

Supplementary Figures and Tables

SLC39A5 mutations interfering BMP/TGF- β pathway in nonsyndromic high myopia

Hui Guo, Xuemin Jin, Tengfei Zhu, Tianyun Wang, Ping Tong, Lei Tian, Yu Peng, Liangdan Sun, Anran Wan, Jingjing Chen, Yanling Liu, Ying Li, Qi Tian, Lu Xia, Lusi Zhang, Yongcheng Pan, Lina Lu, Qiong Liu, Lu Shen, Yunping Li, Wei Xiong, Jiada Li, Beisha Tang, Yong Feng, Xuejun Zhang, Zhuohua Zhang, Qian Pan, Zhengmao Hu, Kun Xia

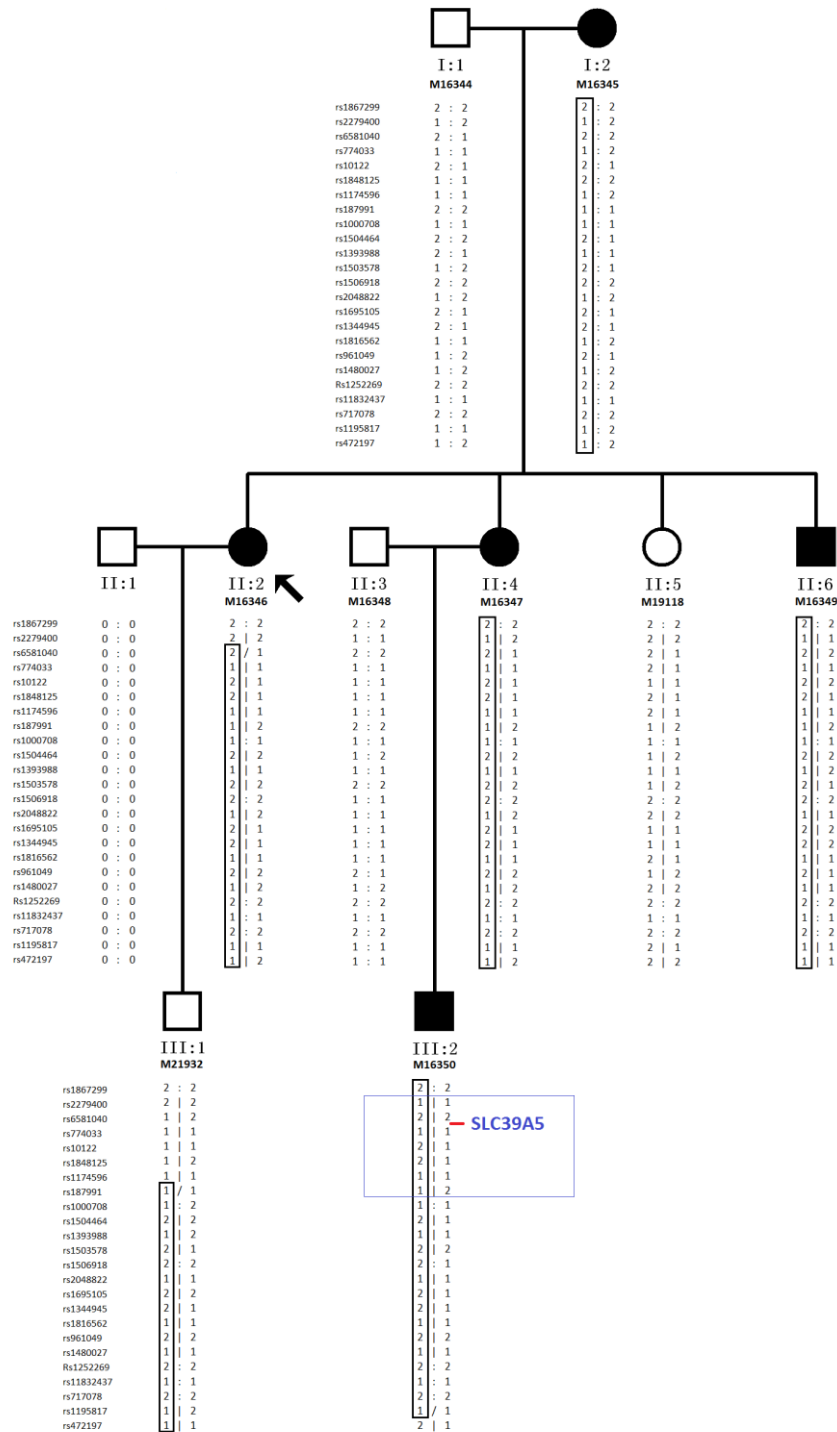


Figure S1. Haplotype analysis for the linkage interval in chromosome 12. The haplotype, highlighted by black square frame, is assumed