Supplementary Data

Supplementary Table 1. Ocular quantitative traits investigated in this study

Trait	Abbreviation	N	Range	Mean±SD	*P_age*[*]	*P_sex*[*]	*Power*
Biometric parameters							
Axial length (mm)	AXL	195	20.5, 26.0	22.7±0.9	<0.0001	<0.0001	1.00
Anterior chamber depth (mm)	ACD	172	2.20, 3.97	3.15±0.37	<0.0001	0.0004	1.00
Lens thickness (mm)	Lens	172	3.40, 5.17	4.24±0.37	<0.0001	0.29	0.95
Intraocular pressure (applanation) (mm Hg)	IOPg	195	8.0, 25.5	14.5±3.1	0.30	0.86	0.87
Goldmann-correlated intraocular pressure (mm Hg)	IOPgc	95	7.2, 26.6	14.4±3.2	0.18	0.99	0.11
Corneal compensated intraocular pressure (mm Hg)	IOPcc	95	8.2, 26.7	15.8±3.4	0.002	0.87	0.00
Corneal parameters							
Central corneal thickness (µm)	CCT	195	433, 608	516.2±30.2	0.004	0.08	0.99
Corneal hysteresis	CH	95	6.0, 13.2	9.69±1.41	<0.0001	0.70	0.99
Corneal resistance factor	CRF	95	5.9, 13.5	9.48±1.40	0.005	0.75	0.99
Horizontal keratometric value (D)	K_H	195	6.80, 8.52	7.65±0.30	<0.0001	0.08	1.00
Vertical keratometric value (D)	K_V	195	6.80, 8.62	7.62±0.29	0.005	0.007	1.00
Optic nerve parameters							
Disc and cup size							
Disc area (mm^2) (HRT_MRA)	DA	165	1.35, 3.50	2.25±0.39	0.03	0.97	0.82
Cup area (mm^2) (HRT_MRA)	CA	165	0.00, 1.67	0.59±0.36	0.48	0.36	0.90
Cup disc area ratio (HRT_MRA)	CDAR	165	0.00, 0.55	0.25±0.13	0.21	0.44	0.93
Cup size (mm^2) (HRT_GPS)	CS	176	0.01, 1.02	0.46±0.20	0.33	0.25	0.99
Cup volume (mm^3) (HRT_MRA)	CV	165	0.00, 1.03	0.15±0.15	0.99	0.17	1.00
Cup contour (All HRT_MRA)							
Cup shape measure	CSM	165	-0.37, 0.02	-0.19±0.07	0.04	0.69	0.16
Contour line modulation temporal to inferior (mm)	CLM_TI	165	-0.05, 0.43	0.21±0.08	0.0003	0.04	0.99
Contour line modulation temporal to superior (mm)	CLM_TS	165	0.01, 0.44	0.22±0.08	<0.0001	0.54	0.69
Maximum contour depression (mm)	Contour_D	165	-0.01, 0.65	0.35±0.12	0.008	0.90	0.99
Maximum contour elevation (mm)	Contour_E	165	-0.29, 0.19	-0.06±0.09	0.26	0.23	0.99
Height variation contour (mm)	HVC	165	0.15, 0.77	0.41±0.10	<0.0001	0.39	0.37
Cup depth							
Cup depth (mm) (HRT_GPS)	CD	176	0.14, 1.18	0.63±0.19	0.009	0.47	0.99
Maximum cup depth (mm) (HRT_MRA)	CD_max	165	0.15, 1.30	0.64±0.22	0.12	0.88	0.99
Mean cup depth (mm) (HRT_MRA)	CD_mean	165	0.05, 0.70	0.23±0.10	0.54	0.54	0.99
Cup disc ratio							
Vertical cup-disc ratio (Fundus photo)	VCDR	191	0.10, 0.95	0.40±0.17	0.05	0.32	0.99
Horizontal cup disc ratio (HRT_MRA)	HCDR_MRA	165	0.00, 0.81	0.49±0.17	0.67	0.09	0.92
Linear cup disc ratio (HRT_MRA)	LCDR_MRA	165	0.04, 0.74	0.48±0.14	0.35	0.55	0.93
Vertical cup disc ratio (HRT_MRA)	VCDR_MRA	165	0.00, 0.78	0.37±0.22	0.07	0.85	0.90
Neural-retinal Rim							
Rim area (mm^2) (HRT_MRA)	RA	165	1.01, 2.57	1.67±0.29	0.0001	0.22	0.97
Rim disc area ratio (HRT_MRA)	RDAR	165	0.45, 1.00	0.75±0.13	0.21	0.44	0.94
Rim steepness (HRT_GPS)	RS	176	-1.21, 1.47	-0.13±0.54	0.01	0.74	0.96
Rim volume (mm^3) (HRT-MRA)	RV	165	0.07, 1.21	0.47±0.17	<0.0001	0.06	0.09

Retinal nerve fiber layer							
Inferior average (µm) (GDx)	Inferior	118	36.9, 94.5	61.6±8.9	0.99	0.91	0.82
Superior average (µm) (GDx)	Superior	118	41.4, 102.9	65.9±9.7	0.35	0.21	0.75
Temporal superior nasal inferior temporal average (µm) (GDx)	TSNIT	118	41.2, 107.3	55.7±7.9	0.02	0.97	0.94
Retinal nerve fiber layer cross sectional area (mm^2) (HRT_MRA)	RNFL_CSA	165	0.19, 3.20	1.45±0.41	<0.0001	0.16	0.56
Mean retinal nerve fiber layer thickness (mm) (HRT_MRA)	RNFL_MT	165	0.04, 0.54	0.27±0.07	<0.0001	0.21	0.22
Horizontal retinal nerve fiber layer curvature (HRT_GPS)	RNFL_HC	176	-0.24, 0.09	-0.03±0.05	0.92	0.81	0.98
Vertical retinal nerve fiber layer curvature (HRT_GPS)	RNFL_VC	176	-0.29, 0.00	-0.12±0.05	0.86	0.82	0.99
Refractive error parameters							
Objective refraction cylindrical distance	ORCD	100	-3.00, -0.25	-0.92±0.58	0.0001	0.29	0.01
Objective refraction spherical distance	ORSD	195	-10.5, 11.5	0.38±1.82	0.01	0.68	0.93
Subjective refraction cylindrical distance	SRCD	70	-3.0, -0.5	-0.99±0.55	0.06	0.70	0.76
Subjective refraction spherical distance	SRSD	195	-6.0, 11.0	0.23±1.54	0.008	0.32	0.70
Subjective refraction spherical near	SRSN	124	0.0, 3.0	2.12±0.87	<0.0001	0.004	0.51

[*] *P* values obtained from multiple regression analysis using general linear models and used to evaluate the association of age and sex with analyzed traits. The trait measurements are the average of both eyes for all the genotyped individuals included in the association study. For some traits measurements were not possible for all study subjects. For a description for how these traits were measured, see Supplementary methods. Power (%) to detect associations with the 4 SNPs used for the PheWAS is shown in the last column. The power calculation methods are included in the methods section.

Abbreviations: N, number of subjects with measurements for the indicated trait; SD, standard deviation.

Supplementary Table 2. Association results for the top 10 *WNT7B* SNPs with central corneal thickness (CCT) in South Indian pedigrees

SNP	Chr	Position[a]	A1/A2[b]	MAF[c]	β[d]	*s.e.*	*p*
rs9330813	22	46364161	A/G	0.495	-0.570	0.107	1.71×10^{-7}
rs9723267	22	46365557	T/G	0.495	-0.530	0.107	1.45×10^{-6}
rs75159625	22	46377008	C/A	0.497	-0.530	0.107	1.46×10^{-6}
rs10453441	22	46363739	A/G	0.358	0.390	0.107	5.85×10^{-4}
rs9330811	22	46362396	A/G	0.338	0.386	0.114	1.02×10^{-3}
rs10453458	22	46360772	C/T	0.406	0.369	0.107	1.30×10^{-3}
rs200329677	22	46369778	C/T	0.277	0.347	0.121	5.85×10^{-3}
rs62226057	22	46368130	A/G	0.190	0.387	0.113	9.98×10^{-3}
rs117979240	22	46348020	A/G	0.035	-0.790	0.309	1.43×10^{-2}
rs62226027	22	46321994	A/G	0.181	0.293	0.142	4.92×10^{-2}

[a]Genomic positions are based on NCBI Build 37/hg19.
[b]A1/A2, minor allele/common allele.
[c]MAF, minor allele frequency.
[d]β models the expected change in mean CCT per increase of one A1 allele.
Chr, chromosome; s.e, standard error.

