Table S1. Mutations in breast cancer genes in Palestinian patients

Subject	Age breast cancer diagnosis	Gene	Position (hg 19)	cDNA change	Molecular consequence	ExAC allele count	Reported here for first time	Study cohort (M/G)	Selection criteria	FH breast cancer	FH ovarian cancer	FH male breast cancer
MK1ES	41	BRCA1	chr17:41,268,824-41,297,565	del exons 1-3	del 28.7 kb	0	Y	M	FH	Y		
MKAH	54	BRCA1	chr17:41,267,756	c.121 C>T	p.His41Tyr	0	Y	M	FH	Y	Y	
MK1	Bi 34, 37	BRCA1	chr17:41,267,746	c.131 G>T	p.Cys44Phe	0		M	FH	Y	Y	
MKUP	35	BRCA1	chr17:41,258,532	c.315insGG	p.Leu52GlyfsX18	0	Y	M	FH	Y		
MKCX	42	BRCA1	chr17:41,247,926	c.607 G>T	p.Glu203Ter	0	Y	M	FH	Y		
MK2	Bi 51, 58	BRCA1	chr17:41,246,326	c.1224delA	p.Val409Ter	0		M	FH	Y		
MKWW	27	BRCA1	chr17:41,246,326	c.1224delA	p.Val409Ter	0		M	FH	Y		
MKPY	48	BRCA1	chr17:41,245,394	c.2291insA	p.Glu720ArgfsX6	0		M	FH	Y	Y	
MKSR	27	BRCA1	chr17:41,243,029	c.4117 C>A	p.Glu1373Ter	0		M	FH	Y		
MKKB	33	BRCA1	chr17:41,219,622	c.5074(+3) A>G	(see note*)	0		M	FH	Y		
MKTC	36	BRCA1	chr17:41,199,683	c.5444 C>T	p.Trp1815Ter	1		M	age			
MKK	33	BRCA2	chr13:32,903,605	c.658 del GT	p.Val220IlefsX4	6		M	age			
MK1EQ	32	BRCA2	chr13:32,907,420	c.1806 ins A	p.Gly602fsX13	0		M	FH	Y		
MKG	32	BRCA2	chr13:32,910,746	c.2482 del GACT	p.Asp752PhefsX19	0		M	FH	Y		
MKDC	31	BRCA2	chr13:32,910,746	c.2482 del GACT	p.Asp752PhefsX19	0		M	age			
MKIP	40	BRCA2	chr13:32,910,746	c.2482 del GACT	p.Asp752PhefsX19	0		M	FH	Y		
MKQV	45	BRCA2	chr13:32,910,746	c.2482 del GACT	p.Asp752PhefsX19	0		M	FH	Y		
MK1EB	66	BRCA2	chr13:32,910,746	c.2482 del GACT	p.Asp752PhefsX19	0		G	-			

