Supplementary Online Content

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eTable 1. Pigmentation phenotype in males and females stratified for Cases and Controls

CASES									
Variable[a]		FEMALES (n=473)		MALES (n=518)		AOR[b]	95%	CI	*P* Value
		n	%	n	%				
Skin Phototype	I/II	409	(77,0)	421	(68,9)	1,33	0,88	2,01	0,180
	III	67	(12,6)	104	(17,0)	0,91	0,54	1,53	0,719
	IV/V	55	(10,4)	86	(14,1)	Ref			
Burning	high	135	(24,8)	118	(18,6)	1,41	0,97	2,06	0,073
	intermediate	292	(53,6)	356	(56,1)	0,99	0,72	1,35	0,949
	low	118	(21,7)	161	(25,4)	Ref			
Tanning	low	66	(12,1)	49	(7,7)	2,03	1,19	3,45	0,009
	intermediate	424	(77,8)	486	(76,5)	1,34	0,91	1,98	0,138
	high	55	(10,1)	100	(15,7)	Ref			
Haircolor	red	57	(10,5)	39	(6,1)	2,22	1,37	3,60	0,001
	blond	156	(28,6)	142	(22,3)	1,75	1,27	2,41	0,001
	light brown	134	(24,6)	144	(22,6)	1,67	1,20	2,32	0,002
	brown/black	198	(36,3)	311	(48,9)	Ref			
Freckles	yes	209	(40,2)	183	(31,0)	1,31	1,00	1,72	0,051
	no	311	(59,8)	407	(69,0)	Ref			
CONTROLS									
Variable[a]		FEMALES (n=432)		MALES (368)		AOR[b]	95%	CI	*P* Value
		n	%	n	%				
Skin Phototype	I/II	332	(63,8)	298	(57,9)	1,47	1,02	2,13	0,039
	III	94	(18,1)	92	(17,9)	1,20	0,75	1,90	0,450
	IV/V	94	(18,1)	125	(24,3)	Ref			
Burning	high	65	(12,0)	59	(11,3)	1,26	0,78	2,04	0,345
	intermediate	291	(53,7)	270	(51,5)	1,00	0,74	1,36	0,999
	low	186	(34,3)	195	(37,2)	Ref			
Tanning	low	48	(8,9)	32	(6,1)	2,72	1,43	5,18	0,002
	intermediate	418	(77,3)	383	(73,1)	1,72	1,18	2,51	0,005
	high	75	(13,9)	109	(20,8)	Ref			
Haircolor	red	36	(6,6)	14	(2,7)	2,81	1,39	5,67	0,004
	blond	100	(18,4)	88	(16,8)	1,50	1,01	2,23	0,043
	light brown	166	(30,6)	152	(29,0)	1,43	1,02	1,99	0,037
	brown/black	241	(44,4)	271	(51,6)	Ref			
Freckles	yes	167	(31,3)	112	(22,9)	1,71	1,23	2,37	0,001
	no	366	(68,7)	378	(77,1)	Ref			

Abbreviations: AOR= adjusted Odds Ratio; CI=Confidence Interval; Ref=Reference group

eTable 2. Frequency of *MC1R* variants in males and females

Variants[a]		FEMALES (n=905)		MALES (n=886)		AOR[e]	0,95	CI	*P* Value
		n	%	n	%				
MC1R	variant	686	(75,8)	694	(78,3)	0,90	0,72	1,12	0,333
	wt	219	(24,2)	192	(21,7)				
						0,94	0,73	1,21	0,636
Number of MC1R variants	≥2	324	(35,8)	316	(35,7)	0,86	0,67	1,10	0,223
	1	362	(40,0)	378	(42,7)				
	0[c]	219	(24,2)	192	(21,7)	0,97	0,62	1,50	0,875
						1,02	0,74	1,41	0,911
Combination of variants[b]	R/R	49	(5,4)	48	(5,4)	0,77	0,58	1,02	0,068
	R/r	113	(12,5)	107	(12,1)	0,92	0,63	1,34	0,654
	R/0	152	(16,8)	187	(21,1)	1,03	0,80	1,32	0,826
	r/r	69	(7,6)	71	(8,0)				
	r/0	273	(30,2)	246	(27,8)	0,90	0,72	1,12	0,333
	0/0[d]	249	(27,5)	227	(25,6)				

