SUPPLEMENTARY DATA

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A. SUPPLEMENTARY METHODS

Definitions of esotropia subtypes:

- Esotropia: Manifest esotropia in primary position.
- Infantile Esotropia: Manifest esotropia that develops within the first six months of life.
- Intermittent Esotropia: Patient has an intermittent esotropia at any point during the examination in primary position.
- Esophoria: Esophoria of 10 prism diopters or more in primary position.
- Acquired Esotropia: Acute acquired non-accommodative esotropia.
- Accommodative Esotropia: Manifest esotropia that reduces with hyperopic correction to a range that fusion may be achieved (less than 10 prism diopters*)* or reliably demonstrate fusion. If bifocals are required to reduce the deviation to 10 prism diopters or less it is acceptable.
- Partially accommodative ETs were manifest esotropias who also had an accommodative component to their deviation. An accommodative component was an eso-deviation that reduced with hyperopic correction or +3.00 lenses by 10 prism diopters or more.

Control cohorts:

Control genotypes generated on Illumina SNP microarrays were derived from the database of Genotypes and Phenotypes (dbGaP) as follows:

- 1877 controls from NEI Age-Related Eye Disease Study (AREDS) Genetic Variation in Refractive Error Substudy (phs000429.v1.p1). Samples were genotyped using Omni 2.5 version: 4v_1D (Mostly orthotropic, personal communication).
- 1264 controls from eMERGE Geisinger eGenomic Medicine (GeM) MyCode Project (phs000381.v1.p1). Samples were genotyped using Omni Express Version: 12-v1_c.

- 3747 cases and controls from the Genome-Wide Association Study of Fuchs' Endothelial Corneal Dystrophy (FECD) (phs000421.v1.p1). Samples were genotyped using Omni 2.5 Version: 4v_1H. This study included samples from the AREDS study, and only non-AREDS samples were used as controls.
- 12595 cases from the Health and Retirement Study (HRS) (phs000428.v1.p1). Samples were genotyped using Omni 2.5 Version: 4v_1D. Only samples of individuals of European origin were used (African Americans and Hispanics were excluded using principal components analysis).

Genotyping:

All cases were processed on Illumina Infinium human Omniexpress_24v1-0 arrays using the automated Infinium HTS Assay at Rutgers University Cell and DNA Repository (RUCDR) (Piscataway, New Jersey, USA). Samples were analyzed in two batches, plates 1-12 and plates 13-24. Plates 23 and 24 were comprised of “repeat” samples that failed during preliminary genotyping analysis. Samples were run against RUCDR technical controls. Genotype calling from intensity data was performed in Illumina GenomeStudio V2011.1, Genotyping module version 1.9.4. Mean genotype call rate among passing samples was 0.99 (SD: 0.0027). The arrays used for genotyping of controls had high number of overlapping SNPs with the Omniexpress_24v1-0 arrays used for cases. This ensured a high SNP coverage in the merged case-control dataset.

Quality Control Procedures:

Initial QC steps were performed in parallel within each of the five datasets (cases and four control sets) using PLINK v1.07[1] and Golden Helix SNP and Variation Suite 8 (SVS) (Golden Helix, Bozeman, MT, USA).

SNP QC: Non-mappable SNPs, and SNPs with overall call rates < 97%, minor allele frequencies (MAF) < 0.01% in autosomal markers, and Hardy Weinberg Equilibrium (HWE) < 1 x 10^{-7} in controls were removed. SNPs were tested for differing missing rates given that different datasets were genotyped on different platforms and at different facilities and times. SNPs with a test *P* value < 1 × 10^{-3} were removed. Because cases were run in two batches, QC metrics, differential missingness, and an association test were performed using batch indicator as a phenotype with case-control status. The resulting Q-Q plot showed no evidence of overdispersion to suggest a batch effect (λ=1.0). SNPs were oriented to genome-forward orientation using SNPs from CEU HapMap3 individuals as a reference dataset (Release 3, NCBI build 36, dbSNP b126). Strand-ambiguous SNPs with an allele frequency difference of > 0.2 between the observed MAF and the HapMap CEU reference data, and strand-ambiguous SNPs not present in the HapMap reference dataset were removed. SNPs passing all these steps were taken forward for imputation and downstream analysis. For X chromosome SNPs, the SNP call rate threshold of 97% was calculated using female samples only. For resolution of strand-ambiguous X chromosome SNPs, allele frequencies were calculated based on female samples only.

Sample QC: Samples with overall call rate < 95% were excluded. X-chromosome heterozygosity rate was used to determine sex. Samples with ambiguous sex or with discrepant sex between reported phenotypic and genomic sex or female samples with a call rate < 95% on the X chromosome were removed from the analysis.

While we allowed for known familial relatedness using a pre-computed kinship matrix, cryptic relatedness for each sample was evaluated using an identity-by-descent (IBD) method on an LD-pruned set of SNPs, and samples that were duplicates or of unknown relatedness were removed. Control datasets were then merged. To ensure that the merged controls did not exhibit population stratification effects, control-control GWASs were performed between each subset of controls, by coding one subset as cases and one as controls, and Q-Q plots were drawn. SNPs showing any significant association and SNPs in regions of extended linkage disequilibrium were removed. Cases and controls were then merged and principal components were computed for all cases and controls with reference samples of known European ancestry (1000G British, CEU and Finland and Italian participants). Individuals causing population stratification and mismatched cases-controls in the merged dataset were removed. Principal components (PC) analysis was conducted using SVS package, which incorporates EIGENSTRAT software[2] based on a pruned set of autosomal SNPs. Participants with PC1 or PC2 values > 4 standard deviations from the known European ancestry group were excluded. The plots for the first principal components were drawn to visualize the genetic variance among the individuals in the merged datasets **(Figure S1).** We finally merged samples from discovery, replication and all control cohorts resulting in 337,204 overlapping SNPs. The reduction in number of overlapping SNPs occurred particularly upon merging of the discovery, replication and eMERGE datasets to the other controls.

Imputation:

Cases and controls were combined into a single dataset for imputation**.**

Pre-imputation QC and pre-phasing: Prior to genotype imputation, several quality control measures were utilized to ensure that the genotyped data were compatible with the reference data set (European phase I integrated variant set release (v3) in NCBI build 37 (hg19) coordinates). First, SNP names and physical locations were updated to NCBI Build 37. Next, Strand orientation was assessed using SHAPEIT[3,4] and alleles were flipped when needed to match the alignment of the 1000G European data. SNPs not in 1000G reference data were excluded. Strand ambiguous genotyped SNPs (for example, A/T or C/G) were dropped from the input genotypes, particularly because they are under-represented on Illumina arrays. Lastly, to produce estimated haplotypes, each chromosome of the correctly aligned GWAS dataset was phased in a single run using SHAPEIT.[3,4]

Imputation: Using the recommended settings, including an effective population size of 20,000, imputation of genotypes was conducted using the IMPUTE2 software program (version 2)[5] and haplotypes from all 379 European individuals in the 1000 Genomes March 2012 Data Release as a reference dataset. To facilitate parallel computation, imputation was run in 1Mb runs. Reference panel SNPs with a European minor allele frequency < 0.001 were not imputed. 14,882,799 SNPs were successfully imputed.

Post-imputation QC: Following imputation, quality score metrics of imputed SNPs were examined. SNPs were excluded for having an IMPUTE2 info score < 0.3 or MAF < 0.01. Mono or multi-allelic variants were also removed. For the purpose of this study, imputed indels and structural variants were excluded from downstream analysis. This resulted in 6,573,381 imputed SNPs that were used for the GWAS.

B. SUPPLEMENTARY FIGURES AND LEGENDS

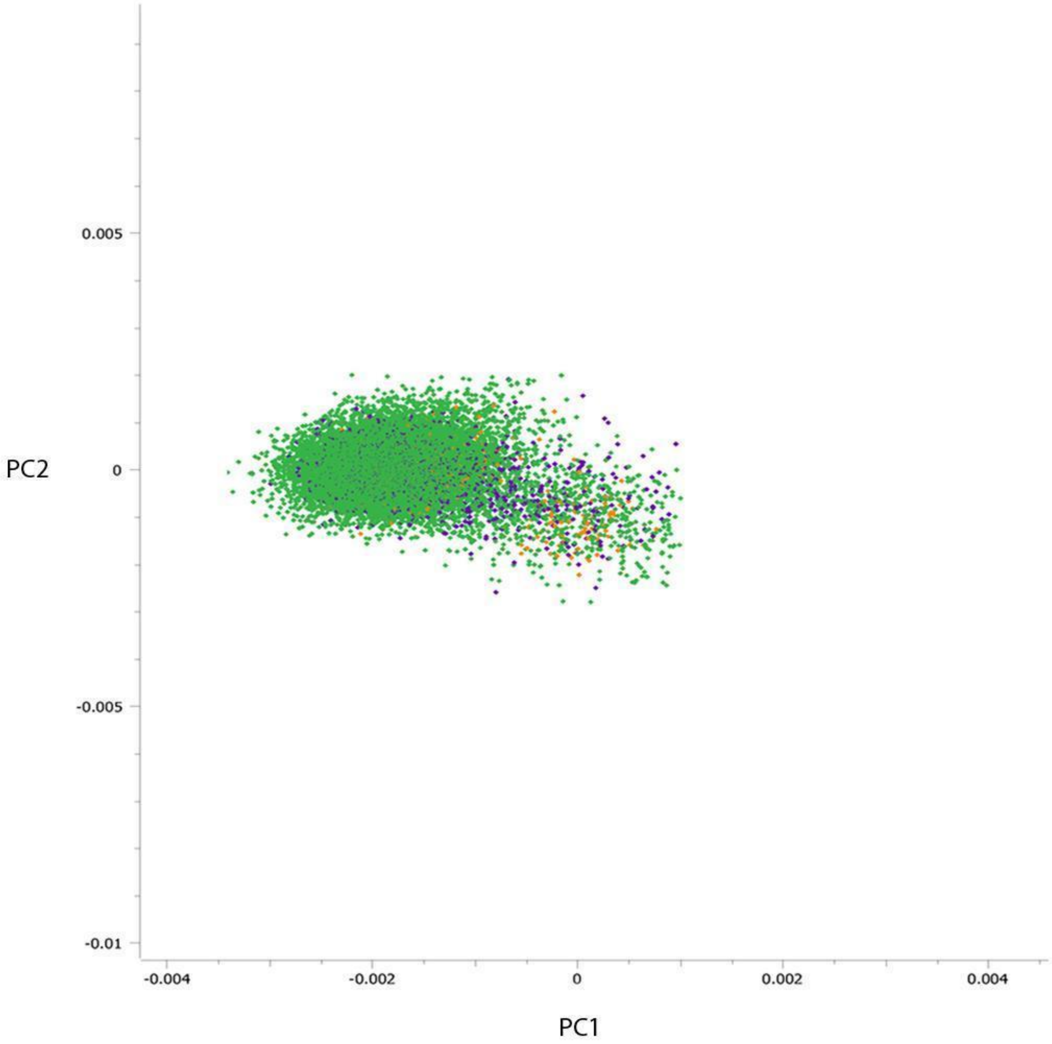

Figure S1: Principal components analysis from all SNPs in the GWAS data set.