Supplementary Table 3. Association results for SNPs previously associated with CCT

SNP ID	Chr	Position	Genes Nearby	Previously Reported			Reference(s)	Indian Dataset				Consistency of Direction	Most Significant Hit ± 100 kb		
				Effect Allele	Freq	β		A1/A2	Freq A1	β	P		SNP ID	Position	P
rs3767703	1	36555758	*COL8A2*	NA	NA	−4.43	Vithana et al. Hum Mol Genet 2011	A/G	0.26	-0.08	0.50	NA	rs538638	36534644	0.036
rs7550047	1	36567343	*COL8A2*	NA	NA	−4.42	Vithana et al. Hum Mol Genet 2011	NA	NA	NA	NA	NA	rs538638	36534644	0.036
rs96067	1	36571920	*COL8A2*	A	080; 0.58	0.03; 0.11	Lu et al. Nat Genet 2013	A/G	0.57	-0.10	0.39	N	rs538638	36534644	0.036
rs10189064	2	219327500	*USP37*	A	0.04	−0.23	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs4674301	219242862	0.019
rs121908120	2	219755011	*WNT10A*	A	0.03	-23.8	Cuellar-Partida et al. Hum Mol Genet 2015	NA	NA	NA	NA	NA	rs860573	219846749	0.030
rs7606754	2	228135180	*COL4A3*	A	0.35; 0.36	−0.07; −0.07	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs13425557	228063071	0.012
rs3749260	3	98250862	*GPR15*	A	0.13	−0.12	Lu et al. Nat Genet 2013	A/C	0.22	0.11	0.42	N	rs6778616	98282957	0.001
rs9822953	3	156472071	*TIPARP*	T	0.67	0.08	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs73019748	156514240	0.039
rs4894535	3	171995605	*FNDC3B*	T	0.17; 0.27	−0.10; −0.09	Lu et al. Nat Genet 2013	T/C	0.25	-0.26	0.05	Y	rs6445054	171992009	0.046
rs7620503	3	177304298	*TBL1XR1-KCNMB2*	T	0.39; 0.51	−0.06; −0.06	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs13091554	177214656	0.009
rs3931397	4	149079497	*NR3C2*	T	0.07; 0.12	−0.12; −0.09	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs7696997	148998566	0.014
rs1117707	5	64389665	*CWC27-ADAMTS6*	A	0.70	−0.09	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs11739329	64429954	0.071
rs2307121	5	64625512	*ADAMTS6*	T	0.34; 0.30	0.09; 0.05	Lu et al. Nat Genet 2013	T/C	0.48	-0.10	0.35	N	rs11957323	64699186	0.023
rs1538138	6	82794594	*FAM46A-IBTK*	T	0.25; 0.23	−0.07; −0.11	Lu et al. Nat Genet 2013	T/C	0.19	-0.19	0.19	Y	rs197246	82883836	0.009

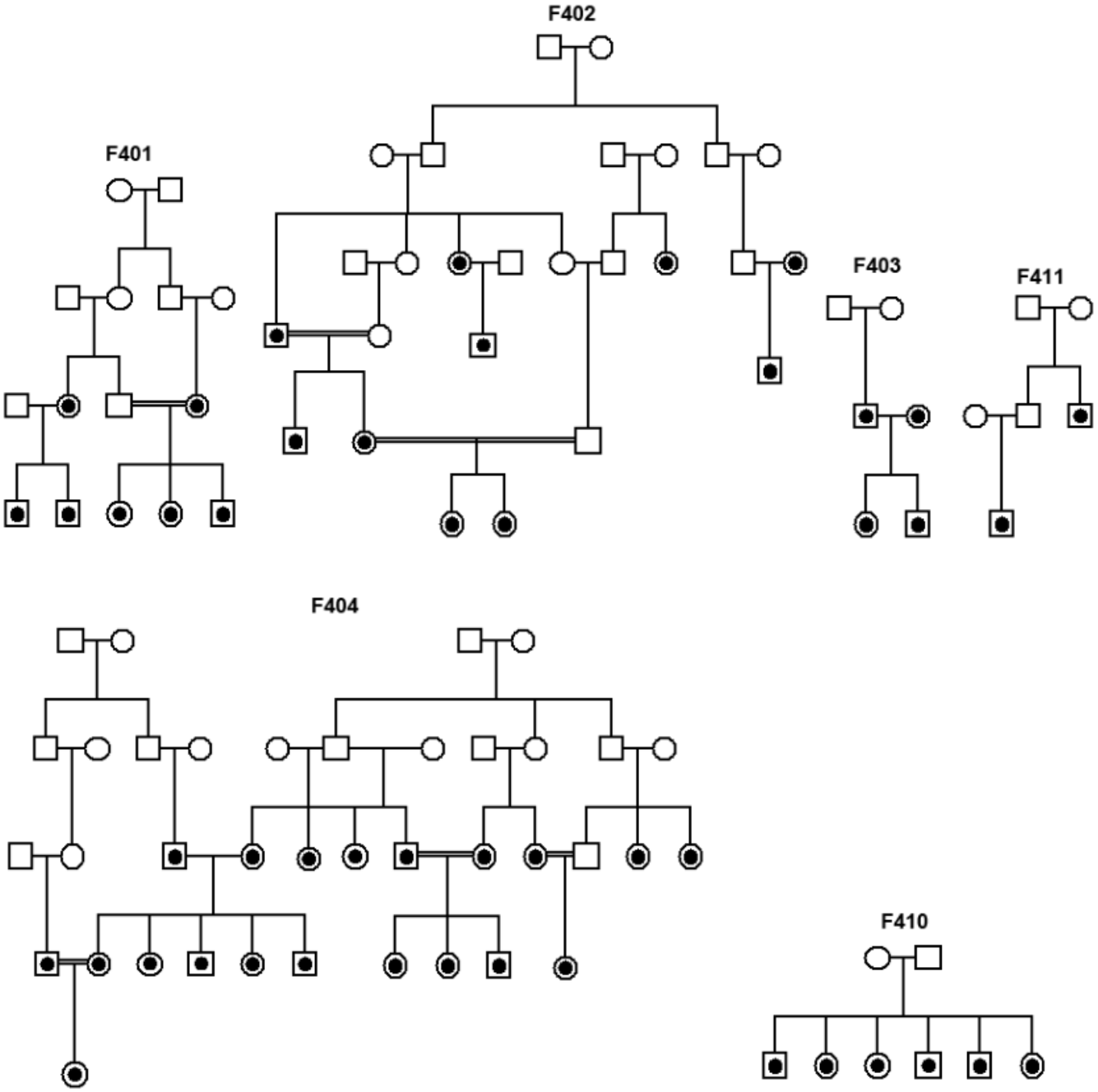
rs11763147	7	65326821	*VKORC1L1*	A	0.45; 0.32	0.07; 0.06	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	NA	NA	NA
rs4718428	7	66421446	*C7orf42*	G	0.46–0.74	−3.18	Cornes et al. Hum Mol Genet 2012	G/T	0.40	0.07	0.55	N	kgp22734253	66503970	0.028
rs1324183	9	13557491	*MPDZ-NF1B*	A	0.20; 0.25	−0.05; −0.10	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs988018	13466788	0.013
rs1007000	9	113662681	*LPAR1*	T	0.22; 0.21	0.07; 0.11	Lu et al. Nat Genet 2013	T/C	0.21	0.09	0.52	Y	rs521803	113565027	0.041
rs1409832	9	137428425	*RXRA-COL5A1*	NA	NA	−3.95	Vithana et al. Hum Mol Genet 2011	G/T	0.50	0.04	0.70	NA	rs34109509	137332109	0.003
rs4842044	9	137431904	*RXRA-COL5A1*	NA	NA	−4.67	Vithana et al. Hum Mol Genet 2011	NA	NA	NA	NA	NA	rs34109509	137332109	0.003
rs1536478	9	137432248	*RXRA-COL5A1*	NA	NA	−4.63	Vithana et al. Hum Mol Genet 2011	NA	NA	NA	NA	NA	rs57557257	137498356	0.004
rs3118515	9	137436314	*RXRA-COL5A1*	A	0.26	−0.23	Gao et al. Invest Ophthalmol Vis Sci 2013	A/G	0.58	0.04	0.75	N	rs57557257	137498356	0.004
rs943423	9	137437183	*RXRA-COL5A1*	C	0.26	−0.21	Gao et al. Invest Ophthalmol Vis Sci 2013	C/T	0.56	0.04	0.74	N	rs57557257	137498356	0.004
rs3118516	9	137439792	*RXRA-COL5A1*	A	0.34	−0.15	Hoehn et al. Hum Genet 2012	NA	NA	NA	NA	NA	rs57557257	137498356	0.004
rs3132306	9	137440212	*RXRA-COL5A1*	T	0.66	0.15	Hoehn et al. Hum Genet 2012	NA	NA	NA	NA	NA	rs57557257	137498356	0.004
rs1536482	9	137440528	*RXRA-COL5A1*	A	0.34; 0.34	−0.12; −0.08	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs57557257	137498356	0.004
rs3118520	9	137441596	*RXRA-COL5A1*	A	0.63	0.13	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs57557257	137498356	0.004
rs7044529	9	137568051	*COL5A1*	T	0.15; 0.20	−0.13; -0.05	Lu et al. Nat Genet 2013	T/C	0.31	-0.06	0.60	Y	rs57557257	137498356	0.004
rs11145951	9	139860264	*LCN12-PTGDS*	T	0.49; 0.69	0.09; 0.04	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	NA	NA	NA
rs7090871	10	63830286	*ARID5B*	T	0.59; 0.64	0.06; 0.07	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs7922024	63763369	0.080
rs1006368	10	126346603	*FAM53B*	A/G	NA	0.22	Lu et al. PLoS Genet 2010	NA	NA	NA	NA	NA	rs10901761	126254468	0.023