Sequencing of MC1R was performed for 1791 participants.
Abbreviations: AOR= adjusted Odds Ratio; CI=Confidence Interval; Ref=Reference group
[a] The single variants do not sum up to the total number of sequenced cases and controls because of missing data
[b] = R= 86_87insA, R142H, R151C, R160W, D294H; r= V60L, D84E, V92M, I155T, R163Q
[c] =wild type [wt]
[d] =participants who did not carry any "r" or "R"
[e] = adjusted for melanoma status

eTable 3a. Sun exposure variables and melanoma risk in males

MALES		CASES (n=518)	CONTROLS (n=368)	AOR[b] (95% CI)	*P* Value
Variable[a]		n (%)	n (%)		
Freckling Face	**++,+++**	214 (41,4)	125 (34,2)	1,93 (1,2-3,1)	0,007
	+	240 (46,4)	161 (44,1)	1,74 (1,14-2,66)	0,010
	0	63 (12,2)	79 (21,6)	Ref	
Freckling Back	**++,+++**	295 (57,3)	140 (38,5)	2,82 (1,73-4,6)	<0,001
	+	169 (32,8)	157 (43,1)	1,43 (0,91-2,25)	0,121
	0	51 (9,9)	67 (18,4)	Ref	
Freckling Hands	**++,+++**	89 (17,2)	39 (10,7)	1,71 (1,05-2,77)	0,030
	+	221 (42,7)	146 (40,1)	1,18 (0,84-1,65)	0,335
	0	207 (40,0)	179 (49,2)	Ref	
Wrinkling Face	**++,+++**	268 (51,8)	155 (42,2)	2,79 (1,58-4,92)	<0,001
	+	200 (38,7)	140 (38,1)	2,22 (1,37-3,61)	0,001
	0	49 (9,5)	72 (19,6)	Ref	
Wrinkling Neck	**++,+++**	279 (54,2)	133 (36,5)	3,65 (2,22-6,02)	<0,001
	+	185 (35,9)	153 (42,0)	1,99 (1,28-3,1)	0,002
	0	51 (9,9)	78 (21,4)	Ref	
Solar lentigines Face	**++,+++**	132 (25,5)	91 (24,9)	2,21 (1,36-3,58)	0,001
	+	292 (56,5)	139 (38,1)	3,14 (2,14-4,6)	<0,001
	0	93 (18,0)	135 (37,0)	Ref	
Solar lentigines Back	**++,+++**	244 (47,5)	114 (31,5)	4,2 (2,6-6,78)	<0,001
	+	210 (40,9)	148 (40,9)	2,65 (1,72-4,07)	<0,001
	0	60 (11,7)	100 (27,6)	Ref	
Solar lentigines Hand	**++,+++**	163 (31,5)	70 (19,3)	3,18 (1,96-5,17)	<0,001
	+	224 (43,3)	146 (40,2)	1,98 (1,35-2,91)	<0,001
	0	130 (25,1)	147 (40,5)	Ref	
Holiday weeks in life	**≥18**	180 (35,0)	138 (37,6)	0,96 (0,68-1,35)	0,820
	9-17	195 (37,9)	120 (32,7)	1,27 (0,9-1,78)	0,175
	<9	139 (27,0)	109 (29,7)	Ref	
Sunburns in life	**≥20**	224 (43,6)	110 (30,0)	2,24 (1,58-3,17)	<0,001
	2-19	165 (32,1)	135 (36,8)	1,37 (0,96-1,94)	0,081
	0-1	125 (24,3)	122 (33,2)	Ref	
Outdoor Occupation in life	**yes**	259 (50,3)	192 (52,3)	0,9 (0,69-1,18)	0,431
	no	256 (49,7)	175 (47,7)	Ref	
RecreationalTime (hours/day)	**> 3**	397 (77,8)	276 (75,0)	0,53 (0,22-1,28)	0,156
	1 - 3	94 (18,4)	85 (23,1)	0,42(0,17-1,05)	0,065
	< 1	19 (3,7)	7 (1,9)	Ref	

Abbreviations: AOR= adjusted Odds Ratio; CI=Confidence Interval; Ref=Reference group
[a] The single variables do not sum up to the total number of females and males because of missing data
[b] =adjusted for age