Scatter plot of cases and controls positions on the first two principal components axes (PC1 and PC2) compared to European ancestry reference samples (1000G British, CEU and Finland and Italian participants). Orange dots represent reference samples, purple dots represent cases, and blue dots represent controls. Cases or controls with PC1 or PC2 values > 4 standard deviations from the European ancestry group were excluded before the association tests (data shown are for the participants that passed the cutoff). PC =principal component.

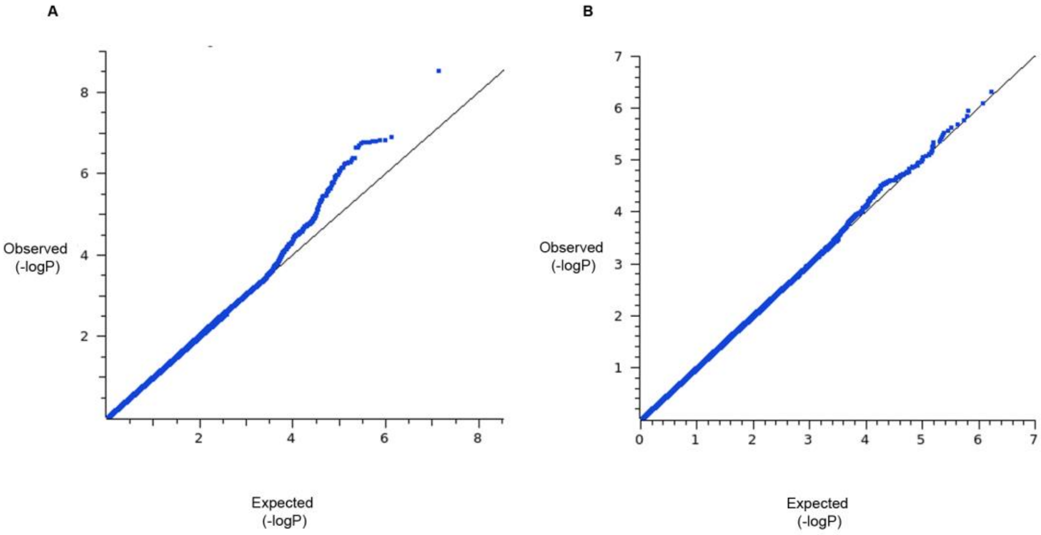

Figure S2: Quantile-quantile (Q-Q) plots of the discovery cohorts.

Q-Q plots created by SVS software for *P*-values obtained from the association analysis of the genotyped and imputed SNPs for **(A)** the 826 cases and 2991 controls in the non-accommodative esotropia discovery cohort, and **(B)** the 224 cases and 749 controls in the accommodative esotropia discovery cohort**.** We conducted genome-wide association testing using EMMAX (Efficient Mixed-Model Association eXpedited) with the first 3 principal components as covariates and a kinship matrix as a random effect. The x-axis shows the expected distribution of -log10(P-values) under the null hypothesis of no association. The y-axis show the observed -log10(P-values) in the association analysis. The curves are made of dots with each dot representing an observed -log10(P-values) calculated for the SNP. The default lines show where x = y.

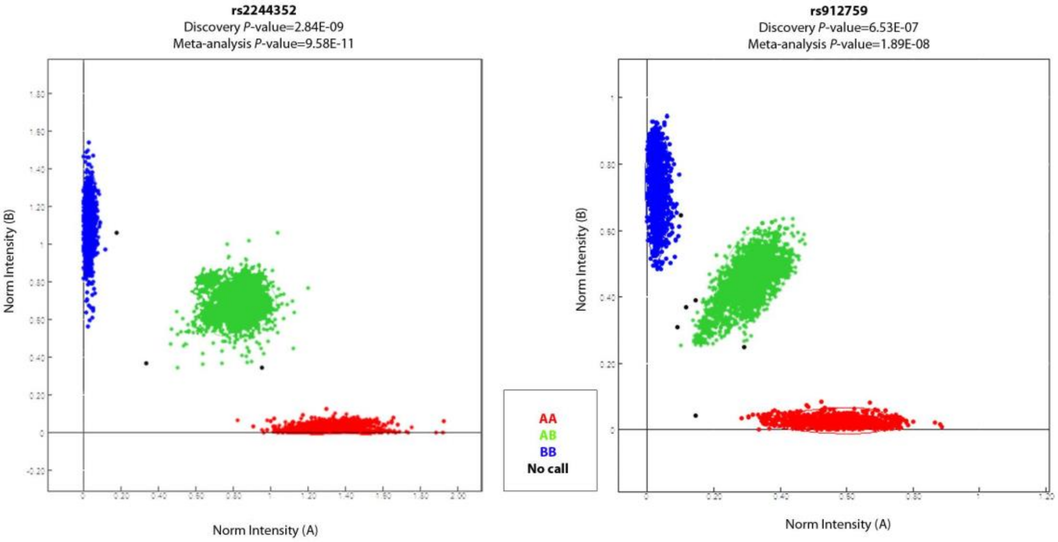

Figure S3: Cluster plots for SNPs rs2244352 and rs912759.

Cluster plots are shown for the most significantly associated SNP in the non-accommodative esotropia study (rs2244352, left) and in the accommodative esotropia cohort (rs912759, right) for all samples that passed quality control. The SNP genotypes were assigned based on cluster formation in scatter plots of normalized alleles A and B intensities. Each circle represents one individual's genotype. Red and blue clouds indicate homozygous genotypes for the SNP (AA, BB respectively), green cloud indicates heterozygous genotypes for the SNP (AB), and black dots indicate individuals with no SNP call.

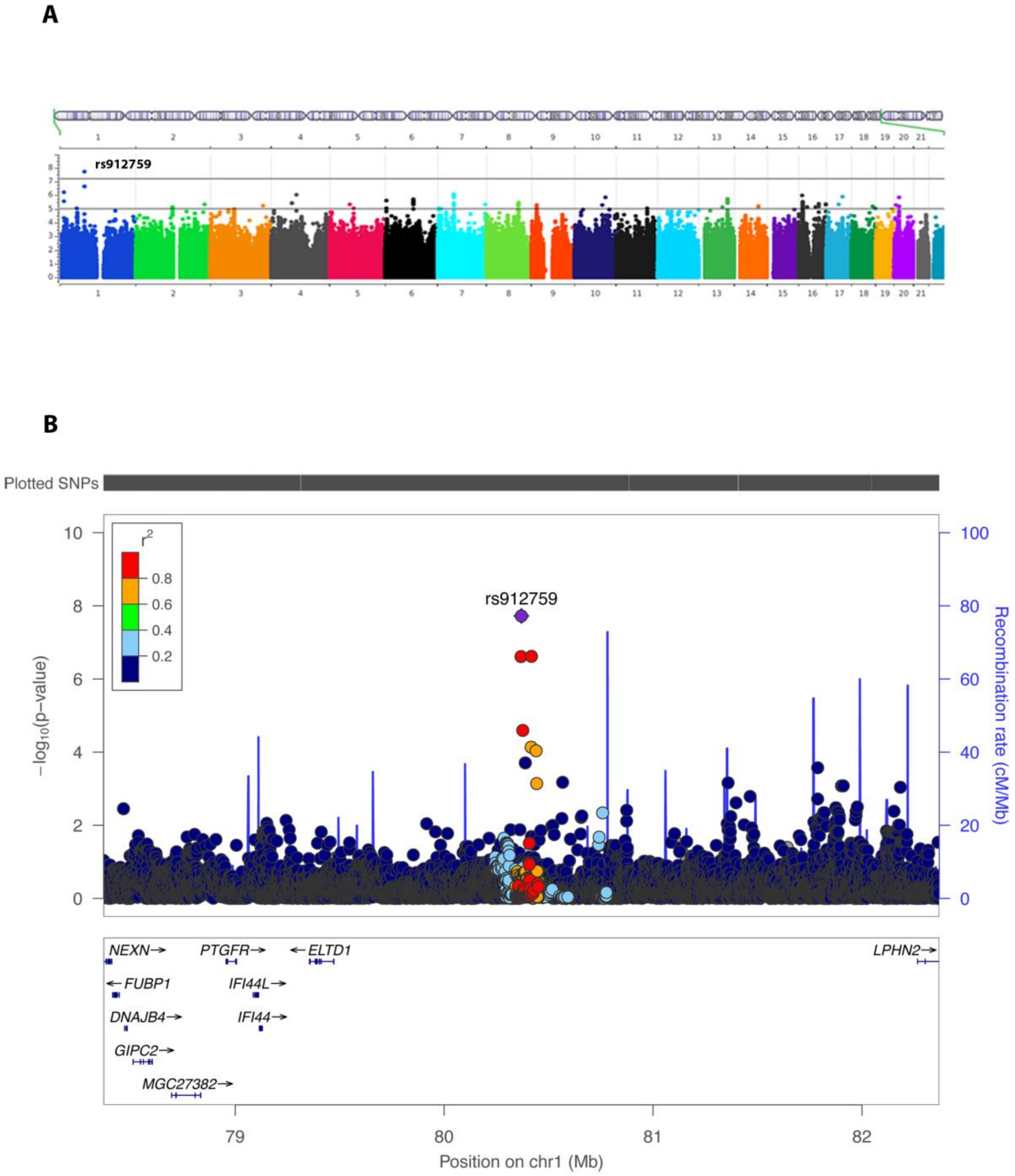

Figure S4: Meta-analysis results of the accommodative esotropia cohort.

(A) Manhattan plot of genome-wide fixed-effect meta-analysis results from the discovery (224 cases and 749 controls) and replication (66 cases and 264 controls) accommodative esotropia cohorts. The SNP rs912759 on chromosome 1p31.1 had a $P = 1.89 \times 10^{-08}$. Chromosomes are represented by alternating colors and labeled on the x-axis. The y-axis represents the –log10 (*P*-values). The upper horizontal line indicates the threshold for genome-wide significance ($P < 5 \times 10^{-8}$) and the lower horizontal line indicates the threshold for suggestive association ($P < 1 \times 10^{-5}$).

