Supplementary Table 1 Genotyping of SNPs for 44 mitotic kinase genes selected by the SNP-tagging approach

Kinome genes	**Mitotic abnormalities**	**Genotyped SNP with valid data**			**HapMap number (NCBI36)**		**% Coverage of HapMap (NCBI36)**		**Genotyped tagSNP density**
	Bettencourt-Dias *et al*., 2004	**Tagged**	**Functional**	**Total**	**SNP**	**Bin**	**Gene**	**Bin**	**TagSNP per kb**
AURKB	8N peak, CYT, CN, ABN, CHR	5	0	5	8	6	88	83	0.31
AURKC	NA	3	0	3	15	5	60	60	0.21
BRD4	S+, aneuploidy, G2/M+, MI, CYT, PM	5	0	5	20	6	80	83	0.09
BUB1	Aneuploidy, ABN	1	0	1	12	1	100	100	0.02
BUB1B	Aneuploidy, MI, PM, ABN, CHR	6	1	7	35	6	100	100	0.08
CDC7	S+, G2/M+	8	0	8	21	9	95	89	0.23
CDK2	G1+, size+, MI, CYT	6	2	6	11	7	91	86	0.38
CDK7	NA	3	0	3	22	5	82	60	0.06
CHEK1	SP, CRAD, CRLC	8	1	8	45	12	87	67	0.20
CIT	8N peak, PM, ABN	13	1	14	114	14	99	93	0.06
CLK2	G1+	1	0	1	4	1	100	100	0.05
CSNK2A1	G2/M+, ABN, CN, CRLC	6	0	6	27	10	81	60	0.08
DBF4	G1+	4	2a	6	8	4	100	100	0.09
EIF2AK4	ABN, SP, CHR, CRAD	4	1	5	117	37	15	11	0.04
IRAK1	CYT	1a	0	1	3	1	100	100	0.05
IRAK4	CYT	7	1	7	29	7	100	100	0.18
KIAA0999	SP, CRAD	22b	1	23	158	23	99	91	0.08
LATS1	G1+	1	3c	4	18	1	100	100	0.06
LATS2	G1+	14	0	14	53	15	94	93	0.14
LRRK1	PM, CN	10	2	12	155	48	31	21	0.06
MAP2K3	G1+, ABN, SP	5	7d	10	22	8	45	63	0.12
MAP2K4	CHR	18	1e	19	63	18	100	100	0.14
MAPKAPK2	SP, CRAD	9	1	10	39	10	97	90	0.15
MAST2	G2/M+, CRAD	10	1a	11	161	10	99	90	0.04
MASTL	NA	11	3f	13	47	12	98	92	0.26
NLK	ABN, SP, CN, CRLC	10	0	10	17	10	100	100	0.06
PAK4	S+, aneuploidy, G2/M+, CRAD	12	0	12	36	8	94	75	0.19
PAK6	S+, aneuploidy, G2/M+, CRAD	17	1a	18	41	20	95	90	0.36
PAK7	S+, aneuploidy, G2/M+, CRAD	1a	3a	3	457	108	9	3	0.02
PKMYT1	G1+	2	0	2	6	5	50	40	0.11
PLK1	G2/M+, MI, CYT, PM, ABN, SP, CN	5	1	5	11	6	91	83	0.23
PRKACB	ABN, SP, CHR	19	4	23	77	20	94	90	0.11
PRKG2	S+, aneuploidy, MI, ABN, SP	10	1a	11	69	13	93	69	0.07
ROCK1	ABN, SP	7	1	7	34	7	100	100	0.04
ROCK2	ABN, SP	9	2a	11	108	10	66	90	0.05

