Table 3. Oligogenotypes significantly associated with variation in breast cancer risk; oligogenic combinations ordered by decreasing maximum *OR*.

						Cases N / Total	Controls N / Total	*OR* (95% C.I.)	*p(assoc.)*	*p(H-W)*	criteria met	*OR* (no epistasis)	*p(epistasis)*	ratio
Two-gene combinations														
GSTP1	A/A	***ERCC2***	C/C			54 / 557	57 / 1202	2.2 (1.8, 2.5)	0.0001	0.11	1	1.5	<.0001	1.4
COMT	*/G	***ERCC2***	C/C			89 / 562	110 / 1209	1.9 (1.7, 2.1)	<.0001	0.17	1	1.7	0.044	1.1
PHB	*/T	***COMT***	*/G			181 / 574	280 / 1233	1.6 (1.4, 1.7)	0.0001	0.20	1	1.5	0.22	1.0
PHB	C/C	***ERCC2***	A/*			276 / 563	719 / 1210	0.7 (0.6, 0.7)	<.0001	0.50	1	0.7	0.48	1.0
Three-gene combinations														
PHB	*/T	***COMT***	G/G	***SULT1A1***	A/A	15 / 555	6 / 1215	5.9 (3.9, 9.4)	<.0001	0.045	1,2	1.5	<.0001	4.0
PHB	C/T	***COMT***	G/G	***SULT1A1***	A/A	13 / 555	6 / 1215	5.1 (3.3, 8.1)	0.0005	0.045	2	1.5	<.0001	3.4
PHB	C/T	***COMT***	*/G	***SULT1A1***	A/A	26 / 555	22 / 1215	2.7 (2.1, 3.4)	0.0007	0.045	2	1.5	<.0001	1.8
PHB	*/T	***COMT***	*/G	***SULT1A1***	A/A	29 / 555	25 / 1215	2.7 (2.1, 3.3)	0.0003	0.045	2	1.5	<.0001	1.8
PHB	*/T	***COMT***	*/G	***SULT1A1***	G/G	83 / 555	122 / 1215	1.6 (1.4, 1.8)	0.0020	0.045	2	1.6	0.43	1.0
PHB	*/T	***COMT***	*/G	***SULT1A1***	*/G	150 / 555	251 / 1215	1.4 (1.3, 1.6)	0.0020	0.045	2	1.5	0.26	1.0
COMT	G/A	***GSTP1***	A/A	***ERCC2***	C/C	33 / 554	23 / 1199	3.3 (2.6, 4.1)	<.0001	0.30	1	1.6	<.0001	2.0
COMT	*/G	***GSTP1***	A/A	***ERCC2***	C/C	44 / 554	36 / 1199	2.8 (2.3, 3.4)	<.0001	0.30	1	1.7	<.0001	1.7
COMT	*/G	***GSTP1***	A/*	***ERCC2***	C/C	81 / 554	96 / 1199	2.0 (1.7, 2.2)	<.0001	0.30	1	1.7	0.0052	1.2
GSTP1	A/A	***ERCC2***	C/C	***HER2***	A/A	32 / 536	26 / 1154	2.8 (2.2, 3.5)	0.0001	0.68	1	1.5	<.0001	1.8
GSTP1	A/A	***ERCC2***	C/C	***HER2***	A/*	49 / 536	54 / 1154	2.1 (1.7, 2.4)	0.0001	0.68	1	1.5	<.0001	1.4
GSTP1	A/A	***ERCC2***	C/C	***NQO1***	C/C	34 / 539	29 / 1178	2.7 (2.2, 3.3)	<.0001	0.30	1	1.5	<.0001	1.9
COMT	G/A	***SULT1A1***	G/G	***ERCC2***	C/C	31 / 546	27 / 1192	2.6 (2.1, 3.3)	0.0001	0.093	1	1.8	<.0001	1.5
