

Supplementary Information

Table S1. Estimation of the statistical power of the unmatched case-control study.

Subjects	MAF	Statistical Power									
		<i>OR</i> = 1.1	<i>OR</i> = 1.2	<i>OR</i> = 1.3	<i>OR</i> = 1.4	<i>OR</i> = 1.5	<i>OR</i> = 1.6	<i>OR</i> = 1.7	<i>OR</i> = 1.8	<i>OR</i> = 1.9	<i>OR</i> = 2.0
530 cases	0.05	0.0782	0.1604	0.2910	0.4492	0.6107	0.7498	0.8535	0.9216	0.9615	0.9825
	0.10	0.1037	0.2599	0.4845	0.7046	0.8616	0.9467	0.9829	0.9953	0.9989	0.9998
	0.15	0.1264	0.3438	0.6217	0.8376	0.9479	0.9873	0.9976	0.9996	0.9999	0.9999
546 controls	0.20	0.1459	0.4115	0.7138	0.9045	0.9778	0.9963	0.9995	0.9999	0.9999	0.9999
	0.25	0.1624	0.4643	0.7745	0.9388	0.9890	0.9986	0.9999	0.9999	0.9999	0.9999
	0.30	0.1756	0.5040	0.8138	0.9569	0.9936	0.9993	0.9999	0.9999	0.9999	0.9999
	0.35	0.1857	0.5322	0.8385	0.9665	0.9956	0.9996	0.9999	0.9999	0.9999	0.9999
	0.40	0.1926	0.5503	0.8526	0.9713	0.9965	0.9997	0.9999	0.9999	0.9999	0.9999
	0.45	0.1965	0.5592	0.8586	0.9730	0.9967	0.9997	0.9999	0.9999	0.9999	0.9999
	0.50	0.1973	0.5595	0.8575	0.9722	0.9965	0.9997	0.9999	0.9999	0.9999	0.9999

Abbreviation: MAF, Minor Allele Frequency; *OR*, Odds Ratio.

Table S2. Characteristics of the study SNPs.

Classification	Gene	Variant	Allele	Chr.	Chr. Position ^a	Call Rate	HWE ^b
Estrogen biosynthesis	<i>CYP17A1</i>	rs743572	A/G	10q24.3	104597152	99.63%	Y
	<i>HSD17B1</i>	rs615942	T/G	17q11-q21	40714804	98.05%	Y
	<i>HSD17B1</i>	rs2830	G/A	17q11-q21	40704563	100%	N
	<i>CYP19A1</i>	rs2414096	A/G	15q21.1	51529779	99.81%	Y
	<i>CYP19A1</i>	rs2445759	T/G	15q21.1	51600841	99.81%	Y
	<i>CYP19A1</i>	rs2446405	T/A	15q21.1	51646793	100%	Y
	<i>CYP19A1</i>	rs700519	T/C	15q21.1	51507968	100%	Y
	<i>CYP19A1</i>	rs10046	T/C	15q21.1	51502986	100%	Y
	<i>CYP19A1</i>	rs749292	G/A	15q21.1	51558731	99.91%	Y
	<i>CYP19A1</i>	rs936306	G/A	15q21.1	51579598	100%	Y

Table S2. Cont.