eTable 3b. Sun exposure variables and melanoma risk in females

FEMALES		CASES (n=473)	CONTROLS (n=432)		AOR[b] (95% CI)	*P* Value
Variable[a]		n (%)	n (%)			
Freckling Face	++,+++	155 (32,8)	148 (34,9)		0,81 (0,53-1,23)	0,328
	+	239 (50,5)	195 (46,0)		1,04 (0,71-1,52)	0,843
	0	79 (16,7)	81 (19,1)		Ref	
Freckling Back	++,+++	187 (39,6)	120 (28,5)		3,02 (1,98-4,62)	<0,001
	+	224 (47,5)	176 (41,8)		2,51 (1,71-3,69)	<0,001
	0	61 (12,9)	125 (29,7)		Ref	
Freckling Hands	++,+++	56 (11,9)	33 (7,8)		2,02 (1,22-3,33)	0,006
	+	211 (44,8)	131 (31,0)		1,94 (1,42-2,67)	<0,001
	0	204 (43,3)	258 (61,1)		Ref	
Wrinkling Face	++,+++	203 (42,9)	175 (40,8)		1,21 (0,73-1,99)	0,456
	+	192 (40,6)	139 (32,4)		1,7 (1,13-2,55)	0,010
	0	78 (16,5)	115 (26,8)		Ref	
Wrinkling Neck	++,+++	120 (25,5)	62 (14,8)		3,68 (2,31-5,85)	<0,001
	+	228 (48,5)	158 (37,6)		2,6 (1,83-3,69)	<0,001
	0	122 (26,0)	200 (47,6)		Ref	
Solar lentigines Face	++,+++	79 (16,7)	65 (15,4)		1,59 (1,01-2,51)	0,046
	+	262 (55,5)	170 (40,3)		2,07 (1,49-2,89)	<0,001
	0	131 (27,8)	187 (44,3)		Ref	
Solar lentigines Back	++,+++	160 (34,0)	88 (21,0)		3,25 (2,14-4,93)	<0,001
	+	226 (48,0)	180 (42,9)		2,24 (1,56-3,23)	<0,001
	0	85 (18,0)	152 (36,2)		Ref	
Solar lentigines Hand	++,+++	152 (32,3)	98 (23,3)		2,18 (1,35-3,52)	0,001
	+	194 (41,2)	152 (36,1)		1,77 (1,22-2,58)	0,003
	0	125 (26,5)	171 (40,6)		Ref	
Holiday weeks in life	≥18	130 (27,8)	130 (30,4)		0,82 (0,59-1,14)	0,237
	9-17	161 (34,4)	140 (32,7)		0,99 (0,72-1,35)	0,931
	<9	177 (37,8)	158 (36,9)		Ref	
Sunburns in life	≥20	164 (34,8)	84 (19,6)		2,41 (1,7-3,42)	<0,001
	2-19	142 (30,1)	166 (38,7)		1,08 (0,78-1,49)	0,633
	0-1	165 (35,0)	179 (41,7)		Ref	
Outdoor Occupation in life	yes	134 (28,3)	156 (36,3)		0,64 (0,48-0,86)	0,003
	no	339 (71,7)	274 (63,7)		Ref	
RecreationalTime (hours/day)	> 3	330 (70,2)	315 (73,1)		0,75 (0,37-1,52)	0,427
	1 - 3	119 (25,3)	102 (23,7)		0,85 (0,41-1,76)	0,654
	< 1	21 (4,5)	14 (3,2)		Ref	

Abbreviations: AOR= adjusted Odds Ratio; CI=Confidence Interval; Ref=Reference group
[a] The single variables do not sum up to the total number of females and males because of missing data
[b] =adjusted for age

