Supplementary Tables

Table S1 – Summary statistics of pigmentation phenotypes for global population. (Related to Figure 1) All statistics relate to M index for baseline pigmentation. Rows with no dataset listed refer to subsets of the dataset in prior rows, e.g. >90% KhoeSan Nama refers to the Nama samples from this study. Cape Verdean samples from (Beleza et al., 2013) were broken into quantiles, labeled Q1 to Q4. μ = mean, σ = standard deviation, and c_V = coefficient of variation (σ/μ), a standardized metric of dispersion.

Dataset	**Population**	**|Latitude|**	**N**	**μ**	**σ**	**c_V**
Candille	Ireland	53.35	42	27.10	1.95	0.07
Candille	Poland	52.23	45	30.54	1.86	0.06
Parra	European	48.14	135	28.32	2.72	0.10
Candille	Italy	41.90	45	31.35	2.06	0.07
Candille	Portugal	41.16	43	30.73	2.46	0.08
Parra	East Asian	35.86	116	31.07	2.98	0.10
Coussens	Xhosa	34.03	50	67.10	7.50	0.11
Coussens	Cape Mixed	33.91	42	53.10	8.50	0.16
Basu Mallick	Ror	29.69	44	42.16	4.11	0.10
This study	Nama	28.82	223	52.12	8.93	0.17
	>90% KhoeSan Nama	28.82	15	51.70	5.74	0.11
This study	Khomani	28.40	278	57.57	10.12	0.18
	>90% KhoeSan Khomani	28.40	41	56.10	6.93	0.12
Sandoval/Moreno	Easter Island	27.13	81	44.27	5.57	0.13
Parra	South Asian	21.13	117	37.48	5.48	0.15
Basu Mallick	Nihali	20.94	33	58.01	6.66	0.11
Basu Mallick	Korku	20.94	35	52.46	7.92	0.15
Basu Mallick	Kapu	17.39	272	43.41	4.87	0.11
Basu Mallick	Naidu	17.39	112	43.57	4.87	0.11
Basu Mallick	Reddy	17.05	844	43.72	4.87	0.11
Sandoval/Moreno	Peruvians	15.85	117	51.88	4.58	0.09
Beleza	Cape Verde	15.11	684	55.39	13.00	0.23
	Q1 African ancestry	15.11	171	46.23	7.73	0.17
	Q2 African ancestry	15.11	171	51.98	9.48	0.18
	Q3 African ancestry	15.11	171	54.31	9.83	0.18
	Q4 African ancestry	15.11	171	69.09	12.10	0.18
Basu Mallick	Toda	11.41	11	42.96	4.12	0.10
Basu Mallick	Kurumba	11.41	24	56.41	5.29	0.09
Basu Mallick	Badaga	11.41	31	46.18	6.15	0.13
Basu Mallick	Kota	11.41	27	45.13	6.30	0.14
Basu Mallick	Saurashtrian	9.92	25	42.36	4.90	0.12
Basu Mallick	Brahmin	9.92	20	41.07	5.51	0.13
Basu Mallick	Yadava	9.92	27	58.21	8.03	0.14
Durazo-Arvizu	Ghana	6.67	237	96.04	10.94	0.11
Norton	Bougainville	6.05	153	89.84	9.52	0.11
Norton	Papua New Guinae	5.90	21	67.94	9.42	0.14
Norton	New Britain	5.56	491	67.92	6.80	0.10
Norton	New Ireland	3.32	242	74.22	8.06	0.11

Norton	Lavongai	2.52	102	77.12	7.51	0.10
Norton	Mussau	1.41	35	65.48	7.95	0.12

Table S2 – Reference and KhoeSan samples included in the ADMIXTURE analysis. (Related to Figure 2)

Population	Country	Region	N	Reference
Khomani	South Africa	Southern Africa	121	Present study
Nama	South Africa	Southern Africa	112	Present study
NamibSan	Namibia	Southern Africa	6	HGDP
Hadza	Tanzania	Southern Africa	17	Henn 2011
Sandawe	Tanzania	Southern Africa	28	Henn 2011
Maasai	Kenya	Eastern Africa	30	HapMap
Bantu (Kenya)	Kenya	Eastern Africa	11	HGDP
Bantu (SA)	South Africa	Southern Africa	8	HGDP
Yoruba	Nigeria	Western Africa	55	HapMap
Mozabite	Algeria	Northern Africa	29	HGDP
CEU	USA	North America	86	HapMap
French	France	Europe	28	HGDP

Table S3 – Heritability estimates by population using multiple approaches. (Related to Table 1) Heritability was assessed separately and jointly in the ‡Khomani and Nama populations. Because of population structure, haplotypes were called separately, (i.e. even when populations were analyzed jointly). N = number of individuals. SNPs = number of SNPs included.

