

A genome-wide association study identifies a susceptibility locus for refractive errors and myopia at 15q14

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Supplementary Table 1. Clinical characteristics of study participants

Abbreviations: GWAS, genome-wide association study; RS-I, Rotterdam Study I; RS-II, Rotterdam Study II; RS-III, Rotterdam Study III; ERF, Erasmus Rucphen Family Study; TwinsUK, the Twin Cohort recruited in London; SD, standard deviation; D, diopters.

	RS-I	RS-II	RS-III	ERF	TwinsUK
Number of individuals in GWAS	5328	2008	1970	2032	4270
Percentage women (%)	58.7	54.1	56.1	56.9	92.6
Mean age in years (SD)	68.5(8.6)	64.2(7.4)	56.2(5.8)	48.5(14.3)	55.0 (12.0)
Refractive error, spherical equivalent mean (SD)	+0.86(2.45)	+0.48(2.51)	-0.35(2.62)	+0.07(2.13)	-0.40 (2.73)
Spherical equivalent categories: n (%)					
• High myopia (<=-6D)	91(1.7)	35 (1.7)	62(3.1)	44 (2.2)	171 (4.0)
• Moderate myopia (-6D:-3D)	271(5.1)	148 (7.4)	244(12.4)	102 (5.0)	410 (9.6)
• Low myopia (-3D:-1.5D)	276(5.2)	141 (7.0)	199(10.1)	138 (6.8)	420(9.8)
• Emmetropia (-1.5D:+1.5D)	2538(47.6)	1024 (51.0)	1089(55.3)	1372 (67.5)	2532(59.3)
• Low hypermetropia (+1.5D:+3D)	1403(26.3)	453 (22.5)	254(12.9)	263 (12.9)	502(11.8)
• Moderate hypermetropia (+3D:+6D)	675(12.7)	189 (9.4)	105(5.3)	98 (4.8)	205(4.8)
• High hypermetropia (>=+6D)	74(1.4)	19 (0.9)	17(0.9)	15 (0.7)	30(0.7)

Supplementary Table 2. Genome-wide association (and replication) for refractive error with 31 SNPs spread across four loci on chromosome 15q14, 14q24, 1q41, and 10p12.3 reaching $P < 10^{-6}$

Abbreviations: RS-I, Rotterdam Study I; RS-II, Rotterdam Study II; RS-III, Rotterdam Study III; ERF, Erasmus Rucphen Family Study; TwinsUK, the Twin Cohort recruited in London; SNP, single nucleotide polymorphism; Chr, chromosome; MA, minor allele; MAF, minor allele frequency; Beta, effect size on spherical equivalent in dioptres; sem, standard error of the mean; -, no data.