COMT	G/A	***SULT1A1***	*/G	***ERCC2***	C/C	53 / 546	58 / 1192	2.1 (1.8, 2.5)	0.0001	0.093	1	1.6	<.0001	1.3
COMT	*/G	***SULT1A1***	*/G	***ERCC2***	C/C	76 / 546	91 / 1192	2.0 (1.7, 2.2)	0.0001	0.093	1	1.7	0.0048	1.2
GSTP1	A/A	***SULT1A1***	*/G	***ERCC2***	C/C	49 / 542	44 / 1187	2.6 (2.2, 3.1)	<.0001	0.0012	1,2	1.5	<.0001	1.7
GSTP1	A/A	***SULT1A1***	G/G	***ERCC2***	C/C	27 / 542	24 / 1187	2.6 (2.0, 3.2)	0.0009	0.0012	2	1.7	<.0001	1.6
GSTP1	A/A	***SULT1A1***	G/A	***ERCC2***	C/C	22 / 542	20 / 1187	2.5 (1.9, 3.2)	0.0020	0.0012	2	1.3	<.0001	1.9
GSTP1	A/*	***SULT1A1***	G/G	***ERCC2***	C/C	48 / 542	50 / 1187	2.2 (1.9, 2.6)	0.0002	0.0012	2	1.6	<.0001	1.4
GSTP1	A/*	***SULT1A1***	*/G	***ERCC2***	C/C	82 / 542	113 / 1187	1.7 (1.5, 1.9)	0.0006	0.0012	2	1.5	0.041	1.1
GSTP1	A/*	***SULT1A1***	A/*	***ERCC2***	A/*	192 / 542	511 / 1187	0.7 (0.7, 0.8)	0.0010	0.0012	2	0.8	0.054	0.9
GSTP1	A/A	***VDR***	*/a	***ERCC2***	C/C	34 / 539	31 / 1162	2.5 (2.0, 3.1)	<.0001	0.25	1	1.5	<.0001	1.7
PHB	*/T	***COMT***	*/G	***ERCC2***	C/C	36 / 557	34 / 1207	2.4 (2.0, 2.9)	0.0001	0.48	1	2.0	0.013	1.2
PHB	C/*	***COMT***	*/G	***ERCC2***	C/C	83 / 557	107 / 1207	1.8 (1.6, 2.1)	<.0001	0.48	1	1.7	0.11	1.1
CYP17	*/T	***SULT1A1***	G/G	***ERCC2***	C/C	48 / 535	48 / 1183	2.3 (2.0, 2.8)	<.0001	0.35	1	1.6	<.0001	1.4
COMT	*/G	***ERCC2***	C/C	***NQO1***	C/C	57 / 543	64 / 1185	2.1 (1.8, 2.4)	<.0001	0.79	1	1.6	<.0001	1.3
COMT	*/G	***ERCC2***	C/C	***NQO1***	C/*	83 / 543	104 / 1185	1.9 (1.7, 2.1)	0.0001	0.79	1	1.7	0.048	1.1
CYP17	*/T	***COMT***	G/A	***ERCC2***	C/C	55 / 545	61 / 1194	2.1 (1.8, 2.5)	0.0001	0.67	1	1.6	<.0001	1.3
CYP17	*/T	***COMT***	*/G	***ERCC2***	C/C	76 / 545	88 / 1194	2.0 (1.8, 2.3)	<.0001	0.67	1	1.7	0.0004	1.2
PHB	C/*	***GSTP1***	A/A	***ERCC2***	C/C	51 / 552	56 / 1200	2.1 (1.8, 2.5)	<.0001	0.39	1	1.5	<.0001	1.4
PHB	C/C	***GSTP1***	A/*	***ERCC2***	A/*	231 / 552	618 / 1200	0.7 (0.6, 0.7)	<.0001	0.39	1	0.7	0.39	1.0
COMT	*/G	***CCND1***	A/*	***ERCC2***	C/C	62 / 546	70 / 1164	2.0 (1.7, 2.3)	<.0001	0.72	1	1.7	0.0095	1.2