Population	Phenotype	Dataset	N	SNPs	Covariates	h^2	s.e
‡Khomani San	Pigmentation	GCTA GRM	107	300370	Euro, Bantu	0.897	0.205
		REAP	107	300370	Euro, Bantu	0.963	0.219
		Exome GRM	82	117132	Euro, Bantu	0.954	0.256
		SOLAR, pedigree	250	NA	Euro, Bantu	0.934	0.165
		KIBD	107	NA	Euro, Bantu	0.957	0.244
	Tanning	GCTA GRM	107	300370	Age, Sex	0.405	0.278
		REAP	107	300370	Age, Sex	0.470	0.305
		Exome GRM	82	117132	Age, Sex	0.373	0.368
		SOLAR, pedigree	276	NA	Age, Sex	0.214	0.137
		KIBD	107	NA	Age, Sex	0.415	0.335
Nama	Pigmentation	GCTA GRM	109	526471	Euro, Bantu	0.953	0.207
		REAP	109	526471	Euro, Bantu	0.981	0.219
		SOLAR, pedigree	168	NA	Euro, Bantu	0.872	0.223
		KIBD	109	NA	Euro, Bantu	0.987	0.247
	Tanning	GCTA GRM	109	526471	Age, Sex	0.405	0.278
		REAP	109	526471	Age, Sex	0.47	0.305
		SOLAR, pedigree	200	NA	Age, Sex	0.128	0.372
		KIBD	109	NA	Age, Sex	0.509	0.337

‡Khomani & Nama	Pigmentation	GCTA GRM	216	241929	Euro, Bantu	0.900	0.150
		REAP	216	217077	Euro, Bantu	0.975	0.152
		SOLAR, pedigree	419	NA	Euro, Bantu	0.959	0.125
		KIBD	216	NA	Euro, Bantu	0.972	0.157
	Tanning	GCTA GRM	216	241929	Age, Sex	0.314	0.195
		REAP	216	217077	Age, Sex	0.411	0.211
		SOLAR, pedigree	477	NA	Age, Sex	0.192	0.116
		KIBD	216	NA	Age, Sex	0.449	0.216

Table S4 – Number of individuals from each population that were phenotyped, genotyped, exome sequenced, or with targeted resequencing data. Pheno = phenotyped, Geno=genotyped, Exome = exome sequenced, Reseq = targeted resequencing. We also indicate the overlap among different genotyping arrays, which are as follows: 550k = Illumina 550k array, OmniEx = Illumina OmniExpress array, OmniExPlus = Illumina OmniExpressPlus array, Omni2.5 = Illumina Omni2.5 array, Mega = Illumina Multi-ethnic genotyping array. Phase 2 of the GWAS analysis consisted of samples genotyped on the MEGA array.

Population		Pheno	Geno	Exome	Reseq	550k	OmniEx	OmniExPlus	Omni2.5	Mega
Combined	Pheno	479	446	84	421	21	68	31	97	301
	Geno	446	465	88	413	35	68	31	100	305
	Exome	84	88	91		23	58	5	0	34
	Reseq	421	413	81	439	25	66	30	87	275
	550k	21	35	23	25	35	0	0	2	10
	OmniEx	68	68	58	66	0	68	0	0	25
	OmniExPlus	31	31	5	30	0	0	31	1	11
	Omni2.5	97	100	0	87	2	0	1	100	25
	Mega	301	305	34	275	10	25	11	25	305
‡Khomani	Pheno	277	261	84	251	21	68	18	0	195
	Geno	261	278	88	248	35	68	18	2	198
	Exome	84	88	91	81	23	58	5	0	34
	Reseq	251	248	81	268	25	66	18	0	180
	550k	21	35	23	25	35	0	0	2	10
	OmniEx	68	68	58	66	0	68	0	0	25
	OmniExPlus	18	18	5	18	0	0	18	0	6
	Omni2.5	0	2	0	0	2	0	0	2	0
	Mega	195	198	34	180	10	25	6	0	198
Nama	Pheno	202	185	0	170	0	0	13	97	106
	Geno	185	187	0	165	0	0	13	98	107
	Exome	0	0	0	0	0	0	0	0	0
	Reseq	170	165	0	171	0	0	12	87	95
	550k	0	0	0	0	0	0	0	0	0
	OmniEx	0	0	0	0	0	0	0	0	0
	OmniExPlus	13	13	0	12	0	0	13	1	5
	Omni2.5	97	98	0	87	0	0	1	98	25
	Mega	106	107	0	95	0	0	5	25	107