(B) SNP rs912759 regional association plot of the genome-wide meta-analysis of the discovery and replication accommodative esotropia cohorts. Rs912759 is shown as a solid purple diamond. The x-axis shows genomic location of SNPs on the chromosome 1p31.1 region, NCBI Build 37, together with the orientation of nearby genes. The y-axis is the −log10 (*P*-value) computed for the displayed SNPs. The color scheme indicates linkage disequilibrium between rs912759 and other SNPs in the region using the r2 value calculated from the 1000 genomes project. Note that rs912759 falls in a gene desert and is separated by ~ 0.9Mb from the nearest telomeric gene (*ELTD1*) and ~1.9 Mb from the nearest centromeric gene (*LPHN2*).

C. SUPPLEMENTARY TABLES

Table S1: Numbers and origin of cases for discovery and replication and control cohorts.

Cases			
	Discovery	**Replication**	
	Origin		
Phenotype	US	UK	Australia
Non-accommodative esotropia			
Esotropia	464	44	448
Infantile Esotropia	164	7	167
Intermittent Esotropia	173	4	12
Acquired Esotropia	11	(-)	1
Esophoria	14	3	3
Accommodative Esotropia	224	36	30
Controls			
Study	Case (included)	Control (included)	Ethnicity
NEI Age-Related Eye Disease Study (AREDS) Genetic Variation in Refractive Error Substudy*	(-)	1877 (1707)	100% Caucasian
eMERGE Geisinger eGenomic Medicine (GeM) MyCode Project Controls	(-)	1264 (1127)	100% Caucasian
Genome-Wide Association Study of Fuchs' Endothelial Corneal Dystrophy (FECD)	3747 (1451)		>99% White
Health and Retirement Study (HRS)	112595 (9287)	(-)	83% White

Table S1: Numbers of cases for discovery and replication broken by phenotype and controls derived from the database of Genotypes and Phenotypes (dbGaP). Numbers in between parenthesis indicate samples that were included in association testing after excluding samples failing quality control, those of non-white ethnicity, or duplicates. *Mostly orthotropic (personal communication). Abbreviations as follows: US: United States; UK: United Kingdom.

Table S2: Analysis results for top SNPs in the non-accommodative esotropia discovery cohort and the matching replication results.

Marker	Chromosome	Position	Minor Allele (Risk Allele)	Major Allele	Gene	P-Value	OR	Allele Freq. (Cases / Controls)	P-Value (Replication)	Odds Ratio (Replication)	Allele Freq. (Replication Cases / Controls)	Replication in same direction
rs12035677	1	232526955	A	G	(-)	2.37E-06	1.56	0.08/0.05	0.36	0.91	0.05/0.06	N
rs748423	2	52571595	A	G	LOC730100	8.26E-06	0.73	0.28/0.35	0.10	0.91	0.33/0.35	Y
rs80238534	2	52620055	G	C	LOC730100	5.92E-06	0.73	0.28/0.35	0.18	0.92	0.33/0.35	Y
rs12468960	2	52623680	A	G	LOC730100	8.47E-06	0.73	0.27/0.34	0.18	0.92	0.32/0.34	Y
rs4971596	2	52624594	A	G	LOC730100	7.31E-06	0.73	0.28/0.35	0.16	0.92	0.33/0.35	Y
rs4971815	2	52624780	G	A	LOC730100	9.83E-06	0.74	0.28/0.35	0.15	0.91	0.33/0.35	Y
rs2276695	2	118814868	T	C	LOC102723413	3.66E-06	1.29	0.41/0.35	0.20	1.07	0.37/0.36	Y
rs2228946	7	116918085	T	C	WNT2	3.30E-06	0.70	0.18/0.24	0.32	1.11	0.23/0.21	N
rs10503319	8	5518699	A	G	(-)	4.50E-06	1.48	0.13/0.09	0.50	1.08	0.11/0.10	Y
rs58555057	8	6002099	G	A	(-)	4.09E-06	0.64	0.07/0.11	0.66	0.98	0.14/0.12	N
rs918924	8	6002470	A	G	(-)	6.84E-06	0.67	0.09/0.13	0.75	0.98	0.11/0.11	Y
rs11136975	8	6006443	G	A	(-)	7.26E-06	0.65	0.08/0.12	0.36	0.93	0.10/0.11	Y
rs12678986	8	6009805	C	G	(-)	5.41E-06	0.66	0.08/0.13	0.40	0.93	0.11/0.11	Y
rs76426181	8	6014282	T	C	(-)	6.41E-06	0.64	0.08/0.12	0.30	0.92	0.10/0.11	Y
rs7948560	11	79169447	C	G	(-)	7.54E-06	0.45	0.01/0.03	0.16	1.22	0.03/0.03	Y
rs10790166	11	116779499	G	A	SIK3	3.02E-06	1.39	0.3/0.24	0.62	0.99	0.23/0.23	Y
rs7123336	11	116782819	C	T	SIK3	1.63E-06	1.41	0.29/0.23	0.82	1.01	0.22/0.22	Y
rs983567	11	116783600	C	T	SIK3	1.63E-06	1.41	0.29/0.23	0.82	1.01	0.22/0.22	Y
rs7107702	11	116804144	C	T	SIK3	5.73E-07	1.44	0.28/0.21	0.82	1.05	0.21/0.20	Y
rs2513094	11	116806412	C	T	SIK3	5.02E-07	1.42	0.3/0.23	0.93	1.03	0.22/0.22	Y
rs61907604	11	116818407	G	A	SIK3	7.97E-07	1.43	0.28/0.21	0.69	1.06	0.21/0.20	Y
rs112704540	11	116818527	G	A	SIK3	7.97E-07	1.43	0.28/0.21	0.69	1.06	0.21/0.20	Y
rs6589580	11	116819873	A	G	SIK3	1.20E-06	1.43	0.30/0.23	0.62	1.09	0.26/0.21	Y
rs1940626	11	116828121	C	T	SIK3	6.94E-07	1.43	0.28/0.21	0.69	1.06	0.21/0.20	Y
rs682048	11	116828320	G	T	SIK3	5.06E-07	1.42	0.30/0.23	0.94	1.04	0.22/0.22	Y
rs1815789	11	116834953	C	T	SIK3	6.94E-07	1.43	0.28/0.21	0.74	1.06	0.21/0.20	Y
rs1815788	11	116834971	C	T	SIK3	6.94E-07	1.43	0.28/0.21	0.74	1.06	0.21/0.20	Y
rs2513097	11	116836212	G	A	SIK3	5.14E-07	1.41	0.29/0.23	0.99	1.03	0.22/0.22	Y
rs1241655	11	116837808	T	G	SIK3	5.88E-07	1.41	0.29/0.23	0.99	1.03	0.22/0.22	Y
rs7941927	11	116838904	G	A	SIK3	4.62E-07	1.44	0.28/0.21	0.69	1.06	0.21/0.20	Y
rs509171	11	116848857	T	C	SIK3	1.23E-07	1.43	0.30/0.23	0.88	1.04	0.22/0.22	Y
rs4938321	11	116852507	T	C	SIK3	1.43E-07	1.45	0.28/0.21	0.63	1.07	0.21/0.20	Y
rs7939934	11	116861268	T	A	SIK3	5.29E-07	1.45	0.28/0.22	0.71	1.06	0.21/0.21	Y
rs6589583	11	116863766	T	C	SIK3	1.58E-07	1.43	0.30/0.23	0.88	1.07	0.22/0.22	Y
rs10892054	11	116868221	T	C	SIK3	1.66E-07	1.45	0.28/0.21	0.61	1.07	0.21/0.20	Y
rs10892055	11	116868371	A	G	SIK3	1.66E-07	1.45	0.28/0.21	0.61	1.07	0.21/0.20	Y
rs7930264	11	116870766	A	G	SIK3	1.58E-07	1.43	0.30/0.23	0.88	1.04	0.22/0.22	Y