RYK	**PM, ABN, CN, SP, CHR**	**8**	**1**	**9**	**61**	**9**	**84**	**89**	**0.08**
SCYL3	**SP**	**12**	**9g**	**20**	**81**	**13**	**99**	**92**	**0.24**
STK11	**ABN, CN, SP**	**1**	**0**	**1**	**6**	**4**	**33**	**25**	**0.03**
STK4	**SP, CRLC**	**8**	**3a**	**11**	**86**	**10**	**97**	**80**	**0.06**
TTK	**MI, PM, SP**	**5**	**4a**	**9**	**71**	**5**	**100**	**100**	**0.10**
WEE1	**G1+**	**6**	**0**	**6**	**12**	**7**	**92**	**86**	**0.22**
CDC42BPA	**MI**	**0**	**6**	**6**	**491**	**42**	**9**	**12**	**NA**
FYN	**MI, ABN**	**0**	**9**	**9**	**210**	**45**	**39**	**18**	**NA**
MAP2K6	**G1+, ABN, SP**	**0**	**6a**	**6**	**125**	**41**	**16**	**7**	**NA**

NOTE: a: all perlegen SNPs; b: 2 SNPs belong to the same bin genotyped; c: 2 perlegen SNPs, 1 HapMap SNP; d: 2 perlegen, 2 HapMap and 3 Ensembl SNPs e: NIEHS SNP; f: 2 perlegen and 1 HapMap SNPs; g: 8 perlegen and 1 HapMap SNPs
Descriptions of phenotypes of mitotic abnormalities listed here were referenced from Bettencourt-Dias *et al*., 2004
For *MAST2*, % coverage is 100% compared to NCBI35 but 90% to NCBI36 because of bin structure change. The same holds true for *PAK4*
In *PAK6*, all 18 snps genotyped account for 18 bins in NCBI36
All 19 *PRKACB* tagSNPs in NCBI35 account for 18 bins in NCBI36
All 10 *PRKG2* tagSNPs in NCBI35 account for only 9 bins in NCBI36 because of bin structure change

Supplementary Table 2 Association of SNPs in mitotic kinase genes with breast cancer risk in pre- and post-menopausal women

Gene Name	rsID	Premenopausal Women		Postmenopausal Women	
		OR (95% CI) Per Allele	P_{trend}	OR (95% CI) Per Allele	P_{trend}
BRD4	rs4808278	1.12 (0.74-1.69)	0.60	1.39 (1.06-1.83)	0.02
*BRD4**	rs8104223	1.08 (0.80-1.47)	0.60	0.79 (0.65-0.96)	0.02
BUB1B	rs7182070	0.82 (0.56-1.19)	0.30	0.77 (0.59-0.99)	0.04
CDC42BPA	rs2802269	0.52 (0.32-0.86)	0.01	0.86 (0.64-1.15)	0.37
CDC42BPA	rs1929860	1.30 (0.97-1.75)	0.08	1.08 (0.89-1.30)	0.43
*CDK2**	rs11171710	1.40 (1.07-1.84)	0.02	0.99 (0.83-1.19)	0.94
*CHEK1**	rs3731399	1.24 (0.84-1.84)	0.27	0.74 (0.56-0.98)	0.04
CIT	rs17496224	1.81 (1.03-3.20)	0.04	1.43 (0.94-2.20)	0.10
*CIT**	rs4766950	1.01 (0.78-1.32)	0.93	1.21 (1.01-1.45)	0.04
DBF4	rs9655955	0.80 (0.48-1.32)	0.38	0.69 (0.48-0.99)	0.04
EIF2AK4	rs2291627	1.30 (0.83-2.05)	0.26	1.25 (0.90-1.73)	0.18
FYN	rs6914091	1.32 (1.00-1.74)	0.05	1.36 (1.13-1.64)	0.001
FYN	rs1465061	1.22 (0.93-1.61)	0.16	1.41 (1.16-1.70)	0.0004
FYN	rs12910	1.20 (0.91-1.57)	0.19	1.31 (1.09-1.57)	0.004
*FYN**	rs13218316	0.58 (0.41-0.83	0.003	0.94 (0.74-1.20)	0.64
KIAA0999	rs10047459	1.67 (1.13-2.45)	0.009	1.11 (0.88-1.40)	0.37
KIAA0999	rs1473177	0.77 (0.50-1.16)	0.21	0.70 (0.52-0.94)	0.02
KIAA0999	rs17120241	0.71 (0.49-1.04)	0.08	0.72 (0.55-0.94)	0.02
*KIAA0999**	rs11216164	0.67 (0.50-0.88)	0.005	1.03 (0.85-1.25)	0.76
*KIAA0999**	rs7120173	1.48 (1.07-2.04)	0.02	1.12 (0.90-1.40)	0.29
*KIAA0999**	rs10502221	0.74 (0.56-0.97)	0.03	1.04 (0.87-1.24)	0.67
*KIAA0999**	rs12225230	0.85 (0.60-1.21)	0.37	0.78 (0.61-0.99)	0.04
*KIAA0999**	rs7928320	0.79 (0.58-1.08)	0.15	0.80 (0.64-0.99)	0.04
*KIAA0999**	rs17120197	0.72 (0.51-1.02)	0.06	0.79 (0.62-0.99)	0.04
*MAP2K4**	rs4791490	0.70 (0.49-0.98)	0.04	1.22 (0.97-1.53)	0.09
*MAPKAPK2**	rs17350838	1.00 (0.73-1.37)	0.99	1.26 (1.01-1.57)	0.04
*MAST2**	rs4660318	0.71 (0.53-0.97)	0.03	1.07 (0.87-1.31)	0.52
*MASTL**	rs12774853	0.68 (0.37-1.26)	0.22	1.91 (1.28-2.85)	0.002
*MASTL**	rs2274636	0.67 (0.42-1.07)	0.09	1.50 (1.07-2.11)	0.02
*MASTL**	rs11015599	0.83 (0.54-1.27)	0.40	1.44 (1.06-1.96)	0.02
*PAK4**	rs7257109	0.74 (0.57-0.97)	0.03	1.10 (0.92-1.32)	0.28
*PAK4**	rs2318902	1.46 (1.01-2.12)	0.05	1.01 (0.80-1.27)	0.92
PAK6	rs4924445	1.14 (0.87-1.51)	0.35	1.24 (1.04-1.49)	0.02