SNP	Chr	Position	Discovery cohort: RS ($n = 5328$)				Replication RS-II ($n = 2008$)		RS-III ($n = 1970$)		ERF ($n = 2032$)		TwinsUK ($n = 4270$)		Meta-analysis ($n = 15608$)	
			MA	MAF	Beta (sem)	P	Beta (sem)	P	Beta (sem)	P	Beta (sem)	P	Beta (sem)	p	Beta (sem)	P
rs688220	15	32786167	A	0.45	-0.27 (0.05)	1.76x10 ⁻⁸	-0.28 (0.08)	3.80x10 ⁻¹	-0.22 (0.08)	9.27x10 ⁻³	-0.03 (0.07)	6.24x10 ⁻¹	-0.15 (0.07)	2.60x10 ⁻²	-0.20 (0.0009)	2.79x10 ⁻¹¹
rs580839	15	32786121	A	0.44	-0.27 (0.05)	1.89x10 ⁻⁸	-0.27 (0.08)	4.96x10 ⁻¹	-0.22 (0.08)	7.95x10 ⁻³	-0.03 (0.07)	6.34x10 ⁻¹	-0.16 (0.07)	1.92x10 ⁻²	-0.20 (0.0009)	2.53x10 ⁻¹¹
rs619788	15	32782398	A	0.44	-0.27 (0.05)	1.92x10 ⁻⁸	-0.27 (0.08)	4.94x10 ⁻¹	-0.22 (0.08)	7.72x10 ⁻³	-0.03 (0.07)	6.27x10 ⁻¹	-0.16 (0.07)	1.85x10 ⁻²	-0.20 (0.0009)	2.53x10 ⁻¹¹
rs4924134	15	32781857	G	0.44	-0.27 (0.05)	2.04x10 ⁻⁸	-0.27 (0.08)	4.76x10 ⁻¹	-0.27 (0.08)	6.58x10 ⁻³	-0.06 (0.07)	4.10x10 ⁻¹	-0.16 (0.07)	1.85x10 ⁻²	-0.21 (0.0009)	1.36x10 ⁻¹²
rs560766	15	32788234	A	0.44	-0.26 (0.05)	4.27x10 ⁻⁸	-0.28 (0.08)	4.54x10 ⁻¹	-0.21 (0.08)	1.29x10 ⁻²	-0.03 (0.07)	6.65x10 ⁻¹	-0.18 (0.07)	7.68x10 ⁻³	-0.20 (0.0009)	2.49x10 ⁻¹¹
rs7176510	15	32786771	T	0.45	-0.26 (0.05)	5.16x10 ⁻⁸	-0.28 (0.08)	5.10x10 ⁻¹	-0.22 (0.08)	9.62x10 ⁻³	-0.02 (0.07)	7.51x10 ⁻¹	-0.16 (0.07)	1.76x10 ⁻²	-0.20 (0.0009)	6.25x10 ⁻¹¹
rs7163001	15	32777866	A	0.44	-0.26 (0.05)	5.23x10 ⁻⁸	-0.28 (0.08)	4.08x10 ⁻¹	-0.23 (0.08)	5.89x10 ⁻³	-0.07 (0.07)	3.01x10 ⁻¹	-0.16 (0.07)	1.87x10 ⁻²	-0.21 (0.0009)	5.61x10 ⁻¹²
rs11073060	15	32777143	A	0.44	-0.26 (0.05)	5.76x10 ⁻⁸	-0.28 (0.08)	4.05x10 ⁻¹	-0.23 (0.08)	5.82x10 ⁻³	-0.08 (0.07)	2.72x10 ⁻¹	-0.16 (0.07)	1.91x10 ⁻²	-0.21 (0.0009)	3.65x10 ⁻¹²
rs8032019	15	32778782	G	0.40	-0.26 (0.05)	6.09x10 ⁻⁸	-0.28 (0.08)	5.57x10 ⁻¹	-0.13 (0.09)	1.30x10 ⁻¹	-0.05 (0.07)	5.12x10 ⁻¹	-0.16 (0.07)	1.96x10 ⁻²	-0.19 (0.0009)	3.71x10 ⁻¹⁰
rs685352	15	32795627	G	0.44	-0.25 (0.05)	8.80x10 ⁻⁸	-0.25 (0.08)	1.28x10 ⁻³	-0.19 (0.08)	1.98x10 ⁻²	-0.07 (0.07)	3.06x10 ⁻¹	-0.24 (0.07)	4.43x10 ⁻⁴	-0.21 (0.0009)	4.19x10 ⁻¹²
rs524952	15	32793178	A	0.47	0.25 (0.05)	1.03x10 ⁻⁷	0.30 (0.08)	2.09x10 ⁻¹	0.19 (0.08)	2.56x10 ⁻²	-0.06 (0.07)	4.13x10 ⁻¹	-0.32 (0.07)	4.15x10 ⁻⁶	-0.23 (0.0009)	3.18x10 ⁻¹⁴
rs634990	15	32793365	C	0.47	0.25 (0.05)	1.03x10 ⁻⁷	0.30 (0.08)	2.15x10 ⁻¹	0.20 (0.08)	2.03x10 ⁻²	-0.05 (0.07)	5.11x10 ⁻¹	-0.33 (0.07)	2.93x10 ⁻⁶	-0.23 (0.0009)	2.21x10 ⁻¹⁴
rs11073059	15	32776966	A	0.44	-0.25 (0.05)	1.20x10 ⁻⁷	-0.28 (0.08)	3.96x10 ⁻¹	-0.23 (0.08)	5.83x10 ⁻³	-0.08 (0.07)	2.72x10 ⁻¹	-0.16 (0.07)	1.91x10 ⁻²	-0.20 (0.0009)	8.45x10 ⁻¹²
rs11073058	15	32776918	T	0.44	-0.25 (0.05)	1.30x10 ⁻⁷	-0.28 (0.08)	3.93x10 ⁻¹	-0.23 (0.08)	5.84x10 ⁻³	-0.08 (0.07)	2.7x10 ⁻¹	-0.16 (0.07)	1.90x10 ⁻²	-0.20 (0.0009)	8.45x10 ⁻¹²