Classification	Gene	Variant	Allele	Chr.	Chr. Position ^a	Call Rate	HWE ^b
	<i>CYP19A1</i>	rs1008805	C/T	15q21.1	51549599	99.91%	Y
	<i>CYP19A1</i>	rs11575899	DEL/TCT	15q21.1	51519949:51519950	99.81%	Y
	<i>STS</i>	rs707762	T/A	Xp22.32	7115093	99.16%	N
	<i>STS</i>	rs17268974	A/T	Xp22.32	7236970	99.72%	N
Estrogen metabolism	<i>CYP11A1</i>	rs1531163	A/G	15q24.1	75113083	100%	Y
	<i>CYP11A1</i>	rs2606345	A/C	15q24.1	75017176	100%	Y
	<i>CYP11A2</i>	rs2069522	T/C	15q24.1	75039233	99.91%	Y
	<i>CYP11A2</i>	rs762551	C/A	15q24.1	75041917	100%	Y
	<i>CYP11B1</i>	rs1056836	C/G	2p22.2	38298203	99.81%	Y
	<i>COMT</i>	rs4680	A/G	22q11.21	19951271	99.81%	N
	<i>GSTP1</i>	rs1695	A/G	11q13	67352689	86.27%	N
Estrogen receptors	<i>ERα</i>	rs728524	G/A	6q25.1	152303437	99.91%	Y
	<i>ERα</i>	rs2234693	T/C	6q25.1	152163335	87.73%	Y
	<i>ERα</i>	rs9340799	G/A	6q25.1	152163381	100%	Y
	<i>ERα</i>	rs3798577	C/T	6q25.1	152421130	99.91%	Y
	<i>ERβ</i>	rs1255998	G/C	14q23.2	64693871	99.91%	Y
	<i>ERβ</i>	rs1256049	A/G	14q23.2	64724051	100%	Y
Estrogen signaling Regulative enzymes	<i>CARM1</i>	rs12460421	A/G	19p13.2	10981352	100%	Y
	<i>CREBBP</i>	rs130021	G/A	16p13.3	3832471	100%	Y
	<i>NQO1</i>	rs1469908	A/G	16q22.1	69764412	99.81%	Y
	<i>SRD5A2</i>	rs523349	G/C	2p23	31805706	99.72%	Y
	<i>SMLT1E1</i>	rs3736599	A/G	4q13.1	70725821	99.81%	Y

Abbreviation: Chr., Chromosome; HWE, Hardy-Weinberg Equilibrium; ^a Information was obtained from the Single Nucleotide Polymorphism database (dbSNP) of NCBI;

^b Y indicates that this SNP was in HWE in the present study, and N means it was not.

Tables S3–S7 only showed the results of codominant model for negative SNPs and five models for the positive SNPs.

Table S3. Single SNPs in estrogen biosynthesis genes and association with breast cancer.

Gene	Variant	Model	Genotype	Control	Case	OR (95% CI) ^a	p ^a
<i>CYP17A1</i>	rs743572	Codominant	G/G	190 (34.9%)	163 (30.9%)	1	
			G/A	254 (46.6%)	273 (51.8%)	1.287 (0.978–1.694)	0.072
			A/A	101 (18.5%)	91 (17.3%)	1.081 (0.756–1.547)	0.669
<i>HSD17B1</i>	rs615942	Codominant	G/G	151 (28.1%)	152 (29.3%)	1	
			G/T	272 (50.6%)	247 (47.7%)	0.927 (0.694–1.237)	0.605
			T/T	114 (21.2%)	119 (23%)	1.077 (0.760–1.526)	0.676
<i>CYP19A1</i>	rs2414096	Codominant	G/G	171 (31.4%)	156 (29.4%)	1	
			G/A	280 (51.5%)	277 (52.3%)	1.099 (0.833–1.451)	0.504
			A/A	93 (17.1%)	97 (18.3%)	1.133 (0.787–1.630)	0.503
<i>CYP19A1</i>	rs2445759	Codominant	G/G	533 (97.8%)	518 (97.9%)	1	
			G/T	11 (2%)	9 (1.7%)	0.888 (0.359–2.193)	0.796
			T/T	1 (0.2%)	2 (0.4%)	1.815 (0.153–21.572)	0.637
<i>CYP19A1</i>	rs2446405	Codominant	T/T	134 (24.5%)	133 (25.1%)	1	
			A/T	288 (52.8%)	290 (54.7%)	0.957 (0.712–1.286)	0.769
			A/A	124 (22.7%)	107 (20.2%)	0.830 (0.579–1.188)	0.307
<i>CYP19A1</i>	rs700519	Codominant	C/C	392 (71.8%)	410 (77.4%)	1	
			C/T	143 (26.2%)	111 (20.9%)	0.723 (0.541–0.965)	0.028
			T/T	11 (2%)	9 (1.7%)	0.845 (0.342–2.085)	0.715
		Dominant	C/C	392 (71.8%)	410 (77.4%)	1	
			C/T-T/T	154 (28.2%)	120 (22.6%)	0.731 (0.552–0.968)	0.029
		Recessive	C/C-C/T	535 (98%)	521 (98.3%)	1	
			T/T	11 (2%)	9 (1.7%)	0.913 (0.371–2.245)	0.842
		Overdominant	C/C-T/T	403 (73.8%)	419 (79.1%)	1	
			C/T	143 (26.2%)	111 (20.9%)	0.726 (0.544–0.968)	0.029
		Log-additive	C	927 (84.9%)	931 (87.8%)	1	
			T	165 (15.1%)	129 (12.2%)	0.772 (0.600–0.993)	0.044

