

**Supplementary Table 1. Hierarchical modeling of associations between MC1R variants and melanoma risk with three different tau<sup>2</sup> values**

tau <sup>2</sup> = 0.025		Val60Leu	Val92Met	Arg151Cys	Ile155Thr	Arg160Trp	Arg163Gln	Asp294His
OR	Equal weighted model	1.70	1.76	2.09	1.86	1.83	1.82	1.98
lower		1.25	1.28	1.51	1.26	1.31	1.27	1.36
upper		2.32	2.41	2.89	2.75	2.56	2.61	2.89
beta		0.53	0.56	0.74	0.62	0.61	0.60	0.68
se		0.16	0.16	0.17	0.20	0.17	0.18	0.19
OR	Model based on MC1R antibody binding	1.70	1.72	2.13	1.95	1.87	1.80	1.90
lower		1.25	1.23	1.50	1.20	1.31	1.25	1.18
upper		2.32	2.42	3.03	3.17	2.68	2.60	3.05
beta		0.53	0.54	0.76	0.67	0.63	0.59	0.64
se		0.16	0.17	0.18	0.25	0.18	0.19	0.24
OR	Model based on MSH ligand binding	1.70	1.74	2.10	1.93	1.85	1.81	1.94
lower		1.25	1.24	1.50	1.06	1.30	1.25	1.22
upper		2.32	2.44	2.95	3.51	2.63	2.62	3.10
beta		0.53	0.56	0.74	0.66	0.61	0.59	0.66
se		0.16	0.17	0.17	0.31	0.18	0.19	0.24
OR	Model based on cAMP response to MSH	1.70	1.64	2.23	1.74	1.94	1.54	2.31
lower		1.25	1.17	1.58	1.16	1.37	0.97	1.47
upper		2.32	2.30	3.13	2.61	2.74	2.45	3.65
beta		0.53	0.50	0.80	0.55	0.66	0.43	0.84
se		0.16	0.17	0.17	0.21	0.18	0.24	0.23
OR	Model based on kinetics - Ki-a-MSH	1.73	1.69	2.14	1.82	1.87	1.81	1.94
lower		1.25	1.16	1.51	1.22	1.32	1.26	1.31
upper		2.38	2.45	3.04	2.72	2.65	2.60	2.87
beta		0.55	0.52	0.76	0.60	0.63	0.59	0.66
se		0.16	0.19	0.18	0.21	0.18	0.19	0.20
OR	Model based on kinetics - Ki-NDP	1.61	1.70	2.31	1.89	1.89	1.91	1.78
lower		1.15	1.23	1.57	1.28	1.35	1.31	1.14
upper		2.24	2.35	3.40	2.79	2.65	2.78	2.77
beta		0.47	0.53	0.84	0.63	0.64	0.65	0.58
se		0.17	0.17	0.20	0.20	0.17	0.19	0.23
OR	Model based on hair color	1.60	1.61	2.21	1.86	2.06	1.71	2.38
lower		1.15	1.14	1.58	1.26	1.42	1.17	1.50
upper		2.21	2.27	3.09	2.75	2.98	2.48	3.79
beta		0.47	0.48	0.79	0.62	0.72	0.53	0.87
se		0.17	0.18	0.17	0.20	0.19	0.19	0.24
OR	Model based on skin color	1.64	1.62	2.30	1.75	1.93	1.53	2.60
lower		1.20	1.16	1.62	1.17	1.37	1.00	1.56
upper		2.25	2.26	3.25	2.61	2.70	2.36	4.34
beta		0.50	0.48	0.83	0.56	0.66	0.43	0.96
se		0.16	0.17	0.18	0.20	0.17	0.22	0.26
OR	Model based on tanning ability	1.62	1.63	2.30	1.94	1.86	1.52	2.76
lower		1.18	1.17	1.63	1.31	1.33	0.99	1.60
upper		2.22	2.27	3.25	2.87	2.60	2.33	4.74
beta		0.48	0.49	0.83	0.66	0.62	0.42	1.01
se		0.16	0.17	0.18	0.20	0.17	0.22	0.28