rs10141617	14	69486195	A	0.32	-0.27 (0.05)	1.45x10 ⁻⁷	-0.10 (0.08)	2.04x10 ⁻¹	-0.05 (0.09)	6.08x10 ⁻¹	-0.05 (0.07)	5.2x10 ⁻¹	0.10 (0.07)	1.46x10 ⁻¹	-0.11 (0.0009)	2.88x10 ⁻⁴
rs12123296	1	214080199	T	0.03	-0.69 (0.14)	3.92x10 ⁻⁷	-0.09 (0.23)	7.07x10 ⁻¹	0.29 (0.26)	2.63x10 ⁻¹	-0.33 (0.22)	1.5x10 ⁻¹	-	-	-0.29 (0.009)	4.50x10 ⁻³
rs12402107	1	214079366	G	0.03	-0.69 (0.14)	3.92x10 ⁻⁷	-0.09 (0.23)	7.07x10 ⁻¹	0.29 (0.26)	2.63x10 ⁻¹	-0.33 (0.22)	1.5x10 ⁻¹	-	-	0.29 (0.009)	4.50x10 ⁻³
rs12132798	1	214087159	G	0.03	-0.70 (0.14)	3.94x10 ⁻⁷	-0.09 (0.23)	7.04x10 ⁻¹	0.29 (0.26)	2.64x10 ⁻¹	-0.33 (0.23)	1.5x10 ⁻¹	-	-	0.29 (0.009)	4.21x10 ⁻³
rs12141208	1	214058683	C	0.03	-0.69 (0.14)	4.02x10 ⁻⁷	-0.09 (0.23)	7.04x10 ⁻¹	0.29 (0.26)	2.55x10 ⁻¹	-0.32 (0.22)	1.5x10 ⁻¹	-	-	-0.29 (0.009)	4.61x10 ⁻³
rs11120645	1	214057102	T	0.03	-0.69 (0.14)	4.03x10 ⁻⁷	-0.09 (0.23)	7.04x10 ⁻¹	0.29 (0.26)	2.54x10 ⁻¹	-0.32 (0.22)	1.5x10 ⁻¹	-	-	-0.29 (0.009)	4.64x10 ⁻³
rs12137796	1	214054933	T	0.03	-0.69 (0.14)	4.05x10 ⁻⁷	-0.09 (0.23)	7.03x10 ⁻¹	0.29 (0.26)	2.54x10 ⁻¹	-0.32 (0.22)	1.5x10 ⁻¹	-	-	-0.28 (0.009)	4.72x10 ⁻³
rs12126346	1	214088575	C	0.03	-0.70 (0.14)	4.07x10 ⁻⁷	-0.10 (0.24)	6.65x10 ⁻¹	0.29 (0.26)	2.67x10 ⁻¹	-0.33 (0.23)	1.5x10 ⁻¹	-	-	-0.29 (0.009)	4.20x10 ⁻³
rs12144789	1	214049058	T	0.03	-0.69 (0.14)	4.21x10 ⁻⁷	-0.09 (0.23)	7.02x10 ⁻¹	0.29 (0.26)	2.50x10 ⁻¹	-0.32 (0.22)	1.5x10 ⁻¹	-	-	-0.28 (0.009)	4.82x10 ⁻³
rs12133551	1	214048165	C	0.03	-0.69 (0.14)	4.24x10 ⁻⁷	-0.09 (0.23)	7.02x10 ⁻¹	0.29 (0.26)	2.50x10 ⁻¹	-0.32 (0.22)	1.5x10 ⁻¹	-	-	0.28 (0.009)	4.81x10 ⁻³
rs12130528	1	214045514	C	0.03	-0.69 (0.14)	4.27x10 ⁻⁷	-0.09 (0.23)	7.00x10 ⁻¹	0.29 (0.26)	2.50x10 ⁻¹	-0.32 (0.22)	1.5x10 ⁻¹	-	-	0.28 (0.009)	4.69x10 ⁻³
rs7416880	1	214038025	A	0.03	-0.70 (0.14)	4.70x10 ⁻⁷	-0.10 (0.24)	6.73x10 ⁻¹	0.30 (0.26)	2.47x10 ⁻¹	-0.33 (0.23)	1.5x10 ⁻¹	-	-	-0.29 (0.009)	4.42x10 ⁻³
rs12129576	1	214038744	C	0.03	-0.70 (0.14)	4.72x10 ⁻⁷	-0.09 (0.24)	6.91x10 ⁻¹	0.30 (0.26)	2.48x10 ⁻¹	-0.32 (0.22)	1.5x10 ⁻¹	-	-	0.28 (0.009)	4.88x10 ⁻³
rs12132110	1	214038803	A	0.03	-0.70 (0.14)	4.77x10 ⁻⁷	-0.09 (0.24)	6.93x10 ⁻¹	0.30 (0.26)	2.49x10 ⁻¹	-0.32 (0.22)	1.5x10 ⁻¹	-	-	-0.28 (0.009)	5.05x10 ⁻³
rs11012633	10	21602727	A	0.12	0.35 (0.07)	8.89x10 ⁻⁷	0.14 (0.12)	2.50x10 ⁻¹	-0.26 (0.12)	3.78x10 ⁻²	-0.06 (0.09)	5.1x10 ⁻¹	-	-	0.17 (0.002)	5.59x10 ⁻⁴
rs12247067	10	21603062	T	0.12	0.35 (0.07)	8.97x10 ⁻⁷	0.14 (0.12)	2.52x10 ⁻¹	-0.26 (0.12)	3.81x10 ⁻²	-0.06 (0.09)	5.2x10 ⁻¹	-	-	0.17 (0.002)	5.77x10 ⁻⁴
rs12252084	10	21607196	G	0.12	0.35 (0.07)	8.97x10 ⁻⁷	0.14 (0.12)	2.53x10 ⁻¹	-0.23 (0.12)	5.98x10 ⁻²	-0.06 (0.09)	5.2x10 ⁻¹	-	-	-0.17 (0.002)	4.36x10 ⁻⁴