rs6589587	11	116875338	G	T	SIK3	1.66E-07	1.45	0.28/0.21	0.61	1.07	0.21/0.20	Y
rs7931398	11	116879676	C	T	SIK3	5.83E-06	1.36	0.31/0.25	0.82	1.05	0.25/0.24	Y
rs7119185	11	116886096	T	C	SIK3	1.48E-07	1.45	0.28/0.21	0.59	1.07	0.21/0.20	Y
rs7128772	11	116889411	A	T	SIK3	1.10E-06	1.40	0.30/0.23	0.96	1.03	0.22/0.21	Y
rs10466590	11	116894413	G	C	SIK3	3.95E-07	1.42	0.30/0.23	0.97	1.04	0.22/0.22	Y
rs11216241	11	116899249	C	A	SIK3	1.67E-07	1.43	0.30/0.23	0.88	1.04	0.22/0.26	Y
rs11600552	11	116900947	C	T	SIK3	3.95E-07	1.42	0.30/0.23	0.97	1.03	0.22/0.22	Y
rs4548653	11	116903316	A	G	SIK3	3.97E-07	1.44	0.28/0.21	0.70	1.07	0.21/0.20	Y
rs4938327	11	116906728	C	T	SIK3	5.44E-07	1.44	0.28/0.21	0.70	1.07	0.21/0.20	Y
rs3181	11	116907043	A	G	SIK3	2.29E-07	1.45	0.28/0.21	0.61	1.07	0.21/0.20	Y
rs721783	11	116907449	T	C	SIK3	2.29E-07	1.45	0.28/0.21	0.61	1.07	0.21/0.20	Y
rs7118591	11	116908457	A	C	SIK3	5.44E-07	1.44	0.28/0.21	0.70	1.07	0.21/0.20	Y
rs11216244	11	116912730	T	C	SIK3	7.34E-07	1.42	0.30/0.23	0.81	1.05	0.22/0.21	Y
rs11216245	11	116913202	T	C	SIK3	8.15E-07	1.41	0.30/0.23	0.83	1.05	0.22/0.22	Y
rs12279066	11	116913909	G	C	SIK3	2.08E-06	1.42	0.29/0.22	0.76	1.05	0.22/0.21	Y
rs10892066	11	116920927	T	C	SIK3	2.27E-06	1.40	0.30/0.23	0.98	1.03	0.22/0.22	Y
rs3886960	11	116924990	T	G	SIK3	2.27E-06	1.40	0.30/0.23	0.99	1.03	0.22/0.22	Y
rs723955	11	116925042	A	G	SIK3	2.27E-06	1.40	0.30/0.23	0.99	1.03	0.22/0.22	Y
rs7108912	11	116925996	A	G	SIK3	2.48E-06	1.40	0.30/0.23	0.99	1.03	0.22/0.22	Y
rs7124872	11	116927951	G	A	SIK3	2.48E-06	1.40	0.30/0.23	0.99	1.03	0.22/0.22	Y
rs7124996	11	116928006	T	C	SIK3	2.21E-06	1.40	0.29/0.23	0.99	1.03	0.22/0.22	Y
rs4938329	11	116928112	T	C	SIK3	2.48E-06	1.40	0.29/0.23	0.99	1.03	0.22/0.22	Y
rs4938330	11	116928514	G	C	SIK3	1.96E-07	1.47	0.26/0.2	0.99	1.03	0.19/0.19	Y
rs11216255	11	116929995	G	A	SIK3	1.53E-06	1.41	0.30/0.23	0.97	1.04	0.22/0.22	Y
rs7101763	11	116941985	T	G	SIK3	1.06E-06	1.43	0.28/0.21	0.97	1.05	0.21/0.20	Y
rs7109649	11	116943544	T	C	SIK3	1.55E-06	1.42	0.30/0.23	0.98	1.04	0.22/0.22	Y
rs1531706	11	116943952	A	C	SIK3	3.41E-06	1.41	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs7935913	11	116944348	A	G	SIK3	3.41E-06	1.41	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs7935834	11	116944437	G	C	SIK3	3.41E-06	1.41	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs1531707	11	116944712	A	G	SIK3	3.41E-06	1.41	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs4620758	11	116945718	A	G	SIK3	9.27E-07	1.43	0.28/0.21	0.97	1.05	0.22/0.22	Y
rs12274388	11	116946238	T	C	SIK3	3.41E-06	1.41	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs7130213	11	116946652	A	C	SIK3	1.04E-06	1.44	0.28/0.21	0.94	1.05	0.22/0.20	Y
rs7484045	11	116946890	T	C	SIK3	3.41E-06	1.41	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs10082609	11	116949074	T	C	SIK3	3.41E-06	1.41	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs11216266	11	116950150	C	T	SIK3	3.41E-06	1.41	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs7106662	11	116951385	C	T	SIK3	3.41E-06	1.41	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs1871756	11	116953645	A	G	SIK3	1.06E-06	1.43	0.28/0.21	0.97	1.04	0.21/0.20	Y
rs10892071	11	116954565	T	C	SIK3	4.09E-06	1.41	0.29/0.23	0.98	1.04	0.22/0.21	Y
rs61903416	11	116955049	C	T	SIK3	3.41E-06	1.41	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs12274465	11	116957189	T	C	SIK3	4.37E-06	1.40	0.29/0.23	0.92	1.03	0.22/0.22	Y
rs7950093	11	116963519	T	G	SIK3	1.90E-06	1.41	0.29/0.23	0.83	1.03	0.22/0.22	Y
rs12269901	11	116973929	C	G	(-)	1.53E-06	1.35	0.34/0.28	0.85	1.06	0.27/0.26	Y
rs4388921	11	116976778	C	T	(-)	1.02E-06	1.44	0.28/0.22	0.76	1.07	0.21/0.20	Y
rs12271169	11	116980021	G	C	(-)	2.39E-06	1.42	0.27/0.21	0.98	1.05	0.21/0.20	Y
rs7112111	11	116980858	G	T	(-)	2.70E-06	1.41	0.27/0.21	0.88	1.06	0.21/0.20	Y
rs7104023	11	116982602	T	A	(-)	2.98E-06	1.41	0.27/0.21	0.72	1.07	0.21/0.20	Y
rs10892075	11	116982821	T	C	(-)	1.75E-07	1.49	0.24/0.18	0.63	1.08	0.18/0.17	Y

rs111765459	11	117083373	C	T	PCSK7	1.70E-06	1.40	0.25/.19	0.46	1.06	0.21/0.19	Y
rs4938358	11	117084091	T	C	PCSK7	1.20E-06	1.40	0.25/.19	0.42	1.06	0.21/0.19	Y
rs12418744	11	117084537	A	G	PCSK7	1.36E-06	1.40	0.25/.19	0.42	1.06	0.21/0.19	Y
rs28704046	11	117086058	T	C	PCSK7	2.99E-06	1.39	0.25/.19	0.34	1.07	0.21/0.19	Y
rs2238006	11	117087792	C	A	PCSK7	5.45E-06	1.39	0.25/0.2	0.41	1.06	0.21/0.20	Y
rs2239012	11	117088362	G	A	PCSK7	4.08E-06	1.38	0.25/0.19	0.34	1.07	0.21/0.19	N
rs2239011	11	117088994	G	A	PCSK7	4.60E-06	1.38	0.25/0.19	0.31	1.07	0.20/0.22	Y
rs2239010	11	117089006	C	G	PCSK7	4.60E-06	1.38	0.25/0.19	0.34	1.07	0.21/0.19	Y
rs3882895	11	117090545	C	T	PCSK7	4.60E-06	1.38	0.25/0.19	0.34	1.07	0.21/0.19	Y
rs3882897	11	117091227	A	G	PCSK7	8.61E-06	1.38	0.25/0.19	0.34	1.07	0.21/0.19	Y
rs4936368	11	117093486	T	C	PCSK7	7.12E-06	1.38	0.25/0.19	0.34	1.07	0.21/0.19	Y
rs4938359	11	117093560	G	A	PCSK7	7.12E-06	1.38	0.25/0.19	0.34	1.07	0.21/0.19	Y
rs3830008	11	117093764	C	A	PCSK7	5.49E-06	1.37	0.25/0.2	0.24	0.91	0.20/0.22	Y
rs74579438	13	68967325	G	A	(-)	4.77E-06	1.77	0.07/0.04	0.52	1.22	0.06/0.05	Y
rs6562524	13	68978085	G	A	(-)	4.77E-06	1.77	0.07/0.04	0.52	1.21	0.06/0.05	Y
rs9541348	13	68984434	G	C	(-)	4.77E-06	1.77	0.07/0.04	0.52	1.22	0.06/0.05	Y
rs12329628	20	60168573	G	A	CDH4	9.50E-06	2.36	0.04/0.02	0.94	0.98	0.01/0.02	N
rs2244352	21	40757973	T	G	WRB	2.84E-09	1.41	0.39/0.31	0.01	1.23	0.37/0.32	Y
rs2837043	21	40851556	T	G	SH3BGR	3.36E-06	1.28	0.52/0.46	0.06	1.14	0.48/0.45	Y

Table S2. Analysis results for top SNPs with $P \leq 1 \times 10^{-05}$ in the non-accommodative esotropia discovery cohort and the matching results from the replication cohort. Abbreviations are as follows: OR, Odds Ratio; Freq, frequency; Y, yes; N, no.

Table S3: Analysis results for the accommodative esotropia discovery and replication cohorts and their meta-analysis:

Marker	Chromosome	Position	Minor Allele (Risk Allele)	Major Allele	Gene	P-Value	OR	MAF Cases/Controls (Discovery)	P-Value (Replication)	OR (Replication)	MAF Cases/Controls (Replication)	Same direction	Overall P-Value	RE Analysis P-Value
rs10874098	1	80367960	C	A	(-)	4.57E-06	0.62	0.39/0.51	0.02	0.62	0.38/0.50	Y	2.43E-07	2.43E-07
rs912759	1	80369902	T	C	(-)	6.53E-07	0.59	0.37/0.50	0.01	0.59	0.37/0.50	Y	1.89E-08	1.89E-08
rs1325201	1	80417950	G	T	(-)	9.17E-07	0.61	0.41/0.53	0.06	1.37	0.57/0.49	N	2.40E-07	2.85E-05
rs10165003	2	2488285	A	G	LOC105373389	1.63E-06	3.20	0.08/0.03	0.83	1.27	0.06/0.05	Y	4.98E-05	2.36E-01
rs13422123	2	2497967	A	T	LOC105373389	8.53E-06	3.00	0.07/0.03	0.83	1.27	0.06/0.05	Y	1.90E-04	2.33E-01
rs57739605	2	64341674	C	T	PELI1	4.44E-06	3.22	0.07/0.03	0.96	0.64	0.03/0.04	N	1.32E-04	3.04E-01
rs148499834	2	166993731	T	C	LOC101929680	3.94E-06	3.23	0.07/0.02	0.44	1.39	0.04/0.03	Y	1.56E-05	6.74E-02
rs72899664	2	188795932	T	C	(-)	7.99E-06	1.79	0.22/0.14	0.24	0.64	0.10/0.14	N	1.43E-03	6.51E-01
rs72899666	2	188797372	T	C	(-)	7.99E-06	1.77	0.22/0.14	0.24	0.63	0.10/0.14	N	1.43E-03	6.51E-01
rs12373649	2	188799373	C	G	(-)	4.73E-06	1.81	0.22/0.13	0.30	0.63	0.10/0.14	N	8.00E-04	6.08E-01
rs12373745	2	188799624	C	T	(-)	2.95E-06	1.90	0.23/0.14	0.29	0.65	0.10/0.14	N	6.28E-04	6.10E-01
rs112142841	3	32206837	T	G	GPD1L	1.44E-06	4.70	0.05/0.02	0.99	0.57	0.01/0.02	N	1.80E-05	2.66E-01
rs4690624	4	179220327	T	G	(-)	3.94E-06	0.61	0.32/0.44	0.69	0.91	0.41/0.44	Y	4.68E-05	1.71E-01
rs7687222	4	179222898	A	G	(-)	5.61E-06	0.61	0.32/0.43	0.69	0.91	0.41/0.44	Y	6.07E-05	1.68E-01
rs56164674	4	179225080	T	C	(-)	9.71E-06	0.63	0.33/0.44	0.65	0.89	0.41/0.44	Y	7.98E-05	1.47E-01
rs2890006	4	179225462	T	C	(-)	5.19E-06	0.62	0.32/0.44	0.65	0.91	0.41/0.44	Y	5.02E-05	1.53E-01
rs62341375	4	179226092	G	A	(-)	8.10E-06	0.62	0.32/0.43	0.65	0.91	0.41/0.44	Y	6.96E-05	1.48E-01
rs9992600	4	179226351	T	C	(-)	5.19E-06	0.63	0.32/0.44	0.65	0.91	0.41/0.44	Y	5.02E-05	1.53E-01
rs1574851	4	179226719	T	C	(-)	9.71E-06	0.62	0.33/0.44	0.65	0.89	0.41/0.44	Y	7.98E-05	1.47E-01
rs1574850	4	179226841	A	G	(-)	6.79E-06	0.62	0.33/0.44	0.65	0.89	0.41/0.44	Y	6.07E-05	1.50E-01
rs6552292	4	179226871	A	G	(-)	5.19E-06	0.62	0.32/0.44	0.65	0.91	0.41/0.44	Y	5.02E-05	1.53E-01
rs1510639	4	179227356	G	A	(-)	5.17E-06	0.62	0.32/0.44	0.65	0.91	0.41/0.44	Y	4.94E-05	1.52E-01
rs1567475	4	179227598	T	C	(-)	8.10E-06	0.62	0.32/0.43	0.65	0.91	0.41/0.44	Y	6.96E-05	1.48E-01
rs6830610	4	179227841	G	A	(-)	8.92E-06	0.62	0.33/0.44	0.65	0.89	0.41/0.44	Y	7.50E-05	1.47E-01
rs1567474	4	179227880	A	G	(-)	5.19E-06	0.62	0.32/0.44	0.77	0.91	0.41/0.44	Y	7.30E-05	1.99E-01
rs2666089	4	179229036	A	C	(-)	5.19E-06	0.62	0.32/0.44	0.65	0.91	0.41/0.44	Y	5.02E-05	1.53E-01
rs1912518	4	179230381	G	T	(-)	9.71E-06	0.63	0.33/0.44	0.65	0.89	0.41/0.44	Y	7.98E-05	1.47E-01
rs1510638	4	179232092	C	A	(-)	9.71E-06	0.63	0.33/0.44	0.65	0.89	0.41/0.44	Y	7.98E-05	1.47E-01
rs6828485	4	179232789	A	G	(-)	5.17E-06	0.62	0.32/0.44	0.65	0.91	0.41/0.44	Y	4.94E-05	1.52E-01
rs10064966	5	9672684	T	C	LOC285692	9.11E-06	1.91	0.24/0.15	0.33	0.91	0.15/0.16	N	1.59E-03	5.88E-01
rs12109904	5	9681798	T	C	LOC285692	1.41E-06	1.97	0.25/0.15	0.33	0.92	0.15/0.16	N	4.48E-04	5.69E-01
rs10039101	5	9689026	T	G	LOC285692	6.13E-06	1.95	0.23/0.13	0.12	0.72	0.11/0.14	N	2.31E-03	7.45E-01
rs1482671	5	44362538	G	A	FGF10	7.99E-06	0.61	0.26/0.37	0.91	0.90	0.36/0.38	Y	1.39E-04	2.48E-01
rs1482672	5	44362769	C	T	FGF10	7.99E-06	0.61	0.26/0.37	0.91	0.90	0.36/0.38	Y	1.39E-04	2.48E-01
rs2121875	5	44365545	C	A	FGF10	9.55E-06	0.60	0.26/0.37	0.91	0.90	0.36/0.38	Y	1.60E-04	2.47E-01
rs6859730	5	44367221	A	T	FGF10	6.33E-06	0.60	0.26/0.37	0.91	0.90	0.36/0.38	Y	1.18E-04	2.49E-01
rs1482673	5	44368123	G	A	FGF10	6.98E-06	0.60	0.26/0.37	0.91	0.90	0.36/0.38	Y	1.28E-04	2.49E-01
rs900379	5	44369656	C	T	FGF10	7.80E-06	0.61	0.26/0.37	0.91	0.90	0.36/0.38	Y	1.39E-04	2.49E-01

