

Supplemental Materials

Supplementary Method

Nominally statistically significant meta-analysis results were graded on the basis of the Human Genome and Epidemiology Network Venice criteria. The amount of evidence, consistency of replication, and protection from bias were considered. We rated the overall epidemiological credibility of nominally statistically significant meta-analysis results as strong (A) if associations received A grades in all three categories, moderate (B) if they received at least one B grade but no C grades, and weak (C) if they received a C grade in any of the three assessment criteria. For the ratings for the amount of evidence, we assigned a grade A when the total number of minor alleles of patients and control subject samples combined in the meta-analyses exceeded 1000 individuals, grade B when the total number was between 100 and 1000 individuals, and grade C when the total number was less than 100 individuals. For consistent replication grading, we assigned a grade A for I^2 point estimates of no more than 25%, a grade B for I^2 values of 25%–50%, and a grade C for I^2 values greater than 50%. Note that this criterion does not apply to meta-analyses with $P < 1 \times 10^{-7}$ after exclusion of the initial dataset(s) (37). For protection from bias, the guidelines propose consideration of various potential sources of bias, including errors in phenotypes, genotypes, and confounding (population stratification).

Furthermore the following potential sources of bias at the meta-analysis level were assessed.

Whenever the summary odds ratio deviated less than 1.15-fold from the null in meta-analyses on the basis of published data, we acknowledged that occult publication and other sources of uncontrollable bias alone may invalidate the association and we therefore assigned a grade C. If the association was no longer nominally statistically significant ($P < .05$) on exclusion of the initial study or on exclusion of studies violating Hardy-Weinberg equilibrium in control subjects, a grade C was assigned as well. Also, we assigned a grade C if the modified regression test (38) showed evidence for publication or small-study

bias, and/or if the excess of statistical significance (39) suggested the possibility of statistical significance-chasing bias. This criterion did not apply to meta-analyses with $P < 1 \times 10^{-7}$ (including all data for prospective analyses such as genome-wide association studies and after exclusion of the initial studies for retrospective analyses).

Supplementary Table 1. Random-effects results of the main meta-analyses using allelic contrasts for all polymorphisms with data from at least four independent case-control datasets, including genome-wide association studies (GWAS) and GWAS replicating studies as of July 31st 2010 †‡

Chromosome	Gene (nearest gene)	Polymorphism	Location (bp) §	Allele contrast	No. of datasets	No. of subjects	MAF	OR (95% CI)	P	Amount of evidence	No. of minor alleles	Venice replication grade	I ²	Venice bias grade	Bias reason	Venice overall grade
1p13.3	<i>GSTM1</i>	GSTM1*0	215276998	wt vs *0	5	2239	0.283	1.12 (0.89 to 1.41)	.321	NA	NA	NA	NA	NA	NA	NA
4q25	<i>EGF</i>	rs4444903	110834110	G vs A	5	2987	0.409	1.14 (0.88 to 1.47)	.314	NA	NA	NA	NA	NA	NA	NA
5p15.33	<i>CLPTMIL</i>	rs401681	1322087	T vs C	7	47195	0.450	1.15 (1.08 to 1.22)	9.6x10 ⁻⁶	A	42771	B	27	C	Low OR	C
5p13.2	<i>SLC45A2</i>	rs16891982	33951693	C vs G	9	14880	0.068	0.40 (0.33 to 0.47)	4x10 ⁻²⁷	A	1644	Al	29	Al	NA	A
9p23	<i>(TYRP1)</i>	rs1408799	12672097	T vs C	4	43166	0.258	0.86 (0.80 to 0.93)	9.1x10 ⁻⁵	A	22196	A	0	A	NA	A
9p21.3	<i>CDKN2A</i>	rs3088440	21968159	T vs C	4	3867	0.077	1.25 (1.03 to 1.51)	.026	B	704	A	24	C	F, HWE	C
9p21.3	<i>CDKN2A</i>	rs11515	21968199	G vs C	4	3867	0.127	1.15 (1.01 to 1.32)	.039	A	1019	A	0	C	F	C
9p21.3	<i>CDKN2A</i>	rs3731249	21970916	A vs G	6	5794	0.025	1.28 (0.84 to 1.97)	.254	NA	NA	NA	NA	NA	NA	NA
11q14.3	<i>TYR</i>	rs1042602	88911696	A vs C	9	53589	0.316	0.95 (0.90 to 0.99)	.021	A	34179	A	0	C	Low OR, F	C
11q14.3	<i>TYR</i>	rs1393350	89011046	A vs G	4	10092	0.269	1.27 (1.16 to 1.39)	8.7x10 ⁻⁸	A	5763	Al	35	Al	NA	A
11q14.3	<i>TYR</i>	rs1126809	89017961	A vs G	6	46939	0.295	1.22 (1.14 to 1.31)	2.7x10 ⁻⁸	A	27940	Al	29	Al	NA	A
12q13.11	<i>VDR</i>	rs731236	48238757	C vs T	6	7070	0.390	0.95 (0.85 to 1.07)	.413	NA	NA	NA	NA	NA	NA	NA
12q13.11	<i>VDR</i>	rs1544410	48239835	A vs G	6	7440	0.400	0.89 (0.82 to 0.97)	.0065	A	5857	A	24	C	Low OR	C
12q13.11	<i>VDR</i>	rs2228570	48272895	A vs G	8	8455	0.387	1.11 (0.98 to 1.24)	.093	NA	NA	NA	NA	NA	NA	NA
12q13.11	<i>(VDR)</i>	rs4516035	48299826	G vs A	7	6566	0.437	1.00 (0.89 to 1.13)	.984	NA	NA	NA	NA	NA	NA	NA
14q32.33	<i>XRCC3</i>	rs861539	104165753	T vs C	5	3607	0.375	1.05 (0.85 to 1.29)	.661	NA	NA	NA	NA	NA	NA	NA
15q13.1	<i>OCA2</i>	rs7495174	28344238	G vs A	5	42367	0.036	0.93 (0.83 to 1.04)	.199	NA	NA	NA	NA	NA	NA	NA
16q24.3	<i>MC1R</i>	rs61996344 (F45L)	89985799	C vs T	4	1333	0.002	1.12 (0.25 to 4.95)	.886	NA	NA	NA	NA	NA	NA	NA
16q24.3	<i>MC1R</i>	rs1805005 (V60L)	89985844	T vs G	21	24816	0.114	1.13 (1.02 to 1.26)	.024	A	5951	C	56	C	Low OR	C
16q24.3	<i>MC1R</i>	rs34474212 (S83P)	89985913	C vs T	5	1264	0.003	2.34 (0.74 to 7.38)	.147	NA	NA	NA	NA	NA	NA	NA
16q24.3	<i>MC1R</i>	rs1805006 (D84E)	89985918	A vs C	19	23336	0.009	1.47 (1.18 to 1.83)	6.4x10 ⁻⁴	B	487	A	0	A	NA	B
16q24.3	<i>MC1R</i>	rs2228479 (V92M)	89985940	A vs G	20	22745	0.076	1.06 (0.97 to 1.15)	.186	NA	NA	NA	NA	NA	NA	NA
16q24.3	<i>MC1R</i>	rs34158934 (T95M)	89985950	T vs C	7	4094	0.001	1.31 (0.47 to 3.65)	.608	NA	NA	NA	NA	NA	NA	NA
16q24.3	<i>MC1R</i>	V122M	89986030	A vs G	5	2268	0.003	1.01 (0.32 to 3.21)	.987	NA	NA	NA	NA	NA	NA	NA
16q24.3	<i>MC1R</i>	rs11547464 (R142H)	89986091	A vs G	16	10606	0.010	1.67 (1.26 to 2.21)	3.7x10 ⁻⁴	B	250	A	7	A	NA	B
16q24.3	<i>MC1R</i>	rs1805007 (R151C)	89986117	T vs C	21	27747	0.078	1.83 (1.56 to 2.15)	2.1x10 ⁻¹³	A	4764	Al	69	Al	NA	A
16q24.3	<i>MC1R</i>	Y152X	89986122	A vs C	8	4193	0.001	1.56 (0.54 to 4.52)	.415	NA	NA	NA	NA	NA	NA	NA

16q24.3	<i>MC1R</i>	rs1110400 (I155T)	89986130	C vs T	19	22506	0.010	1.23 (0.99 to 1.52)	.062	NA	NA	NA	NA	NA	NA	NA
16q24.3	<i>MC1R</i>	rs1805008 (R160W)	89986144	T vs C	22	27368	0.098	1.54 (1.33 to 1.79)	1.7x10 ⁻⁸	A	5526	Al	67	Al	Regr	A
16q24.3	<i>MC1R</i>	rs885479 (R163Q)	89986154	A vs G	20	52153	0.041	1.09 (0.97 to 1.22)	.163	NA	NA	NA	NA	NA	NA	NA
16q24.3	<i>MC1R</i>	R213W	89986303	T vs C	5	2505	0.002	3.04 (1.17 to 7.91)	.023	C	23	A	0	A	NA	C
16q24.3	<i>MC1R</i>	K278E	89986498	G vs A	5	1528	0.003	0.75 (0.17 to 3.31)	.708	NA	NA	NA	NA	NA	NA	NA
16q24.3	<i>MC1R</i>	rs1805009 (D294H)	89986546	C vs G	20	24753	0.015	1.89 (1.51 to 2.38)	3.3x10 ⁻⁸	B	949	Al	42	Al	NA	B
16q24.3	<i>MC1R</i>	rs2228478 (T314T)	89986608	G vs A	10	19013	0.098	1.12 (0.94 to 1.33)	.208	NA	NA	NA	NA	NA	NA	NA
17p13.1	<i>TP53</i>	rs1042522	7579472	C vs G	6	3392	0.231	1.06 (0.84 to 1.34)	.624	NA	NA	NA	NA	NA	NA	NA
19q13.31	<i>XRCC1</i>	rs25487	44055726	A vs G	4	3504	0.364	1.03 (0.93 to 1.14)	.635	NA	NA	NA	NA	NA	NA	NA
19q13.32	<i>ERCC2</i>	rs13181	45854919	C vs A	8	6427	0.382	1.00 (0.87 to 1.13)	.936	NA	NA	NA	NA	NA	NA	NA
19q13.32	<i>ERCC2</i>	rs1799793	45867259	A vs G	5	5027	0.369	1.02 (0.93 to 1.12)	.662	NA	NA	NA	NA	NA	NA	NA
20q11.22	<i>ASIP</i>	rs6058017	32856998	G vs A	7	44247	0.089	0.89 (0.81 to 0.99)	.028	A	7965	A	0	C	Low OR, HWE, Regr	C
20q11.22	<i>PIGU</i>	rs910873	33171772	A vs G	4	6915	0.076	1.52 (1.36 to 1.70)	1.9x10 ⁻¹³	A	1425	Al	0	Al	NA	A
20q11.22	<i>MYH7B</i>	rs1885120	33576989	C vs G	4	6787	0.073	1.59 (1.41 to 1.79)	7.4x10 ⁻¹⁵	A	1306	Al	0	Al	NA	A
22q11.23	<i>GSTT1</i>	GSTT1*0	NA	*0 vs wt	5	2824	0.441	0.98 (0.88 to 1.09)	.709	NA	NA	NA	NA	NA	NA	NA

† CI = confidence interval, F = statistical significance lost excluding first study, HWE = statistical significance lost excluding Hardy-Weinberg equilibrium-violating studies in control subjects, Low OR = an OR less than 1.15, MAF = minor allele frequency in controls when combining all eligible datasets, NA = not applicable, No. of minor alleles = number of minor alleles in patients and control subjects combined across all included datasets, OR = odds ratio, Regr = small-study effect, wt = wild type allele.

‡ Allelic odds ratios, 95% confidence intervals, and *P* values (two-sided) were calculated by the DerSimonian-Lairs random-effects model (32). Analysis included all ethnicities. Venice grading: A = strong epidemiologic credibility, B = modest epidemiologic credibility, C = weak epidemiologic credibility.

