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SNTB1 gene polymorphisms and risk of high myopia: meta-analysis and single-center validation

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Purpose: Genetic polymorphisms in syntrophin beta-1 (SNTB1) have been implicated in altering protein function or expression, potentially influencing ocular growth regulation. Genome-wide association studies (GWASs) suggest that specific *SNTB1* variants may correlate with high myopia susceptibility across diverse populations. However, findings remain inconsistent, highlighting the need for further investigation into population-specific genetic effects and underlying mechanisms.

Methods: Accordingly, the PubMed and Wanfang databases were searched for articles published until June 1, 2025, using the keywords *SNTB1* or *syntrophin beta-1*, *polymorphism*, and *myopia* or *shortsightedness*. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to examine the association. The *SNTB1* rs6469937 polymorphism genotypes were identified with the TaqMan assay.

Results: Four related studies were conducted to better understand the association between *SNTB1* gene polymorphisms and high myopia risk. The *SNTB1* rs4455882 site was associated with a decreased overall high myopia risk (e.g., G vs. A; OR = 0.815; 95% CI, 0.688–0.984; $p_{heterogeneity}$ = 0.465; p = 0.017). Similar trends were detected in the rs4395927 site (e.g., T vs. C; OR = 0.791; 95% CI, 0.670–0.935; $p_{heterogeneity}$ = 0.199; p = 0.006) and rs6469937 site (e.g., A vs. G; OR = 0.811; 95% CI, 0.697–0.944; $p_{heterogeneity}$ = 0.030; p = 0.007). Furthermore, high myopia patients carrying the *SNTB1* rs6469937 AA+AG genotypes exhibited pronounced increases in serum levels of *SNTB1* compared to the GG genotype ($p < 0.01$) but showed an opposite trend compared to genotype-matched normal controls ($p < 0.05$).

Conclusions: The current study suggested that the *SNTB1* rs4455882, rs4395927, and rs6469937 polymorphisms may be potential influencing factors of high myopia. Furthermore, the rs6469937 polymorphism may offer value as a candidate variant requiring validation that can aid in the early identification and prognostic evaluation of high myopia.

High myopia (typically defined as ≤–6.00 diopters) is a severe refractive error marked by excessive axial elongation of the eyeball. It poses significant risks of vision-threatening complications and has become a global public health concern, especially in East Asia. In adults, its prevalence ranges from 0.5% to 9.8%, with considerable regional variations [1].

The etiology of high myopia is complex, involving interactions between genetic and environmental factors. Compared to low-to-moderate myopia, high myopia has a stronger genetic predisposition, while environmental factors play a modulating role. In contrast, the recent rapid increase in low-to-moderate myopia is largely attributed to environmental and lifestyle changes since the mid-20th century [2].

Before the genome-wide association study (GWAS) era, researchers used family linkage analyses and candidate gene approaches to identify high myopia–associated genes in families, twins, and offspring. These studies confirmed that individuals with high myopia in their parents are more likely to develop the condition, highlighting the role of genetic susceptibility [3,4].

GWASs have identified over 200 loci associated with high myopia, including PAX6 and GJD2 [5]. Recently, syntrophin beta-1 (SNTB1) has been widely linked to high myopia susceptibility. SNTB1 encodes a cytoskeleton-associated protein in the syntrophin family, which is involved in cell signaling and structural maintenance. In the retina, SNTB1 may interact with proteins such as the dystrophin complex to influence photoreceptor or retinal neuron stability. Some studies suggest a connection between SNTB1 and retinal development or diseases such as retinal degeneration, although the exact mechanisms remain unclear [6–11].

Currently, no meta-analysis has examined the association between *SNTB1* gene polymorphisms and high myopia risk. Therefore, we performed pooled analyses of all available case-control studies, focusing on four common polymorphisms: rs4455882, rs4395927, rs7839488, and rs6469937. This aims to provide stronger evidence on whether these variants are significantly associated with high myopia [12–15]. Additionally, we explored the relationship between different

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rs6469937 genotypes and SNTB1 expression based on our single-center data.

METHODS

Study selection and data extraction: At the beginning, the PubMed and Wanfang databases were searched for articles published as of June 1, 2025, using the keywords *SNTB1* or *syntrophin beta-1*, *polymorphism*, and *myopia* or *shortsightedness*. No language or publication year restrictions were imposed on the search. The references of retrieved articles and reviews were additionally manually searched for relevant studies.

Eligible studies were those that (a) evaluated correlations between high myopia risk and one or more of the selected polymorphisms, (b) were case-control studies, (c) included age- and gender-matched control groups, and (d) had an available full-text manuscript. Studies were excluded if they (a) lacked a control population, (b) did not provide genotype frequencies, (c) were duplicate studies, or (d) exhibited clear evidence of bias. Literature search results were reviewed by two investigators. Collected data from identified studies included first author, publication year, country, ethnicity, genotypes in the case and control groups, source of controls, Hardy–Weinberg equilibrium analyses of controls, and genotyping methods (polymerase chain reaction, Sequenom MassARRAY System, San Diego, CA, sequencing).

Statistical analyses: Odds ratios (ORs) and 95% confidence intervals (CIs) were used to examine the association between *SNTB1* polymorphisms and the risk of high myopia based on genotypic frequency levels in cases and control subjects. Subgroup analyses were initially conducted based on the source of control subjects, separately assessing population-based and hospital-based studies.

Pooled OR significance was assessed using the *z* test [16]. The χ^2-based *Q* tests were used to assess heterogeneity, with $p < 0.05$ being indicative of significant heterogeneity, in which case pooled ORs were analyzed with a random-effects model [17], whereas a fixed-effects model [18] was otherwise employed [19,20]. For the rs4455882, rs4395927, rs7839488, and rs6469937 polymorphisms in the *SNTB1* gene, associations between genotype and high myopia risk were assessed using dominant, heterozygote comparison, allelic contrast, homozygote comparison, and recessive genetic models. Begg's and Egger's tests were used to evaluate funnel plot asymmetry to detect publication bias [21], with $p < 0.05$ as the cutoff to define significance. The Pearson χ^2 test for goodness of fit was used to detect departures from Hardy–Weinberg equilibrium with respect to the frequencies of *SNTB1* polymorphisms, using $p < 0.05$ as the cutoff to define significance. Stata v11.0 (StataCorp LP, College Station, TX) was used to conduct statistical analyses.