eTable 4a. *MC1R* variants and pigmentation phenotype in males

Combination of *MC1R* variants[a]	Variable[c]							Adjusted for age and melanoma status							
	Skin Phototype							Skin Phototype (IV/V=Ref)							
	I/II		III		IV/V			I/II				III			
	n	%	n	%	n	%		AOR	0,95	CI	*P* Value	AOR	0,95	CI	*P* Value
R/R	34	(6,1)	4	(2,7)	6	(3,9)	R/R	3,17	1,24	8,12	0,016	0,88	0,23	3,34	0,855
R/r	85	(15,3)	10	(6,7)	9	(5,9)	R/r	4,64	2,15	10,02	<0,001	1,31	0,49	3,51	0,596
R/0	123	(22,2)	31	(20,8)	27	(17,8)	R/0	2,30	1,35	3,92	0,002	1,37	0,71	2,62	0,346
r/r	50	(9,0)	11	(7,4)	6	(3,9)	r/r	4,54	1,81	11,38	0,001	2,37	0,81	6,96	0,117
r/0	150	(27,1)	44	(29,5)	45	(29,6)	r/0	1,94	1,21	3,11	0,006	1,31	0,74	2,33	0,356
0/0[b]	112	(20,2)	49	(32,9)	59	(38,8)	0/0[b]	Ref				Ref			
	Tanning							Tanning (high=Ref)							
	low		intermediate		high			low				intermediate			
	n	%	n	%	n	%		OR	0,95	CI	*P* Value	OR	0,95	CI	*P* Value
R/R	15	(23,1)	31	(4,7)	2	(1,3)	R/R	66,92	11,71	382,46	<0,001	4,07	0,94	17,67	0,061
R/r	14	(21,5)	87	(13,1)	6	(3,8)	R/r	19,70	5,19	74,74	<0,001	3,66	1,50	8,92	0,004
R/0	12	(18,5)	137	(20,6)	38	(24,4)	R/0	2,75	0,89	8,52	0,080	0,93	0,57	1,51	0,757
r/r	9	(13,8)	52	(7,8)	10	(6,4)	r/r	7,79	2,14	28,39	0,002	1,34	0,63	2,85	0,441
r/0	10	(15,4)	182	(27,4)	53	(34,0)	r/0	1,76	0,56	5,55	0,331	0,93	0,59	1,45	0,743
0/0[b]	5	(7,7)	175	(26,4)	47	(30,1)	0/0[b]	Ref				Ref			
	Burning							Burning (low=Ref)							
	high		intermediate		low			high				intermediate			
	n	%	n	%	n	%		OR	0,95	CI	*P* Value	OR	0,95	CI	*P* Value
R/R	18	(13,4)	22	(4,5)	8	(3,0)	R/R	11,32	4,28	29,93	<0,001	2,72	1,15	6,43	0,023
R/r	29	(21,6)	59	(12,1)	19	(7,2)	R/r	6,90	3,23	14,76	<0,001	2,82	1,56	5,10	0,001
R/0	32	(23,9)	113	(23,2)	42	(16,0)	R/0	3,59	1,84	7,02	<0,001	2,50	1,59	3,93	<0,001
r/r	13	(9,7)	40	(8,2)	18	(6,8)	r/r	3,47	1,46	8,29	0,005	2,14	1,14	4,01	0,017
r/0	22	(16,4)	148	(30,3)	75	(28,5)	r/0	1,56	0,79	3,09	0,199	2,01	1,35	2,98	0,001
0/0[b]	20	(14,9)	106	(21,7)	101	(38,4)	0/0[b]	Ref				Ref			

Combination of *MC1R* variants[a]	Variable[c]								Adjusted for age and melanoma status											
	Haircolor									Haircolor (brown/black=Ref)											
	red		blond		light brown		brown/black			red				blond				light brown			
	n	%	n	%	n	%	n	%		OR	0,95	CI	*P* Value	OR	0,95	CI	*P* Value	OR	0,95	CI	*P* Value
R/R	18	(40,0)	9	(5,2)	5	(2,5)	16	(3,4)	R/R	51,27	13,54	194,07	<0,001	2,36	0,95	5,82	0,063	0,91	0,32	2,63	0,865
R/r	11	(24,4)	31	(17,9)	23	(11,4)	42	(9,0)	R/r	11,52	3,05	43,51	<0,001	3,12	1,70	5,73	<0,001	1,66	0,90	3,04	0,102
R/0	8	(17,8)	38	(22,0)	47	(23,4)	94	(20,1)	R/0	3,81	0,98	14,77	0,053	1,71	1,00	2,93	0,051	1,49	0,92	2,41	0,102
r/r	1	(2,2)	15	(8,7)	20	(10,0)	35	(7,5)	r/r	1,23	0,12	12,22	0,860	1,73	0,84	3,56	0,134	1,70	0,89	3,22	0,105
r/0	4	(8,9)	47	(27,2)	57	(28,4)	138	(29,6)	r/0	1,34	0,29	6,11	0,705	1,41	0,85	2,35	0,180	1,19	0,76	1,86	0,450
0/0[b]	3	(6,7)	33	(19,1)	49	(24,4)	142	(30,4)	0/0[b]	Ref				Ref				Ref			
	Freckles									Freckles (no=Ref)											
	yes		no							yes											
	n	%	n	%						OR	0,95	CI	*P* Value								
R/R	37	(16,0)	9	(1,5)					R/R	28,36	12,32	65,32	<0,001								
R/r	56	(24,2)	48	(8,1)					R/r	7,51	4,30	13,12	<0,001								
R/0	44	(19,0)	125	(21,2)					R/0	2,29	1,35	3,89	0,002								
r/r	27	(11,7)	39	(6,6)					r/r	4,64	2,45	8,76	<0,001								
r/0	39	(16,9)	180	(30,5)					r/0	1,51	0,89	2,55	0,129								
0/0[b]	28	(12,1)	190	(32,1)					0/0[b]	Ref											