§ Location (in base pairs [bp]) is on the basis of the Human Genome build 19 (40). Note that GSTT1*0 represents a gene deletion and therefore cannot be assigned to a specific location.

|| Criterion does not apply to meta-analysis results ($P < 1 \times 10^{-7}$) after exclusion of the initial study (37).

Supplementary Table 2. Genetic variants associated with cutaneous melanoma identified by random-effects supplementary meta-analyses using allelic contrasts for polymorphisms with three independent case–control datasets available from genome-wide association studies (GWAS) and/or replication studies of GWAS in related traits as supplied in the respective publications as of 31st July 2010 *†

Chromosome	Gene (nearest gene)	Polymorphism	Location (bp)‡	Allele contrast	No. of datasets	No. of subjects§	MAF	OR (95% CI)	P	Amount of evidence	No. of minor alleles	Venice replication grade	I ²	Venice bias grade	Bias reason	Venice overall grade
9p21.3	(<i>MTAP</i>)	rs4636294	21747803	G vs A	3	13005	0.485	0.82 (0.75 to 0.90)	1.4x10 ⁻⁵	A	12930	C	66	A	NA	C
9p21.3	(<i>MTAP</i>)	rs2218220	21756089	T vs C	3	13005	0.487	0.84 (0.80 to 0.89)	5.5x10 ⁻¹¹	A	12930	A	0	A	NA	A
9p21.3	(<i>MTAP</i>)	rs1335510	21757803	G vs T	3	10616	0.417	0.83 (0.78 to 0.89)	5.9x10 ⁻⁹	A	8550	A	0	A	NA	A
9p21.3	<i>MTAP</i>	rs10757257	21806564	A vs G	3	10581	0.415	0.81 (0.76 to 0.86)	3.0x10 ⁻¹¹	A	8442	A#	0	A	NA	A
9p21.3	<i>MTAP</i>	rs7023329	21816528	G vs A	3	12481	0.497	0.84 (0.80 to 0.89)	3.1x10 ⁻¹⁰	A	12194	A	0	A	NA	A
14q32	(<i>SLC24A4</i>)	rs12896399	92773663	G vs T	3	39730	0.452	1.02 (0.86 to 1.21)	.823	NA	NA	NA	NA	NA	NA	NA
15q13.1	<i>OCA2</i>	rs1800407	28230318	T vs C	3	1722	0.070	1.40 (1.07 to 1.82)	.013	B	280	A	0	A	NA	B
16q24.3	<i>CDK10</i>	rs258322	89755903	A vs G	3	8992	0.095	1.66 (1.48 to 1.86)	4x10 ⁻¹⁸	A	2084	A	28	A	NA	A
16q24.3	<i>AFG3L1</i>	rs4785763	90066936	A vs C	3	9158	0.328	1.36 (1.27 to 1.45)	5x10 ⁻²⁰	A	6533	A	0	A	NA	A
20q11.21	<i>C20orf71</i>	rs17305657	31806588	C vs T	3	3937	0.088	1.60 (1.27 to 2.01)	6.3x10 ⁻⁵	B	850	C	59	A	NA	C
20q11.21	(<i>C20orf114</i>)	rs4911310	31861259	G vs A	3	3941	0.292	0.83 (0.75 to 0.92)	2.1x10 ⁻⁴	A	2168	A	0	A	NA	A

20q11.21	<i>C20orf114</i>	rs2253335	31891003	T vs C	3	3916	0.392	1.01 (0.92 to 1.11)	.811	NA	NA	NA	NA	NA	NA	NA
20q11.21	(<i>C20orf114</i>)	rs721970	31903533	A vs G	3	4230	0.070	1.62 (1.35 to 1.95)	3.4×10^{-7}	B	752	B	29	A	NA	B
20q11.21	<i>CDK5RAP1</i>	rs291671	31950845	C vs T	3	3960	0.100	1.46 (1.16 to 1.83)	.0012	B	934	C	63	A	NA	C
20q11.22	<i>E2F1</i>	rs3213182	32263233	G vs T	3	3806	0.111	0.93 (0.77 to 1.34)	.492	NA	NA	NA	NA	NA	NA	NA
20q11.22	<i>E2F1</i>	rs2071054	32265839	C vs T	3	3868	0.298	1.22 (1.11 to 1.34)	5.3×10^{-5}	A	2456	A	0	A	NA	A
20q11.22	(<i>RALY</i>)	rs6142047	32514386	C vs T	3	4273	0.454	1.20 (1.10 to 1.31)	2.5×10^{-5}	A	4074	A	0	A	NA	A
20q11.22	(<i>RALY</i>)	rs17091405	32515916	C vs G	3	4082	0.118	1.00 (0.84 to 1.19)	.972	NA	NA	NA	NA	NA	NA	NA
20q11.22	(<i>RALY</i>)	rs4911379	32535305	A vs C	3	3898	0.336	1.21 (1.10 to 1.33)	6.2×10^{-5}	A	2776	A	0	C	Regr	C
20q11.22	(<i>RALY</i>)	rs6059592	32552643	G vs T	3	4247	0.074	0.82 (0.59 to 1.15)	.241	NA	NA	NA	NA	NA	NA	NA
20q11.22	(<i>RALY</i>)	rs2064348	32564078	T vs C	3	4031	0.100	0.98 (0.79 to 1.22)	.866	NA	NA	NA	NA	NA	NA	NA
20q11.22	<i>RALY</i>	rs2284378	32588095	T vs C	3	3994	0.332	1.21 (1.10 to 1.32)	6.4×10^{-5}	A	2818	A	0	A	NA	A
20q11.22	<i>RALY</i>	rs6141443	32601929	G vs C	3	4039	0.164	0.91 (0.80 to 1.02)	.102	NA	NA	NA	NA	NA	NA	NA
20q11.22	<i>RALY</i>	rs13043392	32606735	C vs A	3	4015	0.362	0.93 (0.85 to 1.20)	.124	NA	NA	NA	NA	NA	NA	NA
20q11.22	<i>RALY</i>	rs2268089	32667298	A vs G	3	4062	0.326	1.23 (1.12 to 1.35)	1.1×10^{-5}	A	2834	A	0	A	NA	A
20q11.22	(<i>ASIP</i>)	rs819163	32842357	G vs T	3	4079	0.124	0.83 (0.70 to 0.99)	.040	B	936	B	36	A	NA	B
20q11.22	(<i>ASIP</i>)	rs6059743	32847711	A vs G	3	3943	0.429	0.91 (0.83 to 0.99)	.036	A	3297	A	0	C	Low OR	C
20q11.22	<i>ASIP</i>	rs819162	32852282	T vs A	3	4158	0.120	0.82 (0.71 to 0.95)	.0094	B	920	A	10	A	NA	B
20q11.22	<i>ITCH</i>	rs7266300	33037408	T vs A	3	3989	0.066	0.80 (0.58 to 1.12)	.201	NA	NA	NA	NA	NA	NA	NA
20q11.22	(<i>MAP1LC3A</i>)	rs6088519	33132191	T vs C	3	4101	0.278	0.95 (0.86 to 1.05)	.291	NA	NA	NA	NA	NA	NA	NA

20q11.22	(<i>MAP1LC3A</i>)	rs6088520	33132364	T vs C	3	4191	0.478	0.88 (0.80 to 0.95)	.0025	A	3866	A	0	C	Low OR	C
20q11.22	(<i>MAP1LC3A</i>)	rs2424994	33132917	T vs C	3	4075	0.174	1.30 (1.15 to 1.47)	2.9×10^{-5}	A	1577	A	18	A	NA	A
20q11.22	<i>PIGU</i>	rs6142206	33212055	T vs C	3	3961	0.413	0.91 (0.83 to 0.99)	.044	A	3189	A	0	C	Low OR	C
20q11.22	<i>TP53INP2</i>	rs6060003	33294945	C vs T	3	4285	0.454	0.86 (0.79 to -0.94)	5.1×10^{-4}	A	3725	A	0	A	NA	A
20q11.22	<i>NCOA6</i>	rs959829	33346047	G vs A	3	4203	0.374	0.96 (0.84 to 1.10)	.495	NA	NA	NA	NA	NA	NA	NA
20q11.22	<i>NCOA6</i>	rs7271289	33397303	A vs G	3	3983	0.182	1.34 (1.11 to 1.62)	.0024	A	1634	C	66	A	NA	C
20q11.22	<i>NCOA6</i>	rs6088619	33411871	C vs T	3	3932	0.132	0.90 (0.78 to 1.05)	.169	NA	NA	NA	NA	NA	NA	NA
20q11.23	<i>PHF20</i>	rs6058339	34460479	C vs T	3	3957	0.102	1.43 (1.25 to 1.64)	2.9×10^{-7}	B	945	A	0	A	NA	B
20q11.23	<i>LOC647979</i>	rs1204552	34638903	A vs T	3	4063	0.070	1.59 (1.36 to 1.87)	7.1×10^{-9}	B	716	A	3	A	NA	B
22q13.1	<i>PLA2G6</i>	rs2284063	38544298	G vs A	3	12690	0.366	0.85 (0.75 to 0.96)	.010	A	8936	C	81	C	F	C
22q13.1	<i>PLA2G6</i>	rs6001027	38545619	G vs A	3	12690	0.363	0.86 (0.77 to 0.96)	.0051	A	8885	C	73	C	F	C

* CI = confidence interval, F = statistical significance lost excluding the first study, Low OR = an OR less than 1.15, MAF = minor allele frequency in controls when combining all eligible datasets, NA = not applicable, No. of minor alleles = number of minor alleles in patients and control subjects combined across all included datasets, OR = odds ratio, Regr = small-study effect.

† Allelic odds ratios, 95% confidence intervals, and *P* values (two-sided) were calculated by the DerSimonian-Lairs random-effects model (32). Analysis included all ethnicities. Venice grading: A = strong epidemiologic credibility, B = modest epidemiologic credibility, C = weak epidemiologic credibility.

‡ Location (in base pairs, bp) is on the basis of the Human Genome build 19 (40).

§ For inclusion of GWAS and other large-scale study data which only provided odds ratios, confidence intervals, and/or P values, we estimated genotype summary counts and the number of analyzed patient and control subjects on the basis of the reported data, control allele frequencies, and overall effective number of subjects for the purpose of Venice grading. Thus the listed number of subjects and the number of minor alleles are only approximations of the real numbers

|| Criterion does not apply to meta-analysis results ($P < 1 \times 10^{-7}$) after exclusion of the initial study (37).

