Supplemental Data

Genome-wide Linkage Scan Reveals

Three Putative Breast-Cancer-Susceptibility Loci

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Table S1: Different combinations of the genotyped members of the BRCA positive families used to calculate the power in linkage detection.

Family	Gene	Combination*	Individual	Status	HLOD
698	*BRCA2*	Original	05S1262	affected	0.50
			05S1263	unaffected	
			05S1264	unaffected	
			04S137	affected	
			05S1261	affected	
		1	05S1262	affected	0.44
			04S137	affected	
			05S1261	affected	
		2	05S1262	affected	0.46
			05S1263	unaffected	
			04S137	affected	
			05S1261	affected	
		3	05S1262	affected	0.46
			04S137	affected	
			05S1264	unaffected	
			05S1261	affected	
		4	05S1262	affected	**-0.76**
			05S1264	**affected**	
			04S137	affected	
			05S1261	affected	
752	*BRCA1*	Original	05S1377	unaffected	0.62
			04S439	affected	
			05S1379	unaffected	
			05S1374	affected	
			05S1375	affected	
			05S1380	affected	
		1	04S439	affected	0.28
			05S1374	affected	
			05S1375	affected	
		2	04S439	affected	0.28
			05S1374	affected	
			05S1380	affected	
		3	05S1374	affected	0.28
			05S1375	affected	
			05S1380	affected	

		4	04S439	affected	0.25
			05S1375	affected	
			05S1380	affected	
		5	04S439	affected	**0.04**
			05S1379	**affected**	
			05S1375	affected	
			05S1380	affected	
		6	04S439	affected	0.25
			05S1374	affected	
			05S1380	affected	
921	*BRCA2*	Original	05S138	affected	0.08
			05S139	affected	
			05S1413	affected	
			05S1414	affected	
		1	05S138	affected	0.26
			05S139	affected	
			05S1413	affected	
		2	05S138	affected	**-0.60**
			05S139	affected	
			05S1414	affected	
		3	05S138	affected	0.24
			05S1413	affected	
			05S1414	affected	
		4	05S139	affected	**-0.20**
			05S1413	affected	
			05S1414	affected	

The pedigrees from the three *BRCA* positive families are represented in Figure 1. In this table we present different combinations (*) used to calculate the maximum HLOD score for each family. For example, in family 698 the combination "original" represents the pedigree used to calculate the HLOD score (shown in the last column, in this case 0.50) using all the genotyped members of this family. In the same family, combination "1" represents the hypothetical case in which only these 3 members from the family were genotyped, obtaining a HLOD score = 0.44. With the combination "4" of family 698 and the combination "5" of family 752 we simulated the phenocopy effect (affected but not mutation carrier individual), and the effect in the HLOD score is notable (highlighted in **bold**). In **bold and red,** we highlight the effect in the HLOD score of the randomness in the genotypes, e.g., the homozygous genotypes on some markers in some individuals could mask the linkage signal. The column *Status* represents the status parameter used for Merlin software.

Table S2: Information of all the STR markers used for the fine-mapping in the three candidate regions.

Chromosome	Marker	Position Mb	Size bp	Expected Heterozygosity	Observed Heterozygosity	Singlepoint HLOD
3	D3S3575	160.83	204-226	0.79	0.79	0.206
	D3S3702	164.88	209-229	0.81	0.77	0.692
	D3S3712	168.45	179-209	0.77	0.82	2.166
	D3S1229	171.85	110-128	0.84	0.86	1.036
6	D6S1703	146.05	135-159	0.77	0.80	0.975/1.499
	D6S311	148.73	219-265	0.93	0.91	1.410/1.735
	D6S1654	149.62	257-279	0.82	0.81	0.545/1.130
	D6S1687	151.06	126-144	0.66	0.41	0.637/0.306
	D6S420	152.51	174-194	0.66	0.72	0.848/0.523
21	D21S1921	35.34	196-214	0.81	0.81	0.118
	D21S1252	36.74	226-254	0.80	0.86	1.449
	D21S267	37.38	177-199	0.88	0.76	2.092
	D21S1883	38.42	227-239	0.73	0.73	0.640

Singlepoint values are extracted from only putative linked families. For the markers located on chromosome 6, singlepoint values are shown for 7/5 (before/after fine-mapping data) putative linked families. We ruled out two families in chromosome 6 because the haplotypical segregation was disrupted when STR markers were added (see Supp. Figure 1).

Table S3: Results of linkage analysis using three different subgroups of families.