MK1CC	48	BRCA2	chr13:32,910,746	c.2482 del GACT	p.Asp752PhefsX19	0		M	FH	Y		
MKDE	36	BRCA2	chr13:32,911,298	c.3033 del AAAC	p.Ala938ProfsX21	2		M	age			
MKZE	61	BRCA2	chr13:32,911,837	c.3345 del T	p.Thr1116LeufsX3	0	Y	M	FH	Y	Y	
MKVI	35	BRCA2	chr13:32,912,110	c.3617 del TTAT	p.Tyr1207Ter	0	Y	M	age			
MKTV	40	BRCA2	chr13:32,912,338	c.3846delTG	p.Val1283LysfsX2	11		M	FH		Y	
MKZT	42	BRCA2	chr13:32,912,338	c.3846delTG	p.Val1283LysfsX2	11		G	-			
MK1CW	Ov38, Br47	BRCA2	chr13:32,912,338	c.3846delTG	p.Val1283LysfsX2	11		M	FH	Y		
MKTO	44	BRCA2	chr13:32,913,559	c.5073 ins A	p.Trp1692MetfsX3	1		M	FH	Y		
MKDO	39	BRCA2	chr13:32,914,954	c.6462 del TC	p.Gln2157IlefsX18	0		M	FH	Y		
MKUQ	29	BRCA2	chr13:32,914,954	c.6462 del TC	p.Gln2157IlefsX18	0		M	FH	Y		
MKEV	58	BRCA2	chr13:32,915,177	c.6685 G>T	p.Glu2229Ter	0		M	FH	Y		
MKQS	40	BRCA2	chr13:32,915,177	c.6685 G>T	p.Glu2229Ter	0		M	FH	Y		
MKFK	47	BRCA2	chr13:32,915,177	c.6685 G>T	p.Glu2229Ter	0		M	FH	Y		
MKCI	50	BRCA2	chr13:32,915,177	c.6685 G>T	p.Glu2229Ter	0		G	-			
MK1DA	26	BRCA2	chr13:32,950,929	c.8754(+1)G>A	splice			M	FH			
MKVL	48	BRCA2	chr13:32,968,951	c.9382C>T	p.Arg3128Ter	2		M	FH	Y		
MK3	35	ATM	chr11:108,128,239	c.2284delCT	p.Leu762ValfsX2	0		M	FH	Y		
MK1C	41	ATM	chr11:108,139,336	c.2838 G>T	splice			M	FH		Y	
MK1O	60	ATM	chr11:108,202,695	c.7720insA	p.Pro2575ThrfsX11	0	Y	M	FH	Y		
MKBH	39	ATM	chr11:108,206,605	c.8185 C>T	p.Gln2729Ter	1		M	age			
MKPB	54	ATM	chr11:108,206,605	c.8185 C>T	p.Gln2729Ter	1		G	-			
MK4	39	ATM	chr11:108,096,223 -108,099,134	del exons 1-2	del 2.9kb	0	Y	M	FH	Y		
MK1DC	36	ATM	chr11:108,096,223 -108,099,134	del exons 1-2	del 2.9kb	0	Y	M	age			
MK5	36	CHEK2	chr22:29,121,058	c.499 G>A	p.Gly167Arg	5		M	FH		Y	
MKUB	43	CHEK2	chr22:29,121,058	c.499 G>A	p.Gly167Arg**	5		M	FH	Y		Y
MKI	42	CHEK2	chr22:29,095,917	c.917 G>C	p.Gly306Ala	7		M	FH	Y		
MKIA	60	CHEK2	chr22:29,095,917	c.917 G>C	p.Gly306Ala	7		M	FH	Y		
MKZD	20	CHEK2	chr22:29,120,962	c.592(+3)T>A	(see note***)	4		M	FH	Y		

MK7	32	TP53	chr17:7,578,389	c.541 G>A	p.Arg181Cys	0		M	FH	Y	
MK8	36	TP53	chr17:7,578,389	c.541 G>A	p.Arg181Cys	0		M	FH	Y	
MK1FJ	68	TP53	chr17:7,578,389	c.541 G>A	p.Arg181Cys	0		M	FH	Y	
MKYE	56	TP53	chr17:7,578,389	c.541 G>A	p.Arg181Cys	0		M	FH	Y	
MK1GG	45	TP53	chr17:7,578,389	c.541 G>A	p.Arg181Cys	0		M	FH	Y	
MKWE	39	TP53	chr17:7,578,389	c.541 G>A	p.Arg181Cys	0		M	age		
MK1FP	27	TP53	chr17:7,578,389	c.541 G>A	p.Arg181Cys	0		M	age		
MK1CL	60	TP53	chr17:7,578,389	c.541 G>A	p.Arg181Cys	0		M	FH	Y	
MKLR	41	TP53	chr17:7,578,389	c.541 G>A	p.Arg181Cys	0		M	FH	Y	
MKUB	43	BARD1	chr2:215,657,138	c.247 A>G	p.Cys83Arg**	0	Y	M	FH	Y	Y
MKPX	34	BARD1	chr2:215,593,531	c.2257 C>T	p.Gln735Ter****	0	Y	M	FH	Y	
MKZO	32	BARD1	chr2:215,593,531	c.2257 C>T	p.Gln735Ter	0	Y	M	age		
MK1EK	29	BARD1	chr2:215,657,157	c.225delACTT	p.Ser76ThrfsX19	0	Y	M	age		
MKPJ	40	BRIP1	chr17:59,934,561	c.237delA	p.Ala80LeufsX21	0	Y	M	age		
MKJ	30	BRIP1	chr17:59,878,628	c.1126 C>T	p.Gln376Ter	0	Y	M	age		
MKHA	42	MRE11A	chr11:94,180,454	c.1714 C>T	p.Arg572Ter	9		M	FH	Y	
MKTJ	40	PALB2	chr16:23,641,218	c.2257 C>T	p.Arg753Ter	4		M	FH	Y	
MK10	35	XRCC2	chr7:152,345,927	c.643 C>T	p.Arg215Ter	5		M	age		