Supplementary Table 3. Comparison of all previously published meta-analysis results and those obtained from the main and supplementary meta-analyses in this study as of July 31st 2010 †,‡

Gene (nearest gene)	Polymorphism	Allele contrast	Prior study author, year (reference)	Prior study funding source	Study design notes	Prior no. of subjects (datasets)	Prior meta OR (95% CI)	Prior P	MelGene no. of subjects
<i>EGF</i>	rs4444903	G vs A	NMA	NA	NA	NA	NA	NA	2987 (5)
<i>CLPTM1L</i>	rs401681	T vs C	NMA	NA	NA	NA	NA	NA	47195 (7)
<i>SLC45A2</i>	rs16891982	C vs G	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	Included a family-based study(49) and six independent datasets from Stacey et al. 2009 (30) as one dataset	17876 (3)	0.38 (0.26 to 0.55)	3.3x10 ⁻⁷	14880 (9)
(<i>TYRP1</i>)	rs1408799	T vs C	NMA	NA	NA	NA	NA	NA	43166 (4)
(<i>MTAP</i>)	rs4636294	G vs A	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	NP	11689 (3)	0.83 (0.76 to 0.91)	5.1x10 ⁻⁵	13005 (3)‡‡
(<i>MTAP</i>)	rs2218220	T vs C	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	NP	11689 (3)	0.83 (0.78 to 0.89)	3.6x10 ⁻⁷	13005 (3) ‡‡
(<i>MTAP</i>)	rs1335510	G vs T	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	NP	11689 (3)	0.84 (0.79 to 0.90)	1.8x10 ⁻⁷	10616 (3) ‡‡
<i>MTAP</i>	rs10757257	A vs G	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	NP	11689 (3)	0.82 (0.77 to 0.88)	6.6x10 ⁻¹⁰	10581 (3) ‡‡
<i>MTAP</i>	rs7023329	G vs A	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	Used a fixed-effect model	11689 (3)	0.83 (0.79 to 0.88)	2.7x10 ⁻¹¹	12481(3) ‡‡
<i>CDKN2A</i>	rs3088440	T vs C	NMA	NA	NA	NA	NA	NA	3867 (4)
<i>CDKN2A</i>	rs11515	G vs C	NMA	NA	NA	NA	NA	NA	3867 (4)
<i>CDKN2A</i>	rs3731249	A vs G	NMA	NA	NA	NA	NA	NA	5794 (6)
<i>TYR</i>	rs1042602	A vs C	NMA	NA	NA	NA	NA	NA	53589 (9)
<i>TYR</i>	rs1393350	A vs G	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	Included replication datasets REP1 and REP2 of Bishop, 2009 (15) as one dataset	10695 (3)	1.21 (1.02 to 1.42)	.02	10092 (4)
<i>TYR</i>	rs1126809 (R402Q)	A vs G	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	Included a family-based study (49), included replication datasets REP1 and	52722 (3)	1.23 (1.16 to 1.29)	1.8x10 ⁻¹⁴	46939 (6)

VDR	rs731236 (TaqI)	C vs T	Mocellin, 2008 (44)	NP	REP2 of Bishop, 2009 (15) as one dataset, and included three independent datasets from Gudbjartsson, 2008 (28) as one dataset	2000 (2)	NP	.07	7070 (6)
VDR	rs731236 (TaqI)	C vs T	Randerson-Moor, 2009 (45)	Cancer Research UK, NIH, ScaRF	Performed meta-analyses by comparing the genotype combinations§	4779 (5)	0.95 (0.75 to 1.20)	.671	7070 (6)
VDR	rs1544410 (BsmI)	A vs G	Mocellin, 2008 (44)	NP	Applied a model-free approach (50), which imposed a recessive genetic model	2896 (3)	1.30 (1.11 to 1.53)	.002	7440 (6)
VDR	rs1544410 (BsmI)	A vs G	Randerson-Moor, 2009 (45)	Cancer Research UK, NIH, ScaRF	Performed meta-analyses by comparing the genotype combinations§	5185 (5)	0.81 (0.72 to 0.92)	.00081	7440 (6)
VDR	rs1544410 (BsmI)	A vs G	Gandini, 2009 (46)	NP	Performed fixed-effect or random-effects meta-analyses#	2896 (3)	0.84 (0.75 to 0.94)	.0021	7440 (6)
VDR	rs2228570 (FokI)	A vs G	Gandini, 2009 (46)	NP	Performed fixed-effect or random-effects meta-analyses#	3318 (4)	1.13 (1.01 to 1.25)	.031	8455 (8)
VDR	rs2228570 (FokI)	A vs G	Mocellin, 2008 (44)	NP	NP	3318 (4)	1.09 (0.99 to 1.21)	.07	8455 (8)
VDR	rs2228570 (FokI)	A vs G	Randerson-Moor, 2009 (45)	Cancer Research UK, NIH, ScaRF	Performed meta-analyses by comparing the genotype combinations§	6114 (7)	1.19 (1.05 to 1.35)	.011	8455 (8)
VDR	rs4516035 (EcoRV)	G vs A	Mocellin, 2008 (44)	NP	NP	1463 (3)	NP	NP	6566 (7)
VDR	rs4516035 (EcoRV)	G vs A	Randerson-Moor, 2009 (45)	Cancer Research UK, NIH, ScaRF	Performed meta-analyses by comparing the genotype combinations§	3754 (5)	1.06 (0.86 to 1.30)	.581	6566 (7)
VDR	rs11568820 (Cdx2)	A vs G	Randerson-Moor, 2009 (45)	Cancer Research UK, NIH, ScaRF	Performed meta-analyses by comparing the genotype combinations§	3347 (3)	0.96 (0.82 to 1.12)	.831	NA
(SLC24A4)	rs12896399	G vs T	NMA	NA	NA	NA	NA	NA	39730 (3) ††
XRCC3	rs861539	T vs C	NMA	NA	NA	NA	NA	NA	3607 (5)
OCA2	rs1800407	T vs C	NMA	NA	NA	NA	NA	NA	1722 (3) ††

<i>OCA2</i>	rs7495174	G vs A	NMA	NA	NA	NA	NA	NA	42367 (5)
<i>C16orf55</i>	rs7188458	A vs G	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	NP	7569 (2)	1.30 (1.21 to 1.40)	1.2x10 ⁻¹²	NA
<i>CDK10</i>	rs258322	A vs G	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	Included replication datasets REP1 and REP2 of Bishop, 2009 (15) as one dataset	10165 (2)	1.67 (1.52 to 1.83)	2.5x10 ⁻²⁷	8992 (3) ‡‡
<i>MC1R</i>	rs61996344 (F45L)	C vs T	NMA	NA	NA	NA	NA	NA	1333 (4)
<i>MC1R</i>	rs1805005 (V60L)	T vs G	Raimondi, 2008 (47)	NP	Included a family-based study (51)	5065 (10)	1.15 (0.92 to 1.43)	.211	24816 (21)
<i>MC1R</i>	rs34474212 (S83P)	C vs T	NMA	NA	NA	NA	NA	NA	1264 (5)
<i>MC1R</i>	rs1805006 (D84H)	A vs C	Raimondi, 2008 (47)	NP	Included a family-based study (51)	3044 (8)	2.40 (1.50 to 3.84)	.00031	23336 (19)
<i>MC1R</i>	rs2228479 (V92M)	A vs G	Raimondi, 2008 (47)	NP	Included a family-based study (51)	4266 (10)	1.22 (0.99 to 1.50)	.061	22745 (20)
<i>MC1R</i>	rs34158934 (T95M)	T vs C	NMA	NA	NA	NA	NA	NA	4094 (7)
<i>MC1R</i>	V122M	A vs G	NMA	NA	NA	NA	NA	NA	2268 (5)
<i>MC1R</i>	rs11547464 (R142H)	A vs G	Raimondi, 2008 (47)	NP	Included a family-based study (51)	2712 (7)	1.66 (1.01 to 2.75)	.051	10606 (16)
<i>MC1R</i>	rs1805007 (R151C)	T vs C	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	Included a family-based study (49) and used a fixed-effect model	17209 (2)	1.49 (1.32 to 1.70)	4.3x10 ⁻¹⁰	27747 (21)
<i>MC1R</i>	rs1805007 (R151C)	T vs C	Raimondi, 2008 (47)	NP	Included a family-based study (51)	5047 (10)	1.78 (1.45 to 2.20)	6x10 ⁻⁸ 1	27747 (21)
<i>MC1R</i>	Y152X	A vs C	NMA	NA	NA	NA	NA	NA	4193 (8)
<i>MC1R</i>	rs1110400 (I155T)	C vs T	Raimondi, 2008 (47)	NP	Included a family-based study (51)	2950 (6)	2.45 (1.32 to 4.55)	.0051	22506 (19)
<i>MC1R</i>	rs1805008 (R160W)	T vs C	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	Included a family-based study (49)	18582(2)	1.42 (1.08 to 1.87)	.01	27368 (22)
<i>MC1R</i>	rs1805008 (R160W)	T vs C	Raimondi, 2008 (47)	NP	Included a family-based study (51)	5064 (10)	1.43 (1.20 to 1.70)	6x10 ⁻⁵ 1	27368 (22)
<i>MC1R</i>	rs885479 (R163Q)	A vs G	Raimondi, 2008 (47)	NP	Included a family-based study (51)	4347 (8)	1.42 (1.09 to 1.85)	.0091	52153 (20)
<i>MC1R</i>	R213W	T vs C	NMA	NA	NA	NA	NA	NA	2505 (5)
<i>MC1R</i>	K278E	G vs A	NMA	NA	NA	NA	NA	NA	1528 (5)
<i>MC1R</i>	rs1805009 (D294H)	C vs G	Raimondi, 2008 (47)	NP	Included a family-based study (51)	4473 (10)	1.77 (1.17 to 2.69)	.0071	24753 (20)
<i>MC1R</i>	rs2228478 (T314T)	G vs A	NMA	NA	NA	NA	NA	NA	19013 (10)
<i>AFG3LI</i>	rs4785763	A vs C	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	Included replication datasets REP1 and REP2 of Bishop, 2009 (15) as one dataset	10165 (2)	1.36 (1.28 to 1.45)	6x10 ⁻²²	9158 (3) ‡‡

<i>TP53</i>	rs1042522	C vs G	NMA	NA	NA	NA	NA	NA	3392 (6)
<i>XRCC1</i>	rs25487	A vs G	Mocellin, 2009 (48)	NP	NP	3504 (4)	1.02 (0.93 to 1.13)	.63	3504 (4)
<i>ERCC2</i>	rs13181	C vs A	Mocellin, 2009 (48)	NP	Applied a model-free approach (50), which imposed an additive model	6006 (8)	1.12 (1.03 to 1.21)	.01	6427 (8)
<i>ERCC2</i>	rs1799793	A vs G	Mocellin, 2009 (48)	NP	NP	3228 (3)	1.04 (0.93 to 1.15)	.50	5027 (5)
<i>GSTM1</i>	GSTM1*0	wt vs *0	NMA	NA	NA	NA	NA	NA	2239 (5)
<i>C20orf71</i>	rs17305657	C vs T	NMA	NA	NA	NA	NA	NA	3937 (3) ††
<i>C20orf114</i>	rs4911310	G vs A	NMA	NA	NA	NA	NA	NA	3941 (3) ††
<i>C20orf114</i>	rs2253335	T vs C	NMA	NA	NA	NA	NA	NA	3916 (3) ††
<i>(C20orf114)</i>	rs721970	A vs G	NMA	NA	NA	NA	NA	NA	4230 (3) ††
<i>CDK5RAP1</i>	rs291671	C vs T	NMA	NA	NA	NA	NA	NA	3960 (3) ††
<i>E2F1</i>	rs3213182	G vs T	NMA	NA	NA	NA	NA	NA	3806 (3) ††
<i>E2F1</i>	rs2071054	C vs T	NMA	NA	NA	NA	NA	NA	3868 (3) ††
<i>(RALY)</i>	rs6142047	C vs T	NMA	NA	NA	NA	NA	NA	4273 (3) ††
<i>(RALY)</i>	rs17091405	C vs G	NMA	NA	NA	NA	NA	NA	4082 (3) ††
<i>(RALY)</i>	rs4911379	A vs C	NMA	NA	NA	NA	NA	NA	3898 (3) ††
<i>(RALY)</i>	rs6059592	G vs T	NMA	NA	NA	NA	NA	NA	4247 (3) ††
<i>(RALY)</i>	rs2064348	T vs C	NMA	NA	NA	NA	NA	NA	4031 (3) ††
<i>RALY</i>	rs2284378	T vs C	NMA	NA	NA	NA	NA	NA	3994 (3) ††
<i>RALY</i>	rs6141443	G vs C	NMA	NA	NA	NA	NA	NA	4039 (3) ††
<i>RALY</i>	rs13043392	C vs A	NMA	NA	NA	NA	NA	NA	4015 (3) ††
<i>RALY</i>	rs2268089	A vs G	NMA	NA	NA	NA	NA	NA	4062 (3) ††
<i>(ASIP)</i>	rs819163	G vs T	NMA	NA	NA	NA	NA	NA	4079 (3) ††
<i>(ASIP)</i>	rs6059743	A vs G	NMA	NA	NA	NA	NA	NA	3943 (3) ††
<i>ASIP</i>	rs819162	T vs A	NMA	NA	NA	NA	NA	NA	4158 (3) ††
<i>ASIP</i>	rs6058017	G vs A	NMA	NA	NA	NA	NA	NA	44247 (7)
<i>ITCH</i>	rs7266300	T vs A	NMA	NA	NA	NA	NA	NA	3989 (3) ††
<i>(MAP1LC3A)</i>	rs6088519	T vs C	NMA	NA	NA	NA	NA	NA	4101 (3) ††
<i>(MAP1LC3A)</i>	rs6088520	T vs C	NMA	NA	NA	NA	NA	NA	4191 (3) ††
<i>(MAP1LC3A)</i>	rs2424994	T vs C	NMA	NA	NA	NA	NA	NA	4075 (3) ††
<i>PIGU</i>	rs910873	A vs G	Gerstenblith, 2010 (43)	Intramural Research	Used a fixed-effect model, included	8388 (4)	1.66 (1.49 to 1.83)	2.5x10 ⁻²²	6915 (4) ††,††