Supplementary Table 3. Human gene expression levels in macular sections of post-mortem donor eyes

All genes represented on the 44k microarray were ranked by increasing expression; rank per gene was calculated as percentile.
Abbreviation: RPE retinal pigment epithelium; SD, standard deviation.

Gene	Photoreceptors	RPE	Choroid
	Mean percentile (SD)	Mean percentile (SD)	Mean percentile (SD)
<i>GOLGA8B</i>	17 (5.0)	14 (5.6)	9 (3.3)
<i>GJD2</i>	30 (2.9)	30 (9.3)	36 (10.3)
<i>ACTC1</i>	85 (8.8)	85 (10.2)	89 (4.0)

Supplementary Table 4. Results of direct sequencing of the coding region of the *GJD2* gene in 47 persons from the discovery cohort (RS-I) by category of refractive error and genotype

Abbreviations: UTR, untranslated region; ORF, open reading frame; SNP, single nucleotide polymorphism; MA, minor allele; MAF, minor allele frequency; AF, allele frequency (total amount of changes (homozygous: single count, heterozygous: double count) per total amount of chromosomes); -, no data.

High myopia: <=-6D, emmetropia: (-1.5D:+1.5D), high hypermetropia (>=+6D)

<i>GJD2</i>		5'UTR		ORF			3'UTR			
2 exons, 8 PCR fragments										
	<i>n</i>	SNP1 A->T 5UTR-127	SNP2 A->T c.333 A->T	SNP3 C->T c.369 C->T	SNP4 C->T c.588 C->T	SNP5 G->A c.888 G->A	SNP6 A->G 3UTR+889	SNP7 C->T 3UTR+1069	SNP8 t->c 3UTR+1087	SNP9 A->G 3UTR+1461
Amino acid change		p.T111T	p.T111T	p.S123S	p.S196S	p.E296E				
SNP		rs2277558	rs651724	rs35174018	rs3743123	rs34964522	-	rs607028	rs792418	rs2339643
		AF	AF	AF	AF	AF	AF	AF	AF	AF
High myopia, homozygous for risk allele rs634990	8	8/16 (0.500)	8/16 (0.500)	0/16 (0.000)	3/16 (0.188)	1/16 (0.063)	0/16 (0.000)	9/16 (0.562)	15/16 (0.938)	8/16 (0.500)
High myopia, homozygous for non risk allele rs634990	8	6/16 (0.375)	10/16 (0.625)	2/16 (0.125)	6/16 (0.375)	4/16 (0.250)	0/16 (0.000)	9/16 (0.562)	15/16 (0.938)	6/16 (0.375)
Emmetropia, homozygous for risk allele rs634990	8	1/16 (0.063)	15/16 (0.938)	1/16 (0.063)	5/16 (0.313)	2/16 (0.125)	0/16 (0.000)	7/16 (0.438)	13/16 (0.813)	1/16 (0.063)
Emmetropia, homozygous for non risk allele rs634990	8	6/16 (0.375)	10/16 (0.625)	2/16 (0.125)	2/16 (0.125)	1/16 (0.063)	0/16 (0.000)	9/16 (0.563)	11/16 (0.688)	6/16 (0.375)
High hypermetropia, homozygous for risk allele rs634990	7	4/14 (0.286)	10/14 (0.714)	0/14 (0.000)	5/14 (0.357)	3/14 (0.214)	0/14 (0.000)	8/14 (0.571)	13/14 (0.929)	4/14 (0.286)
High hypermetropia, homozygous for non risk allele rs634990	8	5/16 (0.313)	10/16 (0.625)	0/16 (0.000)	7/16 (0.438)	5/16 (0.313)	1/16 (0.063)	7/16 (0.438)	15/16 (0.938)	5/16 (0.313)
Total	47	30/94 (0.319)	63/94 (0.670)	5/94 (0.053)	28/94 (0.298)	16/94 (0.170)	1/94 (0.011)	49/94 (0.521)	82/94 (0.872)	30/94 (0.319)
MA		-	T	A	T	T	-	-	-	-
MAF (in NCBI SNP database)		-	0.267	0.059	0.267	0.053	-	-	-	-
Population (in NCBI SNP database*)		-	HapMap CEU European	AGI_ASP population	HapMap CEU European	AGI_ASP population	-	-	-	-
<i>P</i> -value discovery cohort		-	9.45x10 ⁻¹	-	9.83x10 ⁻¹	-	-	-	-	-
MAF discovery cohort		-	0.324	-	0.282	-	-	-	-	-

