Journal of Clinical and Experimental Ophthalmology

OPEN ACCESS Freely available online

Research Article

A Novel NYX Gene Mutation Identified in a Chinese Northeast Han Family with High Myopia and Night Blindness

Xiaoyi*

Department of Ophthalmology, University Hospital and University of Zurich, Zurich, Switzerland

ABSTRACT

Objective: This study aimed to investigate and identify the underlying pathogenic gene mutation responsible for high myopia and congenital night blindness within a family from Northeast China, thereby contributing to a better understanding of the genetic basis and hereditary patterns associated with these ocular disorders.

Methods: Whole-exome sequencing was conducted to screen for genetic variations among family members, while AlphaFold2 was utilized to predict the tertiary structure of the associated protein. This structural analysis was further complemented by molecular dynamics simulations to assess conformational alterations resulting from the identified mutation. In parallel, comprehensive clinical evaluations, including detailed ophthalmic examinations, assessment of refractive status, and fundus imaging, were performed to characterize the phenotypic manifestations and correlate them with the genetic findings.

Results: A novel frame shift mutation, c.264dup (p.R89Afs*26), was identified in exon 3 of the NYX gene, leading to premature truncation of the C-terminal functional domain. The proband presented with extremely high myopia (spherical equivalent<-23.00D) accompanied by classic symptoms of congenital night blindness. Structural analysis revealed pronounced conformational changes in the mutated protein, notably disrupting the interaction interface with mGluR6. Pedigree analysis further supported an X-linked recessive inheritance pattern, aligning with the clinical and genetic findings within the affected family.

Conclusion: This study is the first to report that the NYX c.264dup mutation leads to complete congenital stationary night blindness accompanied by extreme high myopia, thereby expanding the known mutation spectrum of the NYX gene. These findings offer valuable insights for improving molecular diagnosis and facilitating genetic counseling for affected individuals and families, while also providing new perspectives on the molecular mechanisms linking retinal signal transduction to pathological axial elongation.

Keywords: Myopia; NYX gene; Gene mutation; Genome-Wide Association Studies (GWAS)

INTRODUCTION

Myopia is now the leading cause of visual impairment globally, with its prevalence rising rapidly. High myopia, expected to increase from 2.9% to 9.8% by 2050 [1], is linked to severe complications such as retinal detachment, chorioretinal degeneration, and choroidal neovascularization [2]. Understanding its underlying mechanisms is essential for prevention. Both genetic and environmental factors, such as prolonged near work, limited outdoor time, and dim light exposure, contribute to myopia development [3-6]. In recent decades, studies including linkage analysis, whole exome sequencing, meta-analyses, and Genome-Wide Association Studies (GWAS) have identified around 500 candidate genes and 27 loci linked to myopia risk [7,8]. Myopia syndromes are a potential source of genetic variation in the development of myopia [9]. Several well-characterized ophthalmologic syndromes, including Stickler syndrome, Marfan syndrome,

***Correspondence to**: Xiaoyi, Department of Ophthalmology, University Hospital Zurich, Zurich, Switzerland, E-mail: 2230822147@qq.com

Received: 16-Jul-2025, Manuscript No. JCEO-25-38451; **Editor assigned:** 18-Jul-2025, PreQC No. JCEO-25-38451 (PQ); **Reviewed:** 04-Aug-2025, QC No. JCEO-25-38451; **Revised:** 14-Aug-2025, Manuscript No. JCEO-25-38451 (R); **Published:** 24-Aug-2025. DOI: 10.35248/2155-9570.25.16.1002

Citation: Xiaoyi (2025). A Novel NYX Gene Mutation Identified in a Chinese Northeast Han Family with High Myopia and Night Blindness. Clin Exp Ophthalmol.16:1002.

Congenital Stationary Night Blindness (CSNB), Retinitis Pigmentosa (RP) associated with RP2 and RPGR, Bornholm ophthalmopathy , and Cone-Rod Dystrophy (CORD), are associated with high myopia and share common clinical features [10]. These syndromic forms of myopia have provided valuable insights into the genetic architecture of refractive error.

CSNB is a heterogeneous group of non-progressive Inherited Retinal Diseases (IRDs) characterized by rod photoreceptor dysfunction or impaired signaling between photoreceptors and bipolar cells, with diverse clinical features including night blindness, decreased visual acuity, nystagmus, myopia, and strabismus, and exhibits significant genetic heterogeneity [11,12]. Molecular genetic studies have identified cCSNB-causing mutations in the *NYX, GRM6, TRPM1, LRIT3, and SLC24A1* genes [13,14].

In this study, we recruited a family from Northeast China with both high myopia and congenital night blindness to identify the causative genetic variant.

MATERIALS AND METHODS

In patient ascertainment

This study investigated four generations of a Chinese family from Northeast China (Figure 1), recruited through the Second Affiliated Hospital of Harbin Medical University. Informed consent was obtained from all participants in accordance with the declaration of Helsinki, and the study protocol was approved by the Institutional Review Board of the Second Affiliated Hospital, School of Medicine. All experimental procedures adhered to relevant ethical guidelines and regulations. Comprehensive ophthalmologic examinations, including Uncorrected Visual Acuity (UCVA), Best Corrected Visual Acuity (BCVA), slit-lamp biomicroscopy, Intraocular Pressure (IOP) measurement, and fundus evaluation, were conducted by the same team of experienced ophthalmologists. Relevant clinical data are summarized in Table 1. Medical history reviews indicated that the proband (IV4), along with other affected family members (IV3, III2), exhibited clinical features characteristic of CSNB.