				Program of NIH, NCI	replication datasets REP1 and REP2 of Bishop, 2009 (15) as one dataset, and did not exclude overlapping study datasets between Brown et al. 2008 (16) and Bishop et al. 2009 (15)				
<i>PIGU</i>	rs6142206	T vs C	NMA	NA	NA	NA	NA	NA	3961 (3) ‡‡
<i>TP53INP2</i>	rs6060003	C vs T	NMA	NA	NA	NA	NA	NA	4285 (3) ‡‡
<i>NCOA6</i>	rs959829	G vs A	NMA	NA	NA	NA	NA	NA	4203 (3) ‡‡
<i>NCOA6</i>	rs4911442	G vs A	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	Included a family- based study (49), included replication datasets REP1 and REP2 of Bishop, 2009 (15) as one dataset, and did not exclude overlapping study datasets between Brown et al. 2008 (16) and Bishop et al. 2009 (15)	14222 (5)	1.50 (1.32 to 1.71)	5.5x10 ⁻¹⁰	NA
<i>NCOA6</i>	rs7271289	A vs G	NMA	NA	NA	NA	NA	NA	3983 (3) ‡‡
<i>NCOA6</i>	rs6088619	C vs T	NMA	NA	NA	NA	NA	NA	3932 (3) ‡‡
<i>MYH7B</i>	rs1885120	C vs G	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	Used a fixed-effect model, included replication datasets REP1 and REP2 of Bishop et al. 2009 (15) as one dataset, and did not exclude overlapping study datasets between Brown et al. 2008 (16) and Bishop et al. 2009 (15)	8388 (4)	1.69 (1.52 to 1.82)	1.5x10 ⁻²²	6787 (4) ††
<i>PHF20</i>	rs6058339	C vs T	NMA	NA	NA	NA	NA	NA	3957 (3)
<i>LOC647979</i>	rs1204552	A vs T	NMA	NA	NA	NA	NA	NA	4063 (3) ‡‡
<i>ASIP</i>	rs4911414-rs1015362	(haplotype)	Gerstenblith, 2010 (43)	Intramural Research Program of NIH, NCI	NP	43293 (2)	NA	NA	NA
<i>GSTT1</i>	GSTT1*0	*0 vs wt	NMA	NA	NA	NA	NA	NA	2824 (5)
<i>PLA2G6</i>	rs2284063	G vs A	Gerstenblith, 2010 (43)	Intramural Research Program of	NP	11689 (3)	0.84 (0.76 to 0.94)	.003	12690 (3) ‡‡

<i>PLA2G6</i>	rs6001027	G vs A	Gerstenblith, 2010 (43)	NIH, NCI Intramural Research Program of NIH, NCI and Genetics	NP	11689 (3)	0.85 (0.78 to 0.93)	.001	12690 (3) ‡‡
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† CI = confidence interval, NA = not applicable, NCI = National Cancer Institute, NIH = National Institutes of Health, NMA = data did not undergo meta-analyses, NP = not provided in original publication, OR = odds ratio, ScaRF = Skin Cancer Research Fund, UK = United Kingdom.

‡ In order to compare the MelGene results with those from previously published meta-analyses in the field, we collected all relevant articles published before July 31st 2010 and extracted the genetic contrasts and models used (allelic, dominant or recessive, random-effects or fixed-effects) from each publication when provided.

§ Meta-analysis was done by comparing the following genotype combinations: minor/minor versus major/major, minor/major versus major/major, minor/minor + minor/major versus major/major. Only the most statistically significant results are reported.

|| *P* values were not given in original publication and were approximated here for comparison purposes on the basis of the rounded odds ratios and/or confidence intervals provided in the original publication

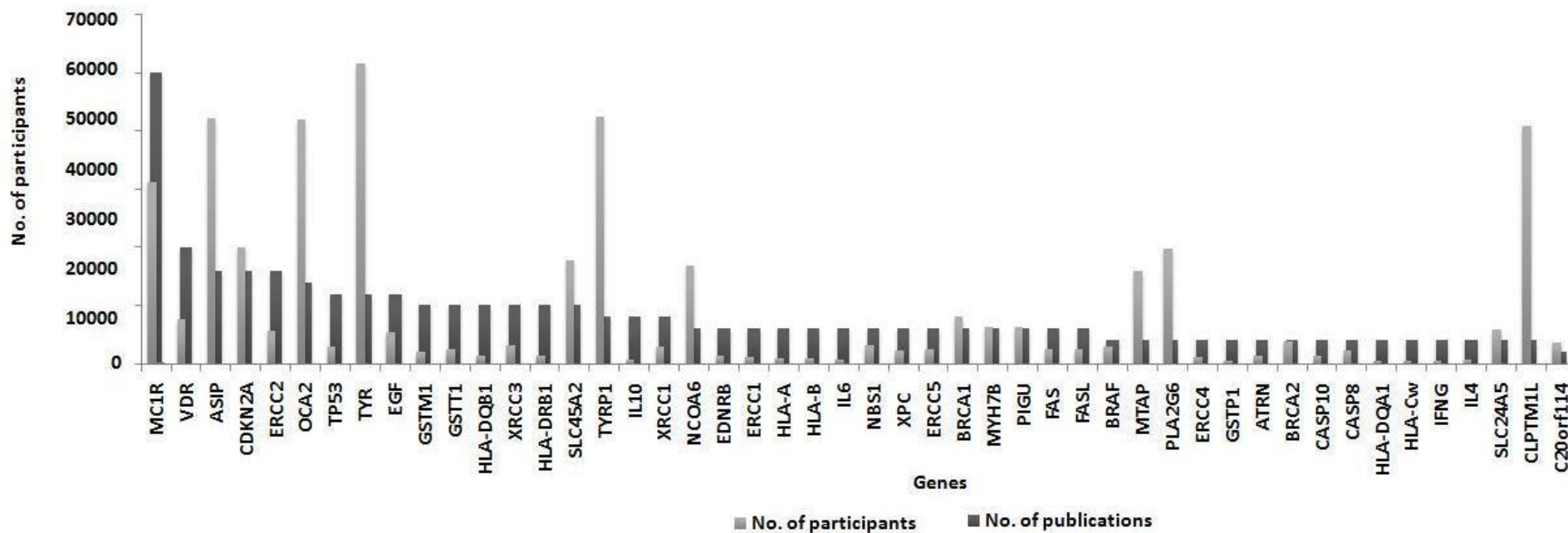
In addition to allelic models, the following genotype combinations were analyzed: minor/minor versus major/major, minor/major versus major/major. Only the allelic result is reported.

†† MelGene meta-analyses included one additional new study (52).

‡‡ Meta-analyses of 3 datasets only including genome-wide association studies (GWAS) and other large-scale replication studies. For the inclusion of data from GWAS and other large-scale studies where only odds ratios,

confidence intervals and/or P values were provided, we estimated genotype summary counts and the number of analyzed subjects on the basis of the reported data, control allele frequencies, and overall effective number of subjects. Therefore the listed number of subjects is only an approximation of the real number.

Supplementary Figure 1



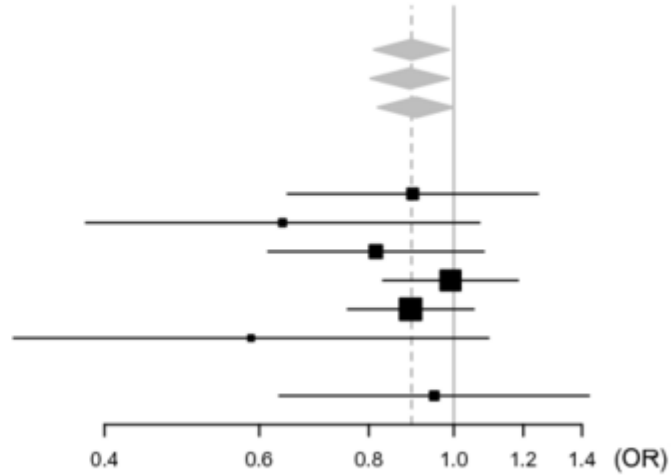
Supplementary Figure 1. The 50 most frequently studied genes in genetic association studies of cutaneous melanoma per aggregate number of study participants and number of publications per gene including genome-wide association studies.

Supplementary Figure 2

A

ASIP (rs6058017): G vs A

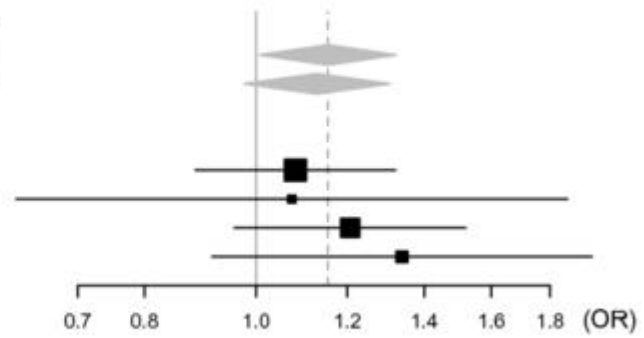
	OR	95% CI	I ²
All studies	0.89	(0.81 to 0.99)	0
All excl initial	0.89	(0.80 to 0.99)	2
All excl HWE violations	0.90	(0.82 to 1.00)	0
Study specific ORs			
Nan, 2009 (C)	0.90	(0.65 to 1.25)	
Brudnik, 2009 (C)	0.64	(0.38 to 1.07)	
Gudbjartsson, 2008, Spain (C)	0.82	(0.61 to 1.08)	
Gudbjartsson, 2008, Iceland (C)	0.99	(0.83 to 1.18)	
Gudbjartsson, 2008, Sweden (C)	0.89	(0.76 to 1.05)	
Meziani, 2005 (C) #	0.59	(0.31 to 1.10)	
Landi, 2005 (C) †	–	–	
Kanetsky, 2002 (C) •	0.95	(0.63 to 1.43)	



B

CDKN2A (rs11515): G vs C

	OR	95% CI	I ²
All studies	1.15	(1.01 to 1.32)	0
All excl initial	1.13	(0.98 to 1.31)	0
Study specific ORs			
Goldstein, 2008 (C)	1.08	(0.89 to 1.32)	
Pjanova, 2007 (C)	1.07	(0.62 to 1.86)	
Debniak, 2005 (C)	1.21	(0.96 to 1.52)	
Kumar, 2001 (C) •	1.34	(0.91 to 1.96)	



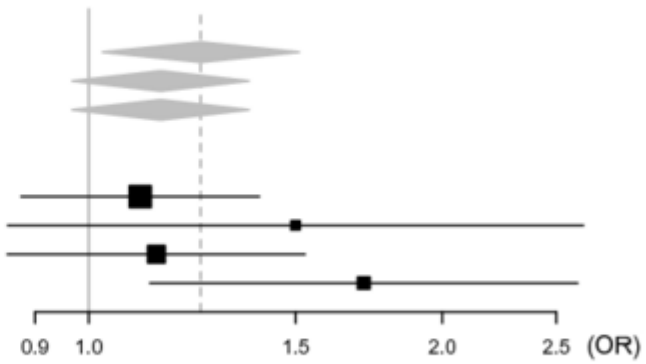
C

CDKN2A (rs3088440): T vs C

	OR	95% CI	I ²
All studies	1.25	(1.03 to 1.51)	24
All excl initial	1.15	(0.97 to 1.37)	0
All excl HWE violations	1.15	(0.97 to 1.37)	0