*NCBI SNP database <http://www.ncbi.nlm.nih.gov/SNP>

Supplementary Table 5. Expression-associated SNPs

We assessed whether the top SNPs (or a proxy if the SNP was not in the database) were found to be associated with gene expression levels in lymphoblastoid cell lines*. The statistical significance threshold was, after applying Bonferroni correction for the number of expression SNPs, defined as a p-value of 3.6×10^{-3} . The r^2 threshold was defined as 0.70.

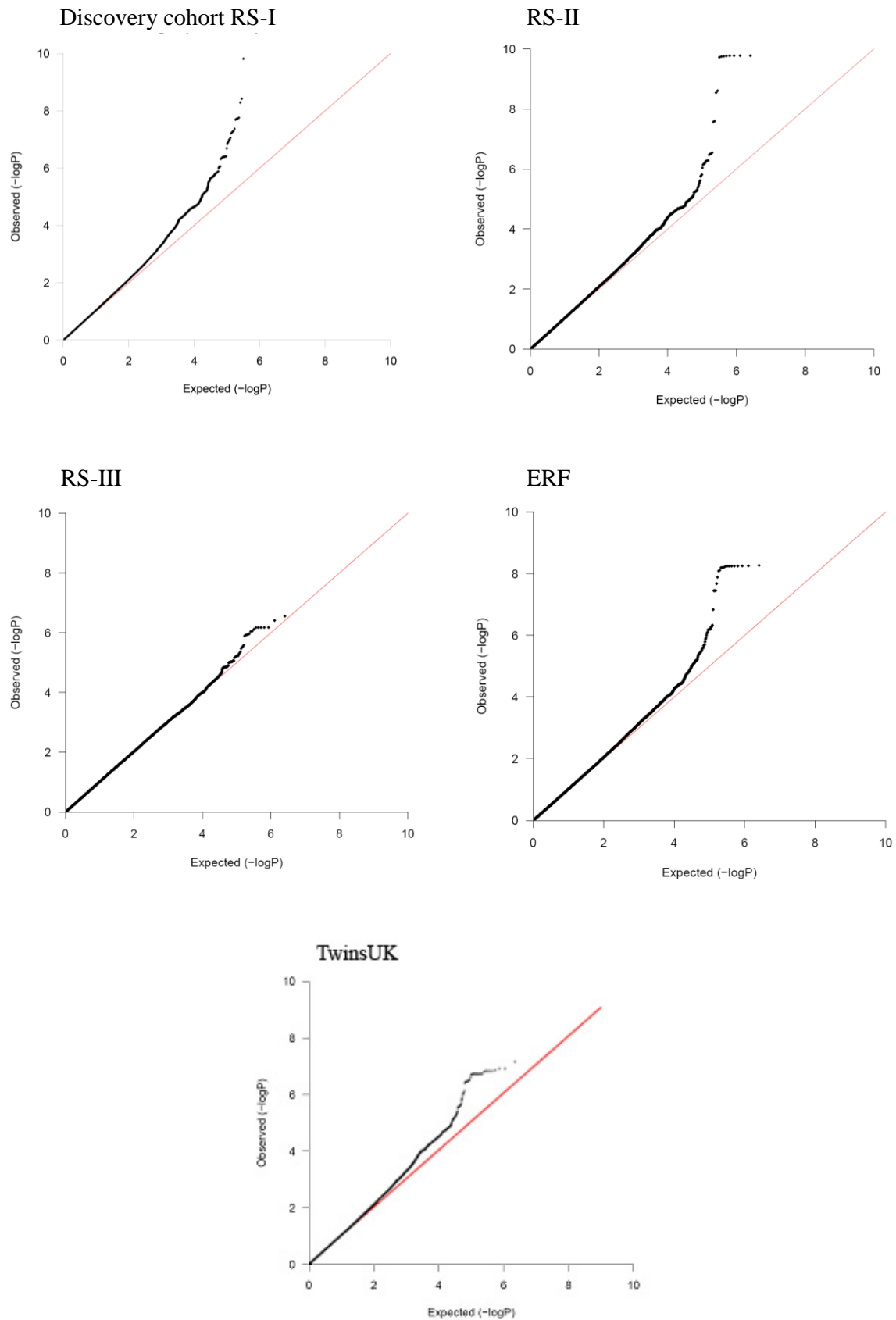
Abbreviations: SNP, single nucleotide polymorphism; -, no data

