

Report

Genetic Variants at 13q12.12 Are Associated

with High Myopia in the Han Chinese Population

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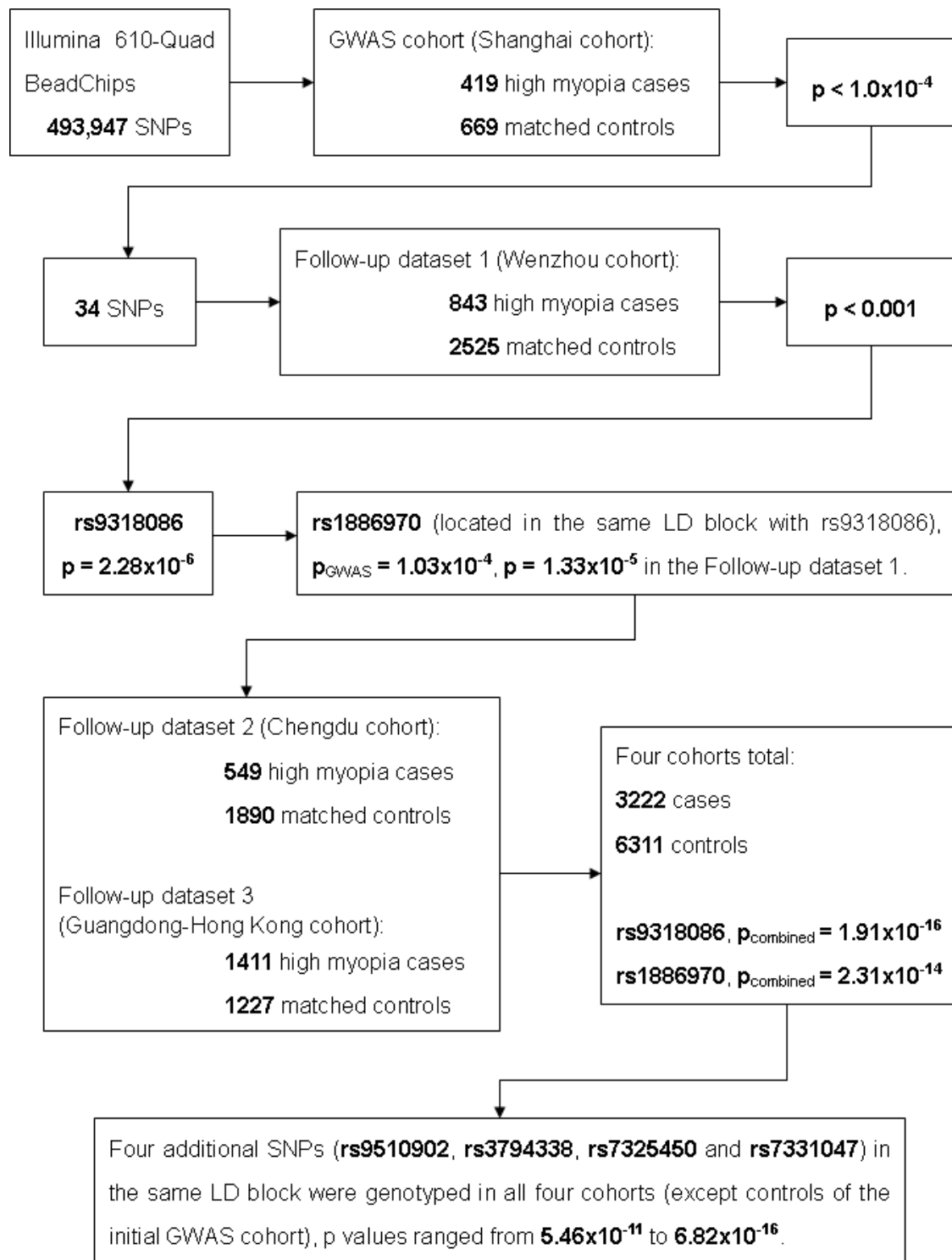


Figure S1. Flow chart of experimental work.