rs4737265	8	69888286	T	C	LINC01592	2.52E-06	1.93	0.25/0.15	0.66	0.79	0.13/0.16	N	1.64E-04	4.28E-01
rs1360136	9	22358389	G	A	(-)	4.19E-06	0.61	0.38/0.50	0.75	0.99	0.49/0.49	Y	4.56E-05	1.81E-01
rs12782324	10	6320019	A	T	(-)	3.42E-06	2.11	0.19/0.10	0.92	0.91	0.13/0.14	N	1.73E-04	3.26E-01
rs1871549	12	67044058	T	C	GRIP1	3.02E-06	0.59	0.33/0.46	0.68	0.91	0.42/0.44	Y	2.82E-05	1.55E-01
rs1904539	12	67045248	A	G	GRIP1	3.98E-06	0.60	0.33/0.45	0.55	0.88	0.41/0.44	Y	2.25E-05	1.03E-01
rs12827280	12	67045424	T	C	GRIP1	4.40E-06	0.60	0.33/0.45	0.55	0.88	0.41/0.44	Y	2.43E-05	1.02E-01
rs9600887	13	78006780	T	C	(-)	3.06E-06	1.64	0.41/0.30	0.32	1.08	0.31/0.29	Y	7.35E-06	3.24E-02
rs72722114	14	69752668	A	C	GALNT16	9.21E-06	0.51	0.12/0.22	0.80	0.84	0.21/0.24	Y	1.42E-04	2.13E-01
rs72722119	14	69752966	A	G	GALNT16	5.00E-06	0.49	0.12/0.22	0.87	0.85	0.21/0.24	Y	1.11E-04	2.43E-01
rs9920512	15	24112081	C	A	(-)	6.64E-06	2.72	0.10/0.04	0.79	0.70	0.05/0.07	Y	9.21E-05	2.05E-01
rs28373973	15	24118536	A	G	(-)	5.42E-06	2.66	0.11/0.05	0.96	0.60	0.05/0.08	N	1.70E-04	3.04E-01
rs111980424	16	66095254	T	G	(-)	7.57E-06	2.25	0.13/0.06	0.10	1.56	0.11/0.08	Y	4.19E-06	1.22E-03

Table S3: Analysis results for the accommodative esotropia discovery and replication cohorts and their meta-analysis (results shown for SNPs with $P \leq 1 \times 10^{-05}$ in the discovery cohort). SNPs rs10874098 and rs912759 had $P < 0.05$ in the replication cohort. Abbreviations as follows: Chr, chromosome; OR, odds ratio; MAF, minor allele frequency; RE, random effect; Y, yes; N, no.

Table S4: Meta-analysis results at rs2244352 and rs912759 in the non-accommodative and accommodative ET cohorts.

	Non-accommodative ET					**Accommodative ET**				
	Fixed Effect OR	**Random Effect OR**	**Fixed Effect P-value**	**Random Effect P-value**	I^2	**Fixed Effect OR**	**Random Effect OR**	**Fixed Effect P-value**	**Random Effect P-value**	I^2
rs2244352	1.33	1.32	9.58 x 10^{-11}	1.09 x 10^{-9}	0.1	1.18	1.18	0.24	0.24	0
rs912759	0.99	0.99	0.82	0.82	0	0.59	0.59	1.89 x 10^{-08}	1.89 x 10^{-08}	0

Table S4: Fixed and random effect meta-analysis results at rs2244352 and rs912759 together with the heterogeneity estimate (I^2). The results are shown for the non-accommodative and accommodative ET cohorts independently. Abbreviations as follows: ET, esotropia; OR, odds ratio.

Table S5: Analysis results for the amblyopia and hyperopia subgroups discovery and replication cohorts and their meta-analysis.

A (Amblyopia)										
Marker	**Chromosome**	**Position**	**P-value discovery**	**OR discovery**	**P-value replication**	**OR replication**	**Overall P-Value**	**RE Analysis P-Value**	I^2	**Risk allele in both cohorts**
rs72922085	1	67261620	6.91E-07	1.63	0.29	1.61	4.15E-07	4.15E-07	0.00	G
rs72671650	1	67265546	7.03E-06	1.60	0.24	1.66	3.40E-06	3.40E-06	0.00	G
rs10910937	1	181397224	8.57E-07	1.71	0.12	1.51	2.31E-07	2.31E-07	0.00	C
rs13434070	3	102424262	3.61E-06	1.75	0.19	1.60	1.39E-06	1.39E-06	0.00	C
rs116450688	6	32716127	7.82E-06	1.84	0.04	2.01	8.57E-07	8.57E-07	0.00	G
rs114299445	6	32719573	9.54E-06	1.83	0.06	1.94	1.39E-06	1.39E-06	0.00	A
rs116931912	6	80846547	5.35E-06	3.35	0.21	2.68	2.46E-06	2.46E-06	0.00	T
rs117563769	6	153541437	1.94E-06	1.89	0.48	0.74	1.84E-05	5.72E-01	0.80	G
rs75627919	6	153544473	1.25E-06	1.89	0.42	0.72	1.50E-05	6.21E-01	0.82	G
rs116211926	6	153546156	1.61E-06	1.88	0.53	0.78	1.35E-05	5.35E-01	0.78	A
rs76180129	6	153546383	1.25E-06	1.89	0.42	0.72	1.50E-05	6.21E-01	0.82	T
rs75896549	6	153550016	7.20E-06	1.94	0.65	0.80	4.58E-05	4.37E-01	0.74	C
rs9479561	6	153550147	5.65E-06	1.83	0.57	1.29	7.31E-06	7.31E-06	0.00	G
rs10965015	9	21473954	9.82E-06	1.37	0.94	0.97	2.28E-05	7.35E-02	0.42	G
rs10965026	9	21485849	4.20E-06	1.42	0.76	0.98	7.62E-06	9.21E-03	0.26	C
rs4978120	9	21486101	6.39E-06	1.41	0.70	1.00	9.98E-06	4.54E-04	0.10	G
rs149407265	9	120745946	2.60E-06	2.66	0.53	1.31	4.00E-06	2.55E-03	0.26	G
rs117507863	9	120747426	2.60E-06	2.66	0.53	1.31	4.00E-06	2.55E-03	0.26	A
rs111486731	10	12482370	1.78E-06	2.68	0.71	1.11	5.49E-06	7.31E-02	0.59	A
rs192756710	10	19209449	7.45E-07	3.24	0.76	1.37	1.55E-06	2.71E-02	0.40	T
rs138421612	10	19213372	1.08E-06	3.16	0.76	1.37	2.16E-06	2.18E-02	0.36	A
rs141331490	10	19216293	3.03E-06	3.05	0.59	1.60	3.73E-06	3.73E-06	0.00	G
rs145426288	10	19219338	1.08E-06	3.17	0.76	1.37	2.16E-06	2.18E-02	0.36	A
rs182698619	10	19223193	1.08E-06	3.17	0.76	1.37	2.16E-06	2.18E-02	0.36	A
rs187902331	10	19223292	1.08E-06	3.17	0.76	1.37	2.16E-06	2.18E-02	0.36	C
rs183317537	10	19226179	7.55E-07	3.21	0.76	1.37	1.51E-06	2.17E-02	0.37	C
rs143658596	10	19226368	7.55E-07	3.21	0.76	1.37	1.51E-06	2.17E-02	0.37	C
rs144479357	10	19237692	7.55E-07	3.20	0.76	1.37	1.51E-06	2.17E-02	0.37	C
rs145822682	10	19242863	7.55E-07	3.20	0.76	1.37	1.51E-06	2.17E-02	0.37	G
rs141412907	10	19243115	7.55E-07	3.20	0.76	1.37	1.51E-06	2.17E-02	0.37	G
rs149020887	10	19246855	7.55E-07	3.20	0.76	1.37	1.51E-06	2.17E-02	0.37	G
rs141211643	10	19247480	7.55E-07	3.20	0.76	1.37	1.51E-06	2.17E-02	0.37	A
rs144292561	10	19248257	7.55E-07	3.20	0.76	1.37	1.51E-06	2.17E-02	0.37	A
rs144777393	10	19252106	1.48E-06	3.13	0.76	1.37	2.81E-06	1.42E-02	0.31	G
rs140364201	10	19253076	1.48E-06	3.13	0.76	1.37	2.81E-06	1.42E-02	0.31	A
rs144481463	10	19256188	1.48E-06	3.13	0.35	2.03	1.13E-06	1.13E-06	0.00	A
rs188992690	10	19262460	1.48E-06	3.13	0.35	2.03	1.13E-06	1.13E-06	0.00	T
rs148951068	10	19262756	1.48E-06	3.13	0.35	2.03	1.13E-06	1.13E-06	0.00	C
rs182167987	10	19278928	1.48E-06	3.13	0.35	2.03	1.13E-06	1.13E-06	0.00	A
rs181048259	10	19279583	1.48E-06	3.13	0.35	2.03	1.13E-06	1.13E-06	0.00	C
rs146205017	10	19288420	1.48E-06	3.13	0.35	2.03	1.13E-06	1.13E-06	0.00	G