Table S3. *Cont.*

Gene	Variant	Model	Genotype	Control	Case	OR (95% CI) ^a	<i>p</i> ^a
<i>CYP19A1</i>	rs10046	Codominant	T/T	130 (23.8%)	155 (29.2%)	1	
			T/C	290 (53.1%)	264 (49.8%)	0.785 (0.587–1.051)	0.103
			C/C	126 (23.1%)	111 (20.9%)	0.748 (0.527–1.064)	0.106
<i>CYP19A1</i>	rs749292	Codominant	G/G	151 (27.7%)	145 (27.4%)	1	
			A/G	279 (51.2%)	264 (49.8%)	0.994 (0.746–1.326)	0.970
			A/A	115 (21.1%)	121 (22.8%)	1.100 (0.777–1.557)	0.593
<i>CYP19A1</i>	rs936306	Codominant	G/G	250 (45.8%)	257 (48.5%)	1	
			A/G	237 (43.4%)	220 (41.5%)	0.869 (0.672–1.125)	0.287
			A/A	59 (10.8%)	53 (10%)	0.869 (0.574–1.317)	0.508
<i>CYP19A1</i>	rs1008805	Codominant	T/T	263 (48.2%)	253 (47.8%)	1	
			C/T	234 (42.9%)	225 (42.5%)	0.990 (0.766–1.278)	0.936
			C/C	49 (9%)	51 (9.6%)	1.138 (0.736–1.758)	0.561
<i>CYP19A1</i>	rs11575899	Codominant	TCT/TCT	265 (48.5%)	255 (48.3%)	1	
			TCT/DEL	230 (42.1%)	228 (43.2%)	1.029 (0.797–1.328)	0.826
			DEL/DEL	51 (9.3%)	45 (8.5%)	0.954 (0.612–1.487)	0.837

Abbreviation: OR, Odds Ratio; 95% CI, 95% confidence interval; Significant values are marked in bold; ^a Adjusted by age.

Table S4. Single SNPs in estrogen metabolism genes and association with breast cancer.

Gene	Variant	Model	Genotype	Control	Case	OR (95% CI) ^a	p ^a
<i>CYP1A1</i>	rs1531163	Codominant	A/A	372 (68.1%)	364 (68.7%)	1	
			A/G	158 (28.9%)	156 (29.4%)	0.996 (0.762–1.303)	0.978
			G/G	16 (2.9%)	10 (1.9%)	0.643 (0.283–1.459)	0.290
<i>CYP1A1</i>	rs2606345	Codominant	C/C	481 (88.1%)	485 (91.5%)	1	
			C/A	63 (11.5%)	44 (8.3%)	0.722 (0.479–1.088)	0.120
			A/A	2 (0.4%)	1 (0.2%)	0.380 (0.034–4.241)	0.432
<i>CYP1A2</i>	rs2069522	Codominant	T/T	463 (85%)	424 (80%)	1	
			T/C	75 (13.8%)	103 (19.4%)	1.500 (1.078–2.087)	0.016
			C/C	7 (1.3%)	3 (0.6%)	0.514 (0.127–2.081)	0.351
		Dominant	T/T	463 (85%)	424 (80%)	1	
			T/C-C/C	82 (15.1%)	106 (20%)	1.421 (1.029–1.961)	0.033
		Recessive	T/T-T/C	538 (98.7%)	527 (99.4%)	1	
			C/C	7 (1.3%)	3 (0.6%)	0.481 (0.119–1.943)	0.304
		Overdominant	T/T-C/C	470 (86.2%)	427 (80.6%)	1	
			T/C	75 (13.8%)	103 (19.4%)	1.510 (1.085–2.101)	0.015
		Log-additive	T	1001 (91.8%)	951 (89.7%)	1	
			C	89 (8.2%)	109 (10.3%)	1.305 (0.968–1.760)	0.081
<i>CYP1A2</i>	rs762551	Codominant	A/A	239 (43.8%)	248 (46.8%)	1	
			C/A	250 (45.8%)	230 (43.4%)	0.876 (0.678–1.133)	0.313
			C/C	57 (10.4%)	52 (9.8%)	0.873 (0.572–1.333)	0.529
<i>CYP1B1</i>	rs1056836	Codominant	C/C	432 (79.3%)	415 (78.5%)	1	
			G/C	101 (18.5%)	106 (20%)	1.073 (0.787–1.462)	0.657
			G/G	12 (2.2%)	8 (1.5%)	0.715 (0.286–1.792)	0.475