SNP	Proxy	r^2	ProbeID	SNP	Allele	Effect	P-value Lymphoblastoid cell line expression	P-value from GWAS spherical equivalent meta-analysis	Gene (chromosome location)
rs11073058	rs560766	0,97	1557338_x_at	rs560766	G	-0,323	1.0×10^{-5}	7.46×10^{-12}	-
rs11073059	rs560766	0,97	1569714_at	rs560766	G	0,28	1.1×10^{-4}	7.46×10^{-12}	ZFYVE20 (3p25.1)
rs11073060	rs560766	0,97	1557338_x_at	rs580839	C	-0,307	9.5×10^{-6}	2.53×10^{-11}	-
rs4924134	rs560766	0,97	227941_at	rs580839	C	-0,268	1.4×10^{-4}	2.53×10^{-11}	LOC339803 (2p15)
rs524952	rs560766	0,71	AVG_TBC1D1	rs580839	C	-0,266	1.9×10^{-4}	2.53×10^{-11}	-
rs560766	-	-	227903_x_at	rs811563	A	0,356	6.8×10^{-6}	6.0×10^{-1}	CI9orf20 (19p13.3)
rs580839	-	-	1563985_at	rs811563	A	-0,34	1.4×10^{-5}	6.0×10^{-1}	-
rs619788	rs580839	1	AVG_ZNF653	rs811563	A	0,331	2.0×10^{-5}	6.0×10^{-1}	-
rs634990	rs560766	0,68	223371_s_at	rs811563	A	0,337	2.3×10^{-5}	6.0×10^{-1}	DNAJC4 (11q13)
rs685352	rs811563	0,6	220077_at	rs811563	A	0,316	5.6×10^{-5}	6.0×10^{-1}	FLJ22349 (22q13.2)
rs688220	rs580839	0,97	1558212_at	rs811563	A	-0,314	6.5×10^{-5}	6.0×10^{-1}	FLJ35024 (9p24.2)
rs7163001	rs560766	0,97	1560199_x_at	rs811563	A	-0,321	6.6×10^{-5}	6.0×10^{-1}	-
rs7176510	rs560766	0,9	234020_x_at	rs811563	A	-0,314	7.1×10^{-5}	6.0×10^{-1}	COMMD1 (2p15)
rs8032019	rs560766	0,78	AVG_HIVEP3	rs811563	A	-0,314	8.7×10^{-5}	6.0×10^{-1}	-
			212349_at	rs811563	A	0,314	9.5×10^{-5}	6.0×10^{-1}	POFUT1(20q11)
			241602_at	rs811563	A	-0,31	1.1×10^{-4}	6.0×10^{-1}	ZNF582 (19q13.43)
			237766_at	rs811563	A	0,298	1.2×10^{-4}	6.0×10^{-1}	ATP9B (18q23)
			206468_s_at	rs811563	A	0,305	1.6×10^{-4}	6.0×10^{-1}	METTL3 (1q24-q25.3)
			244092_at	rs811563	A	-0,293	1.7×10^{-4}	6.0×10^{-1}	ZRANB3(2q21.3)
			207660_at	rs811563	A	-0,293	1.7×10^{-4}	6.0×10^{-1}	DMD (Xp21.2)
			AVG_ALCAM	rs811563	A	-0,293	1.8×10^{-4}	6.0×10^{-1}	-
			227098_at	rs811563	A	-0,298	1.9×10^{-4}	6.0×10^{-1}	DUSP18 (22q12.2)

*Dixon, A.L. et al. A genome-wide association study of global gene expression. *Nat Genet* **39**, 1202-7 (2007).