rs148021190	10	19321086	4.84E-07	3.26	0.35	2.03	3.78E-07	3.78E-07	0.00	T
rs150579085	10	19321516	4.84E-07	3.26	0.35	2.03	3.78E-07	3.78E-07	0.00	C
rs138508566	10	19323165	4.84E-07	3.26	0.35	2.03	3.78E-07	3.78E-07	0.00	G
rs2422455	11	37051498	9.35E-06	1.41	0.12	0.61	1.82E-04	9.47E-01	0.88	A
rs333772	11	37052785	7.53E-06	1.42	0.11	0.60	1.73E-04	9.61E-01	0.88	A
rs2170311	15	78947611	8.15E-06	1.40	0.79	1.40	1.45E-05	6.83E-03	0.21	A
rs61745888	16	57993841	3.57E-07	3.08	0.19	0.00	7.45E-06	8.44E-01	0.87	T
rs76788887	16	57993947	1.60E-06	2.90	0.19	0.00	2.54E-05	8.66E-01	0.86	C
rs7249863	19	23730717	4.01E-06	1.50	0.90	1.02	9.17E-06	5.99E-02	0.42	C
rs2082472	19	23731649	3.83E-06	1.52	0.51	1.14	4.19E-06	4.19E-06	0.00	G
rs8109004	19	23732005	3.83E-06	1.52	0.51	1.14	4.19E-06	4.19E-06	0.00	A
rs12460990	19	23732710	8.61E-06	1.49	0.63	1.14	1.17E-05	1.17E-05	0.00	C
rs62123400	19	23733723	8.61E-06	1.49	0.63	1.14	1.17E-05	1.17E-05	0.00	A
rs62123401	19	23734886	8.61E-06	1.49	0.63	1.14	1.17E-05	1.17E-05	0.00	C
rs55979338	19	23735096	7.18E-06	1.50	0.51	1.14	7.60E-06	7.60E-06	0.00	C
rs62123403	19	23735277	5.65E-06	1.50	0.63	1.14	7.90E-06	7.90E-06	0.00	A
rs12462785	19	23735482	9.40E-06	1.50	0.63	1.14	1.27E-05	1.27E-05	0.00	C
rs12460521	19	23735678	7.86E-06	1.50	0.47	1.19	7.50E-06	7.50E-06	0.00	T
rs2886002	19	23735974	8.61E-06	1.49	0.63	1.14	1.17E-05	1.17E-05	0.00	T
rs12462246	19	23736660	8.34E-06	1.50	0.48	1.16	8.22E-06	8.22E-06	0.00	A
rs12462767	19	23737368	6.96E-06	1.50	0.63	1.14	9.60E-06	9.60E-06	0.00	C
rs12461367	19	23738428	6.96E-06	1.50	0.63	1.14	9.60E-06	9.60E-06	0.00	C
rs2195961	19	23739585	6.96E-06	1.50	0.63	1.14	9.60E-06	9.60E-06	0.00	T
rs62123405	19	23740586	5.09E-06	1.50	0.76	1.12	9.16E-06	8.20E-03	0.25	T
rs59390831	19	23742761	4.40E-06	1.51	0.76	1.12	7.99E-06	9.22E-03	0.26	G
rs2195960	19	23742841	4.82E-06	1.51	0.76	1.12	8.70E-06	8.59E-03	0.25	A
rs2217662	19	23743106	4.82E-06	1.51	0.76	1.12	8.70E-06	8.59E-03	0.25	T
rs62123408	19	23744120	8.51E-06	1.51	0.60	1.14	1.07E-05	1.07E-05	0.00	G
rs17000239	19	23744563	4.82E-06	1.51	0.76	1.12	8.70E-06	8.59E-03	0.25	A
rs35329492	19	23745170	4.82E-06	1.51	0.76	1.12	8.70E-06	8.59E-03	0.25	A
rs12459046	19	23745485	4.82E-06	1.51	0.76	1.12	8.70E-06	8.59E-03	0.25	A
rs10404666	19	23746292	5.85E-06	1.51	0.79	1.07	1.11E-05	1.55E-02	0.29	C
rs2886003	19	23746456	8.53E-06	1.50	0.79	1.04	1.59E-05	1.23E-02	0.26	A
rs10422879	19	23746781	5.85E-06	1.51	0.79	1.07	1.11E-05	1.55E-02	0.29	A
rs10404713	19	23748279	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	G
rs8106780	19	23749345	9.09E-06	1.51	0.63	1.16	1.22E-05	1.22E-05	0.00	G
rs59885226	19	23750703	7.69E-06	1.51	0.63	1.16	1.04E-05	1.04E-05	0.00	G
rs62123411	19	23750818	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	T
rs62123412	19	23750930	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	A
rs10407300	19	23751950	9.09E-06	1.51	0.63	1.16	1.22E-05	1.22E-05	0.00	T
rs4932863	19	23752320	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	T
rs4932864	19	23752621	9.09E-06	1.51	0.63	1.16	1.22E-05	1.22E-05	0.00	A
rs4932865	19	23752627	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	T
rs10414987	19	23753052	9.09E-06	1.51	0.63	1.16	1.22E-05	1.22E-05	0.00	G
rs28561078	19	23753402	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	G
rs4932867	19	23753792	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	T
rs4932868	19	23754021	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	C
rs8101304	19	23754371	5.65E-06	1.52	0.79	1.10	1.08E-05	1.59E-02	0.29	C

rs8100508	19	23754377	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	T
rs8100422	19	23754441	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	C
rs8100711	19	23754442	5.17E-06	1.51	0.79	1.07	9.92E-06	1.67E-02	0.30	A
rs28801777	19	23754846	5.68E-06	1.52	0.79	1.10	1.08E-05	1.58E-02	0.29	G
rs28784951	19	23754939	5.20E-06	1.51	0.79	1.07	9.97E-06	1.67E-02	0.30	A
rs62123413	19	23755017	5.68E-06	1.52	0.79	1.10	1.08E-05	1.58E-02	0.29	A
rs62123414	19	23755550	3.60E-06	1.52	0.79	1.07	7.11E-06	2.09E-02	0.33	T
rs62123415	19	23755564	3.21E-06	1.52	0.79	1.07	6.38E-06	2.21E-02	0.33	G
rs2116911	19	23756666	2.79E-06	1.52	0.79	1.10	5.62E-06	2.40E-02	0.35	G
rs2116910	19	23756821	8.17E-06	1.50	0.66	1.13	1.17E-05	1.17E-05	0.00	C
rs12459435	19	23757169	3.45E-06	1.52	0.79	1.07	6.85E-06	2.20E-02	0.33	T
rs62123416	19	23757362	3.45E-06	1.52	0.79	1.07	6.85E-06	2.20E-02	0.33	A
rs6511445	19	23757705	3.78E-06	1.53	0.79	1.10	7.46E-06	2.11E-02	0.33	G
rs10418784	19	23758443	3.41E-06	1.53	0.79	1.10	6.78E-06	2.22E-02	0.33	T
rs4932869	19	23759524	2.82E-06	1.52	0.79	1.07	5.68E-06	2.42E-02	0.35	A
rs4932708	19	23759573	2.82E-06	1.52	0.79	1.07	5.68E-06	2.42E-02	0.35	A
rs4932709	19	23759591	2.82E-06	1.52	0.79	1.07	5.68E-06	2.42E-02	0.35	A
rs12461255	19	23759956	2.82E-06	1.52	0.79	1.07	5.68E-06	2.42E-02	0.35	T
rs12461720	19	23760412	2.93E-06	1.53	0.63	1.16	4.21E-06	4.24E-05	0.05	A
rs10415081	19	23761513	1.82E-06	1.54	0.72	1.08	3.20E-06	6.29E-03	0.26	G
rs6054501	20	6718939	2.69E-06	1.74	0.36	0.62	2.17E-05	7.02E-01	0.80	C
rs6038600	20	6722376	1.98E-06	1.76	0.20	0.49	2.51E-05	8.68E-01	0.85	G
rs11908452	20	6723240	5.27E-07	1.80	0.18	0.51	8.34E-06	8.75E-01	0.86	G
rs17804047	20	6726127	3.41E-07	1.80	0.18	0.51	5.65E-06	8.71E-01	0.86	T
rs80168499	20	14421257	7.28E-06	3.04	0.31	0.61	6.49E-05	7.56E-01	0.81	T

B (Hyperopia)