to carry the inherited disease allele. Recombination was observed between rs2279400 and rs6581040 on patient M16346 at the top, and between rs1174596 and rs187991 on patient M21932 at the bottom. The minimum haplotype segregating with phenotype carrying the disease allele is from rs2279400 to rs187991 (blue square). SLC39A5 is located between rs6581040 and rs774033.

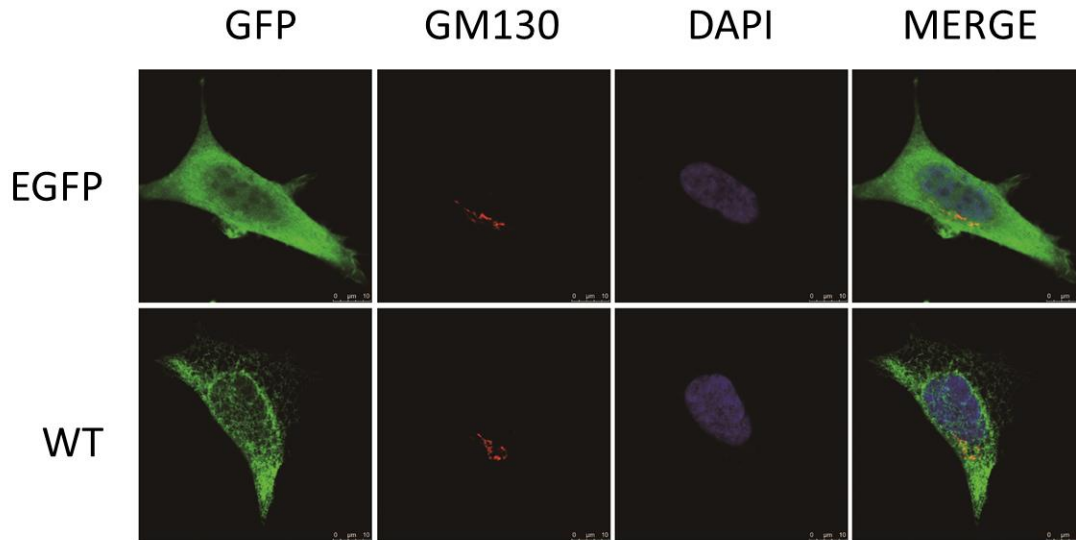


Figure S2. Immunofluorescence showed that SLC39A5 (SLC39A5-GFP: *green*) was not localized in the membrane of Golgi network (GM130 marker: *red*). Blue color indicates the nuclei that were stained with DAPI.