Bioinformatics analyses: Minor allele frequency reports for these four polymorphisms were assessed in six global populations using the 1000 Genomes Browser, which shows different ratios across races for each polymorphism (https://www.ncbi.nlm.nih.gov/snp/). In addition, the genomic locations of the four *SNTB1* polymorphisms (rs4455882, rs4395927, rs7839488, and rs6469937) were visualized using the National Center for Biotechnology Information (NCBI) database. Finally, haplotype analysis was applied, using the LDBlockShow software; the linkage disequilibrium (LD) between single-nucleotide polymorphisms (SNPs) in some gene region was calculated (using the R^2 statistic), and the Solid Spine of LD method (BlockType 2) was employed to identify haplotype blocks.

Genotyping: SNTB1 gene polymorphism genotyping has been performed with a range of techniques across studies, including polymerase chain reaction, the Sequenom MassARRAY System, and sequencing. For the present study, *SNTB1* rs6469937 polymorphism genotypes were assessed with the TaqMan assay using the approach documented by Castro et al. [22]. The power of our study was calculated by the PS: Power and Sample Size Calculation.

Study population: This cross-sectional study recruited 120 treatment-naive patients with high myopia (spherical equivalent ≤−6.00 D) at the Affiliated Hospital of Jiangnan University between April 2023 and December 2024. An age-matched control cohort (n = 120) with emmetropia (spherical equivalent −0.50 to +1.00 D) was concurrently enrolled from routine health screenings. Participants underwent a comprehensive ophthalmic evaluation to exclude confounding pathologies: ocular exclusions, including keratoconus, glaucoma, cataracts, macular degeneration, prior intraocular/refractive surgery, corneal opacities, or strabismus; systemic exclusions, including conditions potentially compromising visual function; and additional exclusions, including an unwillingness to participate or conditions affecting refractive assessment accuracy [23]. Peripheral blood samples (3 ml) were obtained from all participants after written informed consent. The study protocol (Ethical Approval Code: LS202221) received institutional review board approval at Jiangnan University and adhered to the principles of the Declaration of Helsinki.

Enzyme-linked immunosorbent assay: Blood samples were collected in anticoagulant-free tubes, after which serum separator tubes were used and samples were allowed to clot overnight at 4 °C or at room temperature for 2 h. Samples were then centrifuged (1,000 ×*g*, 15 min), after which serum was collected and immediately assessed or stored at −20 °C

or −80 °C for future analyses, minimizing repeated freezing and thawing. Serum levels were detected with an ELISA kit (Yuhengfeng Co. Ltd., Beijing, China). Absorbance at 450 nm was assessed, with correction at 540 or 570 nm. For further details, see the manufacturer's website (ELISA).

RESULTS

Systematic literature review and study selection: Our systematic search strategy retrieved 15 potentially relevant articles from PubMed and Wanfang databases. After rigorous evaluation based on predefined inclusion criteria, four high-quality studies were selected for meta-analysis (Figure 1), including three case-control studies for rs4455882, three case-control studies for rs4395927, four case-control studies for rs6469937, and three case-control studies for rs7839488. The detailed characteristics of the included studies are presented in Table 1.

Minor allele frequency reports for these four polymorphisms were assessed in six global populations using the 1000 Genomes Browser, which shows different ratios across races for each polymorphism (SNP; Figure 2). In addition, through comprehensive database mining, these four polymorphisms (rs4455882, rs4395927, rs7839488, and rs6469937) were located within the promoter region of the SNTB1 gene (Figure 2).

An LD heatmap was then generated, with four SNPs of interest (rs4455882, rs4395927, rs7839488, and rs6469937) annotated in Figure 3. Through the LD plot, we can intuitively visualize the LD structure among SNPs in the target region. rs4395927 and rs7839488 may have an LD relationship. The LD patterns of the four annotated SNPs with surrounding SNPs help elucidate the genetic structure of this region and provide clues for subsequent gene mapping and functional studies.

Pooled analyses: The results of pooled analyses pertaining to the *SNTB1* rs4455882 polymorphism are presented in Table 2. A significant decrease in the association between this polymorphism and high myopia risk was detected in three genetic models (OR = 0.815; 95% CI, 0.688–0.964; $p_{heterogeneity}$ = 0.465; p = 0.017 for G-allele vs. A-allele, Figure 4; OR = 0.569; 95% CI, 0.359–0.903; $p_{heterogeneity}$ = 0.660; p = 0.017 for GG vs. AA; OR = 0.811; 95% CI, 0.658–0.999; $p_{heterogeneity}$ = 0.653; p = 0.049 for GG+GA vs. AA). Similar positive results were observed between the rs4395927 polymorphism and high myopia risk in four genetic models (e.g., OR = 0.791; 95% CI, 0.670–0.935; $p_{heterogeneity}$ = 0.199; p = 0.006 for T-allele vs. C-allele, Figure 5; OR = 0.544; 95% CI, 0.345–0.860; $p_{heterogeneity}$ = 0.775; p = 0.009 for TT vs. CC).