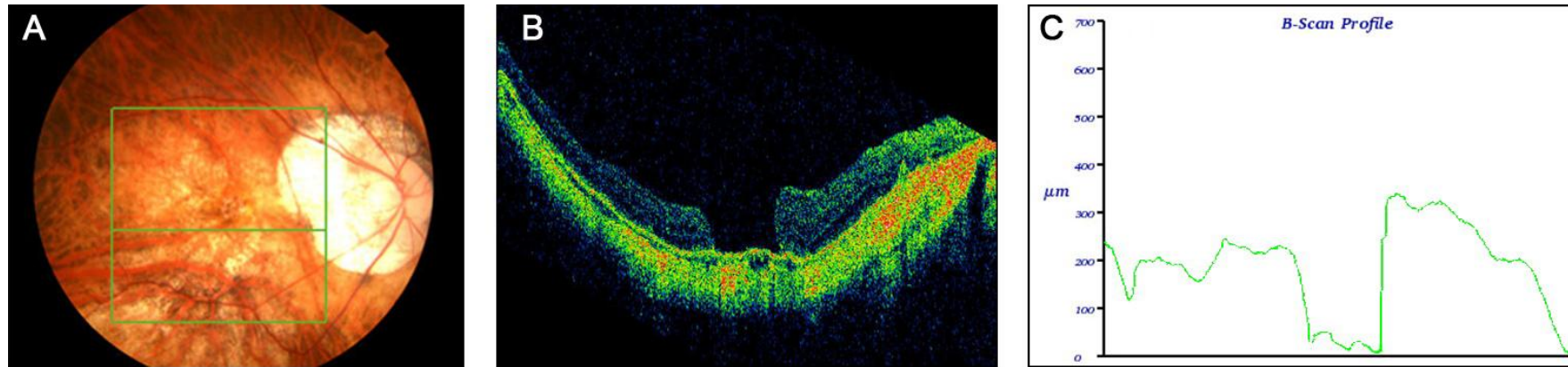


Figure S2. Fundus appearance and OCT of a patient with high myopia. The patient was a 57-year-old male. The refractive error of the left eye was -11.00 diopter sphere. **(A)**. The fundus photograph of the left eye of the patient presented a tigroid or tessellated appearance, circum papillary choriocapillary atrophy, and a macular hole. A Macular hole was also clearly observed in macular region in the OCT test **(B)**, indicating that the RPE layer is very thin at the hole region **(C)**.