tau^2 = 0.10

		Val60Leu	Val92Met	Arg151Cys	Ile155Thr	Arg160Trp	Arg163Gln	Asp294His
OR	Equal weighted model	1.60	1.69	2.30	1.88	1.82	1.78	2.22
lower		1.13	1.18	1.58	1.07	1.22	1.12	1.32
upper		2.28	2.44	3.36	3.31	2.70	2.84	3.72
beta		0.47	0.53	0.83	0.63	0.60	0.58	0.80
se		0.18	0.19	0.19	0.29	0.20	0.24	0.26
OR	Model based on MC1R antibody binding	1.60	1.69	2.31	1.90	1.82	1.78	2.20
lower		1.13	1.17	1.57	1.01	1.22	1.12	1.24
upper		2.28	2.45	3.40	3.58	2.73	2.85	3.92
beta		0.47	0.53	0.84	0.64	0.60	0.58	0.79
se		0.18	0.19	0.20	0.32	0.21	0.24	0.29
OR	Model based on MSH ligand binding	1.60	1.70	2.30	1.87	1.81	1.79	2.22
lower		1.13	1.17	1.57	0.92	1.21	1.12	1.26
upper		2.28	2.45	3.37	3.80	2.71	2.85	3.93
beta		0.47	0.53	0.83	0.63	0.60	0.58	0.80
se		0.18	0.19	0.20	0.36	0.20	0.24	0.29
OR	Model based on cAMP response to MSH	1.60	1.65	2.37	1.79	1.86	1.62	2.46
lower		1.13	1.14	1.61	1.01	1.25	0.96	1.40
upper		2.28	2.39	3.47	3.19	2.78	2.73	4.32
beta		0.47	0.50	0.86	0.58	0.62	0.48	0.90
se		0.18	0.19	0.20	0.29	0.20	0.27	0.29
OR	Model based on kinetics - Ki-a-MSH	1.61	1.67	2.33	1.86	1.83	1.78	2.19
lower		1.13	1.14	1.58	1.05	1.23	1.12	1.30
upper		2.30	2.45	3.43	3.30	2.74	2.84	3.71
beta		0.48	0.51	0.84	0.62	0.61	0.58	0.79
se		0.18	0.20	0.20	0.29	0.20	0.24	0.27
OR	Model based on kinetics - Ki-NDP	1.58	1.68	2.38	1.90	1.84	1.82	2.10
lower		1.10	1.16	1.59	1.08	1.23	1.14	1.20
upper		2.26	2.42	3.56	3.33	2.73	2.92	3.70
beta		0.45	0.52	0.87	0.64	0.61	0.60	0.74
se		0.18	0.19	0.21	0.29	0.20	0.24	0.29
OR	Model based on hair color	1.55	1.63	2.35	1.87	1.92	1.71	2.50
lower		1.09	1.12	1.61	1.06	1.27	1.06	1.42
upper		2.23	2.37	3.44	3.29	2.88	2.75	4.41
beta		0.44	0.49	0.86	0.63	0.65	0.54	0.92
se		0.18	0.19	0.19	0.29	0.21	0.24	0.29
OR	Model based on skin color	1.58	1.63	2.39	1.79	1.86	1.62	2.63
lower		1.11	1.13	1.63	1.01	1.25	0.98	1.45
upper		2.25	2.37	3.51	3.18	2.76	2.68	4.77
beta		0.45	0.49	0.87	0.58	0.62	0.48	0.97
se		0.18	0.19	0.20	0.29	0.20	0.26	0.30
OR	Model based on tanning ability	1.57	1.64	2.39	1.92	1.82	1.61	2.71
lower		1.10	1.13	1.63	1.09	1.23	0.97	1.47
upper		2.23	2.37	3.50	3.38	2.71	2.66	4.98
beta		0.45	0.49	0.87	0.65	0.60	0.47	1.00
se		0.18	0.19	0.20	0.29	0.20	0.26	0.31