Table S5 – Top 50 associations from initial GWAS. (Related to Figure 5) All associations shown are independent ($R^2 \leq 0.5$, window size = 250 kb), and indicate the association between genotype dosages and skin pigmentation M index across the Nama and ‡Khomani datasets. The # tagging column indicates the number of SNPs with an rsID that are tagged by the independent signal.

Chr	**Position**	**SNP**	**Closest_gene**	**Gene_start**	**Gene_end**	**Distance**	**P value**	**# tagging**
5	111622148	rs13170079	EPB41L4A	111478137	111564475	57673	1.08E-06	0
8	72951490	rs10504523	TRPA1	72933485	72987852	0	3.12E-06	1

8	13241026	rs6994536	DLC1	12940869	13372395	0	4.62E-06	3
9	1702573	rs10962731	SMARCA2	2015341	2193624	312768	1.04E-05	0
4	89900558	rs11945054	TIGD2	90033967	90036050	133409	1.59E-05	5
8	529244	rs1703884	TDRP	439802	494998	34246	1.61E-05	0
16	73173205	rs6499616	HCCAT5	73126247	73127673	45532	1.99E-05	0
12	5692000	rs10849298	ANO2	5671816	6055398	0	2.00E-05	0
4	175923101	rs12502984	AC105914.1	175848457	175848542	74559	2.15E-05	1
6	110819059	rs6922009	SLC22A16	110745889	110797844	21215	2.39E-05	0
22	35227406	rs147291650	RP1-272J12.1	35318598	35468259	91192	2.95E-05	3
5	160722863	rs252965	GABRB2	160715435	160973649	0	3.15E-05	0
11	132402910	rs7125438	OPCML	132284870	132813566	0	3.43E-05	0
3	115151361	rs139280087	GAP43	115342170	115440337	190809	3.59E-05	0
5	110506404	rs76678422	WDR36	110427413	110466200	40204	3.79E-05	2
9	2496567	rs872257	VLDLR	2621833	2660053	125266	4.72E-05	0
18	25216159	rs11873957	CDH2	25530929	25757410	314770	4.85E-05	0
12	13248157	rs17820032	GSG1	13236493	13248609	0	4.97E-05	0
14	70466081	rs17107583	SLC8A3	70510933	70655787	44852	5.28E-05	0
16	73185078	rs7190071	HCCAT5	73126247	73127673	57405	5.52E-05	0
15	48595192	rs8025278	SLC12A1	48498497	48596273	0	5.66E-05	10
5	118962245	rs1574641	FAM170A	118965291	118970777	3046	5.82E-05	13
14	64603204	rs11158532	SYNE2	64319682	64693165	0	6.09E-05	3
13	46016101	rs149830128	SLC25A30-AS1	45992296	45994506	21595	6.44E-05	0
7	25272620	rs929255	NPVF	25264188	25268105	4515	6.74E-05	0
9	12048147	rs115075138	TYRP1	12693385	12710266	645238	6.90E-05	2
10	30398791	rs2505115	KIAA1462	30301728	30348453	50338	7.30E-05	26
15	91025830	rs11853271	IQGAP1	90931449	91045475	0	7.33E-05	0
14	31384628	rs7158162	STRN3	31363004	31495607	0	7.75E-05	0
15	63407390	rs4774476	LACTB	63413998	63434260	6608	7.85E-05	1