Supplementary Figure 1. Quantile-quantile plots for discovery and replication studies

SNPs had minor allele frequency ≥ 0.01 . Each black circle represents an observed statistic (defined as $\log_{10} P$) versus the corresponding expected statistic. The red line corresponds to the null distribution. Values were adjusted by genomic controls within each study ($\lambda = 1.054$ for RS-I, 1.012 RS-II, 1.012 RS-III, 1.037 for ERF and 1.04 for TwinsUK).



Supplementary Figure 2. Ingenuity analysis of the *GJD2* gene

Supplementary Figure 2a. *GJD2* and the interaction with eye development genes

Exploration of the Ingenuity database provided a large number of functional links between REST (RE1-silencing transcription factor), insulin, SP1 (Sp1 transcription factor), CAV1 (caveolin 1)). For example, direct protein-protein interaction was found with CAV1, a plasma membrane involved in cellular growth, apoptosis, migration and cell survival during eye development. Interestingly, transcription of *GJD2* is, via SP1, apparently under similar control as growth factors such as VEGFA (vascular endothelial growth factor A) and EGFR (epidermal growth factor receptor), which are also known to be involved in eye growth and development. This analysis suggests that *GJD2* is expressed during eye development and that the protein plays a functional role in this process.

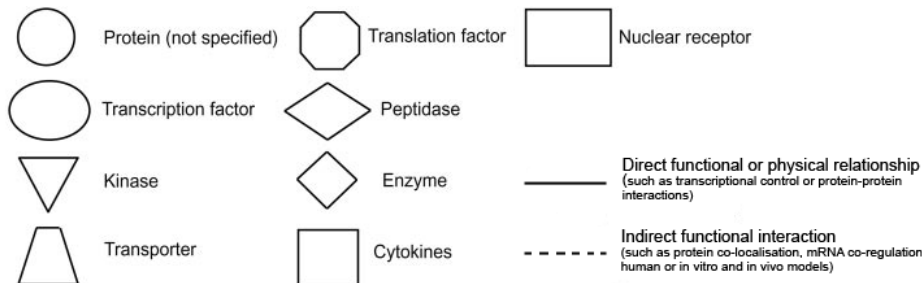
Supplementary Figure 2b. *GJD2* interactions with other membrane-bound and connexin proteins

This search yielded four genes (GJA8 (gap junction protein, alpha 8), VEGFA, FGF2 (fibroblast growth factor 2), RLBP1 (retinaldehyde binding protein 1)). GJA8 is a protein family member of *GJD2* (CX36). We observed a functional molecular network via direct protein-protein interactions, connecting, the gap junction proteins GJA1 (gap junction protein, alpha 1), GJA3 (gap junction protein, alpha 3), GJA8 and *GJD2*, together with TJP1 (tight junction protein 1) and CAV1. Transgenic mouse and in vitro models previously showed that two of the *GJD2* family members (GJA3, GJA8) are involved in eye morphogenesis, determination of eye size, or lens fiber maturation***. Since this network suggests that all molecules shown act in the same or similar molecular complex involved in eye growth and lens fiber maturation, it suggests that *GJD2* is involved in both these mechanisms.