tau^2 = 0.40

		Val60Leu	Val92Met	Arg151Cys	Ile155Thr	Arg160Trp	Arg163Gln	Asp294His
OR	Equal weighted model	1.55	1.66	2.42	1.88	1.80	1.74	2.48
lower		1.07	1.12	1.61	0.91	1.17	1.01	1.33
upper		2.25	2.45	3.63	3.92	2.77	2.98	4.63
beta		0.44	0.50	0.88	0.63	0.59	0.55	0.91
se		0.19	0.20	0.21	0.37	0.22	0.27	0.32
OR	Model based on MC1R antibody binding	1.55	1.66	2.42	1.87	1.80	1.74	2.49
lower		1.07	1.12	1.61	0.87	1.17	1.01	1.30
upper		2.25	2.45	3.63	4.04	2.77	2.98	4.75
beta		0.44	0.51	0.88	0.63	0.59	0.55	0.91
se		0.19	0.20	0.21	0.39	0.22	0.28	0.33
OR	Model based on MSH ligand binding	1.55	1.66	2.42	1.86	1.80	1.74	2.49
lower		1.07	1.12	1.61	0.84	1.17	1.02	1.31
upper		2.25	2.45	3.63	4.14	2.77	2.98	4.75
beta		0.44	0.51	0.88	0.62	0.59	0.55	0.91
se		0.19	0.20	0.21	0.41	0.22	0.28	0.33
OR	Model based on cAMP response to MSH	1.55	1.64	2.44	1.84	1.82	1.68	2.59
lower		1.06	1.11	1.63	0.88	1.18	0.96	1.36
upper		2.25	2.43	3.66	3.86	2.79	2.93	4.93
beta		0.44	0.50	0.89	0.61	0.60	0.52	0.95
se		0.19	0.20	0.21	0.38	0.22	0.29	0.33
OR	Model based on kinetics - Ki-a-MSH	1.55	1.65	2.43	1.87	1.80	1.74	2.47
lower		1.07	1.11	1.61	0.90	1.17	1.01	1.32
upper		2.26	2.45	3.65	3.92	2.78	2.98	4.63
beta		0.44	0.50	0.89	0.63	0.59	0.55	0.90
se		0.19	0.20	0.21	0.38	0.22	0.27	0.32
OR	Model based on kinetics - Ki-NDP	1.54	1.65	2.44	1.89	1.80	1.75	2.45
lower		1.06	1.12	1.61	0.91	1.17	1.02	1.28
upper		2.25	2.44	3.68	3.93	2.77	3.00	4.66
beta		0.43	0.50	0.89	0.64	0.59	0.56	0.89
se		0.19	0.20	0.21	0.37	0.22	0.28	0.33
OR	Model based on hair color	1.53	1.63	2.43	1.87	1.83	1.71	2.61
lower		1.05	1.10	1.62	0.90	1.19	0.99	1.37
upper		2.23	2.42	3.65	3.90	2.82	2.94	4.96
beta		0.43	0.49	0.89	0.63	0.61	0.53	0.96
se		0.19	0.20	0.21	0.37	0.22	0.28	0.33
OR	Model based on skin color	1.54	1.64	2.45	1.84	1.81	1.67	2.66
lower		1.06	1.11	1.63	0.88	1.18	0.96	1.38
upper		2.24	2.42	3.67	3.85	2.78	2.91	5.11
beta		0.43	0.49	0.89	0.61	0.59	0.52	0.98
se		0.19	0.20	0.21	0.38	0.22	0.28	0.33
OR	Model based on tanning ability	1.54	1.64	2.44	1.90	1.80	1.67	2.68
lower		1.06	1.11	1.63	0.91	1.17	0.96	1.39
upper		2.24	2.43	3.67	3.94	2.77	2.91	5.18
beta		0.43	0.49	0.89	0.64	0.59	0.51	0.99
se		0.19	0.20	0.21	0.37	0.22	0.28	0.34