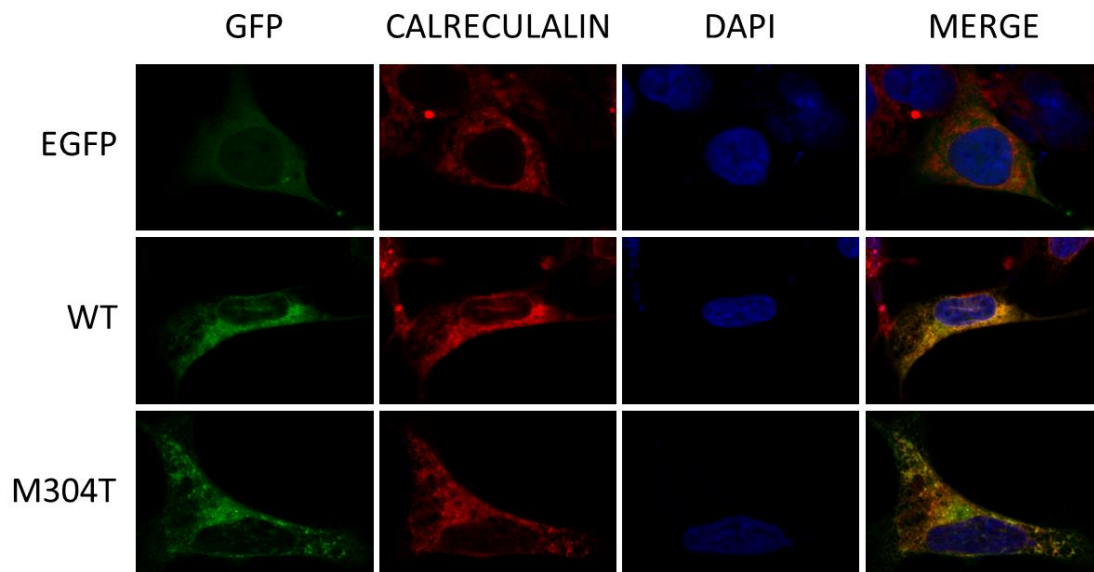


Figure S3. Immunofluorescence showed that SLC39A5 (SLC39A5-GFP: *green*) and the membrane of endoplasmic reticulum (CALRECALIN marker: *red*) are co-localization (Merge: *yellow*). Blue color indicates the nuclei that were stained with DAPI. The missense mutation of *SLC39A5* (M304T) did not influence the membrane localization.

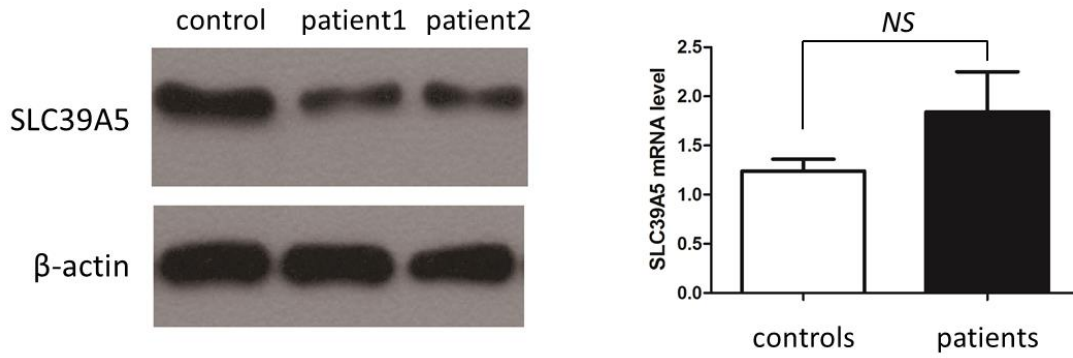


Figure S4. A: Immunoblot showed that the protein expression level of SLC39A5 in patients' lymphocyte cell lines (M16346 and M16350) was decreased as compared to the control. B: Real-time qPCR showed that there is no significant difference of mRNA expression level in lymphocyte cell lines between cases and controls.

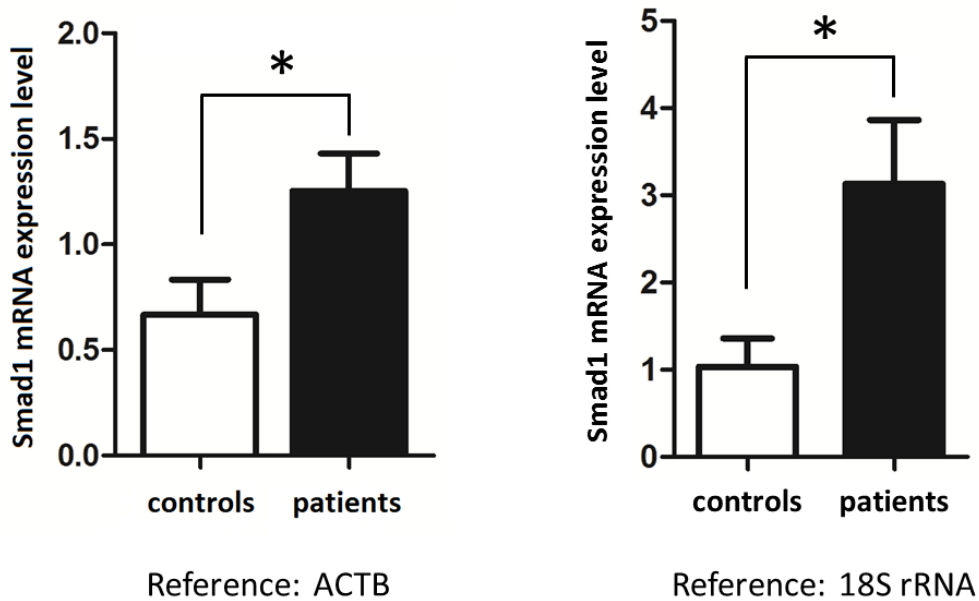


Figure S5. Real-time qPCR revealed that the mRNA expression level of Smad1 is significantly increased in patients as compared to family unaffected controls. Two housekeeping genes, ACTB and 18S rRNA, were used as reference.