Mutations were identified in the mutation discovery cohort (M) by BROCA sequencing and in the general patient cohort (G) by genotyping all alleles found in the mutation discovery cohort. Selection criteria were family history (FH) or age at diagnosis age 40 or younger (age)

* Mutation alters splicing leading to truncation via multiple transcripts (Menendez M et al. Breast Can Res 2012;132:979-992)

** MKUB carries mutations in CHEK2 and BARD1

*** Kraus C et al. Int J Cancer 2017;140(1):95-102.

**** BARD1 Q735X also appeared in 2/100 Palestinian controls.

ExAC database at http://exac.broadinstitute.org/ Accessed 17 December 2016

Bi (bilateral breast cancer), Ov (ovarian cancer), Br (breast cancer), Y (Yes)

Table S2. Previously unreported variants of unknown significance in Palestinian breast cancer patients

Chr	Coordinate	Gene	cDNA	Protein	Transcript	Type	MaxEnt score (ref > mut)	Gerp	Comment
4	84,397,795	FAM175A	c.215(+1)G>A (exon3)		NM_139076	splice	9.66>1.48	5.2	bp completely conserved, exon deletion would be out of frame
11	108,213,947	ATM	c.8269(-2)A>C (exon57)		NM_000051	splice	6.65>-1.39	5.6	bp completely conserved, exon deletion would be inframe
17	59,793,310	BRIP1	c.2492(+2)T>C (exon17)		NM_032043	splice	9.66>1.91	5.6	bp completely conserved, exon deletion would be out of frame
22	29,121,257	CHEK2	c.A547G (exon4)	S183G	NM_001005735	missense	-	5.9	aa completely conserved, PPH2 = 1.0, FHA domain