rs11245330	10	126380338	*FAM53B*	A/G	NA	0.22	Lu et al. PLoS Genet 2010	A/G	0.08	-0.27	0.19	NA	rs4962676	126340892	0.060
rs4938174	11	110913240	*ARHGAP20 -POU2AF1*	A	0.31; 0.15	0.06; 0.11	Lu et al. Nat Genet 2013	A/G	0.19	0.00	0.99	Y	rs17655864	110831371	0.006
rs1564892	12	104445742	*GLT8D2*	A	0.76; 0.43	−0.08; −0.07	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs3817602	104390525	0.001
rs1034200	13	23228691	*FGF9-SGCG*	A	0.23; 0.27	0.10; 0.02	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs9550863	23310550	0.013
rs2755237	13	41109429	*FOXO1*	A/C	NA	0.22	Lu et al. PLoS Genet 2010	C/A	0.08	-0.06	0.75	NA	rs4941980	41058857	0.028
rs2721051	13	41110884	*FOXO1*	T	0.11; 0.03	−0.17; -0.13	Lu et al. Nat Genet 2013	T/C	0.05	0.08	0.75	N	rs4941980	41058857	0.028
rs785422	15	30173885	*TJP1*	T	0.11; 0.08	−0.14; -0.10	Lu et al. Nat Genet 2013	T/C	0.11	-0.32	0.08	Y	rs785425	30178614	0.079
rs12913547	15	67467507	*SMAD3*	T	0.77; 0.64	−0.08; −0.07	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	NA	NA	NA
rs6496932	15	85825567	*AKAP13*	A	0.20; 0.36	−0.11; -0.06	Lu et al. Nat Genet 2013	A/C	0.36	-0.16	0.15	Y	rs16975309	85910978	0.110
rs1828481	15	85840912	*AKAP13*	C	0.45–0.56	3.12	Cornes et al. Hum Mol Genet 2012	NA	NA	NA	NA	NA	rs16975309	85910978	0.110
rs7172789	15	85843517	*AKAP13*	C	0.45–0.56	3.14	Cornes et al. Hum Mol Genet 2012	C/T	0.53	0.12	0.30	Y	rs16975309	85910978	0.110
rs2034809	15	101555399	*LRRK1*	A	0.50	−0.05	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs7183889	101457321	0.011
rs930847	15	101558562	*LRRK1*	T	0.77; 0.73	−0.11; -0.11	Lu et al. Nat Genet 2013	T/G	0.82	-0.11	0.47	Y	rs878274	101551136	0.015
rs4965359	15	101585336	*LRRK1*	A	0.40–0.67	−3.50	Cornes et al. Hum Mol Genet 2012	A/G	0.36	-0.15	0.20	Y	rs878274	101551136	0.015
rs752092	15	101781934	*CHSY1*	A	0.66; 0.78	−0.08; −0.05	Lu et al. Nat Genet 2013	A/G	0.79	-0.07	0.64	Y	rs2124135	101698540	0.036
rs12447690	16	88298124	*ZNF469*	T	0.64	0.16	Hoehn et al. Hum Genet 2012	T/C	0.59	0.14	0.20	Y	rs8051233	88230225	0.005
rs7500824	16	88299491	*ZNF469*	A	0.36	−0.16	Hoehn et al. Hum Genet 2012	A/G	0.30	-0.07	0.56	Y	rs8051233	88230225	0.005

rs7405095	16	88307825	*ZNF469*	A	0.36	−0.16	Hoehn et al. Hum Genet 2012	NA	NA	NA	NA	NA	rs8051233	88230225	0.005
rs7501109	16	88320862	*ZNF469*	C	0.64	0.16	Hoehn et al. Hum Genet 2012	NA	NA	NA	NA	NA	rs8051233	88230225	0.005
rs7501402	16	88320911	*ZNF469*	A	0.36	−0.16	Hoehn et al. Hum Genet 2012	NA	NA	NA	NA	NA	rs8051233	88230225	0.005
rs6540223	16	88321436	*ZNF469*	T	0.64	0.16	Hoehn et al. Hum Genet 2012	T/C	0.77	0.14	0.30	Y	rs8051233	88230225	0.005
rs12448211	16	88330513	*ZNF469*	A	0.62	0.16	Hoehn et al. Hum Genet 2012	NA	NA	NA	NA	NA	rs4072556	88355252	0.008
rs9938149	16	88331640	*ZNF469*	A	0.62; 0.74	0.17; 0.16	Lu et al. Nat Genet 2013	A/C	0.70	0.03	0.81	Y	rs4072556	88355252	0.008
rs9922572	16	88334112	*ZNF469*	A	0.34	−0.14	Hoehn et al. Hum Genet 2012	A/C	0.24	-0.23	0.06	Y	rs4072556	88355252	0.008
rs9925231	16	88338107	*ZNF469*	NA	NA	−4.79	Vithana et al. Hum Mol Genet 2011	NA	NA	NA	NA	NA	rs4072556	88355252	0.008
rs7204132	16	88344517	*ZNF469*	NA	NA	−4.95	Vithana et al. Hum Mol Genet 2011	A/C	0.36	-0.07	0.55	NA	rs4072556	88355252	0.008
rs9927272	16	88346709	*ZNF469*	NA	NA	−3.95	Vithana et al. Hum Mol Genet 2011	A/G	0.36	-0.22	0.05	NA	rs8051681	88445569	0.002
rs2323457	17	14554190	*HS3ST3B1-PMP22*	A	0.29	−0.08	Lu et al. Nat Genet 2013	NA	NA	NA	NA	NA	rs2109174	14513310	0.024
rs12940030	17	14561016	*HS3ST3B1-PMP22*	T	0.71; 0.54	0.08; 0.06	Lu et al. Nat Genet 2013	T/C	0.65	0.15	0.21	Y	rs2109174	14513310	0.024
rs10453441	22	46363739	*WNT7B*	G	0.45	-4.35	Gao et al. Hum Mol Genet 2016	G/A	0.64	-0.39	5.9×10^{-4}	Y	rs9330813	46364161	1.7×10^{-7}

Abbreviations: β, beta; Chr, chromosome; Freq, frequency; A1/A2, allele 1 / allele 2.

A semicolon is used to separate multiple frequencies and betas in previously reported SNPs. For this Indian dataset, the frequency for allele 1 is given and is modeled as the effect allele. The direction of effect was consistent for most SNPs. Most SNPs within the most significant hits ±100 kb region of reported SNPs show a p value of <0.05. SNP positions are according to GRCh37/hg19.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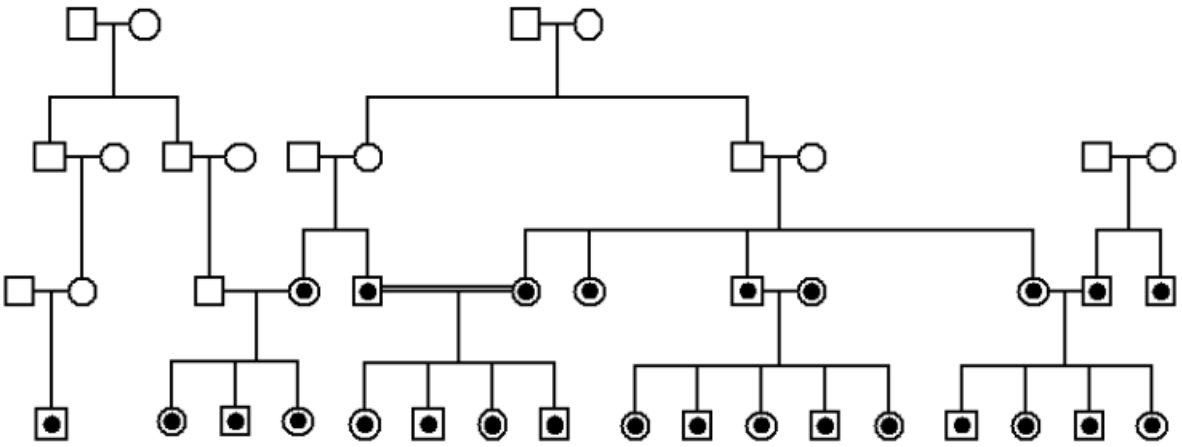