Abbreviation: OR, Odds Ratio; 95% CI, 95% confidence interval; Significant values are marked in bold; ^a Adjusted by age.

Table S5. Single SNPs in estrogen receptors and association with breast cancer.

Gene	Variant	Model	Genotype	Control	Case	OR (95% CI) ^a	p ^a
<i>ERα</i>	rs728524	Codominant	A/A	358 (65.7%)	340 (64.2%)	1	
			G/A	164 (30.1%)	175 (33%)	1.137 (0.873–1.480)	0.340
			G/G	23 (4.2%)	15 (2.8%)	0.628 (0.318–1.239)	0.180
<i>ERα</i>	rs2234693	Codominant	T/T	199 (43%)	202 (42%)	1	
			T/C	194 (41.9%)	214 (44.5%)	1.110 (0.839–1.469)	0.465
			C/C	70 (15.1%)	65 (13.5%)	0.986 (0.663–1.465)	0.944
<i>ERα</i>	rs9340799	Codominant	A/A	343 (62.8%)	337 (63.6%)	1	
			G/A	179 (32.8%)	168 (31.7%)	0.945 (0.726–1.229)	0.671
			G/G	24 (4.4%)	25 (4.7%)	1.222 (0.677–2.207)	0.505
<i>ERα</i>	rs3798577	Codominant	T/T	173 (31.7%)	190 (35.9%)	1	
			T/C	271 (49.6%)	238 (45%)	0.796 (0.605–1.048)	0.104
			C/C	102 (18.7%)	101 (19.1%)	0.927 (0.654–1.314)	0.669
<i>ERβ</i>	rs1255998	Codominant	G/G	206 (37.8%)	209 (39.4%)	1	
			C/G	252 (46.2%)	234 (44.1%)	0.929 (0.712–1.212)	0.585
			C/C	87 (16%)	87 (16.4%)	0.979 (0.683–1.404)	0.908
<i>ERβ</i>	rs1256049	Codominant	G/G	189 (34.6%)	190 (35.9%)	1	
			A/G	266 (48.7%)	243 (45.9%)	0.951 (0.725–1.247)	0.716
			A/A	91 (16.7%)	97 (18.3%)	1.075 (0.753–1.533)	0.692

Abbreviation: OR, Odds Ratio; 95% CI, 95% confidence interval; ^a Adjusted by age.

Table S6. Single SNPs in estrogen signaling-regulatory enzymes and association with breast cancer.

Gene	Variant	Model	Genotype	Control	Case	OR (95% CI) ^a	p ^a
<i>CARM1</i>	rs12460421	Codominant	G/G	147 (26.9%)	127 (24%)	1	
			G/A	267 (48.9%)	290 (54.7%)	1.272 (0.947–1.708)	0.110
			A/A	132 (24.2%)	113 (21.3%)	1.024 (0.720–1.455)	0.896
<i>CREBBP</i>	rs130021	Codominant	A/A	194 (35.5%)	183 (34.5%)	1	
			G/A	259 (47.4%)	264 (49.8%)	1.150 (0.877–1.507)	0.312
			G/G	93 (17%)	83 (15.7%)	0.994 (0.691–1.431)	0.976
<i>NQO1</i>	rs1469908	Codominant	G/G	370 (67.8%)	342 (64.8%)	1	
			G/A	159 (29.1%)	170 (32.2%)	1.142 (0.876–1.490)	0.326
			A/A	17 (3.1%)	16 (3%)	0.889 (0.435–1.819)	0.748
<i>SRD5A2</i>	rs523349	Codominant	G/G	177 (32.4%)	164 (31.1%)	1	
			C/G	266 (48.7%)	263 (49.9%)	1.068 (0.810–1.409)	0.639
			C/C	103 (18.9%)	100 (19%)	1.024 (0.719–1.458)	0.897
<i>SMLT1E1</i>	rs3736599	Codominant	G/G	261 (47.8%)	248 (47%)	1	
			A/G	236 (43.2%)	228 (43.2%)	0.983 (0.761–1.270)	0.896
			A/A	49 (9%)	52 (9.8%)	1.105 (0.717–1.703)	0.652

Abbreviation: OR, Odds Ratio; 95% CI, 95% confidence interval; ^a Adjusted by age.