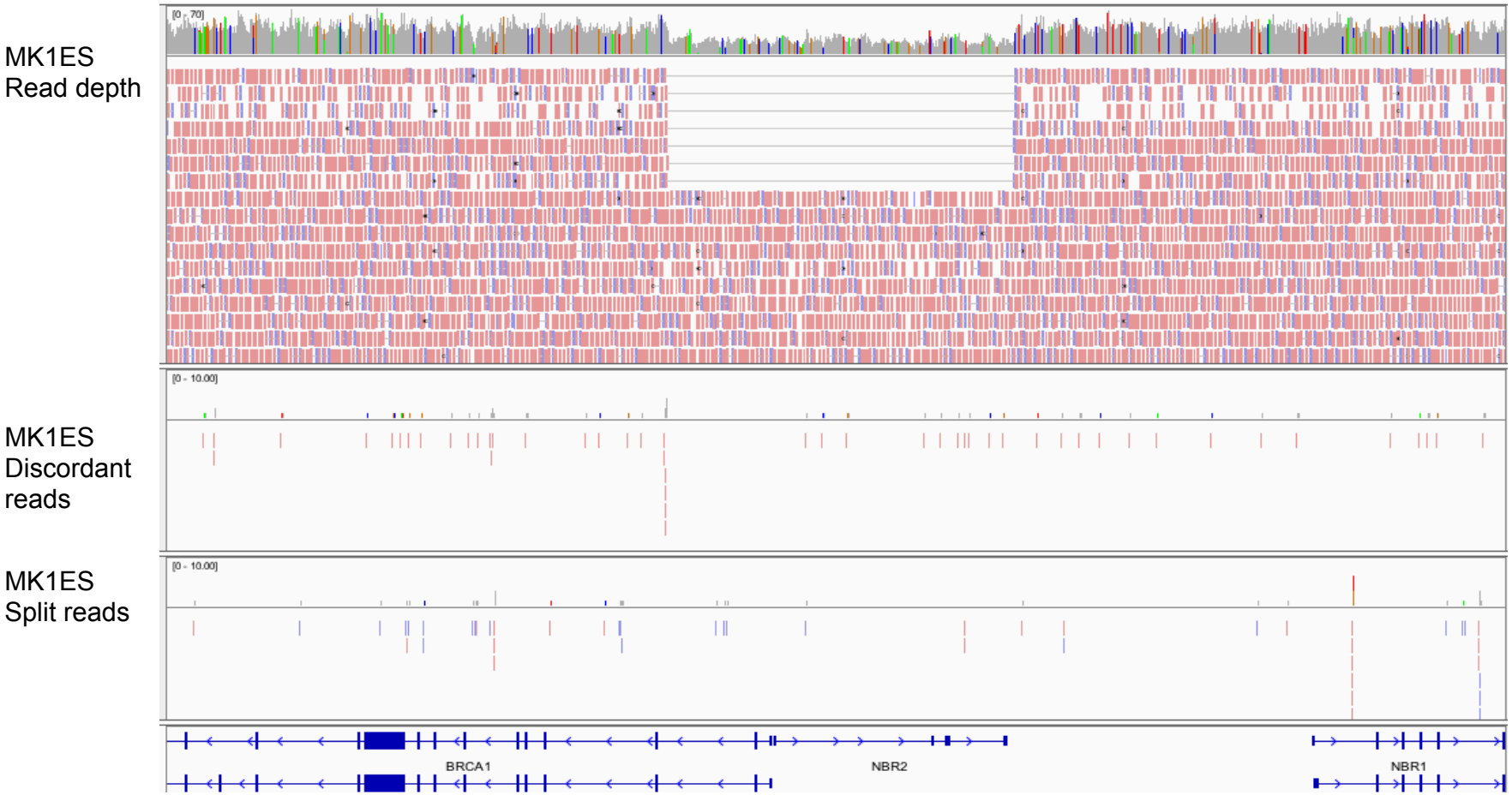
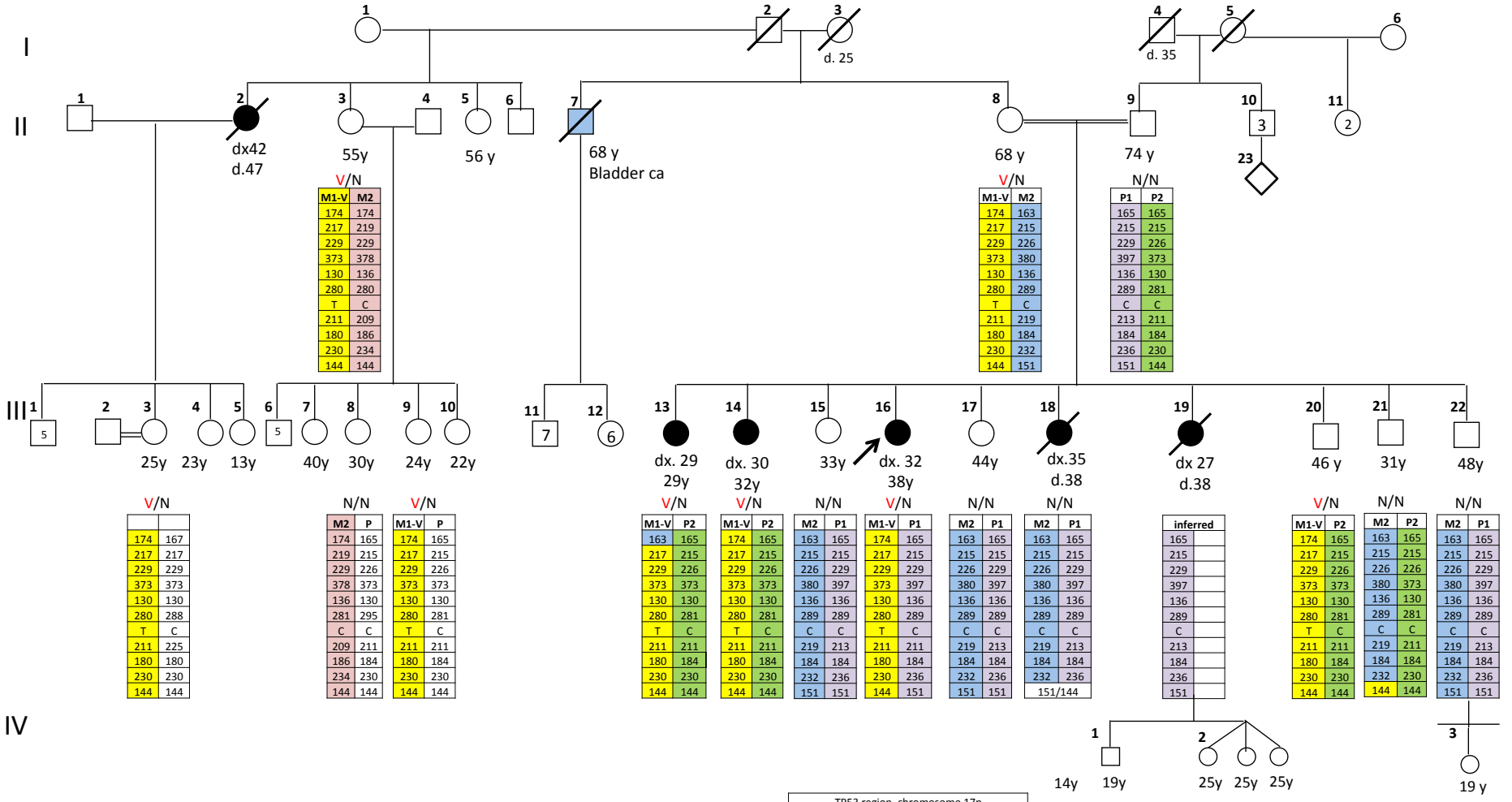