Another potential significant association was found between the rs6469937 polymorphism and high myopia risk in four genetic models in the total group (e.g., OR = 0.811; 95% CI, 0.697–0.944; $p_{heterogeneity}$ = 0.030; p = 0.007 for A-allele vs. G-allele, Figure 6; OR = 0.723; 95% CI, 0.588–0.889; $p_{heterogeneity}$ = 0.136; p = 0.002 for AA vs. GG), and the same associations were found when conducting subgroup analyses based on the source of control subjects both for population-based studies (e.g., OR = 0.824; 95% CI, 0.683–0.994; $p_{heterogeneity}$ = 0.027; p = 0.043 for A-allele vs. G-allele) and hospital-based studies (e.g., OR = 0.853; 95% CI, 0.780–0.932; $p_{heterogeneity}$ = 0.123; p = 0.017 for A-allele vs. G-allele, Figure 7; Table 2). For the three other *SNTB1* rs7839488 polymorphisms, no significant associations with overall high myopia risk were detected for different variant genotypes under the analyzed genetic models (Table 2).

Publication bias analyses: The potential for publication bias was next evaluated with Begg's funnel plots and Egger's test. No publication bias was found in all four polymorphisms (data not shown).

Our own clinical results: The power of our study about rs6469937 was 0.238. In addition, our approach revealed that serum SNTB1 concentrations were significantly higher in high myopia patients harboring the AA+AG genotypes in rs6469937 as compared to the GG genotype ($p < 0.01$), but serum SNTB1 levels in high myopia patients with the AA+AG genotypes were also significantly lower as compared to levels in normal control subjects with the same genotypes ($p < 0.05$; Figure 8).

Network analysis for SNTB1 interaction: STRING database analysis identified 10 potential SNTB1-interacting genes, forming a complex regulatory network (Figure 9). Network topology analysis revealed 10 positive regulatory interactions (SNTB2, SNTG2, DAG1, DTNA, DTNB, UTRN, SGCG, SGCD, DMD, SGCA) with SNTB1. These interactions suggest potential combinatorial biomarker applications for early high myopia detection and provide valuable insights for future mechanistic studies.

DISCUSSION

High myopia affects approximately 2% to 5% of the global population, with prevalence exceeding 20% in East Asia [24]. This condition elevates the risk of sight-threatening complications, including retinal detachment (OR = 10.2), glaucoma (OR = 5.1), and myopic maculopathy, which has a 40% progression risk by age 60 [25].

GWASs have implicated over 25 susceptibility loci. For example, the *PAX6* rs644242 polymorphism was associated

with altered scleral remodeling (OR = 1.28; $p = 3\times10^{-11}$) [5]. The *GJD2* rs634990 polymorphism may disrupt gap junction signaling (β = −0.57D; $p = 4 \times 10^{-10}$) [26]. Furthermore, the *ZC3H11B* rs4373767 polymorphism was a genetic risk factor for moderate and high myopia (OR = 1.42; p = 0.018) and was also associated with excessive axial length in children (β = 0.07; p = 0.002) [27]. Epistatic interactions between *BMP2* and *TGFBR1* variants can also amplify disease severity ($p < 0.001$) [28]. However, polygenic risk scores explain only 12% to 18% of the variance, suggesting that environmental factors play a significant role in the development of high myopia [29].

This meta-analysis is the first to systematically evaluate the relationship between four *SNTB1* polymorphisms and high myopia risk. Our pooled analysis included data from 670 cases and 1,015 controls for rs4455882, 691 cases and 1,022