Table S7. Case-case comparisons for the associations of polymorphisms by subgroups of ER and PR status.

Subgroups	Variant/Gene	Model	Genotype	Group = 0 ^a	Group = 1 ^b	OR (95% CI)	p
ER status	rs2446405 <i>CYP19A1</i>	Codominant	T/T	53 (27.9%)	59 (21.9%)	1	
			A/T	111 (58.4%)	151 (55.9%)	1.217 (0.779–1.900)	0.388
			A/A	26 (13.7%)	60 (22.2%)	2.072 (1.147–3.742)	0.016
		Dominant	T/T	53 (27.9%)	59 (21.9%)	1	
			A/T-A/A	137 (72.1%)	211 (78.2%)	1.381 (0.899–2.121)	0.141
		Recessive	T/T-A/T	164 (86.3%)	210 (77.8%)	1	
			A/A	26 (13.7%)	60 (22.2%)	1.808 (1.092–2.992)	0.021
		Overdominant	T/T-A/A	79 (41.6%)	119 (44.1%)	1	
			A/T	111 (58.4%)	151 (55.9%)	0.899 (0.617–1.310)	0.580
		Log-additive	T	217(57.1%)	269(49.8%)	1	
			A	163(42.9%)	271(50.2%)	1.341 (1.030–1.746)	0.030
	rs17268974 <i>STS</i>	Codominant	T/T	53 (27.9%)	89 (33.2%)	1	
			T/A	109 (57.4%)	157 (58.6%)	0.857 (0.564–1.303)	0.471
			A/A	28 (14.7%)	22 (8.2%)	0.468 (0.243–0.900)	0.023
		Dominant	T/T	53 (27.9%)	89 (33.2%)	1	
			T/A-A/A	137 (72.1%)	179 (66.8%)	0.778 (0.518–1.168)	0.225
		Recessive	T/T-T/A	162 (85.3%)	246 (91.8%)	1	
			A/A	28 (14.7%)	22 (8.2%)	0.518 (0.286–0.936)	0.029
		Overdominant	T/T-A/A	81 (42.6%)	111 (41.4%)	1	
			T/A	109 (57.4%)	157 (58.6%)	1.051 (0.721–1.531)	0.797
		Log-additive	T	215(56.6%)	335(62.5%)	1	
			A	165(43.4%)	201(57.4%)	0.782 (0.598–1.022)	0.072

Table S7. *Cont.*

Subgroups	Variant/Gene	Model	Genotype	Group = 0 ^a	Group = 1 ^b	OR (95% CI)	<i>p</i>
PR status	rs130021 <i>CREBBP</i>	Codominant	A/A	90 (40.4%)	71 (30%)	1	
			G/A	95 (42.6%)	131 (55.3%)	1.756 (1.164–2.648)	0.007
			G/G	38 (17%)	35 (14.8%)	1.188 (0.680–2.076)	0.545
		Dominant	A/A	90 (40.4%)	71 (30%)	1	
			G/A-G/G	133 (59.6%)	166 (70%)	1.594 (1.081–2.351)	0.019
		Recessive	A/A-G/A	185 (83%)	202 (85.2%)	1	
			G/G	38 (17%)	35 (14.8%)	0.856 (0.517–1.416)	0.545
		Overdominant	A/A-G/G	128 (57.4%)	106 (44.7%)	1	
			G/A	95 (42.6%)	131 (55.3%)	1.664 (1.148–2.411)	0.007
		Log-additive	A	275(61.7%)	273(57.6%)	1	
			G	171(38.3%)	201(42.4%)	1.193 (0.915–1.556)	0.192

Abbreviation: ER, estrogen receptor; PR, progesterone receptor; Significant values are marked in bold; ^a ER or PR negative; ^b ER or PR positive.