PAK6	**rs7169803**	**0.92 (0.67-1.26)**	**0.59**	**0.76 (0.61-0.93)**	**0.009**
PKACB	**rs12728744**	**0.56 (0.30-1.06)**	**0.08**	**0.76 (0.50-1.15)**	**0.20**
PKACB*	**rs12129768**	**1.61 (1.04-2.52)**	**0.03**	**0.99 (0.74-1.32)**	**0.93**
PRKG2*	**rs3733553**	**1.46 (1.04-2.05)**	**0.03**	**1.05 (0.86-1.28)**	**0.65**
PRKG2*	**rs7656323**	**1.51 (1.02-2.22)**	**0.04**	**0.90 (0.72-1.13)**	**0.37**
PRKG2*	**rs6827939**	**1.25 (0.83-1.87)**	**0.28**	**0.75 (0.57-0.97)**	**0.03**
ROCK1	**rs17202375**	**0.97 (0.61-1.53)**	**0.89**	**1.72 (1.25-2.37)**	**0.0009**
ROCK1*	**rs288989**	**0.99 (0.75-1.31)**	**0.97**	**0.81 (0.68-0.97)**	**0.02**
ROCK2*	**rs9808232**	**1.39 (1.07-1.82)**	**0.01**	**0.85 (0.71-1.02)**	**0..07**
ROCK2*	**rs978906**	**0.73 (0.57-0.95)**	**0.02**	**1.13 (0.95-1.35)**	**0.18**
ROCK2*	**rs2056103**	**1.37 (1.05-1.79)**	**0.02**	**0.86 (0.72-1.02)**	**0.09**
ROCK2*	**rs2290156**	**1.37 (1.01-1.86)**	**0.05**	**0.91 (0.75-1.10)**	**0.33**
RYK	**rs10935104**	**1.54 (1.03-2.31)**	**0.04**	**1.26 (0.98-1.60)**	**0.07**
RYK	**rs9283588**	**1.47 (0.96-2.25)**	**0.08**	**1.28 (0.98-1.66)**	**0.07**
RYK	**rs1131262**	**1.50 (0.98-2.31)**	**0.06**	**1.24 (0.96-1.61)**	**0.10**
RYK*	**rs12186098**	**2.52 (1.25-5.07)**	**0.01**	**0.99 (0.65-1.49)**	**0.95**
SCYL3*	**rs3817859**	**0.62 (0.39-0.98)**	**0.04**	**0.97 (72-1.32)**	**0.86**
STK4	**rs17420378**	**0.84 (0.63-1.14)**	**0.26**	**0.83 (0.68-1.01)**	**0.06**
STK4	**rs6073636**	**0.84 (0.62-1.13)**	**0.24**	**0.84 (0.69-1.02)**	**0.08**