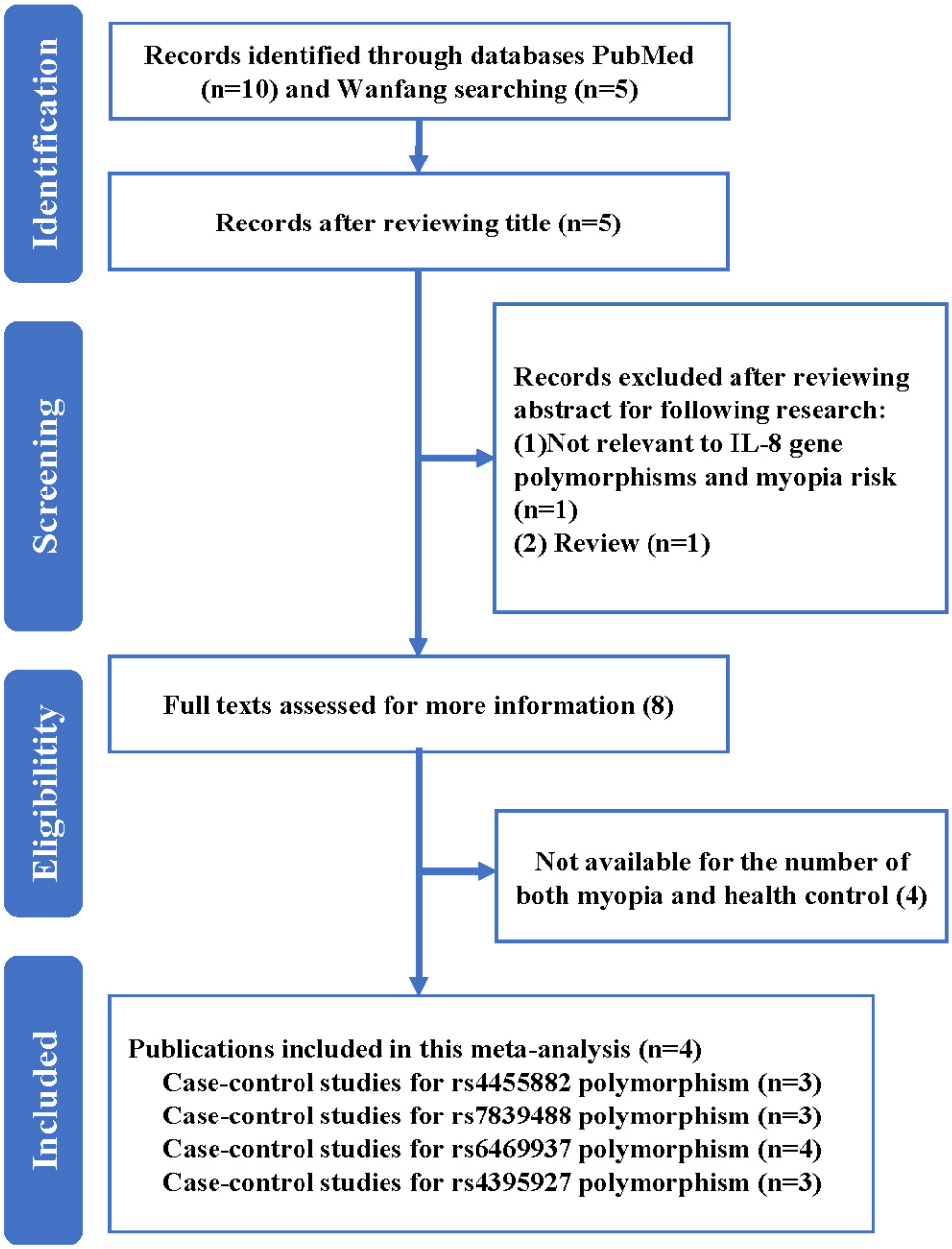

Figure 1. Flowchart depicting the systematic search strategy from different databases about the identification of studies investigating *SNTB1* gene polymorphisms and high myopia risk.

Table 1. Characteristics of included studies about polymorphisms in *SNTB1* gene and myopia risk.

Author	Year	Country	Case	Control	SOC	Case			Control			HWE	Genotype
rs4455882						GG	GA	AA	GG	GA	AA		
Cheong	2020	Singapore	191	135	PB	8	63	120	10	53	72	0.95	Sequenom mass array system
Yang	2023	China	429	830	HB	17	147	265	56	294	480	0.23	Sequenom mass array system
Zhang	2023	China	50	50	HB	32	14	4	30	16	4	0.38	PCR
rs7839488						AA	AG	GG	AA	AG	GG		
Cheong	2020	Singapore	191	135	PB	8	59	124	11	49	75	0.45	Sequenom mass array system
Yang	2023	China	450	837	HB	19	161	270	54	294	489	0.27	Sequenom mass array system
Zhang	2023	China	50	50	HB	34	12	4	27	18	5	0.44	PCR
rs6469937						AA	AG	GG	AA	AG	GG		
Cheong	2020	Singapore	191	134	PB	11	64	116	11	58	65	0.69	Sequenom mass array system
Li	2017	China	299	308	PB	13	110	176	30	121	157	0.34	sequencing
Li	2017	China	95	95	PB	4	33	58	5	46	44	0.11	sequencing
Li	2017	China	526	413	PB	220	230	76	158	194	61	0.91	sequencing
Li	2017	China	562	922	PB	237	246	79	419	401	102	0.68	sequencing
Yang	2023	China	453	831	HB	19	172	262	54	334	443	0.39	Sequenom mass array system
Zhang	2023	China	50	50	HB	2	10	38	5	16	29	0.23	PCR
rs4395927						TT	TC	CC	TT	TC	CC		
Cheong	2020	Singapore	191	135	PB	8	62	121	11	51	73	0.62	Sequenom mass array system
Yang	2023	China	450	840	HB	19	157	274	56	299	485	0.28	Sequenom mass array system
Zhang	2023	China	50	50	HB	2	10	38	4	18	28	0.65	PCR

HB: hospital-based; PB: population-based; SOC: source of control; PCR: polymerase chain reaction; HWE: Hardy–Weinberg equilibrium of the control group.

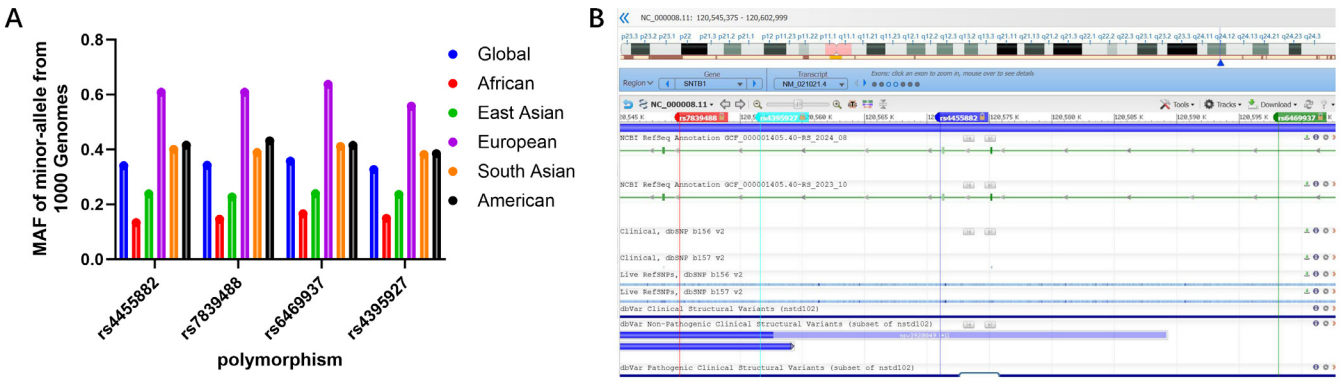

Figure 2. Minor (mutant) allele frequencies for *SNTB1* four polymorphisms based on data from the online 1000 Genomes database. The location and information of four polymorphisms in the *SNTB1* gene from the National Center for Biotechnology (NCBI).

controls for rs7839488, 2,176 cases and 2,753 controls for rs6469937, and 691 cases and 1,025 controls for rs4395927.

We found a significant association between the rs4455882, rs6469937, and rs4395927 polymorphisms and high myopia risk. However, these findings are based on currently limited sample sizes, and further research with larger cohorts is needed.

