116 stop
	3 tandem repeats of exons 14-24 + intron 24 insertion		ins 4776bp, 3098 stop
BRCA2 del exon 1		chr13:32,889,493-32,890,429	
	CF4727		
	promoter deletion, *de novo*		loss of transcript

Table S8. Mutations evaluated by cBROCA

Gene	Genotype	Position hg19	Table
APC	c.532(-1000)delGT	chr5:112,115,487	S5
ATM	c.-30-1G>T	chr11:108,098,321	S4
ATM	c.901G>A; G301S	chr11:108,115,753	S2
ATM	c.1009C>T, p.R337C	chr11:108,117,798	S3
ATM	c.2250G>A; p.K750K	chr11:108,127,067	S2
ATM	c.2638+2T>C	chr11:108,138,071	S2
ATM	c.3154-1G>A	chr11:108,143,448	S4
ATM	c.3963G>A, p.M1321I	chr11:108,155,170	S3
ATM	c.5007-3T>A	chr11:108,170,438	S5
ATM	c.5009C>T, p.A1670V	chr11:108,170,444	S3
ATM	c.5497-2A>C	chr11:108,175,400	S2
ATM	c.5674+1G>T	chr11:108,175,580	S4
ATM	c.5821G>C, p.V1941L	chr11:108,180,945	S3
ATM	c.6976-2A>C	chr11:108,198,370	S2
ATM	c.7089+1del38	chr11:108,198,484	S2
ATM	c.7181C>T, p.S2394L	chr11:108,199,839	S3
ATM	c.7629+2T>C	chr11:108,202,286	S4
ATM	c.8418+1delGTGA	chr11:108,214,099	S2
ATM	c.8787-13G>T	chr11:108,225,525	S5
ATM	c.8988-1G>A	chr11:108,236,051	S2
BARD1	c.159-1G>T	chr2:215,661,842	S4
BARD1	c.1569-12T>G	chr2:215,617,291	S5
BRCA1	c.75C>T, p.P25P	chr17:41,276,039	S3
BRCA1	c.81T>C, p.C27C	chr17:41,2677,96	S3
BRCA1	c.81-6T>C	chr17:41,267,802	S3
BRCA1	c.135-20T>G	chr17:41,258,570	S3
BRCA1	c.190G>T, p.D67Y	chr17:41,258,486	S3
BRCA1	c.212+1G>A	chr17:41,258,472	S4
BRCA1	c.301+55G>A	chr17:41,256,830	S3
BRCA1	c.594-2A>C	chr17:41,247,941	S4
BRCA1	c.4185+1insAdel21	chr17:41,242,939	S4
BRCA1	c.4185+37delTG	chr17:41,242,923	S3
BRCA1	c.4357+518delAAAG	chr17:41,233,900	S3
BRCA1	c.4484G>T; p.R1495M	chr17:41,228,505	S2
BRCA1	c.4485-1G>A	chr17:41,226,539	S4
BRCA1	c.4986+3G>C	chr17:41,222,942	S5
BRCA1	c.4992C>T, p.L1664L	chr17:41,219,707	S6
BRCA1	c.5022C>T, p.I1674I	chr17:41,219,677	S6
BRCA1	c.5072C>T, p.T1691I	chr17:41,219,627	S6
BRCA1	c.5074+1158C>T	chr17:41,218,467	S3
BRCA1	c.5097G>A, p.R1699R	chr17:41,215,946	S3
BRCA1	c.5194-12G>A	chr17:41,209,164	S5
BRCA1	c.5207T>G, p.V1736G	chr17:41,209,139	S3
BRCA1	c.5277+1G>A	chr17:41,209,068	S4
BRCA1	c.5278(-1519)T>C	chr17:41,204,653	S3
BRCA1	c.5406+4delAGTA	chr17:41,201,131	S5