COMT	G/A	***ERCC2***	C/C	***HER2***	A/*	58 / 539	67 / 1158	2.0 (1.7, 2.3)	<.0001	0.42	1	1.6	0.002	1.2
COMT	*/G	***VDR***	A/*	***ERCC2***	C/C	68 / 544	83 / 1169	1.9 (1.6, 2.2)	0.0001	0.22	1	1.6	0.022	1.2
CYP17	*/T	***GSTP1***	A/*	***ERCC2***	C/C	82 / 542	111 / 1189	1.7 (1.5, 2.0)	<.0001	0.34	1	1.5	0.026	1.1
PHB	C/T	***COMT***	*/G	***CCND1***	A/*	118 / 557	159 / 1184	1.7 (1.6, 1.9)	<.0001	0.17	1	1.5	0.0046	1.1
PHB	*/T	***COMT***	*/G	***CCND1***	A/*	127 / 557	175 / 1184	1.7 (1.5, 1.9)	<.0001	0.17	1	1.5	0.0078	1.1
PHB	*/T	***COMT***	*/G	***GSTP1***	A/A	89 / 563	119 / 1221	1.7 (1.5, 2.0)	<.0001	0.22	1	1.4	0.0001	1.2
PHB	C/T	***COMT***	*/G	***NQO1***	C/C	109 / 554	155 / 1208	1.7 (1.5, 1.9)	<.0001	0.29	1	1.4	0.0001	1.2
PHB	C/T	***COMT***	*/G	***NQO1***	C/*	159 / 554	238 / 1208	1.6 (1.5, 1.8)	<.0001	0.29	1	1.5	0.041	1.1
PHB	*/T	***COMT***	*/G	***NQO1***	C/C	119 / 554	173 / 1208	1.6 (1.5, 1.8)	<.0001	0.29	1	1.4	0.0001	1.2
PHB	*/T	***COMT***	*/G	***NQO1***	C/*	174 / 554	264 / 1208	1.6 (1.5, 1.8)	<.0001	0.29	1	1.5	0.043	1.1
PHB	*/T	***COMT***	*/G	***HER2***	A/*	167 / 544	259 / 1176	1.6 (1.4, 1.7)	<.0001	0.63	1	1.5	0.14	1.1
PHB	C/T	***COMT***	*/G	***HER2***	A/*	150 / 544	235 / 1176	1.5 (1.4, 1.7)	0.0001	0.63	1	1.5	0.33	1.0
PHB	C/T	***CYP17***	*/T	***CCND1***	A/*	125 / 541	182 / 1175	1.6 (1.5, 1.8)	0.0001	0.0090	1,2	1.4	0.0003	1.2
PHB	C/T	***CYP17***	*/T	***CCND1***	G/A	95 / 541	143 / 1175	1.5 (1.4, 1.7)	0.0015	0.0090	2	1.3	0.0035	1.2
PHB	*/T	***CYP17***	*/T	***CCND1***	A/*	131 / 541	202 / 1175	1.5 (1.4, 1.7)	0.0002	0.0090	2	1.4	0.011	1.1
PHB	*/T	***CYP17***	*/T	***COMT***	*/G	152 / 553	234 / 1217	1.6 (1.5, 1.8)	<.0001	0.34	1	1.5	0.044	1.1
PHB	C/T	***CYP17***	*/T	***COMT***	*/G	139 / 553	214 / 1217	1.6 (1.4, 1.7)	0.0001	0.34	1	1.5	0.092	1.1
PHB	*/T	***CYP17***	T/T	***VDR***	A/*	81 / 536	120 / 1174	1.6 (1.4, 1.8)	0.0014	0.016	2	1.2	<.0001	1.3
PHB	C/T	***CYP17***	*/T	***VDR***	A/*	144 / 536	234 / 1174	1.5 (1.3, 1.6)	0.0004	0.016	2	1.3	0.011	1.1