Notably, normal individuals with AA/AG genotypes of rs6469937 exhibited higher serum SNTB1 expression than both high myopia patients with the same genotypes and high myopia patients carrying the GG genotype. This suggested

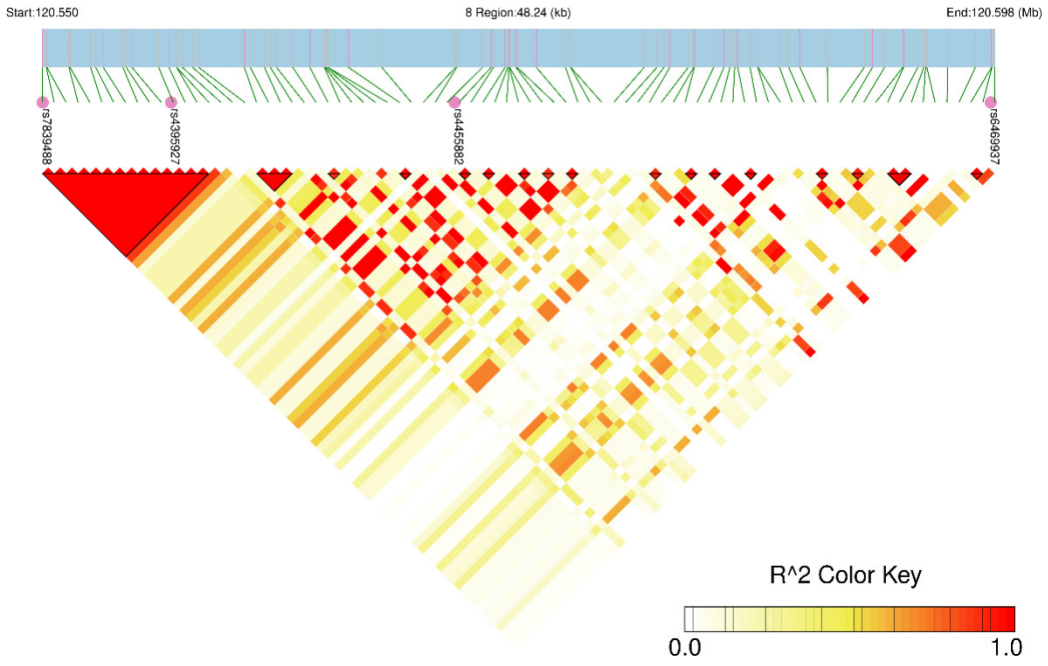

Figure 3. Using the LDBlockShow software, the LD between SNPs in this region was calculated (using the R^2 statistic), and the solid spine of the LD method (BlockType 2) was employed to identify haplotype blocks. LD heatmap: Each square in the figure represents the LD strength (R^2 value) between two SNPs, with colors ranging from white ($R^2 = 0$) to red ($R^2 = 1$). Haplotype blocks: The triangular regions in the figure are divided into multiple blocks, where SNPs within each block exhibit strong LD, representing a potential haplotype. Significant SNPs: The four annotated SNPs are located at specific positions on chromosome 8. Their linkage with other SNPs can be observed through the LD heatmap.

Table 2. Stratified analyses of *SNTB1* gene common polymorphisms on myopia risk.

Variables	No. of studies	Case/ Controls	G-allele versus A-allele	GG versus AA	GA versus AA	GG+GA versus AA	GG versus GA+AA
			OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P
rs4455882							
Total	3	670/1015	0.815 (0.688–0.964) 0.465 0.017	0.569 (0.359–0.903) 0.660 0.017	0.860 (0.692–1.069) 0.676 0.174	0.811 (0.658–0.999) 0.653 0.049	0.679 (0.452–1.020) 0.301 0.062
			A-allele versus G-allele	AA versus GG	AG versus GG	AA+AG versus GG	AA versus AG+GG
			OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P	OR(95%CI) P_h P
rs7839488							
Total	3	691/1022	0.902 (0.651–1.250) 0.095 0.536	0.646 (0.414–1.007) 0.340 0.054	0.929 (0.749–1.150) 0.520 0.497	0.882 (0.719–1.083) 0.391 0.230	0.825 (0.400–1.701) 0.062 0.603
			A-allele versus G-allele	AA versus GG	AG versus GG	AA+AG versus GG	AA versus AG+GG
			OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P
rs6469937							
Total	7	2176/2753	0.811 (0.697–0.944) 0.030 0.007	0.723 (0.588–0.889) 0.136 0.002	0.797 (0.692–0.917) 0.514 0.002	0.769 (0.673–0.880) 0.321 0.000	0.791 (0.601–1.041) 0.069 0.095
Source of control							
PB	5	1673/1872	0.824 (0.683–0.994) 0.027 0.043	0.707 (0.485–1.029) 0.091 0.070	0.773 (0.648–0.923) 0.490 0.004	0.755 (0.638–0.893) 0.306 0.001	0.842 (0.619–1.146) 0.064 0.275
HB	2	503/881	0.853 (0.780–0.932) 0.123 0.017	0.559 (0.333–0.939) 0.466 0.028	0.838 (0.665–1.056) 0.217 0.134	0.796 (0.637–0.995) 0.154 0.045	0.600 (0.360–1.001) 0.566 0.050
			T-allele versus C-allele	TT versus CC	TC versus CC	TT+TC versus CC	TT versus TC+CC
			OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P	OR (95%CI) P_h P
rs4395927							
Total	3	691/1025	0.791 (0.670–0.935) 0.199 0.006	0.544 (0.345–0.860) 0.775 0.009	0.848 (0.687–1.046) 0.187 0.124	0.798 (0.653–0.976) 0.167 0.028	0.579 (0.369–0.907) 0.899 0.017

P_h: value of *Q*-test for heterogeneity test; *P: Z*-test for the statistical significance of the OR; HB: hospital-based; PB: population-based