Gene	Genotype	Position hg19	Table
BRCA1	c.5454C>T, p.D1818D	chr17:41,199,673	S3
BRCA1	c.5468-1G>A	chr17:41,197,820	S2
BRCA2	del exon 1	chr13:32,889,493-32,890,429del	S7
BRCA2	c.28A>G, p.T10A	chr13:32,890,624	S3
BRCA2	c.128A>G, p.N43S	chr13:32,893,274	S3
BRCA2	c.426(-252)G>A	chr13:32,899,986	S3
BRCA2	c.517-2A>G	chr13:32,900,634	S2
BRCA2	c.750G>A, p.V250V	chr13:32,905,124	S3
BRCA2	c.7007G>C, p.R2336P	chr13:32,921,033	S4
BRCA2	c.7007+1G>C	chr13:32,921,034	S4
BRCA2	c.7007+5G>A	chr13:32,921,038	S5
BRCA2	exons 14-24 triplicated	chr13:32,927,735-32,958,445trip	S7
BRCA2	c.7466A>G, p.D2489G	chr13:32,930,595	S3
BRCA2	c.7559G>C, p.R2520P	chr13:32,930,688	S3
BRCA2	c.7618-1G>A	chr13:32,931,878	S2
BRCA2	c.7802A>G, p.Y2601C	chr13:32,932,063	S6
BRCA2	c.7820C>T, p.T2607I	chr13:32,936,674	S3
BRCA2	c.7879A>T, p.I2627F	chr13:32,936,733	S3
BRCA2	c.7902G>A, p.M2634I	chr13:32,936,756	S3
BRCA2	c.7976G>A, p.R2659K	chr13:32,936,830	S4
BRCA2	c.7976+2C>G	chr13:32,936,832	S4
BRCA2	c.7992T>A, p.I2664I	chr13:32,937,331	S6
BRCA2	c.8009C>T, p.S2670L	chr13:32,937,348	S6
BRCA2	c.8206C>T, p.L2736F	chr13:32,937,545	S3
BRCA2	c.8285C>G, p.P2762R	chr13:32,937,624	S3
BRCA2	c.8331+3A>C	chr13:32,937,673	S5
BRCA2	c.8350C>T, p.R2784W	chr13:32,944,557	S3
BRCA2	c.8359C>T, p.R2787C	chr13:32,944,566	S3
BRCA2	c.8510G>T, p.G2837V	chr13:32,945,115	S3
BRCA2	c.9076C>G, p.Q3026E	chr13:32,954,009	S3
BRCA2	c.9117G>A, p.P3039P	chr13:32,954,050	S2
BRCA2	c.9344A>G, p.K3115R	chr13:32,968,913	S3
BRCA2	c.9648(+127)G>A	chr13:32,971,308	S3
BRIP1	c.82A>G, p.M28V	chr17:59,938,819	S6
BRIP1	c.93+1G>A	chr17:59,938,807	S2
BRIP1	c.93+1G>A	chr17:59,938,807	S4
BRIP1	c.297C>T, p.D99D	chr17:59,934,501	S3
BRIP1	c.626A>G, p.K209R	chr17:59,924,463	S4
BRIP1	c.2372A>T, p.D791V	chr17:59,820,381	S3
BRIP1	c.2309A>G, p.K797R	chr17:59,793,414	S3
BRIP1	c.2765T>C, p.L922S	chr17:59,763,337	S3
CDH1	c.1565+1G>A	chr16:68,849,663	S2
CDH1	c.1565+1G>A	chr16:68,849,663	S4
CDH1	c.1711G>A; G571S	chr16:68,853,328	S2
CDH1	c.2296-670T>A	chr16:68,862,887	S3
CDH1	c.2440-6C>G	chr16:68,867,187	S3
CHEK2	c.246-260del15	chr22:29,130,450-29,130,464del	S3
CHEK2	c.320-5T>A	chr22:29,121,360	S5

Gene	Genotype	Position hg19	Table
CHEK2	c.444+1G>A	chr22:29,121,230	S2
CHEK2	c.592+3A>T	chr22:29,120,962	S5
CHEK2	c.846+4delAGTA	chr22:29,105,987	S5
CHEK2	c.1130A>G, p.E377G	chr22:29,091,827	S3
GEN1	c.1072-185G>A	chr2:17,955,353	S3
MLH1	c.678-481C>T	chr3:37,055,442	S3
MLH1	c.1732-264A>T	chr3:37,088,746	S5
MSH2	c.2635-24A>G	chr2:47,709,894	S5
PALB2	c.46A>G, p.K16E	chr16:23,652,433	S3
PALB2	c.1551A>G, p.K517K	chr16:23,646,316	S3
PALB2	c.1699C>T, p.H567T	chr16:23,641,776	S3
PALB2	c.2204C>T, p.P735L	chr16:23,641,271	S3
PALB2	c.2289G>C, p.L763F	chr16:23,641,186	S3
PALB2	c.2515-1G>T	chr16:23,640,597	S2
PALB2	c.2559C>T, p.G853G	chr16:23,640,552	S6
PALB2	c.2587-703G>A	chr16:23,638,421	S3
PALB2	c.2752C>T, p.P918S	chr16:23,635,412	S3
PALB2	c.2835-1G>C	chr16:23,634,452	S2
PALB2	c.2835-1G>C	chr16:23,634,452	S4
PALB2	c.3113G>A, p.W1038X	chr16:23,632,683	S4
PTEN	c.79+4229A>T	chr10:89,628,534	S3
PTEN	c.79+11548A>G	chr10:89,638,942	S3
PTEN	c.210-7del5	chr10:89,690,796	S5
PTEN	c.492+7414A>G	chr10:89,700,422	S3
RAD51C	c.904+5G>T	chr17:56,798,178	S5
RAD51C	c.1026+5delGTA	chr17:56,809,910	S5
RAD51D	c.904-2A>T	chr17:33,428,057	S2
RAD51D	c.904-3C>T	chr17:33,428,059	S3
TP53	c.786(-60)G>A	chr17:7,577,215	S3

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Table S4

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