NOTE: OR, odds ratio; CI, confidence interval.
Logistic regression analysis adjusted for age, geographical region, menopausal status, age at menarche, oral contraceptive use, age first birth, hormone replacement therapy and pack-years cigarette smoking.
*Non-significant association in the complete case-control study population.

Supplementary Table 3 Haplotype blocks identified in nine genes associated with breast cancer risk

Haplotypes and Blocks	Haplotype	Hap-Frequency	Hap-Score	*P*-value
***BRD4* block 1**	**21111**	**0.164**	**-1.62**	**0.10**
	11211	**0.200**	**-1.58**	**0.11**
	11221	**0.104**	**-0.41**	**0.68**
	22111	**0.179**	**0.28**	**0.78**
	11111	**0.238**	**1.39**	**0.16**
	21112	**0.115**	**2.04**	**0.04**
***BUB1B* block 1**	**1122**	**0.147**	**-2.04**	**0.04**
	1111	**0.245**	**-0.42**	**0.68**
	1211	**0.318**	**0.82**	**0.41**
	1121	**0.009**	**0.89**	**0.37**
	2121	**0.280**	**0.98**	**0.33**
***DBF4* block 1**	**21122**	**0.068**	**-2.31**	**0.02**
	12111	**0.063**	**-0.54**	**0.59**
	11211	**0.055**	**0.07**	**0.95**
	11122	**0.115**	**0.15**	**0.88**
	11111	**0.697**	**1.30**	**0.19**
***KIAA0999* block 1**	**11121**	**0.110**	**-2.10**	**0.04**
	12111	**0.349**	**-1.54**	**0.12**
	21112	**0.050**	**-0.14**	**0.89**
	11211	**0.070**	**0.10**	**0.92**
	11221	**0.002**	**0.50**	**0.61**
	11112	**0.166**	**1.46**	**0.14**
	11111	**0.251**	**1.69**	**0.09**
***MAST2* block 1**	**12112122**	**0.066**	**-2.08**	**0.04**
	11222111	**0.005**	**-1.80**	**0.07**
	11211111	**0.152**	**-1.20**	**0.23**
	11111111	**0.003**	**-0.46**	**0.65**
	12112222	**0.098**	**0.20**	**0.84**
	11221111	**0.134**	**0.59**	**0.56**
	21111111	**0.260**	**0.89**	**0.38**
	11112122	**0.280**	**1.16**	**0.25**
***MAP2K4* block 1**	**1211112**	**0.007**	**-1.80**	**0.07**
	2211111	**0.143**	**-1.51**	**0.13**
	1112111	**0.100**	**-1.47**	**0.14**
	1111122	**0.003**	**-1.16**	**0.25**
	1112122	**0.214**	**-0.63**	**0.53**
	1111112	**0.002**	**-0.62**	**0.54**
	1221111	**0.108**	**-0.02**	**0.99**
	1111212	**0.245**	**1.06**	**0.29**
	1211111	**0.178**	**2.76**	**0.006**
***ROCK1* block 1**	**1211**	**0.459**	**-1.69**	**0.09**
	1112	**0.216**	**-0.79**	**0.43**
	2112	**0.092**	**-0.19**	**0.85**
	1111	**0.139**	**1.13**	**0.26**