Marker	Chromosome	Position	P-value discovery	OR discovery	P-value replication	OR replication	Overall P-Value	RE Analysis P-Value	I^2	Risk allele in both cohorts
rs113877316	3	80129340	7.96E-06	2.57	0.34	0.64	8.63E-04	0.60	0.90	A
rs1435382	4	37238386	5.22E-06	0.69	0.82	1.01	1.79E-04	0.36	0.85	G
rs1023730	4	37240580	3.09E-06	0.66	0.92	1.01	9.38E-05	0.32	0.85	T
rs1656197	4	37244135	3.95E-06	0.67	0.89	1.01	1.20E-04	0.33	0.85	A
rs78011035	5	50177455	1.87E-06	2.47	0.25	1.52	2.50E-06	0.01	0.50	A
rs10795300	10	986429	6.98E-06	1.60	0.02	0.67	1.08E-02	0.88	0.95	G
rs11253524	10	986459	5.21E-06	1.60	0.03	0.68	8.64E-03	0.87	0.95	T
rs11201870	10	87768614	9.21E-07	1.67	0.31	1.14	2.49E-06	0.03	0.68	A
rs2352179	10	87790080	2.77E-06	1.67	0.02	1.41	1.62E-07	0.00	0.00	T
rs1147601	10	90608238	6.29E-06	0.59	0.67	0.97	6.53E-05	0.16	0.79	G
rs77403571	11	45913607	2.34E-06	2.30	0.49	0.81	3.84E-04	0.50	0.90	A
rs10771886	12	32045777	4.52E-06	1.42	0.98	0.91	1.03E-04	0.28	0.84	T
rs10771887	12	32045784	4.52E-06	1.42	0.98	0.91	1.03E-04	0.28	0.84	T
rs4759700	12	130973555	7.97E-06	1.71	0.39	1.24	2.03E-05	0.04	0.62	T
rs9560962	13	92836123	7.79E-06	0.57	0.23	0.84	9.75E-06	0.01	0.49	T
rs74064178	14	82929718	2.38E-06	2.77	0.50	0.73	3.44E-04	0.49	0.90	A
rs1237957	16	10096870	7.66E-06	1.71	0.71	1.08	8.44E-05	0.17	0.79	C
rs3104709	16	10097944	7.66E-06	1.71	0.71	1.08	8.29E-05	0.17	0.79	T
rs863283	16	10103435	7.09E-06	1.70	0.75	1.07	9.34E-05	0.19	0.80	A

rs837690	16	10103724	6.40E-06	1.70	0.67	1.09	6.61E-05	0.16	0.79	A
rs865101	16	10104243	8.31E-06	1.67	0.94	1.05	1.75E-04	0.26	0.83	C
rs3104710	16	10104257	8.31E-06	1.67	0.94	1.05	1.75E-04	0.26	0.83	T
rs837691	16	10105143	8.31E-06	1.67	0.94	1.04	1.75E-04	0.26	0.83	G
rs1448273	16	10146237	5.31E-06	1.69	0.97	1.00	1.76E-04	0.30	0.85	T
rs79262004	16	10162462	6.13E-06	1.68	0.90	0.95	2.20E-04	0.33	0.86	T
rs61366236	18	33315471	7.79E-06	2.86	0.33	0.58	1.15E-03	0.60	0.90	T
rs10153386	18	68615592	8.93E-06	2.01	0.17	1.37	7.67E-06	0.00	0.42	G
rs429358	19	45411941	7.16E-07	1.77	0.03	1.46	1.00E-07	0.00	0.06	C
rs6049216	20	2442273	6.28E-06	0.54	0.82	1.05	2.30E-04	0.36	0.86	C
rs11908452	20	6723240	5.39E-06	1.77	0.43	0.84	3.78E-04	0.55	0.89	G
rs17804047	20	6726127	6.56E-06	1.76	0.45	0.84	3.90E-04	0.54	0.88	T
rs11910551	21	43213700	9.62E-06	3.02	0.05	0.70	2.25E-03	0.92	0.93	T
rs73373447	21	43215744	7.79E-06	3.12	0.05	0.70	2.06E-03	0.91	0.93	C

Table S5: Analysis results for the amblyopia and hyperopia subgroups discovery and replication cohorts and their meta-analysis (Results shown for SNPs with $P \leq 1 \times 10^{-05}$ in the discovery cohort). Abbreviations as follows: OR, Odds ratio; RE, random effect.

Table S6: SNPs in high linkage disequilibrium (LD) with rs2244352.

Marker	Gene	Chromosome: position	Alleles	MAF	Distance	D'	R^2	P-value	RegulomeDB score
rs2244352	WRB	21:40757973	T/G	0.32	0	1	1	2.84E-09	1b
rs3787924	WRB	21:40761307	A/G	0.31	3334	1	0.71	1.50E-05	7
rs6517547	WRB	21:40755994	T/C	0.29	-1979	1	0.74	2.07E-05	7
rs2837006	WRB	21:40772436	T/C	0.31	14463	0.95	0.7	1.07E-05	1f
rs2837001	WRB	21:40763895	T/C	0.31	5922	0.95	0.7	1.11E-05	5
rs2837005	WRB	21:40769807	T/C	0.31	11834	0.95	0.7	1.16E-05	5
rs8131718	WRB	21:40766181	G/T	0.31	8208	0.95	0.7	1.40E-05	7
rs1060180	WRB	21:40769017	G/T	0.31	11044	0.95	0.7	1.40E-05	7
rs13230	WRB	21:40769290	A/G	0.31	11317	0.95	0.7	1.40E-05	5
rs9974828	WRB	21:40772045	C/T	0.31	14072	0.95	0.7	1.53E-05	7
rs2837000	WRB	21:40762255	G/A	0.31	4282	0.95	0.7	1.64E-05	5
rs2836999	WRB	21:40761545	T/G	0.31	3572	0.95	0.7	1.71E-05	1f
rs3787923	WRB	21:40761056	G/C	0.31	3083	0.95	0.7	2.01E-05	7
rs7277602	SH3BGR	21:40828145	C/G	0.48	70172	0.95	0.54	3.18E-05	7
rs10775662	WRB	21:40756675	G/A	0.29	-1298	0.95	0.7	3.40E-05	4
rs2837007	WRB	21:40772484	C/T	0.31	14511	0.95	0.7	3.80E-05	1f
rs2837008	WRB	21:40773487	C/T	0.31	15514	0.95	0.7	4.20E-05	7
rs13051142	LCA5L	21:40817430	G/A	0.48	59457	0.95	0.52	4.75E-05	2b
rs13050837	LCA5L	21:40817356	C/T	0.48	59383	0.95	0.54	5.33E-05	4
rs9983100	LCA5L	21:40808508	C/T	0.48	50535	0.95	0.54	5.65E-05	7
rs4816626	LCA5L	21:40809364	C/T	0.48	51391	0.95	0.54	5.68E-05	7
rs9983404	LCA5L	21:40817127	G/C	0.48	59154	0.95	0.54	5.65E-05	2b
rs9983435	LCA5L	21:40816631	T/C	0.48	58658	0.95	0.5	5.33E-05	1f
rs9305674	WRB	21:40764049	G/A	0.31	6076	0.9	0.66	1.64E-05	5
rs13051949	WRB	21:40760605	A/T	0.31	2632	0.9	0.66	3.01E-05	4
rs2837002	WRB	21:40763986	T/G	0.31	6013	0.9	0.66	3.41E-05	5
rs9983180	LCA5L	21:40817071	C/A	0.48	59098	0.9	0.54	5.33E-05	1f
rs9983716	LCA5L	21:40816940	T/C	0.48	58967	0.9	0.5	5.33E-05	5
rs13051054	LCA5L	21:40817507	C/A	0.48	59534	0.85	0.48	4.84E-05	4
rs8131355	SH3BGR	21:40867016	G/A	0.47	109043	0.82	0.34	4.38E-05	6
rs2837051	SH3BGR	21:40869246	G/A	0.47	111273	0.82	0.34	5.16E-05	7
rs8126729	SH3BGR	21:40867559	C/T	0.47	109586	0.82	0.34	6.23E-05	7
rs2009713	SH3BGR	21:40866086	C/T	0.5	108113	0.82	0.33	1.23E-05	6
rs2837043	SH3BGR	21:40851556	T/G	0.48	93583	0.76	0.31	3.36E-06	5

Table S6: SNPs in high linkage disequilibrium (LD) with rs2244352, the significant SNP resulting from the association test of the non-accommodative esotropia discovery cohort. LD calculated using SNAP: SNP Annotation and Proxy Search tool version 2.2. Regulome DB[6] scores are assigned to variants based on the number of datatypes supporting its functionality; smaller scores indicate more evidence. Abbreviations are as follows: MAF, minor allele frequency; DB: database.

Table S7: Single Tissue eQTL analysis for rs2244352

Gene	P-Value	Effect Size	Tissue
WRB	8.60E-34	-0.63	Artery - Tibial
WRB	1.40E-31	-0.65	Adipose - Subcutaneous
LCA5L	9.90E-29	-0.82	Nerve - Tibial
WRB	3.80E-28	-0.4	Nerve - Tibial
LCA5L	1.40E-27	-0.79	Esophagus - Muscularis
LCA5L	2.90E-27	-0.75	Skin - Sun Exposed (Lower leg)
LCA5L	1.10E-26	-0.76	Skin - Not Sun Exposed (Suprapubic)
WRB	5.70E-26	-0.56	Cells - Transformed fibroblasts
LCA5L	6.40E-26	-0.61	Thyroid
WRB	3.00E-24	-0.53	Skin - Sun Exposed (Lower leg)
WRB	3.20E-24	-0.49	Esophagus - Mucosa
WRB	5.20E-23	-0.32	Lung
WRB	1.50E-22	-0.37	Esophagus - Muscularis
WRB	9.90E-22	-0.54	Adipose - Visceral (Omentum)
LCA5L	4.10E-21	-0.79	Artery - Aorta
WRB	7.90E-20	-0.58	Breast - Mammary Tissue
LCA5L	1.60E-18	-0.64	Esophagus - Mucosa
WRB	3.70E-18	-0.34	Thyroid
WRB	5.60E-18	-0.42	Skin - Not Sun Exposed (Suprapubic)
LCA5L	1.20E-16	-0.73	Heart - Left Ventricle
LCA5L	1.20E-16	-0.43	Muscle - Skeletal
LCA5L	2.40E-16	-0.6	Artery - Tibial
LCA5L	4.60E-16	-1	Brain - Cerebellar Hemisphere
LCA5L	8.20E-16	-0.64	Adipose - Subcutaneous
LCA5L	1.00E-15	-0.65	Stomach
LCA5L	1.70E-15	-0.69	Pancreas
LCA5L	3.40E-15	-0.83	Colon - Sigmoid
LCA5L	8.20E-15	-0.69	Heart - Atrial Appendage
WRB	3.00E-14	-0.53	Colon - Sigmoid
LCA5L	4.00E-14	-0.39	Cells - Transformed fibroblasts
WRB	4.40E-14	-0.41	Artery - Aorta
LCA5L	7.20E-14	-0.66	Esophagus - Gastroesophageal Junction
WRB	1.10E-13	-0.24	Whole Blood
LCA5L	1.60E-13	-0.32	Lung
LCA5L	2.10E-13	-0.53	Adipose - Visceral (Omentum)
LCA5L	2.70E-13	-0.52	Breast - Mammary Tissue
WRB	8.70E-13	-0.46	Esophagus - Gastroesophageal Junction
WRB	4.20E-12	-0.56	Artery - Coronary
SH3BGR	2.50E-11	-0.35	Skin - Sun Exposed (Lower leg)
LCA5L	4.60E-11	-0.95	Brain - Cerebellum
WRB	4.80E-11	-0.58	Ovary
SH3BGR	1.60E-10	-0.57	Pancreas
LCA5L	2.00E-10	-0.79	Spleen
SH3BGR	4.00E-10	-0.32	Nerve - Tibial
LCA5L	7.50E-10	-0.81	Brain - Cortex