Table S1. Four linkage regions with maximum LOD score more than 1.

CHR	snpID	Position(cM)	Position(bp)	LOD	ALPHA	HLOD
Linkage Region 1						
chr2	rs714393	208.0927	212698718	-1.583	0	0
chr2	rs2054615	209.1377	213484752	0.799	1	0.799
chr2	rs931218	209.1535	213496624	0.808	1	0.808
chr2	rs1397354	210.4696	214916394	1.3	1	1.3
chr2	rs1880586	211.9134	216195171	1.415	1	1.415
chr2	rs1525351	211.9945	216263366	1.415	1	1.415
chr2	rs1851328	213.9884	217180532	1.414	1	1.414
chr2	rs750365	216.01	218391463	1.413	1	1.413
chr2	rs921970	217.5207	219209796	1.413	1	1.413
chr2	rs9076	217.5223	219210781	1.413	1	1.413
chr2	rs585185	217.9054	219457741	1.412	1	1.412
chr2	rs1554622	218.1358	219606218	1.412	1	1.412
chr2	rs746233	219.8353	220384126	1.41	1	1.41
chr2	rs1378011	221.572	221231032	1.41	1	1.41
chr2	rs1463991	222.5677	221703746	1.411	1	1.411
chr2	rs1002742	223.789	222133254	1.412	1	1.412
chr2	rs348971	225.0195	222918191	1.414	1	1.414
chr2	rs1438620	225.1031	223038461	1.402	1	1.402
chr2	rs6756323	226.1572	223785740	1.208	1	1.208
chr2	rs2028383	226.2017	223823132	1.198	1	1.198
chr2	rs17203808	226.6372	224189533	1.08	1	1.08
chr2	rs1045654	228.0278	225630233	-1.46	0	0
Linkage Region 2						
chr2	rs1469375	244.998	235950187	-1.461	0	0
chr2	rs11680844	246.1844	236261524	0.667	1	0.667
chr2	rs1569125	247.446	236556537	0.928	1	0.928
chr2	rs1728291	247.7624	236668638	0.966	1	0.966
chr2	rs729454	249.1315	237851338	1.074	1	1.074
chr2	rs1198823	251.5616	238760118	1.127	1	1.127
chr2	rs1198826	251.6564	238793068	1.126	1	1.126
chr2	rs895572	251.7202	238815252	1.121	1	1.121
chr2	rs472357	253.1288	239355454	0.997	1	0.997
chr2	rs6431603	253.4846	239492882	0.959	1	0.959
chr2	rs291335	255.1809	240147847	0.712	1	0.712
chr2	rs731161	256.5374	240671768	0.304	1	0.304
chr2	rs2083411	257.3843	240961728	-1.362	0	0
Linkage Region 3						
chr10	rs1041226	19.60313	6643851	-1.164	0	0
chr10	rs2439903	20.05396	6831860	0.566	1	0.566
chr10	rs942432	20.8777	7162564	1.012	1	1.012
chr10	rs1969825	21.00757	7221320	1.054	1	1.054
chr10	rs942434	21.03659	7237007	1.063	1	1.063
chr10	rs1537626	21.80639	7653124	1.249	1	1.249
chr10	rs3858256	22.02301	7770222	1.289	1	1.289
chr10	rs1244459	22.31534	7928240	1.339	1	1.339
chr10	rs2671303	22.58606	8074577	1.38	1	1.38
chr10	rs516769	22.841	8212168	1.415	1	1.415
chr10	rs1663691	25.24088	9023732	1.415	1	1.415
chr10	rs2589569	25.38377	9071968	1.415	1	1.415
chr10	rs1033912	25.99346	9592521	1.414	1	1.414