	1122	0.091	2.70	0.007
RYK block 1	1111112	0.128	-1.35	0.18
	1121121	0.002	-1.24	0.21
	1111211	0.346	-1.19	0.23
	1112111	0.323	-0.63	0.53
	1111111	0.002	0.33	0.74
	1112211	0.002	0.81	0.42
	1121111	0.018	0.82	0.41
	2111211	0.054	1.68	0.09
	1221121	0.125	2.47	0.01
STK4 block 1	1122111122	0.139	-2.41	0.02
	2121112221	0.115	-0.57	0.57
	1122121122	0.157	-0.40	0.69
	1211111111	0.078	0.48	0.63
	1121111121	0.003	0.49	0.63
	1111211111	0.152	0.68	0.50
	1111111111	0.283	0.81	0.42
	1121112221	0.065	1.43	0.15
	1111111121	0.004	1.47	0.14

NOTE: 1=major allele, 2=minor allele; Hap-Frequency: frequency of each haplotype in the controls; Hap-Score: statistical measurement of association of each specific haplotype with breast cancer risk

Supplementary Table 4 Pair-wise combinations of SNPs that displayed significant associations with breast cancer risk (Chi-square $P \leq 0.0001$)

SNP 1	SNP 2	Gene 1	Gene 2	$OR_{1/0\ copies}$	$OR_{2/0\ copies}$	$OR_{0/1\ copies}$	$OR_{1/1\ copies}$	$OR_{2/1\ copies}$	$OR_{0/2\ copies}$	$OR_{1/2\ copies}$	$OR_{2/2\ copies}$
rs7928320	rs278123	*KIAA0999*	*CIT*	1.00 (0.73, 1.39)	1.12 (0.62, 2.02)	1.16 (0.90, 1.49)	0.61 (0.43, 0.86)	1.72 (0.89, 3.36)	1.15 (0.76, 1.74)	0.25 (0.12, 0.53)	3.10 (0.62, 15.48)
rs7928320	rs17409442	*KIAA0999*	*CIT*	0.98 (0.72, 1.33)	1.18 (0.67, 2.07)	1.22 (0.95, 1.56)	0.62 (0.44, 0.87)	1.87 (0.96, 3.65)	1.18 (0.75, 1.85)	0.20 (0.08, 0.49)	2.10 (0.38, 11.55)
rs7928320	rs175877	*KIAA0999*	*CIT*	0.50 (0.38, 0.66)	1.27 (0.78, 2.07)	0.81 (0.62, 1.05)	0.80 (0.56, 1.15)	0.96 (0.42, 2.18)	0.40 (0.19, 0.83)	1.40 (0.46, 4.28)	(,)
rs7928320	rs278126	*KIAA0999*	*CIT*	0.94 (0.69, 1.29)	1.16 (0.66, 2.04)	1.19 (0.93, 1.53)	0.64 (0.46, 0.90)	1.92 (0.98, 3.73)	1.03 (0.67, 1.59)	0.21 (0.09, 0.48)	1.55 (0.26, 9.40)
rs4660891	rs6914091	*MAST2*	*FYN*	1.86 (1.29, 2.68)	0.60 (0.28, 1.28)	1.58 (1.16, 2.14)	1.86 (1.34, 2.58)	1.22 (0.64, 2.33)	2.20 (1.49, 3.26)	1.77 (1.13, 2.77)	3.34 (1.30, 8.56)
rs7928320	rs633	*KIAA0999*	*IRAK1*	0.50 (0.38, 0.67)	1.30 (0.78, 2.17)	1.03 (0.80, 1.34)	1.12 (0.77, 1.62)	1.20 (0.56, 2.58)	0.84 (0.46, 1.54)	0.96 (0.40, 2.32)	3.85 (0.43, 34.54)
rs7928320	rs570278	*KIAA0999*	*PAK4*	0.71 (0.56, 0.89)	1.22 (0.79, 1.88)	1.37 (0.86, 2.17)	0.27 (0.10, 0.74)	(,)	1.00 (,)	1.00 (,)	1.00 (,)