PHB	*/T	***CYP17***	*/T	***VDR***	A/*	155 / 536	256 / 1174	1.5 (1.3, 1.6)	0.0007	0.016	2	1.3	0.013	1.1
PHB	C/T	***CYP17***	*/T	***NQO1***	C/*	174 / 540	285 / 1199	1.5 (1.4, 1.7)	0.0001	0.085	1	1.4	0.013	1.1
PHB	C/C	***ERCC2***	A/*	***HER2***	A/*	245 / 537	642 / 1160	0.7 (0.6, 0.7)	0.0001	0.28	1	0.7	0.39	1.0
PHB	C/C	***ERCC2***	A/*	***NQO1***	C/*	248 / 539	675 / 1187	0.7 (0.6, 0.7)	0.0001	0.48	1	0.7	0.23	1.0
PHB	C/C	***ERCC2***	A/*	***NQO1***	C/C	167 / 539	488 / 1187	0.6 (0.6, 0.7)	<.0001	0.48	1	0.7	0.035	0.9
PHB	C/C	***GSTP1***	A/*	***NQO1***	C/C	180 / 548	487 / 1201	0.7 (0.7, 0.8)	0.0007	0.050	2	0.8	0.061	0.9
PHB	C/C	***SULT1A1***	*/G	***ERCC2***	A/*	236 / 545	630 / 1193	0.7 (0.6, 0.7)	0.0001	0.16	1	0.7	0.44	1.0
PHB	C/C	***SULT1A1***	A/*	***ERCC2***	A/*	138 / 545	409 / 1193	0.7 (0.6, 0.7)	0.0001	0.16	1	0.7	0.12	1.0
PHB	C/C	***SULT1A1***	A/*	***NQO1***	C/*	157 / 541	449 / 1196	0.7 (0.6, 0.7)	0.0001	0.23	1	0.7	0.022	0.9
PHB	C/C	***CCND1***	A/*	***NQO1***	C/C	135 / 540	383 / 1165	0.7 (0.6, 0.8)	0.0001	0.24	1	0.8	<.0001	0.8
PHB	C/C	***VDR***	A/*	***ERCC2***	A/*	195 / 541	537 / 1170	0.7 (0.6, 0.7)	0.0001	0.52	1	0.7	0.093	1.0
PHB	C/C	***VDR***	A/a	***ERCC2***	A/*	114 / 541	350 / 1170	0.6 (0.6, 0.7)	<.0001	0.52	1	0.7	0.0094	0.9
PHB	C/C	***CYP17***	*/T	***ERCC2***	A/*	215 / 544	610 / 1196	0.6 (0.6, 0.7)	<.0001	0.43	1	0.7	0.010	0.9
COMT	A/A	***VDR***	A/a	***NQO1***	C/C	26 / 545	107 / 1166	0.5 (0.4, 0.6)	0.0007	0.0030	2	0.7	<.0001	0.7

OR = Odds Ratio; C.I. = Confidence Interval; *p(assoc.)* = empirical *p*-value for association with breast cancer risk; *p(H-W)* = empirical *p*-value for test for Hardy-Weinberg equilibrium in cases; Criteria met: criteria 1 is *p(assoc)* ≤ 0.0001, criteria 2 is *p(H-W)* ≤ 0.05 AND *p(assoc.)* ≤ 0.002; *OR(no epistasis)* = *OR* calculated under assumption of no epistasis; *p(epistasis)* = empirical *p*-value for evidence of epistasis; ratio = *OR* / *OR(no epistasis)*; "*" under gene combinations denotes both alleles, for example, *COMT* */G is the combination of *COMT* G/G and *COMT* C/G.