eTable 4b. *MC1R* variants and pigmentation phenotype in females

Combination of *MC1R* variants[a]	Variable[c]								Adjusted for age and melanoma status							
	Skin Phototype								Skin Phototype (IV/V=Ref)							
	I/II		III		IV/V				I/II				III			
	n	%	n	%	n	%			AOR	0,95	CI	*P* Value	AOR	0,95	CI	*P* Value
R/R	43	(6,9)	3	(2,3)	2	(1,7)	R/R		6,26	1,45	26,98	0,014	1,56	0,25	9,83	0,637
R/r	96	(15,4)	9	(6,9)	6	(5,2)	R/r		4,88	1,99	11,96	0,001	1,75	0,57	5,37	0,330
R/0	107	(17,1)	22	(16,8)	18	(15,7)	R/0		1,87	1,02	3,43	0,042	1,41	0,66	3,00	0,371
r/r	54	(8,6)	8	(6,1)	5	(4,3)	r/r		3,51	1,32	9,36	0,012	1,86	0,56	6,17	0,308
r/0	181	(29,0)	46	(35,1)	36	(31,3)	r/0		1,57	0,96	2,56	0,073	1,40	0,76	2,57	0,276
0/0[b]	144	(23,0)	43	(32,8)	48	(41,7)	0/0[b]		Ref				Ref			
	Tanning								Tanning (high=Ref)							
	low		intermediate		high				low				intermediate			
	n	%	n	%	n	%			OR	0,95	CI	*P* Value	OR	0,95	CI	*P* Value
R/R	12	(12,5)	33	(4,7)	4	(3,7)	R/R		10,56	2,77	40,31	0,001	1,37	0,46	4,13	0,573
R/r	23	(24,0)	84	(12,0)	6	(5,6)	R/r		12,55	3,98	39,55	<0,001	2,41	0,97	5,98	0,058
R/0	20	(20,8)	112	(16,0)	19	(17,6)	R/0		3,50	1,36	9,02	0,010	1,03	0,56	1,90	0,916
r/r	8	(8,3)	58	(8,3)	3	(2,8)	r/r		9,00	2,00	40,50	0,004	3,41	1,01	11,50	0,048
r/0	23	(24,0)	209	(29,9)	40	(37,0)	r/0		1,99	0,83	4,77	0,121	0,90	0,55	1,48	0,680
0/0[b]	10	(10,4)	203	(29,0)	36	(33,3)	0/0[b]		Ref				Ref			

Combinati	Variable[c]		Adjusted for age and melanoma status

		Burning							Burning (low=Ref)						
		high		intermediate		low			high				intermediate			
		n	%	n	%	n	%		OR	0,95	CI	*P* Value	OR	0,95	CI	*P* Value
R/R		19	(11,4)	24	(5,0)	6	(2,4)	R/R	10,87	3,87	30,57	<0,001	2,61	1,02	6,67	0,046
R/r		30	(18,0)	65	(13,5)	18	(7,1)	R/r	5,31	2,51	11,22	<0,001	2,49	1,37	4,51	0,003
R/0		30	(18,0)	81	(16,8)	41	(16,2)	R/0	2,46	1,27	4,75	0,008	1,39	0,87	2,22	0,166
r/r		14	(8,4)	42	(8,7)	13	(5,1)	r/r	3,76	1,54	9,13	0,004	2,31	1,17	4,58	0,016
r/0		50	(29,9)	140	(29,0)	81	(32,0)	r/0	2,17	1,22	3,87	0,009	1,18	0,80	1,74	0,401
0/0[b]		24	(14,4)	131	(27,1)	94	(37,2)	0/0[b]	Ref				Ref			

on of MC1R variants[a]	Haircolor								Haircolor (brown/black=Ref)											
	red		blond		light brown		brown/black			red				blond				light brown			
	n	%	n	%	n	%	n	%		OR	0,95	CI	P Value	OR	0,95	CI	P Value	OR	0,95	CI	P Value
R/R	32	(40,0)	9	(4,3)	4	(1,6)	4	(1,1)	R/R	135,61	37,26	493,55	<0,001	5,57	1,63	19,03	0,006	1,79	0,43	7,41	0,419
R/r	12	(15,0)	43	(20,7)	34	(13,8)	24	(6,5)	R/r	8,04	2,84	22,73	<0,001	4,11	2,24	7,54	<0,001	2,57	1,40	4,72	0,002
R/0	10	(12,5)	36	(17,3)	46	(18,7)	60	(16,2)	R/0	2,75	0,99	7,63	0,052	1,41	0,83	2,42	0,207	1,38	0,85	2,25	0,194
r/r	5	(6,3)	17	(8,2)	19	(7,7)	28	(7,6)	r/r	2,98	0,88	10,13	0,080	1,45	0,73	2,90	0,292	1,22	0,63	2,35	0,553
r/0	14	(17,5)	55	(26,4)	73	(29,7)	130	(35,1)	r/0	1,82	0,71	4,68	0,213	1,04	0,65	1,65	0,880	1,01	0,67	1,52	0,973
0/0[b]	7	(8,8)	48	(23,1)	70	(28,5)	124	(33,5)	0/0[b]	Ref				Ref				Ref			
	Freckles								Freckles (no=Ref)												
	yes		no							yes											
	n	%	n	%						OR	0,95	CI	P Value								
R/R	41	(12,7)	7	(1,3)					R/R	35,50	14,59	86,41	<0,001								
R/r	70	(21,7)	40	(7,2)					R/r	11,37	6,60	19,61	<0,001								
R/0	68	(21,1)	78	(14,1)					R/0	5,58	3,40	9,16	<0,001								
r/r	22	(6,8)	44	(8,0)					r/r	3,11	1,65	5,86	<0,001								
r/0	86	(26,6)	178	(32,2)					r/0	2,80	1,80	4,38	<0,001								
0/0[b]	36	(11,1)	205	(37,1)					0/0[b]	Ref											