rs7928320	rs4427776	*KIAA0999*	*LRRK1*	0.61 (0.46, 0.82)	1.61 (0.88, 2.96)	0.99 (0.77, 1.27)	0.68 (0.47, 0.98)	0.84 (0.46, 1.54)	0.44 (0.25, 0.75)	0.51 (0.23, 1.17)	(,)
rs10929728	rs12915781	*ROCK2*	*LRRK1*	0.96 (0.74, 1.26)	0.80 (0.53, 1.20)	1.25 (0.92, 1.70)	0.97 (0.71, 1.33)	2.45 (1.36, 4.42)	0.95 (0.46, 1.96)	0.32 (0.15, 0.65)	3.95 (1.08, 14.40)
rs1465061	rs4924445	*FYN*	*PAK6*	1.50 (1.05, 2.13)	1.52 (0.91, 2.53)	1.48 (1.05, 2.09)	1.42 (1.01, 1.98)	3.55 (2.17, 5.79)	1.49 (0.95, 2.33)	2.20 (1.43, 3.39)	1.60 (0.82, 3.12)
rs10929728	rs2924848	*ROCK2*	*LRRK1*	0.55 (0.37, 0.82)	2.17 (1.18, 3.99)	0.98 (0.69, 1.39)	1.13 (0.80, 1.60)	1.11 (0.67, 1.84)	1.21 (0.80, 1.83)	0.83 (0.54, 1.27)	0.63 (0.32, 1.26)
rs6914091	rs2707736	*FYN*	*CIT*	0.99 (0.73, 1.35)	1.31 (0.89, 1.94)	0.66 (0.45, 0.95)	0.97 (0.71, 1.35)	1.37 (0.89, 2.12)	0.38 (0.19, 0.75)	1.93 (1.11, 3.33)	1.13 (0.51, 2.47)
rs6914091	rs2242119	*FYN*	*PAK6*	1.38 (0.96, 1.99)	1.34 (0.83, 2.14)	1.12 (0.76, 1.64)	1.43 (1.01, 2.01)	3.00 (1.91, 4.71)	1.26 (0.77, 2.06)	1.79 (1.14, 2.81)	0.96 (0.50, 1.84)
rs12910	rs633	*FYN*	*IRAK1*	1.80 (1.35, 2.41)	1.81 (1.27, 2.58)	2.30 (1.49, 3.55)	1.71 (1.22, 2.40)	2.12 (1.38, 3.26)	1.75 (0.60, 5.14)	0.83 (0.36, 1.89)	3.69 (1.62, 8.41)
rs7928320	rs9899521	*KIAA0999*	*MAP2K3*	0.64 (0.48, 0.86)	1.34 (0.73, 2.47)	0.73 (0.57, 0.94)	0.64 (0.45, 0.91)	0.97 (0.51, 1.86)	1.40 (0.86, 2.28)	0.25 (0.10, 0.63)	2.06 (0.53, 7.95)
rs1112880	rs7928320	*PRKG2*	*KIAA0999*	0.95 (0.66, 1.35)	4.80 (0.56, 41.4)	0.61 (0.47, 0.77)	0.96 (0.57, 1.60)	(,)	1.58 (0.99, 2.53)	0.72 (0.25, 2.07)	(,)
rs6914091	rs4924445	*FYN*	*PAK6*	1.57 (1.08, 2.28)	1.53 (0.96, 2.45)	1.37 (0.93, 2.02)	1.57 (1.10, 2.22)	3.12 (1.99, 4.90)	1.57 (0.94, 2.61)	2.32 (1.48, 3.64)	1.49 (0.79, 2.78)
rs12526265	rs616495	*TTK*	*LATS2*	1.21 (0.93, 1.58)	1.62 (1.05, 2.49)	1.91 (1.40, 2.60)	1.01 (0.74, 1.38)	1.48 (0.86, 2.57)	1.91 (1.04, 3.51)	0.88 (0.45, 1.76)	(,)
rs7928320	rs2297345	*KIAA0999*	*PAK7*	0.87 (0.63, 1.20)	1.23 (0.71, 2.13)	1.16 (0.90, 1.48)	0.70 (0.50, 0.99)	2.03 (0.93, 4.45)	1.83 (1.17, 2.88)	0.33 (0.15, 0.71)	1.61 (0.45, 5.74)

NOTE: q values for all the interactions shown in the table are 0.329