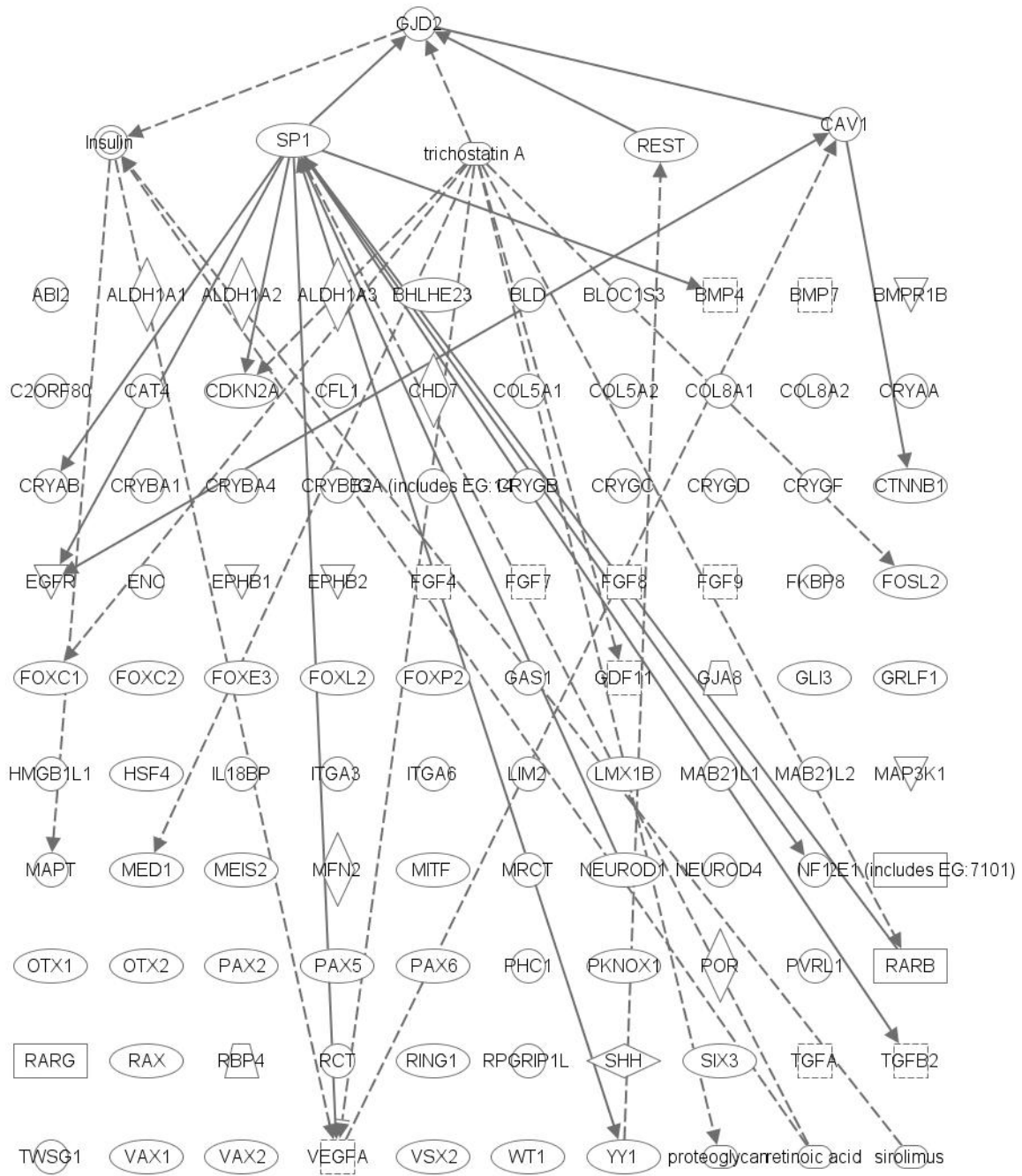
*Rong P. et al. Disruption of Gja8 ($\alpha 8$ connexin) in mice leads to microphthalmia associated with retardation of lens growth and lens fiber maturation. *Development* **129**, 167-174 (2002).

White, T.W. et al. Targeted Ablation of Connexin50 in Mice Results in microphthalmia and Zonular Pulverulent Cataracts. *J Cell Biol* **143, 815-825 (1998).

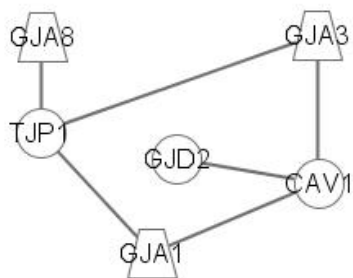
Legend



Supplementary Figure 2a.



Supplementary Figure 2b.



Supplementary Figure 3. Regulatory elements on the 15q14 associated locus

Regional map of the associated locus based on UCSC Genome browser views (Mar. 2006 (hg 18), NCBI Build 36.1, chr15:32766300-32820148 bp, and May 2004 (hg17), NCBI Build 35, chr15:32766300-32820148 bp) with used border SNP nr rs7494782-rs644339 with accompanying DNase I hypersensitive sites (represented by the grey blocks), sequence conservation (represented by the blue peaks) and the insulator site in terms of CTCF binding (illustrated in light blue)*.

*Heintzman, N.D. & Ren, B. Finding distal regulatory elements in the human genome. *Curr Opin Genet Dev* **19**, 541-9 (2009).