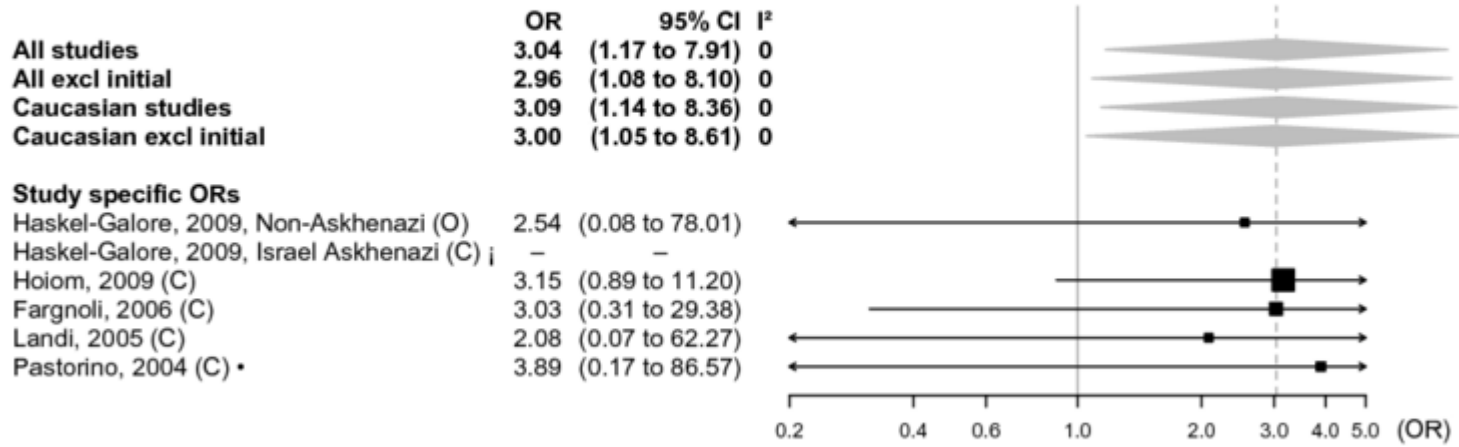
Study specific ORs

Goldstein, 2008 (C)	1.11	(0.88 to 1.40)
Pjanova, 2007 (C)	1.50	(0.85 to 2.64)
Debniak, 2005 (C)	1.14	(0.85 to 1.53)
Kumar, 2001 (C) • #	1.71	(1.13 to 2.61)



D

MC1R (R213W): T vs C



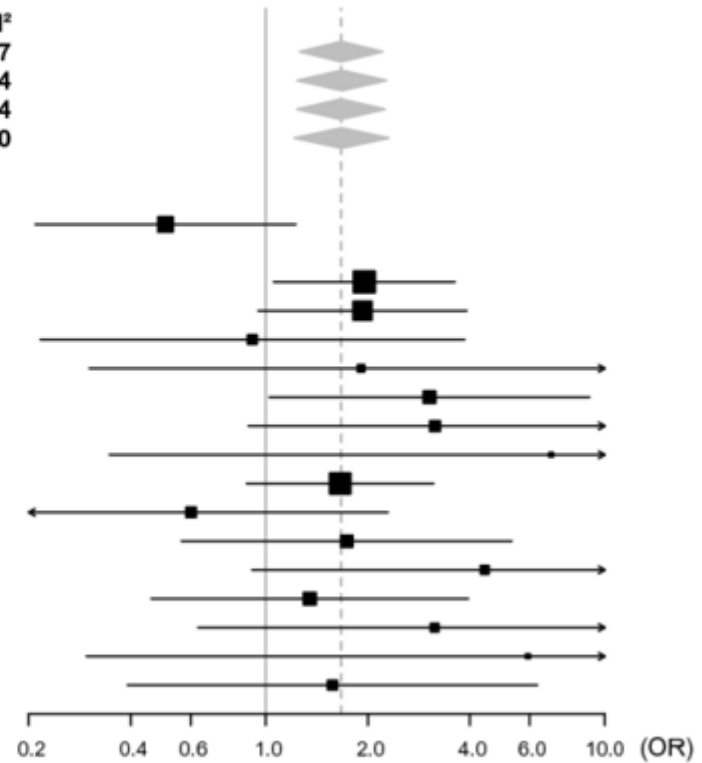
E

MC1R (rs11547464): A vs G

	OR	95% CI	I²
All studies	1.67	(1.26 to 2.21)	7
All excl initial	1.68	(1.24 to 2.27)	14
Caucasian studies	1.67	(1.23 to 2.25)	14
Caucasian excl initial	1.67	(1.21 to 2.31)	20

Study specific ORs

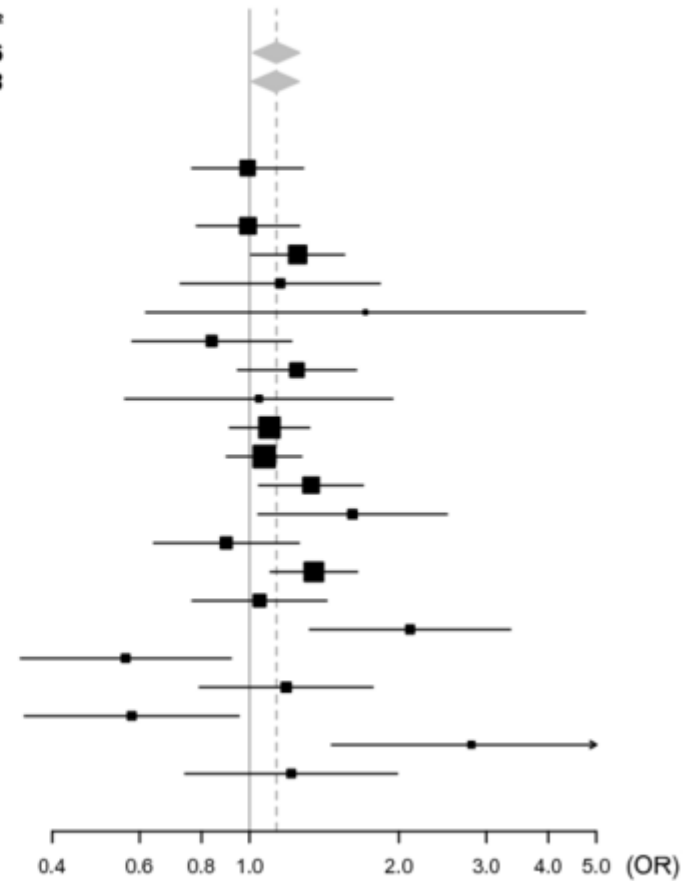
Kanetsky, 2010 (C)	0.51	(0.21 to 1.23)
Duffy, 2009 (C) †	–	–
Scherer, 2009, Germany (C)	1.95	(1.05 to 3.62)
Scherer, 2009, Spain (C)	1.93	(0.95 to 3.92)
Council, 2009 (C)	0.91	(0.22 to 3.86)
Haskel-Galore, 2009, Non-Askhenazi (O)	1.91	(0.30 to 12.10)
Haskel-Galore, 2009, Israel Askhenazi (C)	3.04	(1.02 to 9.01)
Hoiom, 2009 (C)	3.15	(0.89 to 11.20)
Brudnik, 2009 (C)	6.94	(0.35 to 139.41)
Guedj, 2008 (C)	1.66	(0.88 to 3.13)
Fernandez, 2007 (C)	0.60	(0.16 to 2.29)
Mossner, 2007 (C)	1.73	(0.56 to 5.33)
Stratigos, 2006 (C)	4.42	(0.91 to 21.49)
Fargnoli, 2006 (C)	1.35	(0.46 to 3.96)
Landi, 2005 (C)	3.15	(0.63 to 15.71)
Matichard, 2004 (C)	5.93	(0.30 to 119.10)
Kennedy, 2001 (C) •	1.57	(0.39 to 6.33)