10	57701140	rs2050724	MTRNR2L5	57358749	57360488	340652	7.92E-05	2
10	97539140	rs10882664	ENTPD1	97471535	97629452	0	8.42E-05	0
18	25162200	rs1008854	CDH2	25530929	25757410	368729	8.53E-05	1
11	13864951	rs111514753	RNA5SP331	13929030	13929137	64079	8.76E-05	1
6	6359328	rs75063567	LY86-AS1	6346697	6622977	0	8.77E-05	7
22	37381451	rs5756452	TEX33	37387165	37403839	5714	8.99E-05	2
14	79237349	rs8011930	NRXN3	78870092	80328786	0	9.22E-05	0
4	58768454	rs10517418	IGFBP7-AS1	57975927	58071465	696989	9.36E-05	0
3	188124354	rs1559810	LPP	187871071	188430630	0	9.60E-05	6
9	2179528	rs146831108	SMARCA2	2015341	2193624	0	9.89E-05	3
15	48433494	rs2470102	SLC24A5	48413168	48434869	0	0.000102	1
18	8713088	rs593582	SOGA2	8705658	8828944	0	0.000105	0
2	200698610	rs17628965	FTCDNL1	200625266	200715896	0	0.000106	0
3	165374980	rs17706250	BCHE	165490691	165555260	115711	0.000106	0
2	59771224	rs2058591	AC007179.1	59662347	59669396	101828	0.000107	31
13	38449344	rs9548088	TRPC4	38210772	38444562	4782	0.000107	1
18	34002578	rs10853434	FHOD3	33877676	34360018	0	0.000109	1
6	21016532	rs201311	CDKAL1	20534687	21232635	0	0.000113	0
13	70728411	rs10507781	ATXN8OS	70681344	70713561	14850	0.000115	1
7	21142846	rs2893030	AC006481.1	20875049	21062767	80079	0.000117	1

Table S6 – Summary statistics and regulator information for known and novel pigmentation SNPs. (Related to Table 2 and Figure 5) A) P-value, effect size and standard error, and frequency are shown for known pigmentation loci (including skin, eye, and hair color phenotypes) in the ‡Khomani, Nama, and jointly analyzed samples. B) Regulatory information including conservation, functional class, motif changes, etc, indentified via HaploReg are shown for resequencing variants in 6 of the targeted regions.

*Provided as Excel spreadsheet due to size constraints

Table S7 – Regions selected for targeted resequencing. (Related to Figure 5)
Resequencing was successfully performed for a total of 441 KhoeSan individuals.

Chromosome	Start position	Stop position	Region name
1	213124065	213129065	rs3002288_VASH2
3	69778586	70581155	MITF_reg
3	183312675	183402304	KLHL24_reg
5	33946089	33954193	rs35395_rs16891982_SLC45A2
6	393821	398821	rs12203592_IRF4
6	468636	473636	rs12202284_IRF4
6	132705804	132878234	STX7_reg
6	145550394	145806673	EPM2A_reg
6	154719057	154724057	rs6917661_OPRM1
7	55106677	55111677	rs12668421_EGFR
9	1597299	2688571	FLJ35024_reg
9	12051391	12710266	TYRP1_reg
9	12394231	12399231	rs13289810_TYRP1
9	14724664	14910993	FREM1_reg
9	16882517	16887517	rs12350739_BNC2
10	6087269	6140602	IL2RA_reg
10	8100798	8105798	rs376397_GATA3
11	68843899	68848899	rs35264875_TCPN2
11	89015461	89020461	rs1126809_TYR
12	48235320	48346831	VDR_gene
12	89325835	89330835	rs12821256_KITLG
12	117890817	118406028	KSR2_reg
13	42004631	43096387	VWA8_reg
13	78378646	78383646	rs975739_EDNRB
14	52307604	52312604	rs8015138_GNG2
14	64565582	64619850	SYNE2_reg
14	72388817	73033238	RGS6_gene
15	28000021	28567298	OCA2_HERC2
15	48403169	48434869	SLC24A5_gene
15	48430994	48435994	rs2470102_SLC24A5
15	63345526	63633034	RAB8B_reg
15	69186598	69357389	NOX5_reg
16	89983617	89988644	rs1805008_rs1805007_MC1R
17	12328143	12363103	MAP2K4_reg
18	61581324	61780587	CHD7_gene
20	32736112	32741112	rs1015362_ASIP

Table S8 – Power to detect loci with suggestive and genome-wide significance for effect sizes previously associated with skin pigmentation. A previous study by Beleza et al, 2013 showed that 4 loci explained 35% of the variation in skin color. We show power for the approximate sample sizes in phase 1, phase 2, and the resequencing analysis.

Alpha	**% variance explained by locus**	**Power with N=233**	**Power with N=440**	**Sample size for 80% power**
p = 5e-8	0.1	0.31	0.91	376
	0.09	0.22	0.84	420
	0.08	0.15	0.73	475
	0.07	0.09	0.58	546
	0.06	0.05	0.41	640
	0.05	0.02	0.24	772
p = 1e-5	0.1	0.70	0.99	263
	0.09	0.61	0.98	293
	0.08	0.50	0.95	332
	0.07	0.38	0.89	381
	0.06	0.27	0.79	447
	0.05	0.17	0.63	539