chr10	rs1535976	29.10913	11850132	1.413	1	1.413
chr10	rs1892302	30.42805	12446572	1.414	1	1.414
chr10	rs1111060	30.71605	12576812	1.414	1	1.414
chr10	rs652029	32.08619	13064407	1.414	1	1.414
chr10	rs7899305	32.49754	13199611	1.415	1	1.415
chr10	rs1890876	33.35893	13482731	1.416	1	1.416
chr10	rs1001201	34.76352	14043452	1.416	1	1.416
chr10	rs873849	36.16506	14509807	1.416	1	1.416
chr10	rs2298033	37.67526	15649710	1.416	1	1.416
chr10	rs1341106	37.81187	15701278	1.416	1	1.416
chr10	rs1341100	37.95056	15753837	1.416	1	1.416
chr10	rs780838	40.7268	16921370	1.414	1	1.414
chr10	rs1810205	40.83673	16965227	1.414	1	1.414
chr10	rs1276709	41.01948	17038138	1.414	1	1.414
chr10	rs359280	41.72523	17319707	1.414	1	1.414
chr10	rs359327	41.82716	17398870	1.414	1	1.414
chr10	rs729245	43.47998	18741794	1.415	1	1.415
chr10	rs10740828	43.86	19320865	1.415	1	1.415
chr10	rs949857	45.14854	20525737	1.416	1	1.416
chr10	rs4748722	45.52962	21073521	1.416	1	1.416
chr10	rs10828183	45.72443	21353551	1.416	1	1.416
chr10	rs8341	46.38657	22825133	1.416	1	1.416
chr10	rs927751	46.52325	23506529	1.387	1	1.387
chr10	rs442463	47.94854	24614557	0.763	1	0.763
chr10	rs1928365	49.57619	25782764	-0.958	0	0
Linkage Region 4						
chr12	rs2279400	69.47428	54581314	-1.461	0	0
chr12	rs6581040	70.80205	55790945	1.12	1	1.12
chr12	rs774033	72.09882	56825311	1.416	1	1.416
chr12	rs10122	72.76	58350631	1.416	1	1.416
chr12	rs1848125	72.81748	58519811	1.39	1	1.39
chr12	rs1174596	72.96262	58761336	1.332	1	1.332
chr12	rs187991	73.85646	59962305	0.421	1	0.421
chr12	rs1000708	73.92	60083488	0.421	1	0.421
chr12	rs1504464	73.95303	60743179	0.421	1	0.421
chr12	rs1393988	74.06718	60987363	0.421	1	0.421
chr12	rs1503578	74.07032	60991716	0.421	1	0.421
chr12	rs1506918	74.51395	61606297	0.421	1	0.421
chr12	rs2048822	74.63473	61773625	0.421	1	0.421
chr12	rs1695105	77.63686	64597579	0.421	1	0.421
chr12	rs1344945	78.7658	65675628	0.422	1	0.422
chr12	rs1816562	80.26799	66678337	0.422	1	0.422
chr12	rs961049	80.39421	66762591	0.422	1	0.422
chr12	rs1480027	80.93679	67124761	0.421	1	0.421
chr12	rs1252269	81.14355	67262772	0.396	1	0.396
chr12	rs11832437	81.32215	67381992	0.373	1	0.373
chr12	rs717078	82.47697	68131676	0.182	1	0.182
chr12	rs1195817	84.43761	69330932	-1.037	0	0

Table S2. Summary statistics for exome sequencing for the two individuals from HM-FR3 family

Sample	Bases	Map Bases	Map Bases Rate	Target Map Base	Target Map Bases Rate	Target Length	Coverage	Mean Depth
M16346	6.83 Gbp	5.22 Gbp	78.2%	2.91 Gbp	67.7%	62 Mbp	95.1%	46.9X
M16350	13.03 Gbp	9.89 Gbp	77.4%	5.66 Gbp	70.1%	62 Mbp	95.6%	91.2X

Table S3. Clinical description for the 180 family probands or sporadic cases

StatItems	Age	Refractive Error [DS]		Axial Length[mm]	
		OD	OS	OD	OS
Min	3	6.40	6.50	26.50	26.20
Max	77	30.00	30.00	44.38	35.00
Mid	41	11.75	12.00	27.52	27.46
Avg	39	13.64	14.31	28.07	27.99