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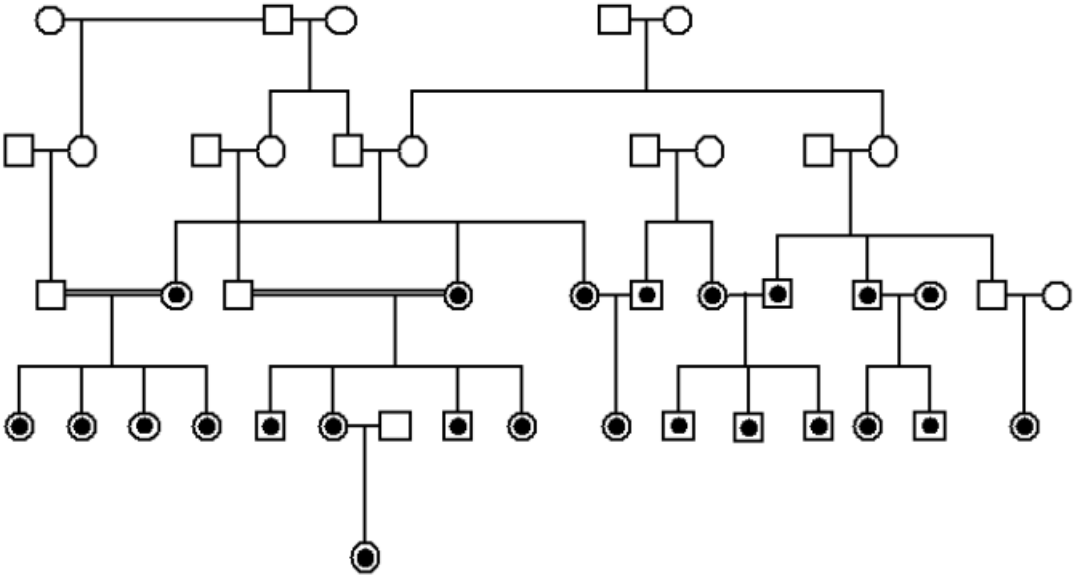

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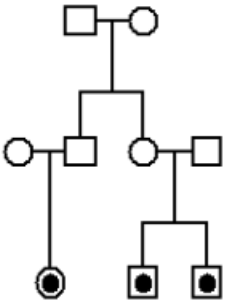

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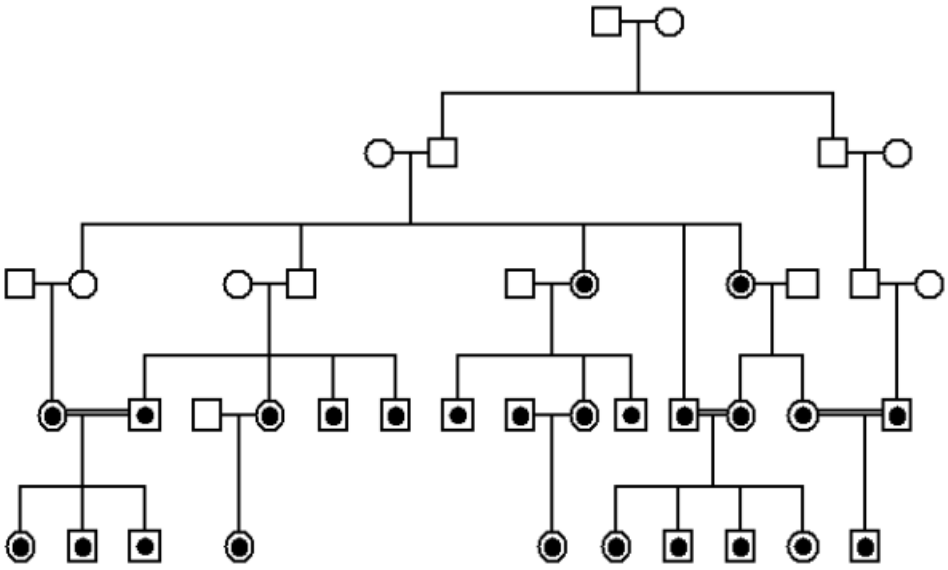

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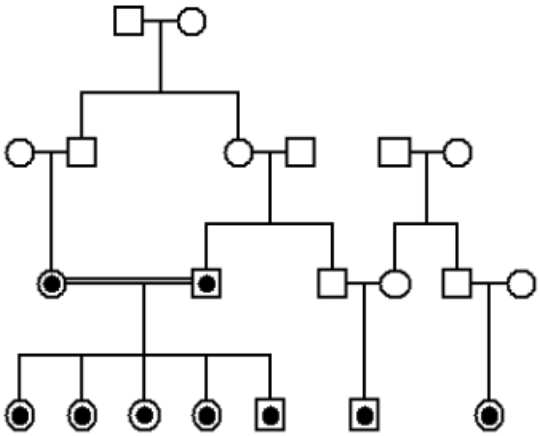

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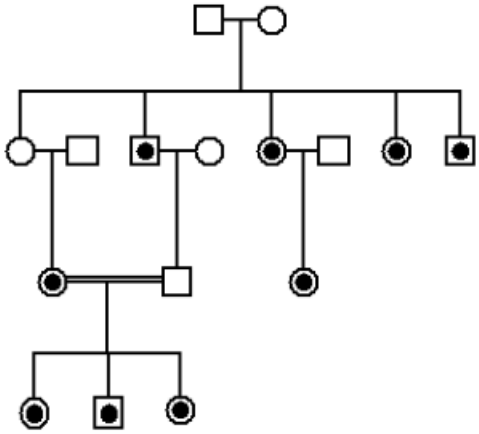

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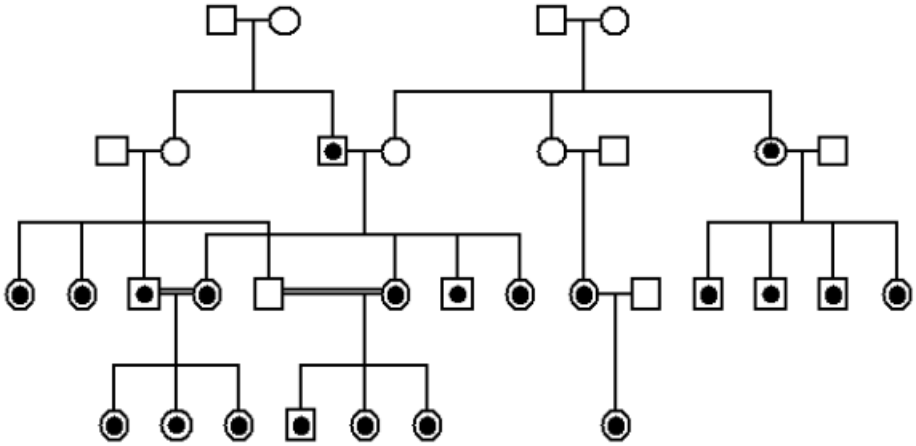