F

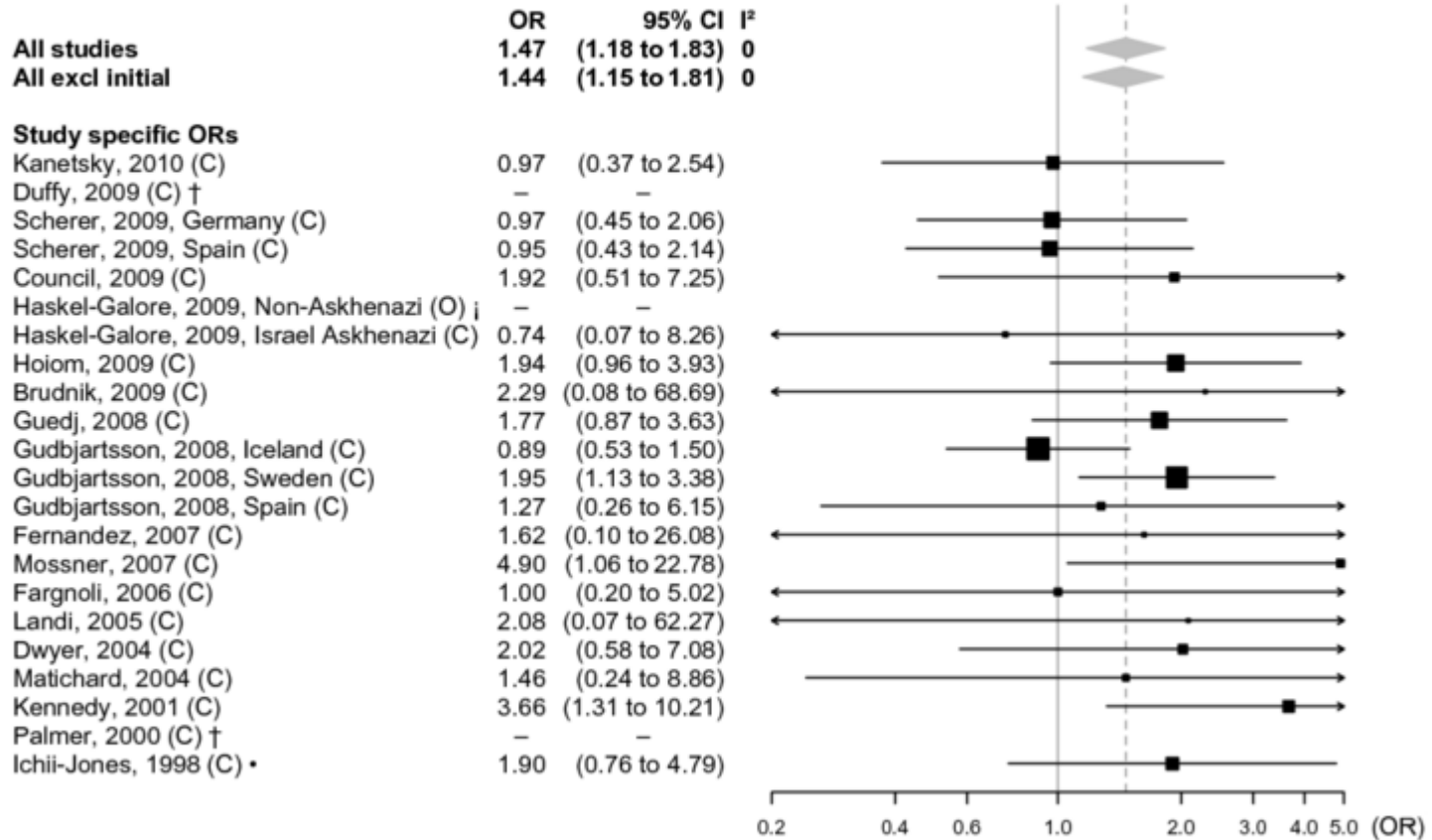
MC1R (rs1805005): T vs G

	OR	95% CI	I ²
All studies ø	1.13	(1.02 to 1.26)	56
Caucasian studies	1.13	(1.01 to 1.26)	58
Study specific ORs			
Kanetsky, 2010 (C)	0.99	(0.76 to 1.28)	
Duffy, 2009 (C) †	-	-	
Scherer, 2009, Germany (C)	0.99	(0.78 to 1.26)	
Scherer, 2009, Spain (C)	1.25	(1.01 to 1.55)	
Council, 2009 (C)	1.15	(0.72 to 1.83)	
Haskel-Galore, 2009, Non-Askhenazi (O)	1.71	(0.62 to 4.74)	
Haskel-Galore, 2009, Israel Askhenazi (C)	0.84	(0.58 to 1.21)	
Hoiom, 2009 (C)	1.25	(0.94 to 1.64)	
Brudnik, 2009 (C)	1.04	(0.56 to 1.94)	
Gudbjartsson, 2008, Sweden (C)	1.10	(0.91 to 1.32)	
Gudbjartsson, 2008, Iceland (C)	1.07	(0.90 to 1.27)	
Gudbjartsson, 2008, Spain (C)	1.33	(1.04 to 1.70)	
Fernandez, 2007 (C)	1.61	(1.04 to 2.50)	
Mossner, 2007 (C)	0.90	(0.64 to 1.26)	
Debniak, 2006 (C)	1.35	(1.10 to 1.65)	
Han, 2006 (C)	1.05	(0.77 to 1.43)	
Stratigos, 2006 (C)	2.11	(1.32 to 3.36)	
Fargnoli, 2006 (C)	0.56	(0.34 to 0.92)	
Landi, 2005 (C)	1.19	(0.79 to 1.77)	
Dwyer, 2004 (C)	0.58	(0.35 to 0.95)	
Matichard, 2004 (C)	2.80	(1.46 to 5.36)	
Kennedy, 2001 (C)	1.21	(0.74 to 1.99)	
Palmer, 2000 (C) • †	-	-	



G

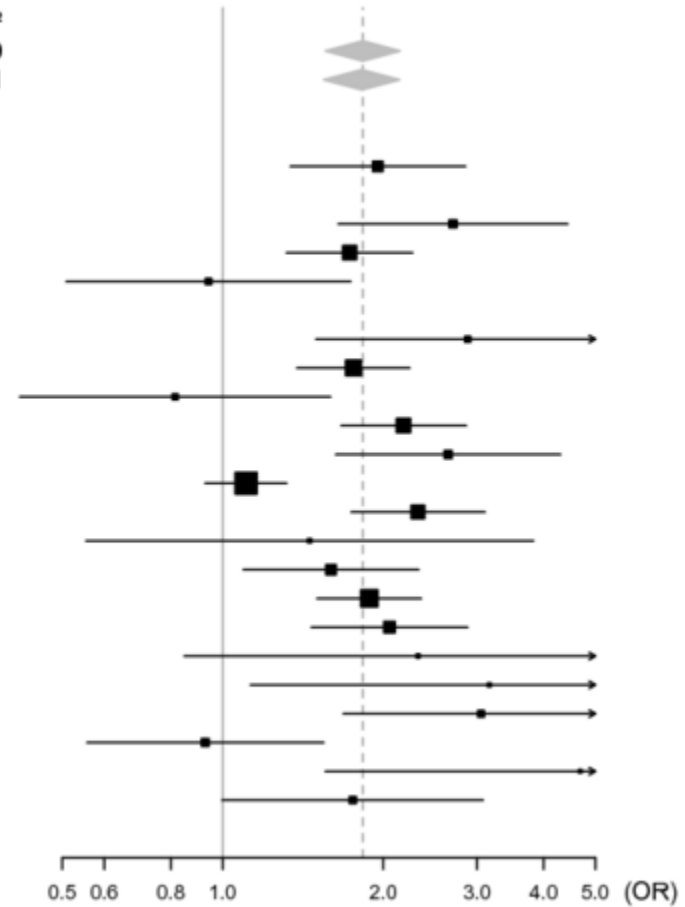
MC1R (rs1805006): A vs C



H

MC1R (rs1805007): T vs C

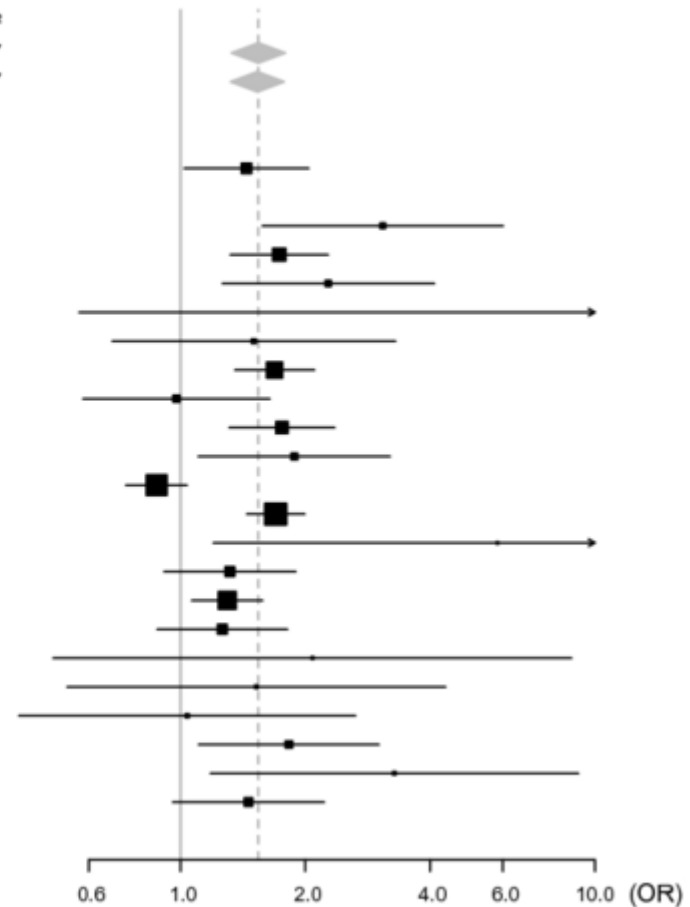
	OR	95% CI	I ²
All studies ø	1.83	(1.56 to 2.15)	69
All excl HWE violations	1.82	(1.55 to 2.15)	71
Study specific ORs			
Kanetsky, 2010 (C)	1.96	(1.34 to 2.86)	
Duffy, 2009 (C) †	–	–	
Scherer, 2009, Spain (C)	2.70	(1.65 to 4.44)	
Scherer, 2009, Germany (C)	1.73	(1.32 to 2.27)	
Council, 2009 (C)	0.94	(0.51 to 1.74)	
Haskel-Galore, 2009, Non-Askhenazi (O) j	–	–	
Haskel-Galore, 2009, Israel Askhenazi (C)	2.88	(1.50 to 5.56)	
Hoiom, 2009 (C)	1.76	(1.38 to 2.25)	
Brudnik, 2009 (C)	0.81	(0.42 to 1.59)	
Guedj, 2008 (C)	2.18	(1.67 to 2.86)	
Gudbjartsson, 2008, Spain (C)	2.65	(1.63 to 4.30)	
Gudbjartsson, 2008, Iceland (C)	1.11	(0.93 to 1.32)	
Gudbjartsson, 2008, Sweden (C)	2.32	(1.74 to 3.10)	
Fernandez, 2007 (C)	1.46	(0.55 to 3.83)	
Mossner, 2007 (C)	1.60	(1.09 to 2.33)	
Debniak, 2006 (C)	1.88	(1.50 to 2.36)	
Han, 2006 (C)	2.06	(1.47 to 2.88)	
Stratigos, 2006 (C) #	2.32	(0.85 to 6.38)	
Fargnoli, 2006 (C)	3.16	(1.13 to 8.87)	
Landi, 2005 (C)	3.05	(1.68 to 5.54)	
Dwyer, 2004 (C)	0.93	(0.56 to 1.55)	
Matichard, 2004 (C)	4.68	(1.56 to 14.08)	
Kennedy, 2001 (C)	1.75	(1.00 to 3.08)	
Palmer, 2000 (C) • †	–	–	



I

MC1R (rs1805008): T vs C

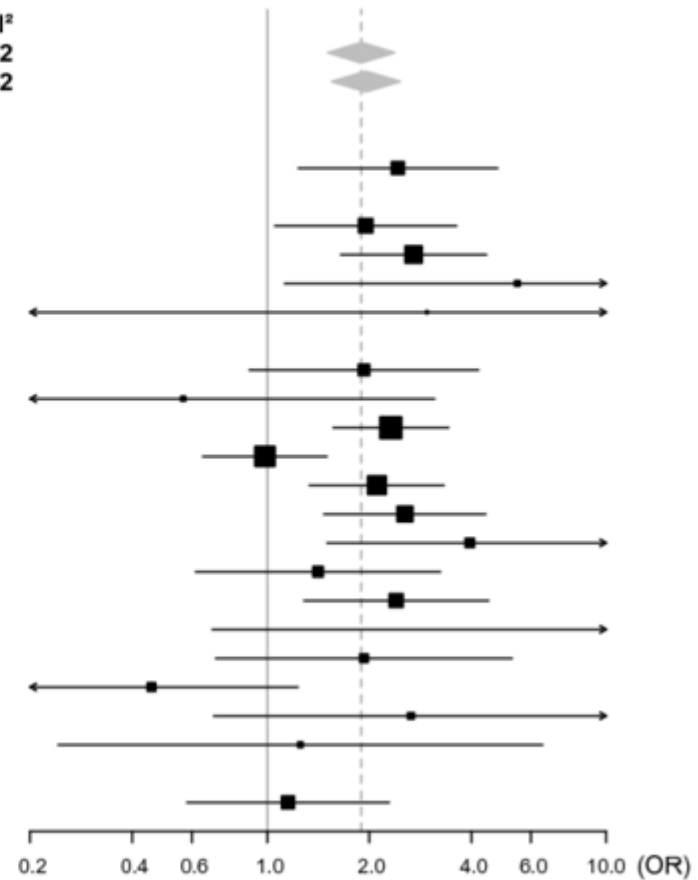
	OR	95% CI	I ²
All studies ø	1.54	(1.33 to 1.79)	67
Caucasian studies	1.53	(1.32 to 1.78)	67
Study specific ORs			
Kanetsky, 2010 (C)	1.44	(1.02 to 2.04)	
Duffy, 2009 (C) †	-	-	
Scherer, 2009, Spain (C)	3.08	(1.57 to 6.01)	
Scherer, 2009, Germany (C)	1.73	(1.32 to 2.27)	
Council, 2009 (C)	2.27	(1.26 to 4.10)	
Haskel-Galore, 2009, Non-Askhenazi (O)	11.12	(0.57 to 217.91)	
Haskel-Galore, 2009, Israel Askhenazi (C)	1.50	(0.68 to 3.31)	
Hoiom, 2009 (C)	1.69	(1.35 to 2.10)	
Brudnik, 2009 (C)	0.98	(0.58 to 1.64)	
Guedj, 2008 (C)	1.76	(1.31 to 2.36)	
Gudbjartsson, 2008, Spain (C)	1.88	(1.10 to 3.21)	
Gudbjartsson, 2008, Iceland (C)	0.87	(0.74 to 1.04)	
Gudbjartsson, 2008, Sweden (C)	1.70	(1.44 to 2.00)	
Fernandez, 2007 (C)	5.82	(1.20 to 28.25)	
Mossner, 2007 (C)	1.32	(0.91 to 1.90)	
Debniak, 2006 (C)	1.30	(1.06 to 1.58)	
Han, 2006 (C)	1.26	(0.88 to 1.81)	
Stratigos, 2006 (C)	2.08	(0.49 to 8.80)	
Fagnoli, 2006 (C)	1.52	(0.53 to 4.36)	
Landi, 2005 (C)	1.04	(0.41 to 2.65)	
Dwyer, 2004 (C)	1.83	(1.11 to 3.02)	
Matichard, 2004 (C)	3.28	(1.18 to 9.12)	
Kennedy, 2001 (C)	1.46	(0.96 to 2.22)	
Palmer, 2000 (C) • †	-	-	