Abbreviations: AOR= adjusted Odds Ratio; CI=Confidence Interval; Ref=Reference group
[a]= R= 86_87insA, R142H, R151C, R160W, D294H; r= V60L, D84E, V92M, I155T, R163Q
[b]=participants who did not carry any "r" or "R"
[c] The single variables do not sum up to the total number of females and males because of missing data

eTable 5a. *MC1R* variants and pigmentation phenotype in Cases

Combination of *MC1R* variants[a]	Variable[c]							Adjusted for age and sex							
	Skin Phenotype							Skin Phenotype (IV/V=Ref)							
	I/II		III		IV/V			I/II				III			
	n	%	n	%	n	%		AOR	0,95	CI	P Value	AOR	0,95	CI	P Value
R/R	48	(6,8)	2	(1,4)	5	(4,5)	R/R	3,35	1,24	9,03	0,017	0,38	0,07	2,08	0,265
R/r	131	(18,6)	11	(8,0)	6	(5,4)	R/r	7,44	3,05	18,20	0,000	1,68	0,57	4,98	0,346
R/0	148	(21,1)	32	(23,2)	21	(18,9)	R/0	2,55	1,43	4,56	0,002	1,46	0,73	2,93	0,287
r/r	63	(9,0)	11	(8,0)	4	(3,6)	r/r	5,75	1,96	16,82	0,001	2,71	0,80	9,20	0,111
r/0	192	(27,3)	37	(26,8)	32	(28,8)	r/0	2,08	1,24	3,49	0,005	1,10	0,58	2,09	0,764
0/0[b]	121	(17,2)	45	(32,6)	43	(38,7)	0/0[b]	Ref				Ref			
	Tanning							Tanning (high=Ref)							
	low		intermediate		high			low				intermediate			
	n	%	n	%	n	%		OR	0,95	CI	P Value	OR	0,95	CI	P Value
R/R	16	(15,5)	40	(5,3)	3	(2,4)	R/R	27,94	6,36	122,79	0,000	2,70	0,79	9,24	0,113
R/r	27	(26,2)	121	(15,9)	4	(3,1)	R/r	35,02	9,27	132,37	0,000	6,05	2,10	17,48	0,001
R/0	27	(26,2)	152	(20,0)	30	(23,6)	R/0	4,79	1,82	12,59	0,001	1,06	0,62	1,80	0,837
r/r	12	(11,7)	67	(8,8)	5	(3,9)	r/r	12,57	3,34	47,28	0,000	2,84	1,07	7,56	0,037
r/0	14	(13,6)	206	(27,1)	49	(38,6)	r/0	1,40	0,51	3,83	0,513	0,85	0,52	1,36	0,492
0/0[b]	7	(6,8)	173	(22,8)	36	(28,3)	0/0[b]	Ref				Ref			
	Burning							Burning (low=Ref)							
	high		intermediate		low			high				intermediate			
	n	%	n	%	n	%		OR	0,95	CI	P Value	OR	0,95	CI	P Value
R/R	28	(13,3)	24	(4,4)	7	(3,0)	R/R	11,06	4,33	28,21	0,000	2,39	0,98	5,85	0,056
R/r	47	(22,4)	88	(16,1)	17	(7,3)	R/r	7,53	3,72	15,24	0,000	3,57	1,96	6,48	0,000
R/0	50	(23,8)	113	(20,7)	46	(19,8)	R/0	3,08	1,70	5,55	0,000	1,74	1,11	2,74	0,016
r/r	15	(7,1)	54	(9,9)	15	(6,5)	r/r	2,82	1,22	6,52	0,015	2,63	1,38	5,02	0,003
r/0	42	(20,0)	158	(28,9)	69	(29,7)	r/0	1,65	0,92	2,94	0,091	1,62	1,08	2,44	0,021