Table 6. Association of single gene polymorphisms with breast cancer risk in women under age 53 years

	N cases	N controls	*OR*	(95% CI)	*p*	*OR*B		N cases	N controls	*OR*	(95% CI)	*p*	*OR*B
PHB							***GSTP1***						
C/*	598	1450	0.9	(0.7, 1.1)	0.30	-	***A/****	500	1079	1.0	(0.9, 1.1)	0.41	-
C/C	375	1024	0.7	(0.7, 0.8)	**0.0003**	1	***A/A***	249	524	1.0	(1.0, 1.1)	0.37	1
C/T	223	426	1.4	(1.3, 1.5)	**0.0008**	1.4	***A/G***	251	555	1.0	(0.9, 1.0)	0.31	1.0
T/T	23	49	1.2	(0.9, 1.4)	0.30	1.3	***G/G***	72	150	1.0	(0.9, 1.2)	0.41	1.0
****/T***	246	475	1.4	(1.3, 1.5)	**0.0003**	1.4	****/G***	323	705	1.0	(0.9, 1.1)	0.37	-
Total	621	1499					***Total***	572	1229				
HER2							***ERCC2***						
A/*	520	1114	1.0	(0.8, 1.2)	0.39	-	***A/****	461	1056	0.6	(0.6, 0.7)	**0.0009**	-
A/A	327	696	1.0	(0.9, 1.1)	0.48	1	***A/A***	204	473	0.9	(0.8, 1.0)	0.11	1
G/A	193	418	1.0	(0.9, 1.1)	0.42	1.0	***A/C***	257	583	0.9	(0.8, 1.0)	0.14	1.0
G/G	33	67	1.1	(0.9, 1.3)	0.39	1.0	***C/C***	107	157	1.6	(1.4, 1.8)	**0.0009**	1.6
****/G***	226	485	1.0	(0.9, 1.1)	0.48	-	****/C***	364	740	1.1	(1.1, 1.3)	0.11	-
Total	553	1181					***Total***	568	1213				
CCND1							***VDR***						
G/*	453	963	0.9	(0.8, 1.0)	0.22	-	***A/****	435	935	1.0	(0.9, 1.1)	0.34	-
G/G	168	382	0.9	(0.8, 1.0)	0.12	1	***A/A***	180	351	1.1	(1.0, 1.2)	0.13	1
G/A	285	581	1.0	(1.0, 1.1)	0.33	1.1	***A/a***	255	584	0.9	(0.8, 1.0)	0.083	0.9
A/A	119	229	1.1	(1.0, 1.2)	0.22	1.2	***a/a***	125	256	1.1	(1.0, 1.2)	0.34	1.0
****/A***	404	810	1.1	(1.0, 1.2)	0.12	-	****/a***	380	840	0.9	(0.8, 1.0)	0.13	-
Total	572	1192					***Total***	560	1191				
SULT1A1							***CYP17***						
G/*	494	1078	0.9	(0.8, 1.1)	0.30	-	***T/****	477	1041	1.0	(0.9, 1.1)	0.45	-
G/G	264	522	1.2	(1.1, 1.3)	0.062	1	***T/T***	208	464	1.0	(0.9, 1.1)	0.36	1
G/A	230	556	0.8	(0.8, 0.9)	0.030	0.8	***T/C***	269	577	1.0	(1.0, 1.1)	0.39	1.0
A/A	71	143	1.1	(1.0, 1.2)	0.30	1.0	***C/C***	85	182	1.0	(0.9, 1.2)	0.45	1.0
****/A***	301	699	0.9	(0.8, 0.9)	0.062	-	****/C***	354	759	1.0	(1.0, 1.1)	0.36	-
Total	565	1221					***Total***	562	1223				
NQO1							***COMT***						
C/*	546	1171	1.1	(0.9, 1.4)	0.43	-	***A/****	434	951	0.9	(0.8, 1.0)	0.16	-
C/C	369	824	0.9	(0.8, 1.0)	0.15	1	***A/A***	128	346	0.7	(0.7, 0.8)	**0.0041**	1
C/T	177	347	1.1	(1.0, 1.3)	0.13	1.1	***A/G***	306	605	1.2	(1.1, 1.3)	0.065	1.4
T/T	18	41	1.0	(0.7, 1.2)	0.43	1.0	***G/G***	146	285	1.1	(1.0, 1.2)	0.16	1.4
****/T***	195	388	1.1	(1.0, 1.2)	0.15	-	****/G***	452	890	1.4	(1.3, 1.5)	**0.0041**	1.4
Total	564	1212					***Total***	580	1236				