J

MC1R (rs1805009): C vs G

	OR	95% CI	I ²
All studies	1.89	(1.51 to 2.38)	42
All excl initial	1.96	(1.55 to 2.47)	42
Study specific ORs			
Kanetsky, 2010 (C)	2.43	(1.23 to 4.79)	
Duffy, 2009 (C) †	–	–	
Scherer, 2009, Germany (C)	1.95	(1.05 to 3.62)	
Scherer, 2009, Spain (C)	2.70	(1.65 to 4.44)	
Council, 2009 (C)	5.47	(1.13 to 26.60)	
Haskel-Galore, 2009, Israel Askhenazi (C)	2.96	(0.10 to 88.72)	
Haskel-Galore, 2009, Non-Askhenazi (O) †	–	–	
Hoiom, 2009 (C)	1.93	(0.89 to 4.21)	
Brudnik, 2009 (C)	0.57	(0.10 to 3.12)	
Guedj, 2008 (C)	2.32	(1.56 to 3.43)	
Gudbjartsson, 2008, Iceland (C)	0.99	(0.65 to 1.50)	
Gudbjartsson, 2008, Sweden (C)	2.11	(1.33 to 3.33)	
Gudbjartsson, 2008, Spain (C)	2.55	(1.47 to 4.41)	
Fernandez, 2007 (C)	3.96	(1.50 to 10.46)	
Mossner, 2007 (C)	1.41	(0.62 to 3.25)	
Han, 2006 (C)	2.40	(1.28 to 4.50)	
Fagnoli, 2006 (C)	12.40	(0.69 to 223.55)	
Landi, 2005 (C)	1.93	(0.71 to 5.28)	
Dwyer, 2004 (C)	0.46	(0.17 to 1.23)	
Matichard, 2004 (C)	2.65	(0.69 to 10.14)	
Kennedy, 2001 (C)	1.25	(0.24 to 6.51)	
Palmer, 2000 (C) †	–	–	
Ichii-Jones, 1998 (C) •	1.15	(0.58 to 2.29)	



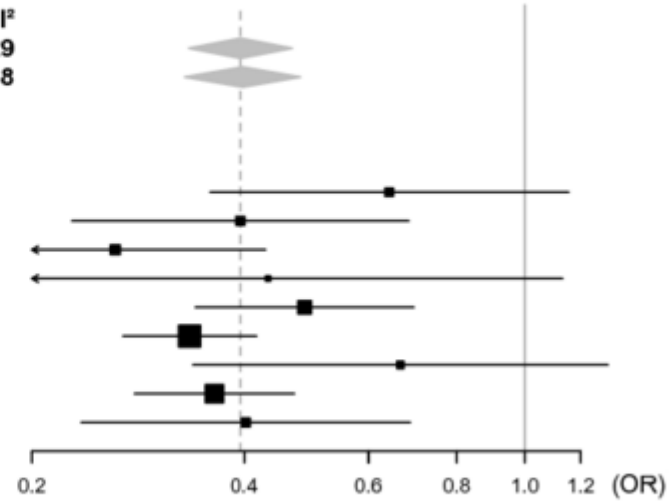
K

SLC45A2 (rs16891982): C vs G

	OR	95% CI	I ²
All studies	0.40	(0.33 to 0.47)	29
All excl initial	0.40	(0.33 to 0.48)	38

Study specific ORs

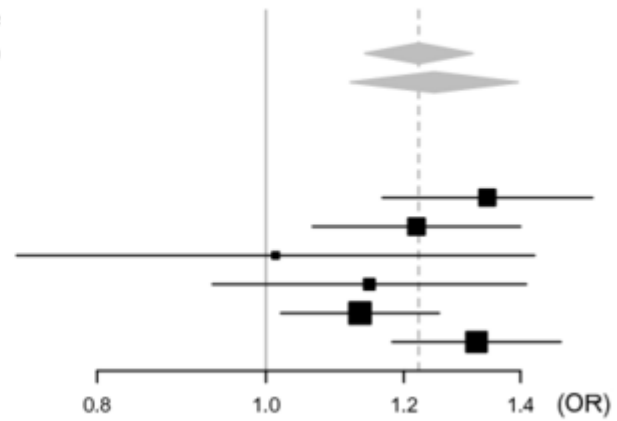
Duffy, 2009 (C) †	–	–	
Stacey, 2009, Iceland (C)	0.64	(0.36 to 1.15)	
Stacey, 2009, Holland (C)	0.39	(0.23 to 0.68)	
Stacey, 2009, Sweden (C)	0.26	(0.16 to 0.43)	
Stacey, 2009, Austria (C)	0.43	(0.17 to 1.13)	
Stacey, 2009, Italy (C)	0.49	(0.34 to 0.70)	
Stacey, 2009, Spain (C)	0.33	(0.27 to 0.42)	
Nan, 2009 (C)	0.67	(0.34 to 1.31)	
Guedj, 2008 (C)	0.36	(0.28 to 0.47)	
Fernandez, 2008 (C) •	0.40	(0.23 to 0.69)	



L

TYR (rs1126809): A vs G

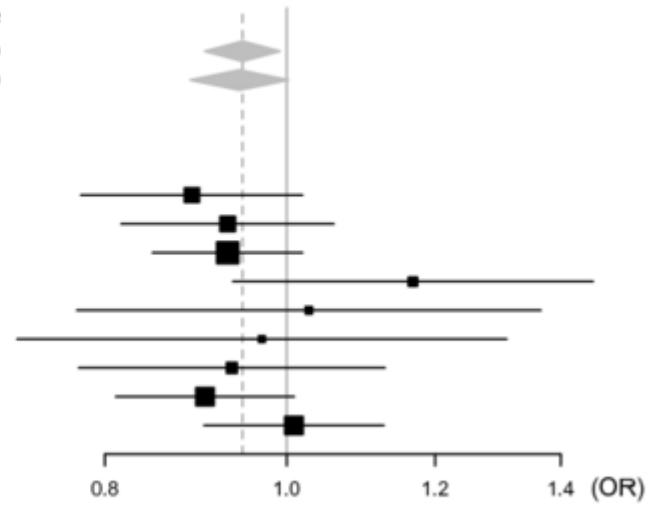
	OR	95% CI	I ²
All studies	1.22	(1.14 to 1.31)	29
All excl initial	1.25	(1.12 to 1.40)	21
Study specific ORs			
Duffy, 2009 (C) †	–	–	
Bishop, 2009, GenoMEL REP1 (C) ¶¶	1.34	(1.17 to 1.54)	
Bishop, 2009, Leeds REP2 (C) ¶¶	1.22	(1.06 to 1.40)	
Fernandez, 2008 (C)	1.01	(0.72 to 1.43)	
Gudbjartsson, 2008, Spain (C) •	1.15	(0.93 to 1.41)	
Gudbjartsson, 2008, Iceland (C) •	1.13	(1.02 to 1.26)	
Gudbjartsson, 2008, Sweden (C) •	1.32	(1.18 to 1.48)	



M

TYR (rs1042602): A vs C

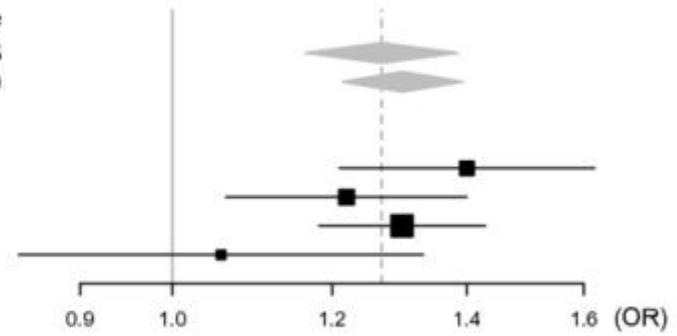
	OR	95% CI	I ²
All studies	0.95	(0.90 to 0.99)	0
All excl initial	0.94	(0.89 to 1.00)	0
Study specific ORs			
Duffy, 2009 (C) †	–	–	–
Bishop, 2009, GenoMEL REP1 (C) ††	0.89	(0.78 to 1.02)	
Bishop, 2009, Leeds REP2 (C) ††	0.93	(0.82 to 1.06)	
Bishop, 2009, GenoMEL GWAS (C) ††	0.93	(0.85 to 1.02)	
Nan, 2009 (C)	1.17	(0.94 to 1.46)	
Council, 2009 (C)	1.03	(0.77 to 1.37)	
Fernandez, 2008 (C)	0.97	(0.72 to 1.31)	
Gudbjartsson, 2008, Spain (C) •	0.93	(0.77 to 1.13)	
Gudbjartsson, 2008, Iceland (C) •	0.90	(0.81 to 1.01)	
Gudbjartsson, 2008, Sweden (C) •	1.01	(0.90 to 1.13)	



N

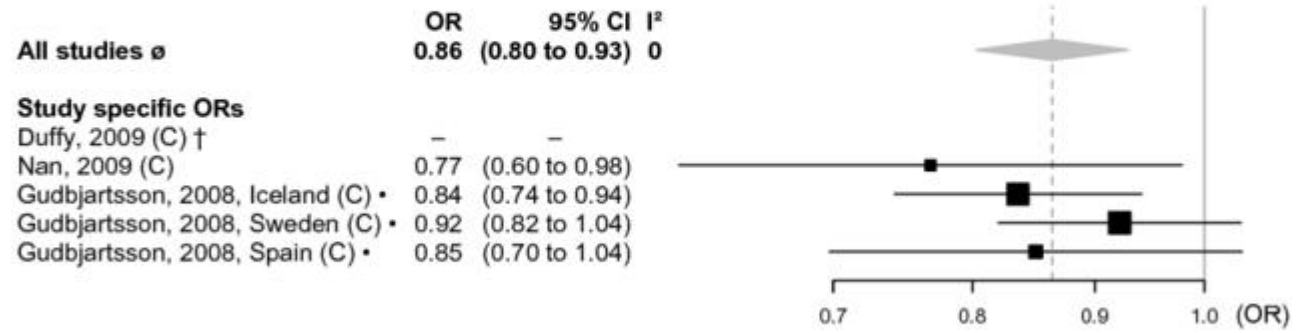
TYR (rs1393350): A vs G

	OR	95% CI	I²
All studies	1.27	(1.16 to 1.39)	35
All excl initial	1.30	(1.21 to 1.39)	0
Study specific ORs			
Bishop, 2009 [Replication GenoMEL (REP1)] (C) ¶	1.40	(1.21 to 1.62)	
Bishop, 2009 [Replication Leeds (REP2)] (C) ¶	1.22	(1.06 to 1.40)	
Bishop, 2009 [GWAS] (C) ¶	1.30	(1.18 to 1.43)	
Nan, 2009 (C) •	1.06	(0.84 to 1.33)	