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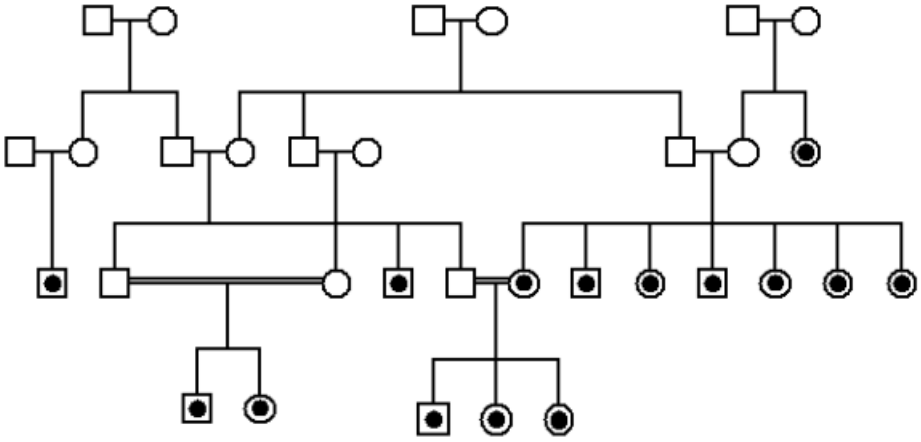
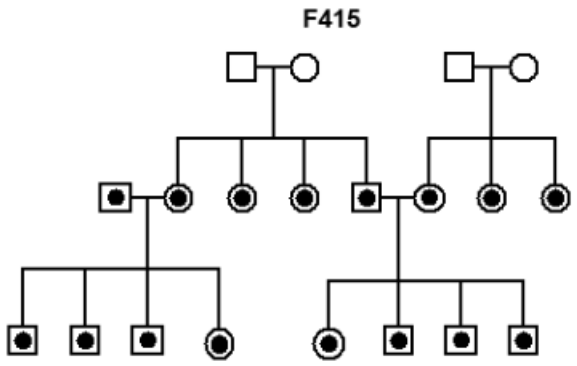
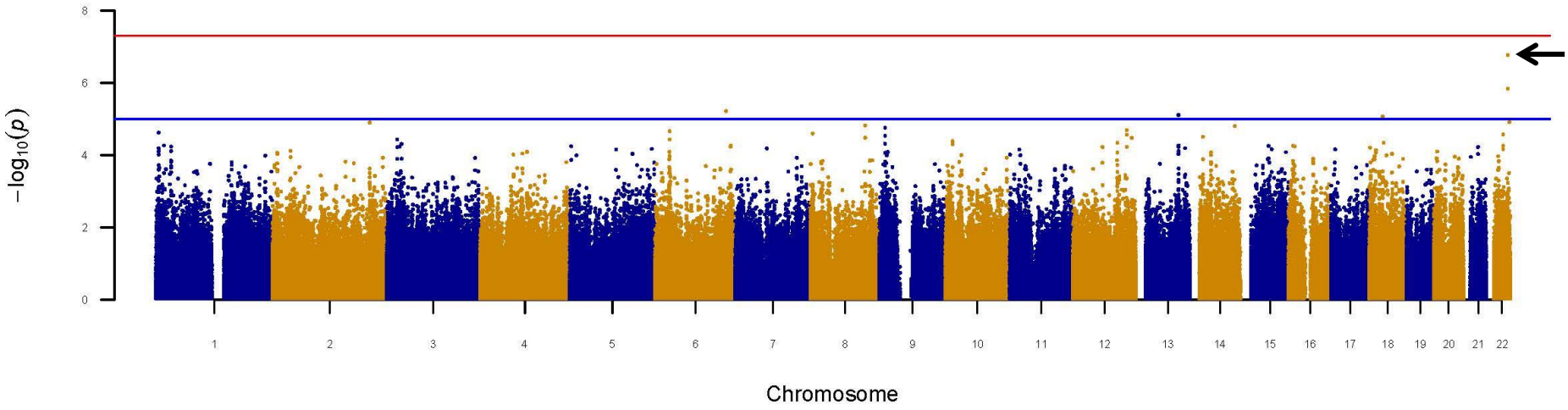
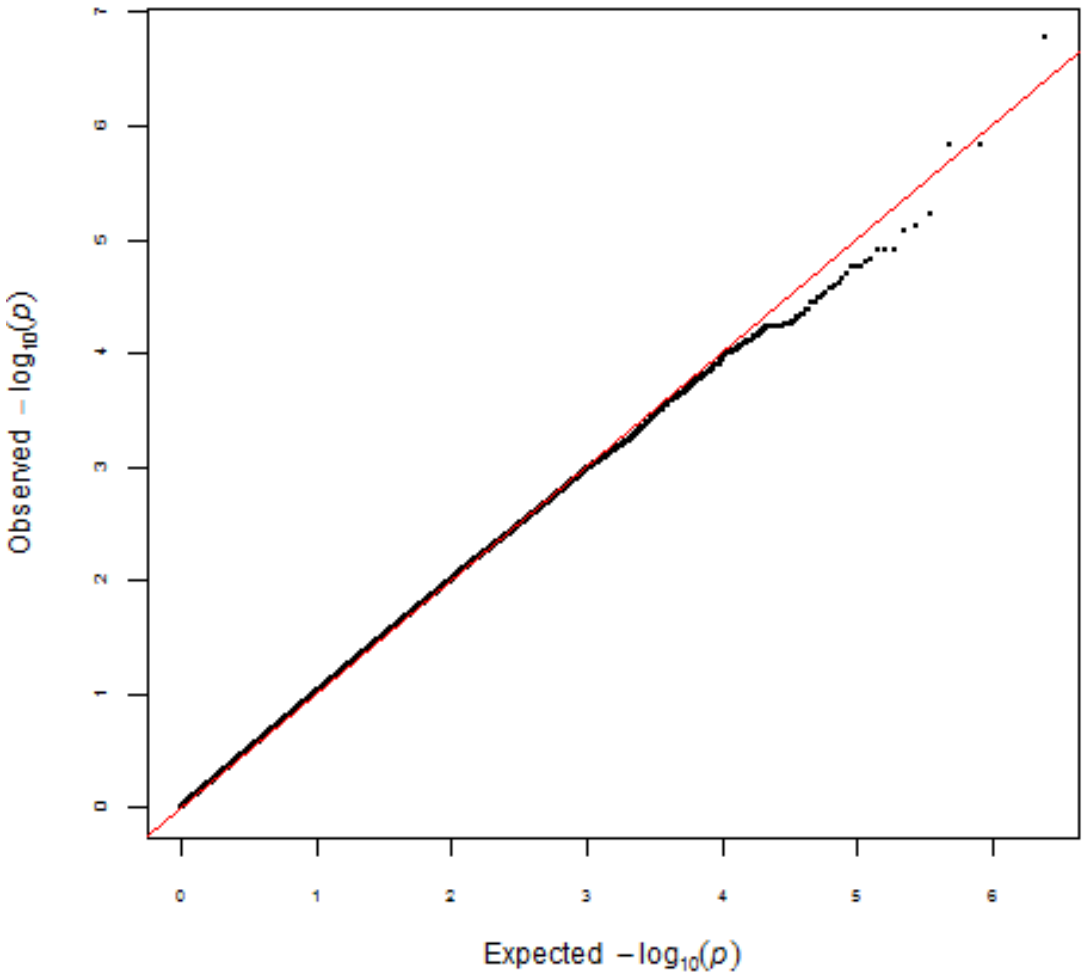




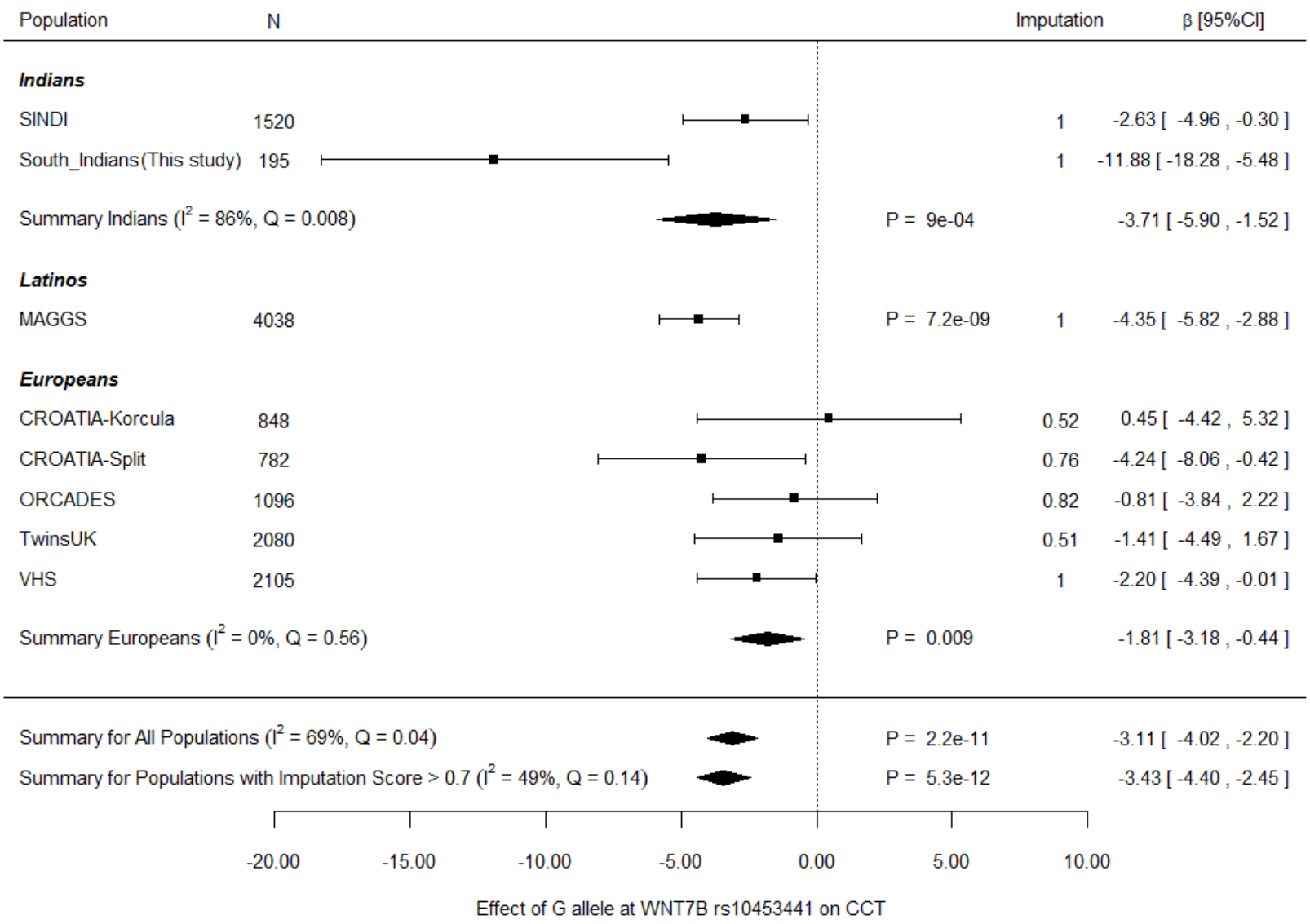
Supplementary Figure 1. **South Indian pedigrees investigated in this study.** Individuals marked with a dot inside the symbol have clinical trait measurements and are genotyped. Double lines between individuals represent consanguineous marriages.