Figure S1. Deletion of the *BRCA1* promoter at chr17:41,268,824-41,297,565 in patient MK1ES, with breakpoints identified by whole genome sequencing and analysis by MANTA-SV



TP53 region, chromosome 17p		
D17S---	Genomic position hg19	Distance from gene (bp)
796	6,251,594	-1,326,795
1881	6,527,835	-1,050,554
516	6,653,622	-924,767
578	6,823,888	-754,501
960	7,257,773	-320,616
15TG	7,431,324	-147,065
c.541 C>T	7,578,389	0
1353	7,617,423	39,034.0
1796	7,787,271	208,882
1812	8,261,908	683,519
786	8,811,780	1,233,391

Figure S2 Haplotype analysis of family MK7 for markers on chromosome 17p flanking TP53 p.R181C. Markers are indicated in the table; numbers on each haplotype represent allele sizes. The haplotype of TP53 p.R181C is in yellow. III-18 does not carry TP53 p.R181C despite her young age at breast cancer diagnosis. DNA from III-19 was not available, and her children all inherited the haplotype of their maternal grandfather (II-9), so the TP53 genotype of III-19 cannot be inferred.

			Family			
			MK7	**MK8**	**MK1CL**	
Marker order	Marker	Position (hg19)	Genotype	Genotype	Genotype	Shared haplotype
1	D17S796	6,251,594	**174**/165	165/165	**174**/169	**174**
2	D17S1881	6,527,835	**217**/215	224/225	**217**/211	**217**
3	D17S516	6,653,622	**229**/229	227/240	**229**/229	**229**
4	D17S578	6,823,888	**373**/379	**373**/373	**373**/373	**373**
5	D17S960	7,257,773	**130**/136	**130**/136	**130**/136	**130**
6	15TG	7,431,324	**280**/289	**280**/289	**280**/297	**280**
TP53 at 7,571,720 – 7,590,868; R181C at 7,578,389						
7	D17S1353	7,617,423	**211**/211	**211**/211	**211**/219	**211**
8	D17S1796	7,787,271	**180**/184	**180**/184	**180**/184	**180**
9	D17S1812	8,261,908	**230**/236	**230**/234	**230**/236	**230**
10	D17S786	8,811,780	**144**/151	**144**/144	**144**/144	**144**

Figure S3. Genotypes at chromosome 17p markers of patients heterozygous for TP53 p.R181C. For each STR marker, allele sizes are indicated in basepairs. The shared haplotype is shown in the blue shaded column.