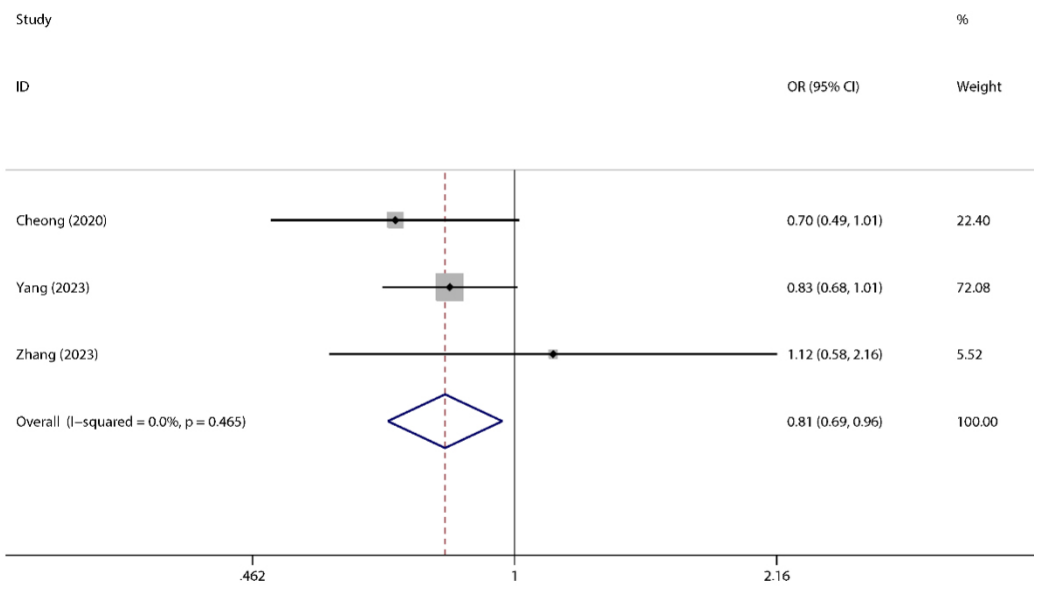

Figure 4. Forest plots corresponding to high myopia risk between the *SNTB1* rs4455882 polymorphism in the G-allele versus the A-allele in total. The squares and horizontal lines respectively correspond to the study-specific ORs and 95% CIs, with the square area being indicative of weight (the inverse of the variance). Diamonds additionally reflect the summary OR and 95% CI.

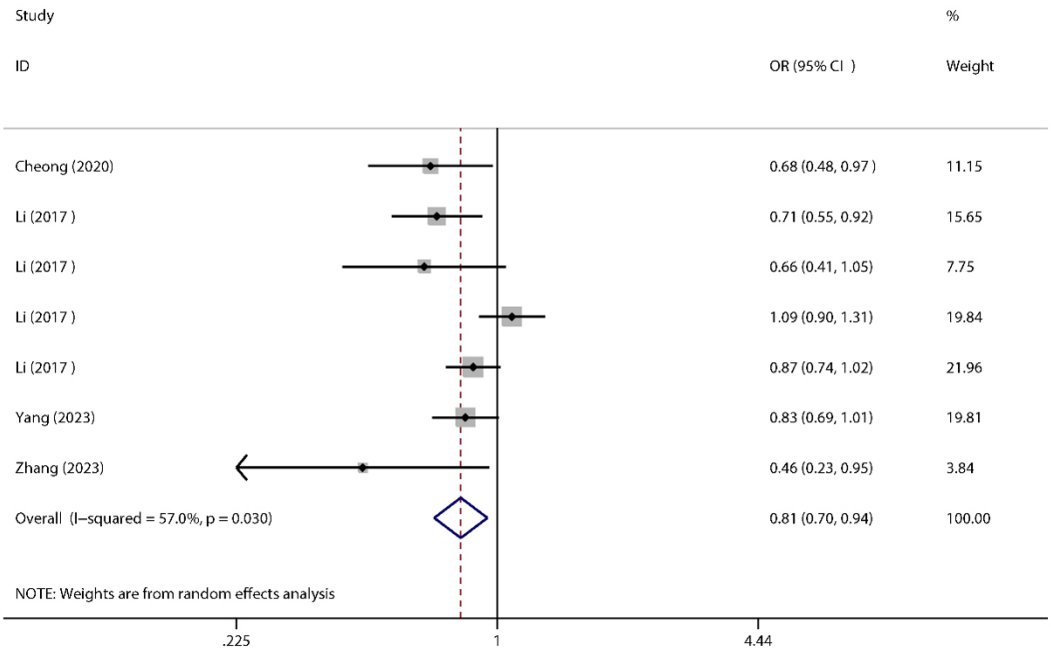

Figure 5. Forest plots corresponding to high myopia risk between the *SNTB1* rs4395927 polymorphism in the T-allele versus the C-allele in total.