Subgroup	Number of families	Chromosome	HLOD
Bilaterality	13	3	3.13
		12	1.78
≤ 50 years	21	21	2.40
		6	1.31
		3	1.22
≥ 4 BC cases	23	3	2.78
		6	1.78
		21	1.37

Results from the three subgroups of families, families with members affected by bilateral breast cancer, families with mean age lower or equal than 50 years and families with 4 or more breast cancer cases, are represented in this table. We would like to highlight the HLOD score obtained from the subset of bilateral families in chromosome 3 (HLOD=3.13).

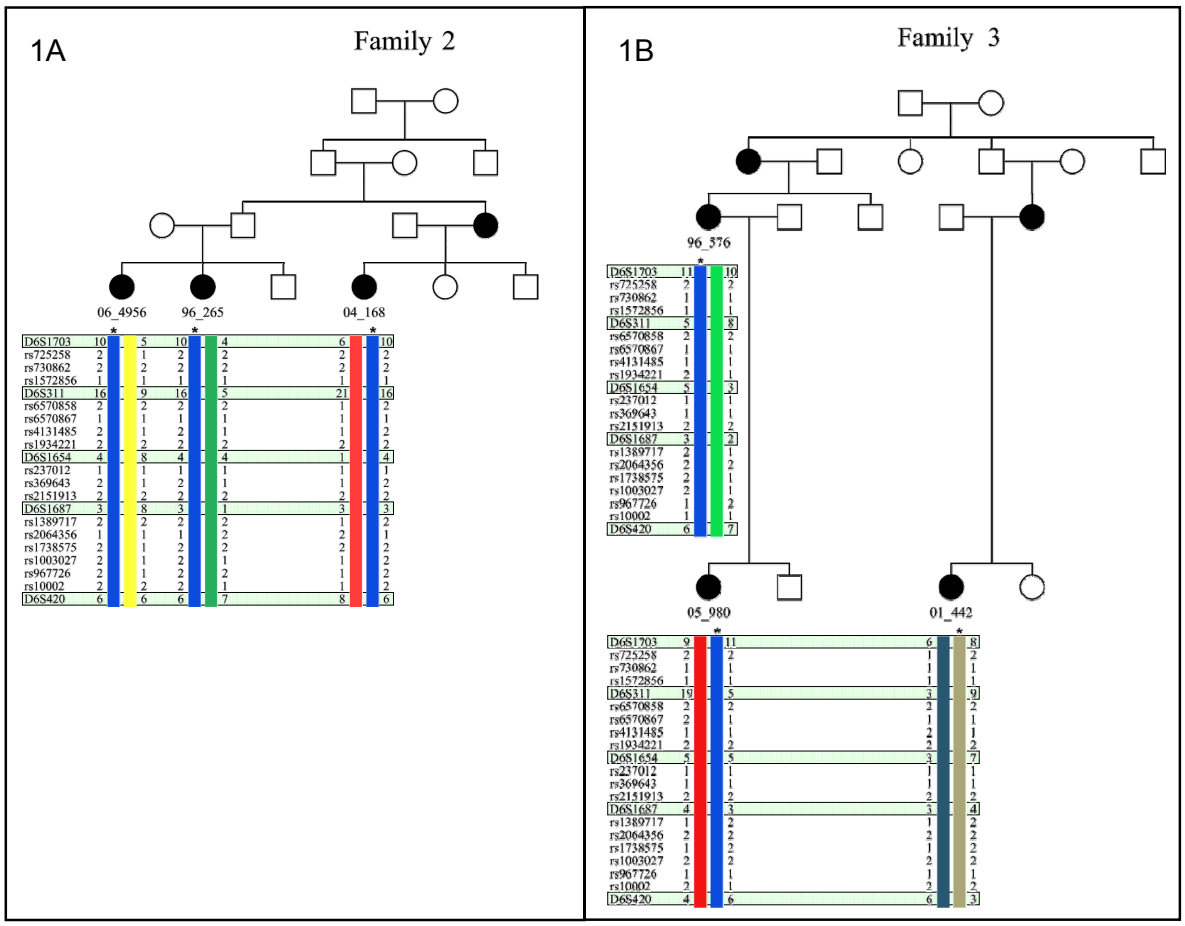

Figure S1: Fine Mapping: Representation of the pedigrees of two families identified by SNP markers as putative linked to region on chromosome 6. We used five STR markers to confirm the segregation of the shared haplotypes identified by SNP markers. In Family 2 (1A) the segregation is confirmed whereas in Family 3 (1B) the segregation is ruled out. STR markers are shadowed in light green.