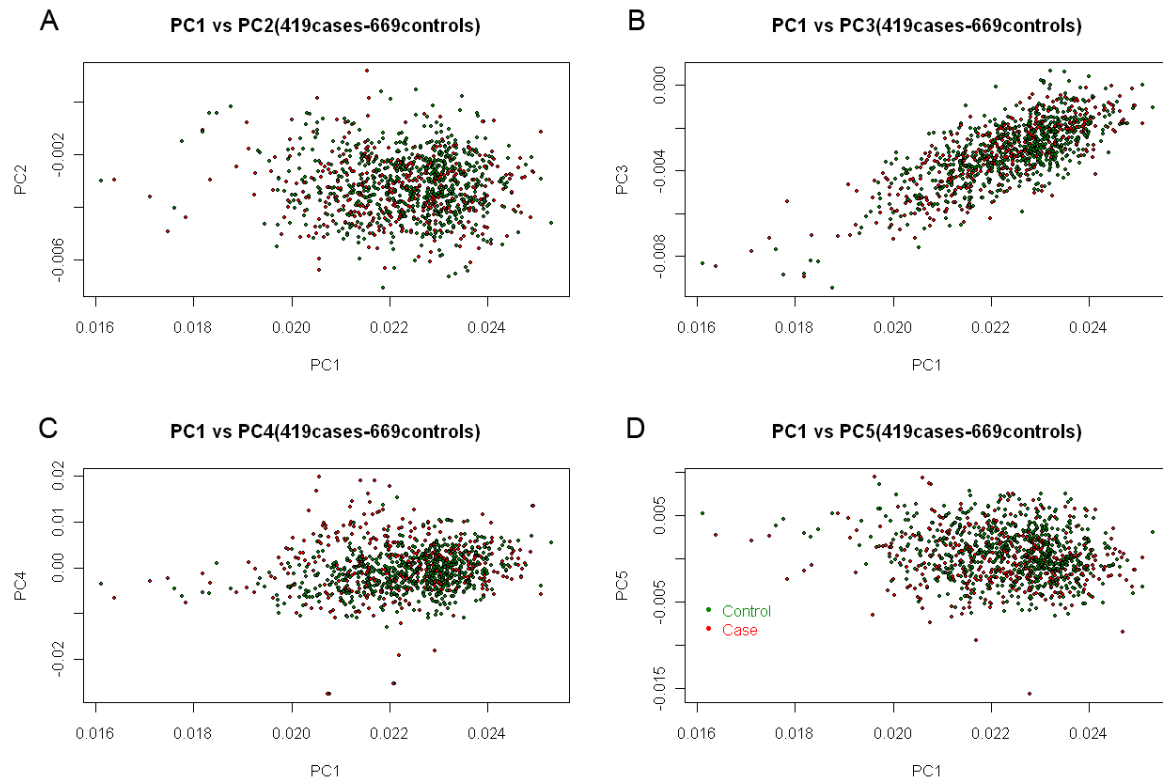


Figure S3. Plots of the first five principal components from the principal components analysis using 1088 participant samples (419 cases, 669 controls). The red points are cases and the green points are controls. **A.** PCA plot of the first and second components; **B.** plot of the first and third components; **C.** plot of the first and fourth components; and **D.** plot of the first and fifth components.

Table S1. Loci with p values less than 1.0×10^{-4} at GWAS and their follow-up studies in the follow-up dataset 1.

CHR	SNP	Position	Allele	GWAS dataset (SH) ^a			Follow-up dataset 1 (WZ) ^a			Gene_symbol	Location
				F_A	F_U	p	F_A	F_U	p		
1	rs2184345	230877734	A	0.4845	0.4155	1.64E-05	0.4195	0.4338	0.5284	<i>LOC729336</i>	flanking_5UTR
1	rs1891927	163404870	A	0.07757	0.1271	5.83E-05	0.1061	0.1353	0.04716	<i>LMX1A</i>	flanking_3UTR
1	rs3752606	166025408	G	0.06786	0.1181	6.35E-05	0.1051	0.1147	0.4996	<i>MPZL1</i>	3UTR
1	rs7523061	245828951	G	0.4393	0.5209	8.74E-05	0.4112	0.3955	0.5122	<i>OR2G3</i>	flanking_5UTR
1	rs16832771	189027411	A	0.2076	0.1413	9.05E-05	0.2237	0.2554	0.2516	<i>FAM5C</i>	flanking_5UTR
2	rs4662459	146800145	G	0.4179	0.3326	5.84E-06	0.3669	0.3353	0.1522	<i>PABPC1P2</i>	flanking_5UTR
2	rs6719401	238500934	A	0.07197	0.01732	1.96E-05	0.01427	0.01618	0.7317	<i>RAMP1</i>	flanking_3UTR
3	rs3887345	75886161	G	0.42	0.5135	5.12E-05	0.4788	0.4635	0.5333	<i>NULL</i>	flanking_5UTR
3	rs6549245	69788306	G	0.3043	0.3752	9.90E-05	0.3701	0.3706	0.9827	<i>MITF</i>	flanking_5UTR
4	rs16995877	33517230	A	0.1103	0.04795	5.97E-07	0.1191	0.1132	0.6903	<i>RPL31P31</i>	flanking_5UTR
4	rs6823909	158547155	A	0.1849	0.1037	4.28E-06	0.1728	0.1632	0.5823	<i>GRIA2</i>	flanking_3UTR
5	rs1353492	92471800	A	0.235	0.2882	6.80E-05	0.2996	0.3083	0.6839	<i>POLD2P1</i>	flanking_5UTR
5	rs730870	125902892	G	0.4143	0.4903	8.79E-05	0.4292	0.425	0.853	<i>ALDH7A1</i>	flanking_3UTR
6	rs2181938	23824132	G	0.2927	0.2163	6.65E-05	0.2461	0.2368	0.6369	<i>NRSN1</i>	flanking_5UTR
8	rs7003102	126372675	G	0.1065	0.1737	3.46E-06	0.1478	0.1206	0.08827	<i>NSMCE2</i>	intron
8	rs1979221	126689885	G	0.331	0.2511	1.07E-05	0.3077	0.3118	0.8483	<i>TRIB1</i>	flanking_3UTR
8	rs4870938	126421004	A	0.1036	0.1644	3.13E-05	0.1338	0.1176	0.2951	<i>NSMCE2</i>	intron
10	rs7899695	94419074	G	0.04317	0.01149	8.30E-06	0.06126	0.05588	0.6222	<i>KIF11</i>	flanking_3UTR
13	rs6561323	46083602	A	0.0631	0.1054	3.41E-05	0.09486	0.07396	0.1114	<i>LRCH1</i>	intron
13	rs6561321	46059561	C	0.06548	0.1061	7.60E-05	0.09221	0.07647	0.2262	<i>LRCH1</i>	intron
13	rs9316222	46112691	A	0.07262	0.1173	8.12E-05	0.09363	0.075	0.1532	<i>LRCH1</i>	intron
13	rs9318086	23330467	A	0.5143	0.4469	8.14E-05	0.4987	0.4327	2.28E-06	<i>MIPEP</i>	intron