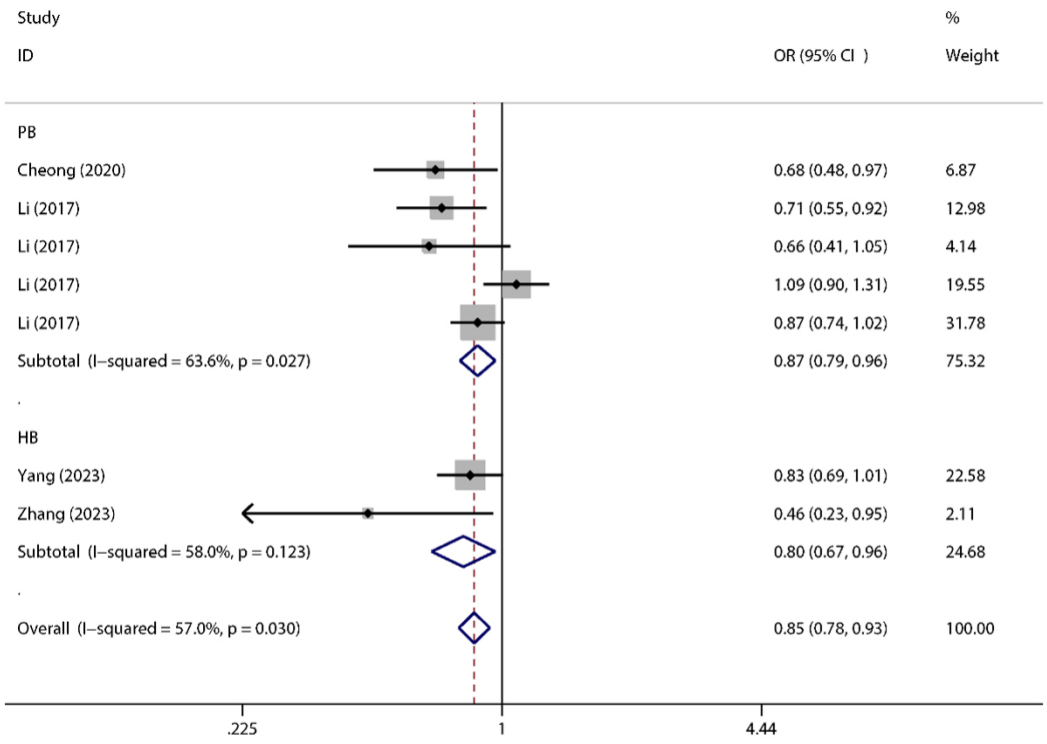

Figure 6. Forest plots corresponding to high myopia risk between the *SNTB1* rs6469937 polymorphism in the A-allele versus the G-allele in total.

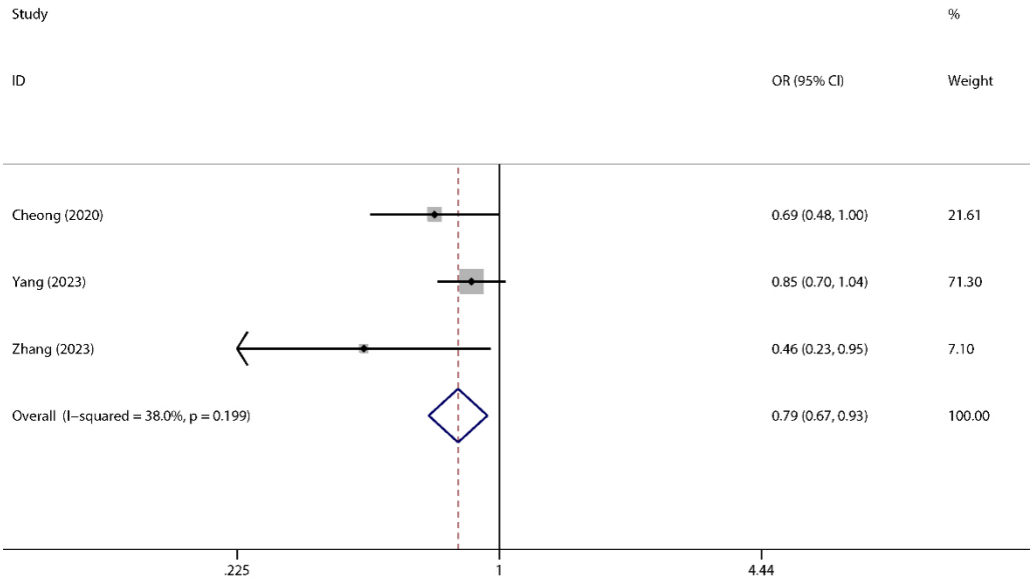

Figure 7. Forest plots corresponding to high myopia risk between the *SNTB1* rs6469937 polymorphism in the A-allele versus the G-allele in the hospital-based subgroup.

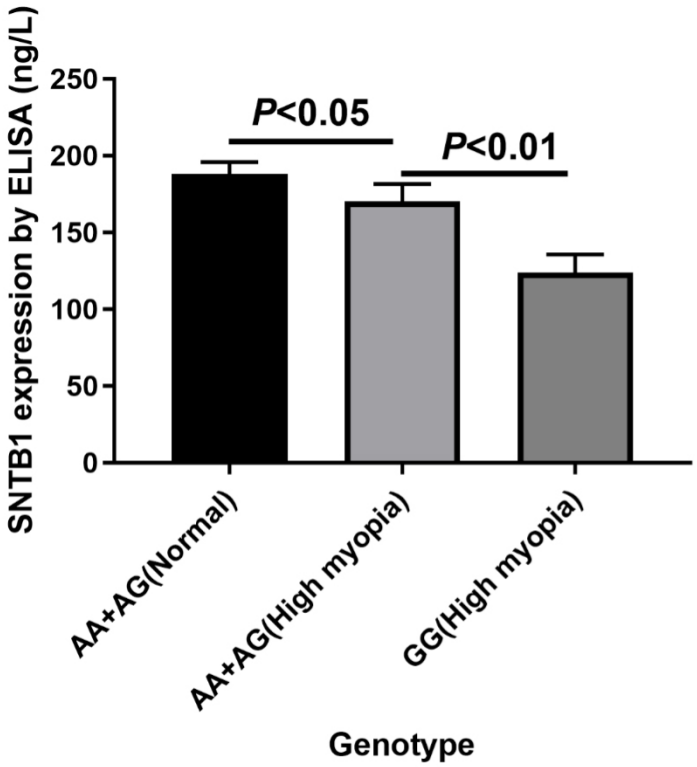

Figure 8. Networks showing the interactions between the SNTB1 gene and other genes as predicted using the STRING database, with details provided for 10 core genes.

that the rs6469937 polymorphism could enable early risk assessment in the population, allowing for early interventions like promoting eye hygiene, avoiding prolonged eye use, and increasing participation in sports activities to reduce the incidence of high myopia.