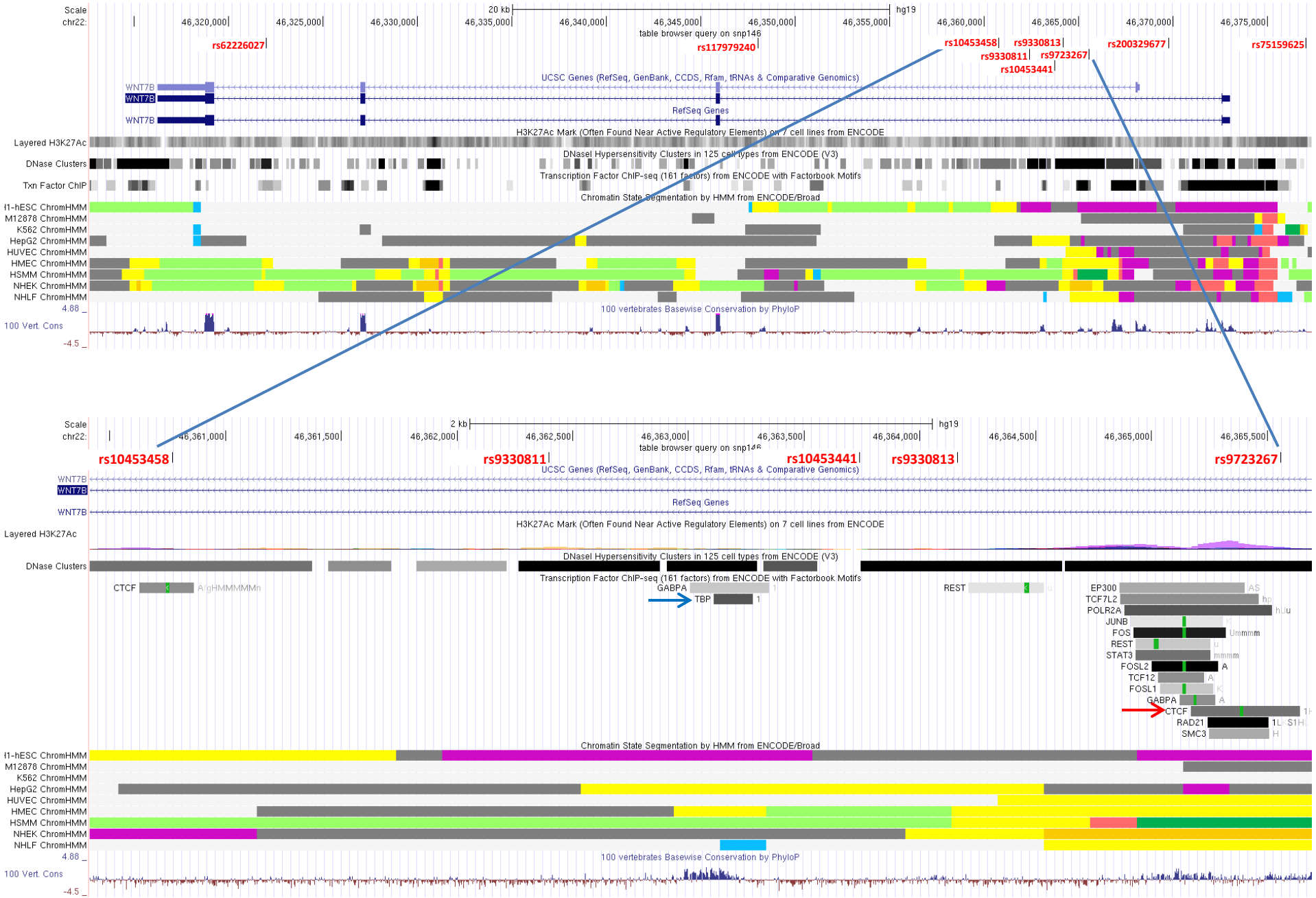
Supplementary Figure 2. Genome-wide association results for CCT in the South Indian pedigrees**.** The results for the 1,223,314 SNPs after data cleaning are plotted as $-\log_{10}(p)$ by genomic position. The horizontal red line indicates the formal threshold for genome-wide significance at $p = 5.0\times10^{-8}$. The horizontal blue line denotes suggestive evidence of association at $p = 1.0\times10^{-5}$. The top SNP, rs9330813 is indicated by the arrow.



Supplementary Figure 3. Q-Q plot of the genome-wide *p* values for CCT in the South Indian pedigrees**.** The results for the 1,223,314 SNPs after data cleaning are plotted as observed $-\log_{10}(p)$ by expected $-\log_{10}(p)$. The diagonal red line indicates the observed $-\log_{10}(p)$ equals to the expected $-\log_{10}(p)$. The genomic inflation factor is 1.05.


Population
N
Imputation
β [95%CI]
Indians
SINDI 1520 1 -2.63 [-4.96 , -0.30]
South_Indians(This study) 195 1 -11.88 [-18.28 , -5.48]
Summary Indians (I2 = 86%, Q = 0.008) P = 9e-04 -3.71 [-5.90 , -1.52]
Latinos
MAGGS 4038 P = 7.2e-09 1 -4.35 [-5.82 , -2.88]
Europeans
CROATIA-Korcula 848 0.52 0.45 [-4.42 , 5.32]
CROATIA-Split 782 0.76 -4.24 [-8.06 , -0.42]
ORCADES 1096 0.82 -0.81 [-3.84 , 2.22]
TwinsUK 2080 0.51 -1.41 [-4.49 , 1.67]
VHS 2105 1 -2.20 [-4.39 , -0.01]
Summary Europeans (I2 = 0%, Q = 0.56) P = 0.009 -1.81 [-3.18 , -0.44]
Summary for All Populations (I2 = 69%, Q = 0.04) P = 2.2e-11 -3.11 [-4.02 , -2.20]
Summary for Populations with Imputation Score > 0.7 (I2 = 49%, Q = 0.14) P = 5.3e-12 -3.43 [-4.40 , -2.45]
-20.00
-15.00
-10.00
-5.00
0.00
5.00
10.00
Effect of G allele at WNT7B rs10453441 on CCT

Supplementary Figure 4. Meta-analysis for rs10453441 and CCT. Forest plot showing effect estimates for the South Indian pedigrees, as well as for the replication effort. Pooled estimates for β and 95% confidence interval (95%CI) were calculated by fixed effects, inverse variance weighting meta-analysis. Reduced evidence for association but similiar overall effects was observed if the meta-analysis was completed using the random effects model: $P=1.0x10^{-4}$, β = -3.44, 95%CI: -5.21, -1.68. Individual dataset results are indicated by black squares and summary values are indicated by black diamonds. Abbreviations: MAGGS, Mexican American Glaucoma Genetic Study; SINDI, Singapore Indian Eye Study; ORCADES, Orkney Complex Disease Study; TwinsUK, UK Twin Study; VHS, Viking Health Study.