16	rs9923450	9009889	A	0.3595	0.4425	5.97E-05	0.414	0.4015	0.5794	<i>LOC729913</i>	intron
16	rs462407	82380105	A	0.07279	0.1233	7.29E-05	0.1054	0.1162	0.4512	<i>CDH13</i>	intron
17	rs7946	17350285	A	0.2405	0.1794	5.64E-05	0.1726	0.1721	0.9754	<i>PEMT</i>	coding
18	rs10514157	70994152	A	0.3294	0.2549	7.49E-05	0.3112	0.3	0.5984	<i>ZADH2</i>	flanking_3UTR
19	rs285680	38969526	C	0.2488	0.1647	7.16E-06	0.2322	0.2544	0.2571	<i>KCTD15</i>	flanking_5UTR
20	rs6066502	45911998	C	0.4381	0.3617	1.96E-05	0.389	0.3897	0.9761	<i>SULF2</i>	flanking_5UTR
20	rs6122616	45872639	G	0.1869	0.2511	6.32E-05	0.2165	0.2059	0.573	<i>SULF2</i>	flanking_5UTR
22	rs3827410	45258351	C	0.06905	0.03064	9.86E-06	0.0461	0.05735	0.2602	<i>CELSR1</i>	intron
22	rs9628484	47538566	A	0.07194	0.119	3.24E-05	0.1017	0.09706	0.7376	<i>FAM19A5</i>	flanking_3UTR
22	rs13057753	47541323	A	0.07399	0.1203	6.35E-05	0.1039	0.09706	0.7376	<i>FAM19A5</i>	flanking_3UTR
22	rs1077166	43489769	G	0.2917	0.3475	8.40E-05	0.3149	0.3294	0.5011	<i>PRR5</i>	intron
22	rs131021	47559621	G	0.07775	0.1218	9.13E-05	0.1034	0.1059	0.8602	<i>FAM19A5</i>	flanking_3UTR

^aGWAS, genome-wide association study; GWAS dataset, Shanghai cohort; Follow-up dataset 1, Wenzhou cohort; F_A, the allele frequency of the affected patients; F_U, the allele frequency of the unaffected controls; The p value was corrected by age and gender.

Table S2. SNPs associated with high myopia at 13q12.12 from GWAS.

SNP	Position (Chr.13)	Allele	F_A ^a	F_U ^b	p ^c	OR ^d	Gene_symbol
rs2861537	23204049	A	0.4405	0.4043	0.027	1.239	intron 18 (<i>MIPEP</i>)
rs1536299	23216963	C	0.4405	0.4051	0.028	1.238	intron 18 (<i>MIPEP</i>)
rs4770489	23224754	G	0.356	0.3954	0.014	0.783	intron 17 (<i>MIPEP</i>)
rs7319884	23285412	A	0.327	0.3617	0.026	0.799	intron 14 (<i>MIPEP</i>)
rs9318086	23330467	A	0.5143	0.4469	8.14X10 ⁻⁵	1.471	intron 10 (<i>MIPEP</i>)
rs1886970	23338498	G	0.5155	0.4507	1.03X10 ⁻⁴	1.462	intron 7 (<i>MIPEP</i>)
rs1977381	23368554	A	0.5024	0.4419	3.60X10 ⁻⁴	1.417	intron 1 (<i>C1QTNF9B</i>)
rs716608	23374045	A	0.5324	0.467	1.47X10 ⁻⁴	1.444	downstream of <i>C1QTNF9B</i>
rs2077709	23374073	A	0.531	0.4678	1.79X10 ⁻⁴	1.437	downstream of <i>C1QTNF9B</i>

^aF_A, the allele frequency of the affected patients; ^bF_U, the allele frequency of the unaffected controls; ^cThe p value was corrected by age, gender and genomic control; ^dOR, odds ratio.