O

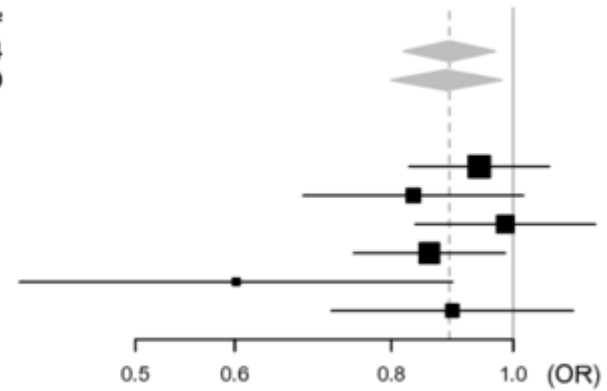
TYRP1 (rs1408799): T vs C



P

VDR (rs1544410): A vs G

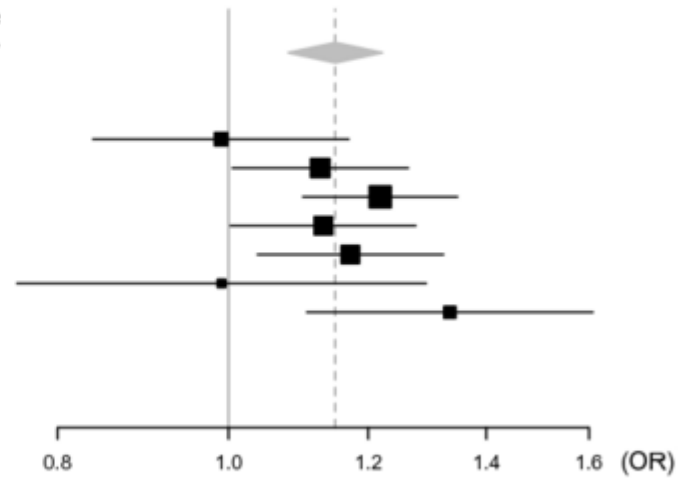
	OR	95% CI	I ²
All studies	0.89	(0.82 to 0.97)	24
All excl initial	0.88	(0.80 to 0.98)	39
Study specific ORs			
Gapska, 2009 (C)	0.94	(0.83 to 1.07)	
Randerson-Moor, 2009, UK (Leeds CCS2) (C)	0.83	(0.68 to 1.02)	
Randerson-Moor, 2009, UK (Leeds CCS1) (C)	0.99	(0.84 to 1.16)	
Li, 2008 (C)	0.86	(0.75 to 0.99)	
Santonocito, 2007 (C)	0.60	(0.40 to 0.90)	
Han, 2007 (C) •	0.89	(0.72 to 1.12)	



Q

CLPTM1L (rs401681): T vs C

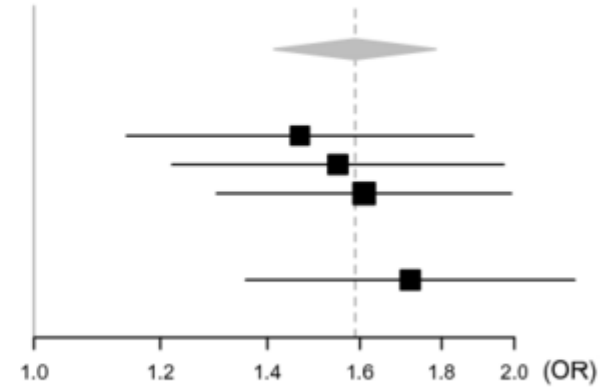
	OR	95% CI	I ²
All studies ø	1.15	(1.08 to 1.22)	27
Study specific ORs			
Pooley, 2010 (C) ¶¶	0.99	(0.84 to 1.17)	
Stacey, 2009, Iceland (C)	1.13	(1.00 to 1.26)	
Stacey, 2009, Sweden (C)	1.22	(1.10 to 1.35)	
Stacey, 2009, Spain (C)	1.13	(1.00 to 1.28)	
Stacey, 2009, Holland (C)	1.17	(1.04 to 1.32)	
Stacey, 2009, Austria (C)	0.99	(0.76 to 1.29)	
Stacey, 2009, Italy (C)	1.33	(1.11 to 1.61)	
Rafnar, 2009 (C) • ‡	-	-	
Rafnar, 2009 (C) • ‡	-	-	
Rafnar, 2009 (C) • ‡	-	-	



R

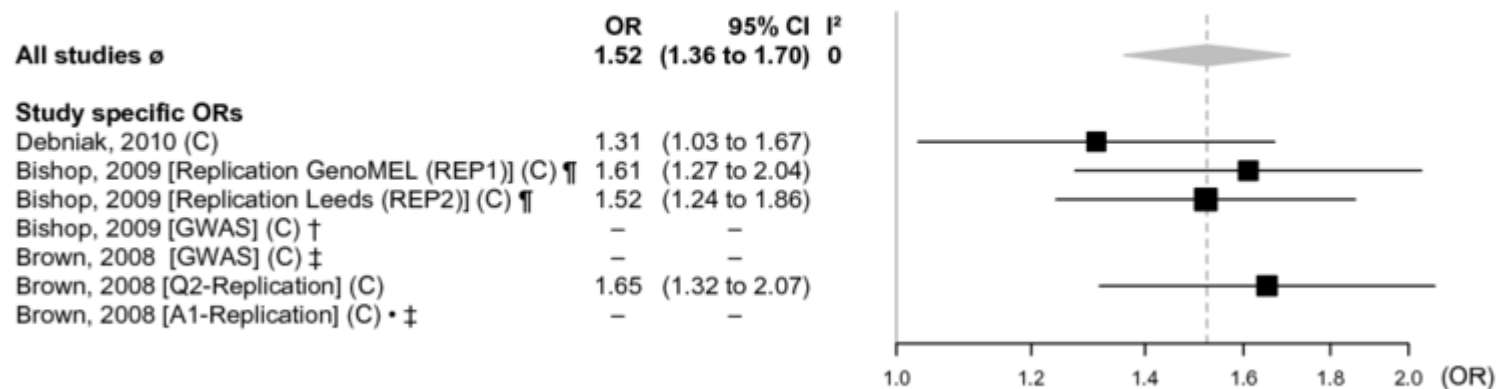
MYH7B (rs1885120): C vs G

	OR	95% CI	I²
All studies \emptyset	1.59	(1.41 to 1.79)	0
Study specific ORs			
Debniak, 2010 (C)	1.47	(1.14 to 1.88)	
Bishop, 2009 [Replication GenoMEL (REP1)] (C) ¶	1.55	(1.22 to 1.97)	
Bishop, 2009 [Replication Leeds (REP2)] (C) ¶¶	1.61	(1.30 to 1.99)	
Bishop, 2009 [GWAS] (C) †	–	–	
Brown,2008 [GWAS] (C) ‡	–	–	
Brown, 2008 [Q2-Replication] (C)	1.72	(1.36 to 2.18)	
Brown, 2008 [A1-Replication] (C) • ‡	–	–	



S

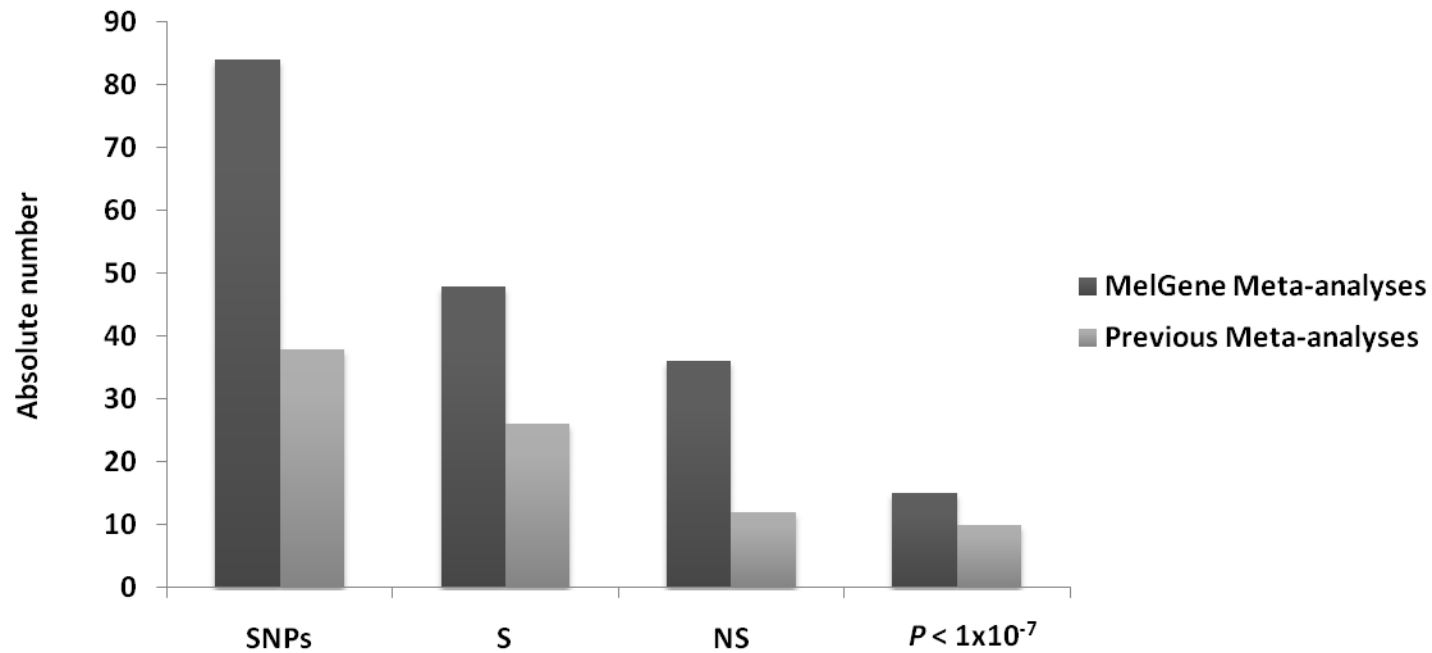
FIGU (rs910873): A vs G



Supplementary Figure 2. Forest plots of random-effects meta-analyses using allelic contrasts for polymorphisms showing statistically nominally significant ($P < .05$) summary odds ratios (ORs). Random-effects summary odds ratios and 95% confidence intervals (CIs) were calculated by the DerSimonian Laird model (29). Data from reports published before July 31, 2010 were included in the meta-analyses for **A)** *ASIP* (rs6058017), **B)** *CDKN2A* (rs11515), **C)** *CDKN2A* (rs3088440), **D)** *MC1R* (R213W), **E)** *MC1R* (rs11547464 [R142H]), **F)** *MC1R* (rs1805005 [V60L]), **G)** *MC1R* (rs1805006 [D84E]), **H)** *MC1R* rs1805007 (R151C), **I)** *MC1R* (rs1805008 [R160W]), **J)** *MC1R* (rs1805009 [D294H]), **K)** *SLC45A2* (rs16891982), **L)** *TYR* (rs1126809), **M)** *TYR* (rs1042602), **N)** *TYR* (rs1393350), **O)** *TYRP1* (rs1408799), **P)**

VDR (rs1544410), **Q**) *CLPTMIL* (rs401681), **R**) *MYH7B* (rs1885120), and **S**) *PIGU* (rs910873). All studies and All excl initial denote the summary odds ratios and 95% confidence intervals after meta-analysis of all studies displayed on the forest plots, and after exclusion of the initial study, respectively. The dotted vertical line indicates the summary odds ratio of the meta-analysis of All studies. I^2 was calculated by the estimate of percentage of between-study heterogeneity that is beyond chance. GWAS = genome-wide association studies, HWE = Hardy Weinberg Equilibrium. • denotes the initial study. † No data was provided or data was not eligible for inclusion in the meta-analysis. ‡ This dataset was excluded from the meta-analysis because of overlap of patients and/or control subjects in this study with subjects included in another study for the same polymorphism. # A Hardy-Weinberg violation was observed in the controls ($P \leq .05$). ¶ The published odds ratio and 95% confidence interval were used for analysis. i The polymorphism was monomorphic in the respective dataset. ø Meta-analysis of this polymorphism after excluding the initial study was not applicable because of missing data for the initial study or less than three remaining datasets after exclusion of the initial dataset. C indicates the population was of European ancestry. O indicates the study population was of other or mixed ethnicity.

Supplementary Figure 3



Supplementary Figure 3. Comparison of the number of variants, as well as the number of statistically and non-statistically significant results between previously published meta-analyses and meta-analyses performed for this study as of July 31, 2010. SNPs = number of single nucleotide polymorphisms, S = nominally statistically significant results ($P < .05$), NS = non-statistically significant results, $P < 1 \times 10^{-7}$ = single nucleotide polymorphisms that reached genome-wide significance.