LCA5L	8.30E-10	-0.65	Pituitary
LCA5L	1.10E-09	-0.86	Vagina
SH3BGR	1.40E-09	-0.28	Thyroid
LCA5L	4.90E-09	-0.43	Whole Blood
LCA5L	6.30E-09	-0.47	Adrenal Gland
LCA5L	6.40E-09	-0.7	Artery - Coronary
LCA5L	9.30E-09	-0.63	Brain - Nucleus accumbens (basal ganglia)
LCA5L	2.20E-08	-0.52	Brain - Hippocampus
LCA5L	3.10E-08	-0.73	Ovary
LCA5L	3.20E-08	-0.81	Brain - Frontal Cortex (BA9)
LCA5L	9.20E-08	-0.77	Uterus
LCA5L	1.50E-07	-0.58	Small Intestine - Terminal Ileum
LCA5L	2.10E-07	-0.65	Prostate
LCA5L	3.80E-07	-0.46	Brain - Caudate (basal ganglia)
LCA5L	4.20E-07	-0.75	Brain - Anterior cingulate cortex (BA24)
WRB	4.50E-07	-0.64	Uterus
WRB	4.80E-07	-0.41	Vagina
WRB	6.60E-07	0.45	Brain - Cerebellar Hemisphere
SH3BGR	1.10E-06	-0.28	Skin - Not Sun Exposed (Suprapubic)
LCA5L	1.40E-06	-0.72	Brain - Putamen (basal ganglia)
WRB	2.10E-06	-0.43	Spleen
WRB	2.70E-06	-0.22	Stomach
SH3BGR	3.60E-06	-0.38	Colon - Sigmoid
SH3BGR	4.20E-06	-0.26	Adipose - Visceral (Omentum)
SH3BGR	8.20E-06	-0.25	Adipose - Subcutaneous
WRB	1.20E-05	-0.29	Prostate
WRB	1.70E-05	-0.4	Brain - Spinal cord (cervical c-1)
WRB	3.40E-05	-0.31	Pancreas
LCA5L	5.10E-05	-0.49	Minor Salivary Gland
SH3BGR	1.40E-04	-0.34	Adrenal Gland
LCA5L	1.80E-04	-0.42	Brain - Hypothalamus
SH3BGR	2.00E-04	-0.18	Artery - Tibial
SH3BGR	2.00E-04	-0.22	Esophagus - Muscularis
WRB	2.20E-04	-0.42	Brain - Substantia nigra
SH3BGR	2.30E-04	-0.18	Stomach
SH3BGR	2.60E-04	-0.37	Brain - Nucleus accumbens (basal ganglia)
WRB	3.50E-04	-0.43	Minor Salivary Gland
SH3BGR	3.80E-04	-0.19	Artery - Aorta
SH3BGR	3.80E-04	-0.2	Lung
PSMG1	1.10E-03	-0.14	Whole Blood
LCA5L	1.20E-03	-0.49	Brain - Substantia nigra
WRB	1.50E-03	-0.27	Brain - Cortex
WRB	1.60E-03	-0.27	Brain - Caudate (basal ganglia)
WRB	2.50E-03	-0.15	Heart - Atrial Appendage
SH3BGR	2.90E-03	-0.21	Breast - Mammary Tissue
LCA5L	3.40E-03	-0.41	Cells - EBV-transformed lymphocytes
SH3BGR	3.40E-03	-0.16	Cells - Transformed fibroblasts
LCA5L	3.50E-03	-0.58	Brain - Spinal cord (cervical c-1)

WRB	3.50E-03	-0.28	Brain - Putamen (basal ganglia)
HMGN1	3.60E-03	-0.08	Whole Blood
WRB	4.20E-03	-0.19	Small Intestine - Terminal Ileum
LCA5L	5.10E-03	0.059	Testis
WRB	5.70E-03	-0.3	Cells - EBV-transformed lymphocytes
LCA5L	6.30E-03	-0.28	Liver
SH3BGR	6.50E-03	-0.3	Uterus
PSMG1	7.60E-03	0.24	Brain - Nucleus accumbens (basal ganglia)
WRB	8.70E-03	-0.26	Brain - Hippocampus
SH3BGR	9.50E-03	-0.2	Vagina
WRB	9.60E-03	0.26	Brain - Frontal Cortex (BA9)
PSMG1	9.90E-03	0.19	Brain - Cortex
PSMG1	1.10E-02	0.14	Esophagus - Gastroesophageal Junction
SH3BGR	1.40E-02	-0.29	Brain - Hippocampus
PSMG1	1.40E-02	0.09	Esophagus - Muscularis
SH3BGR	1.60E-02	-0.25	Pituitary
HMGN1	1.60E-02	0.2	Brain - Caudate (basal ganglia)
PSMG1	1.80E-02	0.2	Brain - Cerebellum
SH3BGR	2.20E-02	-0.08	Muscle - Skeletal
HMGN1	2.30E-02	0.13	Cells - EBV-transformed lymphocytes
SH3BGR	2.40E-02	-0.24	Brain - Hypothalamus
WRB	2.50E-02	-0.11	Adrenal Gland
PSMG1	2.90E-02	0.25	Brain - Putamen (basal ganglia)
BRWD1	3.10E-02	-0.06	Cells - Transformed fibroblasts
WRB	3.30E-02	-0.14	Pituitary
SH3BGR	3.40E-02	-0.26	Brain - Putamen (basal ganglia)
PSMG1	3.40E-02	0.07	Muscle - Skeletal
PSMG1	4.50E-02	-0.06	Thyroid
BRWD1	4.70E-02	0.06	Muscle - Skeletal
PSMG1	4.90E-02	0.14	Brain - Frontal Cortex (BA9)
BRWD1	4.90E-02	0.06	Esophagus - Muscularis
BRWD1	5.00E-02	0.08	Esophagus - Gastroesophageal Junction

Table S7: Single Tissue eQTL analysis for rs2244352. Only genes that were sufficiently expressed or with associations < 0.05 based on GTEx analysis release V7 (http://gtexportal.org/) are reported. Note that the risk allele of rs2244352 in the GWAS study is the reference allele [T]. Abbreviations as follows: BA9, Brodmann area 9; BA24, Brodmann area 24.

Table S8: Effect sizes for Single Tissue eQTL analysis of rs2244352 in different brain subregions.

	Gene				
Brain region	**WRB**	**LCA5L**	**SH3BGR**	**HMGN1**	**PSMG1**
Cortex	-0.27	-0.81	(-)	(-)	0.19
Caudate (basal ganglia)	-0.27	-0.46	(-)	0.2	(-)
Nucleus accumbens (basal ganglia)	(-)	-0.63	-0.37	(-)	0.24
Putamen (basal ganglia)	-0.28	-0.72	-0.26	(-)	0.25
Hippocampus	-0.26	-0.52	-0.29	(-)	(-)
Cerebellar Hemisphere	0.45	-1.00	(-)	(-)	(-)
Cerebellum	(-)	-0.95	(-)	(-)	0.2
Frontal Cortex (BA9)	0.26	-0.81	(-)	(-)	0.14
Amygdala	(-)	(-)	(-)	(-)	(-)
Anterior cingulate cortex (BA24)	(-)	-0.75	(-)	(-)	(-)
Hypothalamus	(-)	-0.42	-0.24	(-)	(-)
Spinal cord (cervical c-1)	-0.4	-0.58	(-)	(-)	(-)
Substantia nigra	-0.42	-0.49	(-)	(-)	(-)

Table S8: Effect sizes for Single Tissue eQTL analysis of rs2244352 in different brain regions (only reported for those with *P* < 0.05). Note that the risk allele of rs2244352 in the GWAS study is the reference allele [T]. Data based on GTEx analysis release V7 (http://gtexportal.org/). Abbreviations are as follows: BA9, Brodmann area 9; BA24, Brodmann area 24.

Table S9: Expression and function of the genes within the topologically associating domain (TAD) that includes rs2244352.

Gene	**Expression**			**Function**	**Effect of rs2244352 [T] on expression**
	Fetal Tissues	**Adult Tissues**	**Spatial**		
WRB[7-10]	Yes	Yes	High in brain, heart, liver, skeletal muscle and pancreas	Post-translational TRC40-mediated insertion of tail-anchored proteins into the ER membrane	Increase
LCA5L[11]	NA	Yes	High in testis, lung, retina, heart and brain	Localizes to motile cilia and/or flagella, potentially involved in ciliopathies	Increase
SH3BGR[7,12-14]	Yes	Yes	High in CNS, heart, sarcomere and visceral organs	Not characterized	Increase
HMGN1[15-19]	Yes	Restricted to cells committed to active differentiation	Ubiquitous	Member of HMGN family. Modulators of cellular differentiation and enhance the ability to repair damaged DNA	Increase/ decrease
BRWD1[7,20,21]	Yes	Yes	High in brain, kidney, testes, pancreas, and muscle	Transcriptional regulator involved in chromatin remodeling complexes	Increase

PSMG1[7,22,23]	Yes	yes	High in testis, kidney, liver, brain, heart, skeletal muscle, and pancreas	Possible function in cell proliferation	Decrease

Table S9: Expression and function of the genes within the topologically associating domain (TAD) where the significant SNP rs2244352 resides. The risk allele in the GWAS which is also the reference allele [T] of rs2244352 was found to be associated with increased expression of most of the genes except *HMGN1* where it exerted effect in both directions and *PSMG1* where it decreased the expression; data based on GTEx analysis release V7 (http://gtexportal.org/).

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