Scale
chr22:
20 kb
hg19
46,320,000
46,325,000
46,330,000
46,335,000
46,340,000
46,345,000
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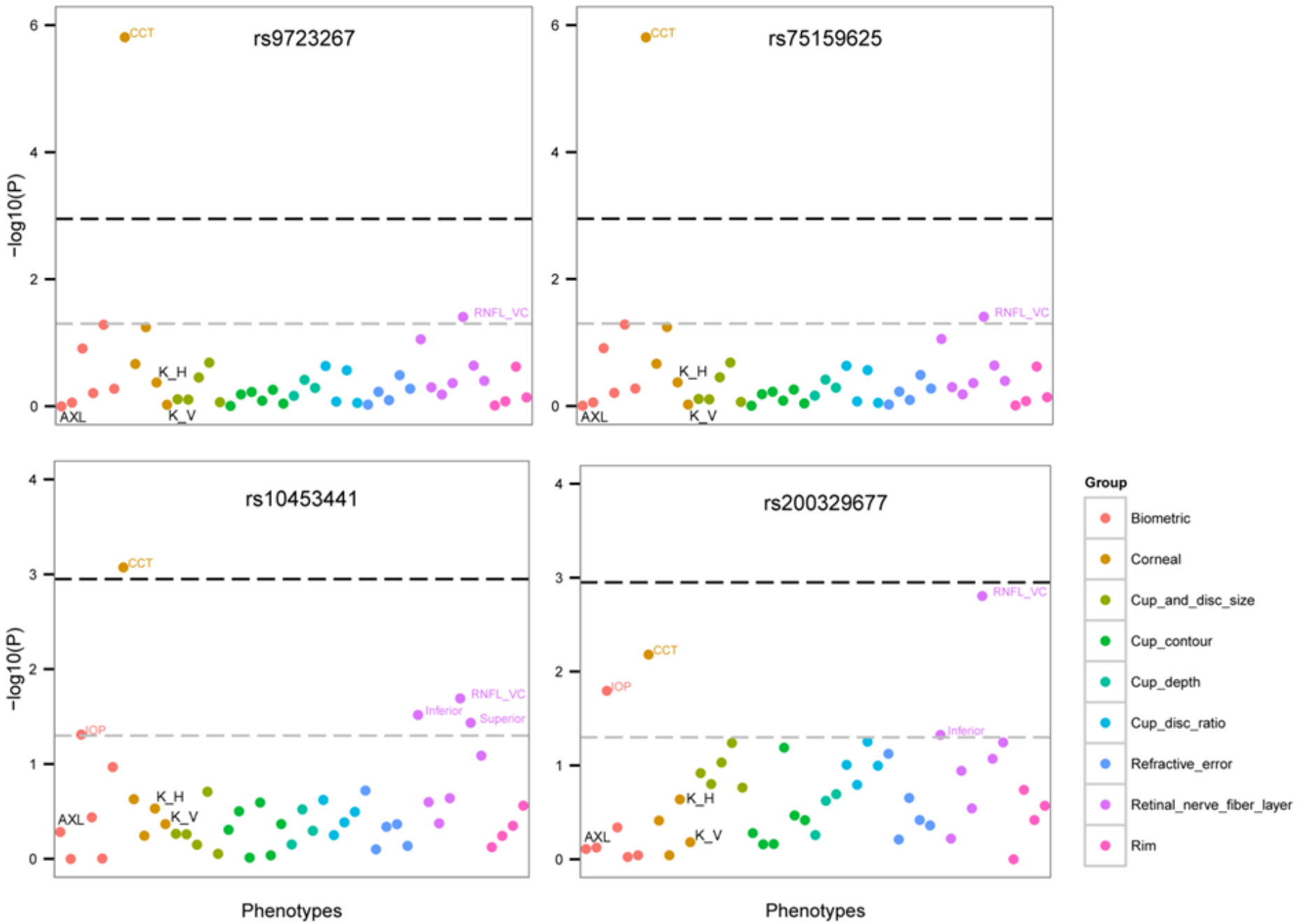
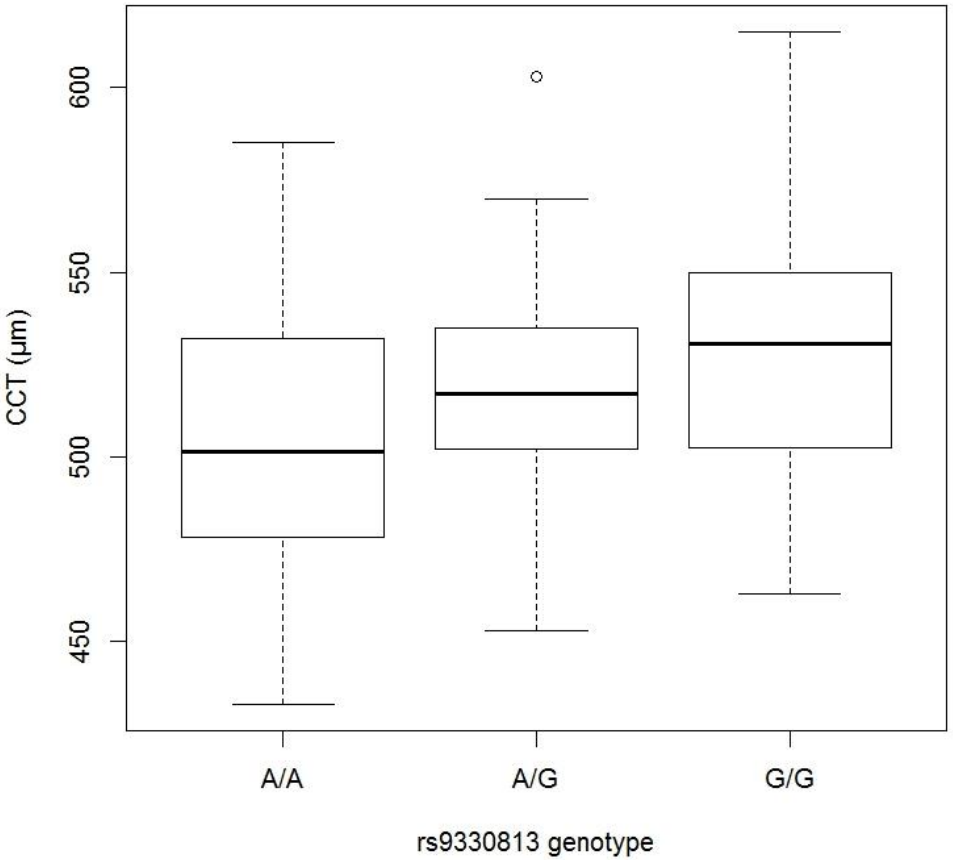
46,355,000
46,360,000
46,365,000
46,370,000
46,375,000
table browser query on snp146
rs62226027
rs117979240
rs10453458
rs9330813
rs200329677
rs75159625
rs9330811
rs9723267
rs10453441
UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
WNT7B
RefSeq Genes
H3K27Ac Mark (Often Found Near Active Regulatory Elements) on 7 cell lines from ENCODE
Layered H3K27Ac
DNaseI Hypersensitivity Clusters in 125 cell types from ENCODE (V3)
DNase Clusters
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs
Txn Factor ChIP
Chromatin State Segmentation by HMM from ENCODE/Broad
H1-hESC ChromHMM
M12878 ChromHMM
K562 ChromHMM
HepG2 ChromHMM
HUVEC ChromHMM
HMEC ChromHMM
HSMM ChromHMM
NHEK ChromHMM
NHLF ChromHMM
4.88
100 vertebrates Basewise Conservation by PhyloP
100 Vert. Cons
-4.5
Scale
chr22:
2 kb
hg19
46,361,000
46,361,500
46,362,000
46,362,500
46,363,000
46,363,500
46,364,000
46,364,500
46,365,000
46,365,500
table browser query on snp146
rs10453458
rs9330811
rs10453441
rs9330813
rs9723267
UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
WNT7B
RefSeq Genes
H3K27Ac Mark (Often Found Near Active Regulatory Elements) on 7 cell lines from ENCODE
Layered H3K27Ac
DNaseI Hypersensitivity Clusters in 125 cell types from ENCODE (V3)
DNase Clusters
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs
CTCF
GABPA
TBP
REST
EP300
TCF7L2
POLR2A
JUNB
FOS
REST
STAT3
FOSL2
TCF12
FOSL1
GABPA
CTCF
RAD21
SMC3
Chromatin State Segmentation by HMM from ENCODE/Broad
H1-hESC ChromHMM
M12878 ChromHMM
K562 ChromHMM
HepG2 ChromHMM
HUVEC ChromHMM
HMEC ChromHMM
HSMM ChromHMM
NHEK ChromHMM
NHLF ChromHMM
4.88
100 vertebrates Basewise Conservation by PhyloP
100 Vert. Cons
-4.5