Table S3. Primers for genotyping by the SNaPshot method

SNP	PCR primers	SNaP shot primer
rs9510902	Forward: GAGGGTCCAGAATGTTTGT Reverse: CCTCCCTGGTTTGTCTTAC	CACAGGCTGTTAAGCACAGC
rs3794338	Forward: GTCCTTATTTTACTTC Reverse: GCTTCTTGCTTAGATTTAG	ACCTACCCCAGAATCTGGGGAAAAGA
rs1886970	Forward: AGGGAGGTGGAAAGTGAT Reverse: TGGCATTGTTTTGTCTGT	TGTATTGGCAGGGGGCTGTTGTGCACATCATC
rs7331047	Forward: GTGCCAGGTTTCCATTCT Reverse: GATGGGTTGGGATGTAGTC	TCACCTACGGAAGTGGGGTGATAAACTACCTAGTGTC
rs9318086	Forward: CAACCTTAACTCTCCTACTT Reverse: CGCTCTTATGTTTTCTCA	AATAAACACAGGAGGATATAGAAGCCAGAGGAGTACTTCTGTCA
rs7325450	Forward: GTCAGGGCTCACATTAGA Reverse: GCAGCAAGGTTTCTGTAG	AGGAGGTTTTTAGAGGATGTCACGACTAGGGTTGAGTGTCAGTTAATCTG

Table S4. Primers for gene expression by RT-PCR.

Gene name	Gene id	Primer sequences	Product length
<i>MIPEP</i>	NM_005932.3	Forward: CTCCACGCAGAATCACCA Reverse: TCCCTCGTATCATCTCAAAA	272
<i>C1QTNF9B</i>	NM_001007537.1	Forward: TGCTTGCCATTGAAATCTGC Reverse: TCTCCACTCGTCCCATCCTT	196
<i>C1QTNF9B-AS1</i>	NM_001135816.1	Forward: ACCAAAGACACCTGAACATT Reverse: TAAGAGGCTGGAAAGGAGAT	181
<i>GAPDH</i>	NM_002046.3	Forward: GAAGGTGAAGGTCGGAGTC Reverse: GAAGATGGTGATGGGATTTTC	226

TableS 5. GWAS Results in this study of previous identified myopia associated SNPs by GWASs.

Gene	Location	SNP	Sample Size	Ethnicity	p	Reference	Minor Allele	GWAS data in this study				
								F_A	F_U	CHISQ	p	OR
<i>CTNND2</i>	5p15	rs6885224	4153	Singapore Chinese & Japanese	7.84E-06	Li YJ, et al. Ophthalmology. 2010 Nov 20.	G	0.2124	0.2003	0.4638	0.4958	1.077
		rs12716080	4155		1.05E-05		C	0.2255	0.2175	0.1941	0.6595	1.048
<i>BLID & MIR100HG</i>	11q24.1	rs10892819	2741	Japanese	0.04	Hideo Nakanishi, et al. PLoS Genet. 2009 Sep 25.	C	0.2368	0.2571	1.128	0.2882	0.8968
		rs577948			2.22E-07		A	0.5012	0.4888	0.3172	0.5733	1.051
		rs11218553			8.28E-03		G	0.3067	0.3154	0.1822	0.6695	0.9602
		rs11218544			5.48E-06		C	0.4069	0.4111	0.03652	0.8484	0.983
<i>RASGRF1</i>	15q25	rs939661	14105	European	3.85E-09	Pirro G Hysi, et al. Nat Genet. 2010 Sep 12.	G	0.3592	0.4103	5.658	0.01738	0.8056
		rs8027411			2.07E-09		C	0.3974	0.4544	4.358	0.03680	0.817
near <i>GJD2 & ACTC1</i>	15q14	rs560766	15608	European	2.49E-11	Abbas M Solouki, et al. Nat Genet. 2010 Sep 12.	A	0.4486	0.4275	0.9283	0.3353	1.089
		rs580839			2.53E-11		A	0.4462	0.4279	0.6909	0.4058	1.077