Combination of	Variable[c]							Adjusted for age and sex				
0/0[b]		28	(13,3)	110	(20,1)	78	(33,6)	0/0[b]	Ref			Ref		

MC1R variants[a]

MC1R variants[a]	Haircolor							Haircolor (brown/black=Ref)											
	red		blond		light brown		brown/black			red				blond				light brown		
	n	%	n	%	n	%	n	%		OR	0,95	CI	P Value	OR	0,95	CI	P Value	OR	0,95	CI	P Value
R/R	36	(43,9)	11	(4,6)	2	(,9)	10	(2,2)	R/R	239,29	49,55	1155,68	0,000	3,46	1,36	8,79	3,46	0,50	0,11	2,38	0,385
R/r	16	(19,5)	57	(23,8)	40	(17,9)	39	(8,8)	R/r	25,36	5,56	115,73	0,000	4,44	2,58	7,66	4,44	2,48	1,43	4,31	0,001
R/0	15	(18,3)	48	(20,0)	54	(24,2)	92	(20,7)	R/0	10,56	2,35	47,48	0,002	1,61	0,98	2,66	1,61	1,45	0,91	2,33	0,122
r/r	3	(3,7)	18	(7,5)	26	(11,7)	37	(8,3)	r/r	5,04	0,81	31,44	0,083	1,46	0,75	2,84	1,46	1,70	0,93	3,10	0,086
r/0	10	(12,2)	65	(27,1)	50	(22,4)	145	(32,6)	r/0	3,93	0,84	18,34	0,081	1,29	0,81	2,04	1,29	0,79	0,50	1,26	0,329
0/0[b]	2	(2,4)	41	(17,1)	51	(22,9)	122	(27,4)	0/0[b]	Ref				Ref				Ref			

	Freckles								Freckles (no=Ref)				
	yes		no							yes			
	n	%	n	%						OR	0,95	CI	P Value
R/R	51	(15,2)	6	(1,0)					R/R	49,62	19,51	126,18	0,000
R/r	87	(26,0)	60	(10,0)					R/r	7,96	4,80	13,19	0,000
R/0	67	(20,0)	125	(20,9)					R/0	3,01	1,86	4,89	0,000
r/r	26	(7,8)	53	(8,9)					r/r	2,81	1,53	5,15	0,001
r/0	72	(21,5)	178	(29,8)					r/0	2,15	1,34	3,45	0,001
0/0[b]	32	(9,6)	176	(29,4)					0/0[b]	Ref			

Abbreviations: AOR= adjusted Odds Ratio; CI=Confidence Interval; Ref=Reference group

eTable 5b. *MC1R* variants and pigmentation phenotype in Controls

Combination of *MC1R* variants[a]	Variable[c]								Adjusted for age and sex							
	Skin Phenotype								Skin Phenotype (IV/V=Ref)							
	I/II		III		IV/V				I/II				III			
	n	%	n	%	n	%			AOR	0,95	CI	P Value	AOR	0,95	CI	P Value
R/R	29	(6,1)	5	(3,5)	3	(1,9)		R/R	4,95	1,44	17,02	0,011	2,46	0,56	10,91	0,236
R/r	50	(10,5)	8	(5,6)	9	(5,8)		R/r	3,03	1,39	6,59	0,005	1,43	0,51	4,04	0,494
R/0	82	(17,2)	21	(14,8)	24	(15,4)		R/0	1,78	1,02	3,09	0,042	1,31	0,65	2,65	0,455
r/r	41	(8,6)	8	(5,6)	7	(4,5)		r/r	3,06	1,29	7,27	0,011	1,75	0,59	5,21	0,316
r/0	139	(29,2)	53	(37,3)	49	(31,4)		r/0	1,46	0,93	2,29	0,099	1,61	0,93	2,79	0,090
0/0[b]	135	(28,4)	47	(33,1)	64	(41,0)		0/0[b]	Ref				Ref			
	Tanning								Tanning (high=Ref)							
	low		intermediate		high				low				intermediate			
	n	%	n	%	n	%			OR	0,95	CI	P Value	OR	0,95	CI	P Value
R/R	11	(19,0)	24	(4,0)	3	(2,2)		R/R	23,70	5,33	105,51	0,000	1,92	0,55	6,66	0,305
R/r	10	(17,2)	50	(8,3)	8	(5,8)		R/r	7,35	2,19	24,62	0,001	1,46	0,65	3,31	0,362
R/0	5	(8,6)	97	(16,1)	27	(19,7)		R/0	1,16	0,34	3,94	0,809	0,86	0,50	1,47	0,579
r/r	5	(8,6)	43	(7,1)	8	(5,8)		r/r	3,70	0,95	14,37	0,058	1,25	0,55	2,84	0,597
r/0	19	(32,8)	185	(30,6)	44	(32,1)		r/0	2,66	1,05	6,74	0,039	0,99	0,63	1,57	0,974
0/0[b]	8	(13,8)	205	(33,9)	47	(34,3)		0/0[b]	Ref				Ref			
	Burning								Burning (low=Ref)							
	high		intermediate		low				high				intermediate			