Supplementary Figure 5. *WNT7B* genomic region associated with ocular traits as annotated by ENCODE. The top SNP in this family-based South Indian study associated with CCT (rs9330813) and the top SNPs associated with corneal curvature and axial length in a recent Japanese study (Miyake et al., 2015) (rs10453441, rs200329677) as well as the top SNP associated with CCT in a Latino study (Gao et al., 2016) (rs10453441) fall within a 10Kb region in intron 1 (top panel). The lower panel shows the SNPs that flank a cluster of transcription factor binding sites including the top SNP in our study (rs9330813) and rs10453441, the top SNP in the other two studies. Of these, rs9723267, which is in complete linkage disequilibrium with rs9330813, overlaps a CTCF/Rad21 binding site (red arrow) that may have enhanced activity because of the presence of a nearby TBP binding site (blue arrow) (Roy et al., 2015). The region also includes multiple DNaseI sites that in most cell types are annotated as enhancers by ENCODE. Cell types: GM12878 (B-lymphocyte, lymphoblastoid), H1-hESC (embryonic stem cells), K562 (leukemia), HepG2 (hepatocellular carcinoma), HUVEC (umbilical vein endothelial cells), HMEC (mammary epithelial cells), HSMM (skeletal muscle myoblasts), NHEK (epidermal keratinocytes), NHLF (lung fibroblasts). ENCODE annotation: Bright Red, Active Promoter; Light Red, Weak Promoter; Purple, Inactive/poised Promoter; Orange, Strong enhancer; Yellow, Weak/poised enhancer; Blue, Insulator; Dark Green, Transcriptional transition and Transcriptional elongation; Light Green, Weak transcribed; Gray, Polycomb-repressed; Light Gray, Heterochromatin, low signal. Data is taken from a UCSC genome browser screen shot (http://genome.ucsc.edu).


rs9723267
rs75159625
rs10453441
rs200329677
−log10(P)
Phenotypes
CCT
IOP
AXL
K_H
K_V
RNFL_VC
Inferior
Superior
Group
Biometric
Corneal
Cup_and_disc_size
Cup_contour
Cup_depth
Cup_disc_ratio
Refractive_error
Retinal_nerve_fiber_layer
Rim

Supplementary Figure 6. PheWAS plots for top SNPs associated with CCT in the South Indian population (rs9723267 and rs75159625, top panels) and top SNPs associated with corneal curvature and axial length in the Japanese population (rs10453441 and rs2000329677, bottom panels). The association results for each measured trait (Supplementary Table 1) were plotted with the phenotypes (ocular traits) grouped along the x-axis and the –log10(P) value for association analysis on the y-axis. The phenotype group is indicated by the color of the graph point as indicated by the side panel. The lower grey dashed line indicates P = 0.05. The upper black dashed line indicates a single-SNP Bonferroni correction for 45 traits, P = 0.001 (0.05/45). Abbreviations: CCT, central corneal thickness; IOP, intraocular pressure measured by Goldman applantation; AXL axial length; K_H, corneal curvature horizontal; K_V, corneal curvature, vertical; Inferior, average retinal nerve fiber layer thickness in the inferior quadrant as measured by HRT (Heidelberg Retina Tomograph) and analyzed with the Moorfields regression analysis; Superior, average nerve fiber layer thickness in the superior quandrant as measured by the HRT and analyzed with the Moorfields regression analysis; RNFL_VC, retinal nerve fiber layer curvature as measured by the HRT and analyzed by using Glaucoma Probability Score (GPS). Other traits were not labeled in these figures due to limited space.



Supplementary Figure 7. CCT boxplot for three genotypes of top SNP rs9330813 in the South Indian population. The CCT boxplot for three genotypes of top SNP rs9330813 was consistent with an additive model in this South Indian dataset.

SUPPLEMENTARY METHODS

Measurement of ocular quantitative traits:

After informed written consent, 45 selected ocular quantitative traits (Supplementary Table 1) were measured in individuals enrolled in this study. Not all traits could be measured in every enrolled subject and the N (number) of subjects with the measured trait is indicated in Supplementary Table 1. The traits are grouped as biometric parameters (6 traits), corneal parameters (5 traits), optic nerve parameters (29 traits) and refractive error parameters (5 traits). For all traits measurements were made separately for each eye and then the average value of both eyes was used for the analyses. Methods to measure each trait are described in the following sections:

Biometric traits: **Axial length** (AXL) was measured using Digital Biometry Reading (DBR; Ocuscan, Alcon Laboratories Inc, Fort Worth, TX). **Anterior chamber depth** (ACD) was graded using the modified van Herrick technique using a set of reference images and slit lamp biomicroscopy. **Intraocular pressure** (IOPg) was measured using the Goldman applanation tonometer (Zeiss AT 030 Applanation Tonometer, Carl Zeiss, Jena, Germany) while seated at the slit lamp. IOP measurements were also obtained from the Ocular Response Analyzer (Goldmann-correlated intraocular pressure (IOPgc, mm Hg) and Corneal compensated intraocular pressure (IOPcc, mm Hg). **Lens thickness** (Lens) was measured using the Pentacam (Oculus, Inc., Lynnwood, WA).

Cornea traits: **Central corneal thickness** (CCT) was measured by an ultrasound pachymeter (Dicon P55; Paradigm Medical Industries Inc., Salt Lake City, UT). **Corneal curvature** (CC, K_H and K_V) was evaluated using the Javal–Schiotz keratometer (Haag-Streit AG, Köniz, Switzerland). **Corneal hysteresis** (CH) and **corneal resistance factor** (CRF) were measured by Ocular Response Analyzer (ORA; Reichert Inc., Depew, NY).

Optic nerve traits: VCDR (vertical cup-to-disc ratio) was graded using fundus photography (Zeiss FF450-plus fundus camera, Carl Zeiss, Jena, Germany). **Inferior, superior and TSNIT (temporal, superior, nasal, inferior, temporal) nerve fiber layer thickness** was measured by Glaucoma Diagnostics (GDx; Carl Zeiss Meditec AG, Jena, Germany). **Other optic nerve parameters** were measured by Heidelberg Retina Tomograph (HRT; Heidelberg Engineering, Dossenheim, Germany). All HRT measurements were analyzed using Moorfields Regression Analysis (MRA) except cup size, cup depth, rim steepness and retinal nerve fiber layer curvature, which were analyzed using Glaucoma Probability Score (GPS).

Refractive error traits: The ETDRS distance acuity chart was used to measure visual acuity. **Objective refractive error** measurements (Objective refraction cylindrical distance, ORCD; Objective refraction spherical distance, ORSD) were made using the autorefractor (Topcon RM A 7000 Auto refractometer) and by retinoscopy (Optotechnik, Herrsching, Germany). Subjective refractive error measurements were made by manual refinement of the objective measures using trial frame and lenses.

Collection of samples and genotyping for the replication cohorts:

Three of European studies used for replication, CROATIA-Korčula, CROATIA-Split, and ORCADES, are healthy adult volunteers from the Croatian island of Korčula, the Croatian urban city of Split and the northern isles of Orkney (Orkney Complex Disease Study, ORCADES, Scotland, UK). Samples were collected and genotyped as previously described (Vitart et al., 2010). Genotype data imputed using IMPUTE2 to the 1000 genomes phase 1 (integrated variant set- March 2012 release) was used for replication. Imputation scores for the SNPs investigated (rs9330813 and rs10453441) were >.50 for each dataset. VHS, the Viking Health Study, is a cross-sectional study of the UK population from the Northern isles of Shetland with eye examination

and measurements identical to those carried out in the ORCADES study (http://www.orcades.ed.ac.uk/orcades/VHSS.html). 2179 individuals genotyped with the HumanOmniExpressExome-8v1 genome-wide Illumina array passed quality controls (no mismatch between reported and genotyped gender, genotyping call per individual > 97%, with genotyping call per SNP > 98% and variants with large departure from Hardy-Weinberg equilibrium removed). The variant rs10453441 was present on the genotyping array, therefore data presented for VHS is from direct genotypes.

The Twins UK cohort was collected and genotyped as previously described (Lu et al., 2013). Genotype data imputed using IMPUTE2 to the 1000 genomes phase 1 (integrated variant set- March 2012 release) was used for replication. Imputation scores for the SNPs investigated (rs9330813 and rs10453441) were >.500.

The Singaporean Indian population (SINDI) was collected and genotyped as previously described (Vithana et al., 2011). SNPs rs9330813 and rs10453441 were not included in the Illumina Human610-Quad platform used for genotyping and the *WNT7B* genomic region imputed poorly in this population. For replication for this study a TaqMan assay was designed for rs10453441 and successfully used for genotyping. A similar assay for rs9330813 failed design.

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