Single genes often harbor multiple polymorphic loci that confer different disease susceptibilities. These loci can modulate disease risk independently or synergistically through distinct mechanisms: first, functional domain specificity: in the *CFH* gene, the rs1061170 variant increases age-related macular degeneration risk (OR = 2.5) by impairing Bruch's membrane binding, while the rs800292 variant confers protection (OR = 0.6) via enhanced C3b cleavage [30]. Second, transcriptional versus coding effects: for *IL6*, the promoter SNP rs1800795 alters cytokine levels in atherosclerosis (β = 0.8 pg/ml; $p = 1 \times 10^{-6}$) [31], whereas the coding SNP rs2069845 affects chronic hepatitis C risk via receptor binding [32]. Third, allelic interaction patterns: in *TP53*, the rs1042522 variant enhances apoptosis in cancer (hazard ratio = 1.4), while the intronic rs17878362 variant influences messenger RNA splicing efficiency ($\Delta\Psi = 0.21$, $p < 0.01$) [33]. Fourth, spatial segregation: variants can occur in different regulatory regions (*FTO* rs1421085 [obesity] vs. rs9939609 [metabolic rate]) [34] and for the haplotype effects: *CYP2D6* rs3892097 (poor metabolizer) negates rs1135840 (ultrarapid) [35]. Our study on SNTB1 reflects a similar complexity.

To investigate the mechanism of the SNTB1 protein, we used the STRING online system to identify potential interacting proteins. We detected 10 proteins that may contribute to myopia through syntrophin-mediated signaling, extracellular matrix (ECM) remodeling, and scleral biomechanics. Further research should explore their specific interactions in retinal dopamine signaling and scleral collagen regulation, which could reveal new therapeutic targets.

This study had several limitations. First, although we incorporated all relevant articles, the overall sample size remains relatively small. This limitation was compounded when stratifying data by age, sex, race, eye axis length, and myopia degree. Second, the risk of high myopia associated with these polymorphisms may be influenced by gene–gene, gene–environment, and other polymorphic interactions. Future efforts should aim to collect details data on these factors. Third, more in-depth research into the mechanisms by which these polymorphic loci lead to disease susceptibility is needed. Such research would strengthen the rationale for genetic testing, provide more convenient clinical detection methods, and offer potential intervention targets for

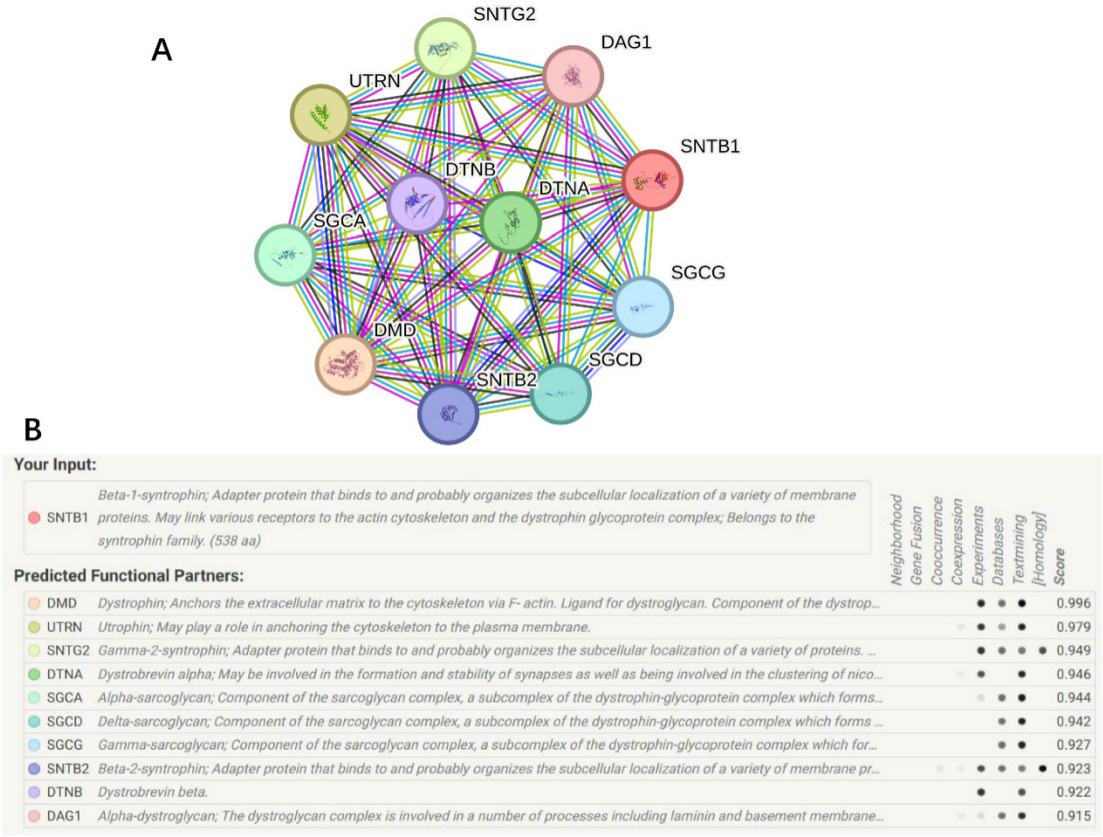

Figure 9. Serum analysis of SNTB1 expression level in rs6469937 genotypes of high myopia using mean values (horizontal lines, mean values). Serum SNTB1 levels in high myopia patients carrying AA/AG genotypes were significantly higher than those carrying GG genotypes ($p < 0.01$), but the same genotypes were significantly lower than those in healthy controls carrying AA/AG genotypes ($p < 0.05$).

treatment. Fourth, the generalizability of results is limited, as most included studies were from East Asian populations (Han Chinese, Singaporean Chinese). Finally, future directions should include longitudinal studies to assess whether these SNPs predict incident high myopia or its progression rate, expansion to multiethnic cohorts to determine whether the protective association holds across different genetic backgrounds, and larger, multicenter studies to increase statistical power and reduce sampling bias.

Conclusion: The results of the present meta-analysis support a potential link between the *SNTB1* rs4455882, rs6469937, and rs4395927 polymorphisms and an overall decrease in high myopia risk. The rs6469937 polymorphism was additionally established as a potential risk indicator/candidate variant requiring validation for high myopia. Large-scale studies with larger sample sizes and environmental factors will be essential to clarify the susceptibility of the SNTB1 gene to high myopia.

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