Combination of MC1R	Variable[c]			Adjusted for age and sex

	n	%	n	%	n	%		OR	0,95	CI	P Value	OR	0,95	CI	P Value
R/R	9	(9,9)	22	(5,2)	7	(2,5)	R/R	9,65	3,15	29,57	0,000	2,99	1,23	7,28	0,016
R/r	12	(13,2)	36	(8,5)	20	(7,0)	R/r	4,50	1,84	10,97	0,001	1,83	1,00	3,37	0,051
R/0	12	(13,2)	81	(19,1)	37	(13,0)	R/0	2,45	1,06	5,66	0,036	2,13	1,33	3,40	0,002
r/r	12	(13,2)	28	(6,6)	16	(5,6)	r/r	5,59	2,24	13,97	0,000	1,71	0,87	3,33	0,117
r/0	30	(33,0)	130	(30,7)	87	(30,6)	r/0	2,59	1,33	5,06	0,005	1,44	0,99	2,10	0,056
0/0[b]	16	(17,6)	127	(30,0)	117	(41,2)	0/0[b]	Ref				Ref			

variants[a]

Haircolor counts and odds ratios (Haircolor brown/black=Ref)

variants[a]	red n	red %	blond n	blond %	light brown n	light brown %	brown/black n	brown/black %		red OR	red 0,95 CI		red P Value	blond OR	blond 0,95 CI		blond P Value	light brown OR	light brown 0,95 CI		light brown P Value
R/R	14	(32,6)	7	(5,0)	7	(3,1)	10	(2,6)	R/R	29,26	9,68	88,46	0,000	2,64	0,94	7,43	0,066	1,55	0,56	4,27	0,394
R/r	7	(16,3)	17	(12,1)	17	(7,6)	27	(6,9)	R/r	4,69	1,54	14,28	0,007	2,10	1,03	4,27	0,041	1,36	0,69	2,68	0,371
R/0	3	(7,0)	26	(18,4)	39	(17,4)	62	(15,8)	R/0	0,94	0,24	3,68	0,928	1,50	0,84	2,69	0,172	1,38	0,84	2,26	0,207
r/r	3	(7,0)	14	(9,9)	13	(5,8)	26	(6,6)	r/r	2,10	0,52	8,53	0,300	1,87	0,88	3,94	0,101	1,07	0,52	2,22	0,853
r/0	8	(18,6)	37	(26,2)	80	(35,7)	123	(31,4)	r/0	1,23	0,45	3,40	0,688	1,06	0,64	1,77	0,819	1,41	0,94	2,11	0,099
0/0[b]	8	(18,6)	40	(28,4)	68	(30,4)	144	(36,7)	0/0[b]	Ref				Ref				Ref			

Freckles counts and odds ratios (Freckles no=Ref)

variants[a]	yes n	yes %	no n	no %		yes OR	yes 0,95 CI		yes P Value
R/R	27	(12,3)	10	(1,8)	R/R	21,92	9,48	50,72	0,000
R/r	39	(17,8)	28	(5,1)	R/r	11,60	6,17	21,82	0,000
R/0	45	(20,5)	78	(14,3)	R/0	4,56	2,67	7,80	0,000
r/r	23	(10,5)	30	(5,5)	r/r	5,94	3,02	11,68	0,000
r/0	53	(24,2)	180	(33,0)	r/0	2,17	1,33	3,53	0,002
0/0[b]	32	(14,6)	219	(40,2)	0/0[b]	Ref			

Abbreviations: AOR= adjusted Odds Ratio; CI=Confidence Interval; Ref=Reference group
[a]= R= 86_87insA, R142H, R151C, R160W, D294H; r= V60L, D84E, V92M, I155T, R163Q

[b]=participants who did not carry any "r" or "R"
[c] The single variables do not sum up to the total number of controls because of missing data