Whole exome sequencing

Genomic DNA was extracted from peripheral blood samples using standard protocols. Whole-exome sequencing was performed for seven family members (III-2, III-4, III-5, IV-1, IV-2, IV-3, and IV-4) using the Illumina NovaSeq 6000 platform (San Diego, USA) at the Wenzhou Genomics Institute. The raw sequencing reads were aligned to the human reference Genome (GRCh37) using the Burrows-Wheeler Aligner (BWA), and variant calling was conducted using the Genome Analysis Toolkit (GATK), following established best practices. Identified variants were subsequently annotated with ANNOVAR to facilitate downstream interpretation.

Validation and screening of NYX mutation

Genomic DNA from all available family members was extracted from peripheral blood using the Qiagen DNA Blood Midi Kit (Qiagen GmbH, Hilden, Germany), following the manufacturer's instructions. The exon and exon-intron boundary sequences of the NYX gene were retrieved from the Ensembl Genome Browser, and specific primers were designed using Primer-BLAST. All coding regions and splice site sequences of the NYX gene were amplified and sequenced for each individual. The resulting sequence data were analyzed using Mutation Surveyor software (SoftGenetics, USA) to identify potential pathogenic variants.

Homology analysis

Sequence homology analysis of the NYX protein was conducted using Molecular Evolutionary Genetics Analysis version 7 (MEGA7). Amino acid sequences of NYX were retrieved from the National Center for Biotechnology Information (NCBI) public database and subsequently used for multiple sequence alignment. The alignment of selected homologous sequences was performed using the ClustalW algorithm integrated within the 'Align' function of the MEGA7 software, allowing for comparative analysis of sequence conservation across species.

Phylogenetic tree analysis

Phylogenetic analysis of the NYX gene was carried out using MEGA version 7.0. Amino acid sequences from ten distinct species were used to construct an optimal phylogenetic tree employing the Neighbor Joining (NJ) method. Evolutionary distances were calculated using the Poisson correction model and expressed as the number of amino acid substitutions per site. To evaluate the robustness of the tree topology, 1,000 bootstrap replicates were conducted, and the resulting confidence values (expressed as percentages) were annotated at each corresponding branch node.

Protein structure prediction and comparative analysis

The three-dimensional structures of the wild-type NYX protein and its mutant variant were predicted using the AlphaFold3 platform by inputting their respective amino acid sequences into the system. Utilizing advanced deep learning algorithms, AlphaFold3 inferred the protein conformations directly from sequence data. The accuracy and reliability of predicted structural models were evaluated using integrated quality metrics: predicted Local Distance Difference Test (pLDDT) scores, Predicted Aligned Error (PAE), and Predicted Distance Error (PDE). For detailed structural and atomic-level analysis, models were processed and visualized with PyMOL, enabling comparison of wild-type and mutant protein tertiary structures.

Comparative analysis of amino acid variations

The coding sequence (CDS) of the mutant NYX protein was analyzed using the ExPASy Translate tool (https://web.expasy.org/translate/) to predict its primary amino acid structure. The translated sequence was compared with the wild-type to identify mutation sites and characterize amino acid substitutions, enabling precise determination of altered residues and their potential structural and functional impacts.

Table 1: Clinical characteristics of the high myopia with night blindness pedigree.

Subject No.	Gender	UCVA (OD/OS)	BCVA (OD/OS)	Refractive error(OD/OS)	IOP (OD/OS)	Slit-lamp (OD/OS)	Night Blindness	Additional Findings
III2	F	1.0/0.8	1.0/0.8	0/-0.25	11.0/10.0	OB/OB	+	Laser surgery
III4	F	0.25/0.3	0.8/0.6	0.8	12.0/14.0	High density of the lenses in both eyes	-	
III5	F	0.3/0.25	1.2/1.0	0.909090909	13.0/11.0	OB/OB	-	Polio
III6	M	1.2/1.2	1.2/1.2	0.25/0	12.0/14.0	Corneal scarring	-	
IV1	F	0.1/0.2	1.0/1.0	1.166666667	14.0/15.0	OB/OB	-	
IV2	M	0.1/0.12	1.0/1.2	1.222222222	14.0/14.0	OB/OB	-	
IV3	M	0.01/0.01	0.6/0.6	1.040816327	16.0/13.0	OB/OB	+	Suspected keratoconus
IV4	M	0.01/0.01	0.6/0.6	1.031914894	14.2/12.0	OB/OB	+	Leukodermia

Footnote to Table 1: Subject No. refers to the family member identifier; Gender is indicated as M for male and F for female; UCVA represents uncorrected visual acuity; BCVA denotes best corrected visual acuity; Refractive error is expressed as the spherical equivalent in diopters; IOP refers to intraocular pressure measured in mmHg; Slit-lamp indicates the findings from anterior segment examination; Night blindness is marked as "+" if present and "-" if absent; OB indicates optic disc appearance within normal limits; OD and OS refer to the right eye and left eye, respectively. proband:IV4.

RESULTS

Baseline demographic characteristics

Overall cohort: The proband (IV4), a 21-year-old male, exhibited progressive high myopia with a Spherical Equivalent (SE) of -24.25 D in the right eye (OD) and -23.50 D in the left eye (OS). Onset of myopia occurred before the age of four (SE<-6.00 D), accompanied by classic symptoms of night blindness, including impaired vision under low-light conditions, difficulty navigating in the dark, and inability to ascend or descend stairs without auxiliary lighting. Fundus examination revealed hallmark features of high myopia, such as tilted optic discs with peripapillary atrophy, tessellated fundus, prominent choroidal vessels, absent foveal reflex, and peripheral retinal lattice degeneration with pigmentary deposition. Notably, the proband also presented with cutaneous vitiligo, primarily affecting the hands and scalp. His monozygotic twin brother (IV3) exhibited even more severe myopia (OD: -25.50 D; OS: -24.50 D), with fundus imaging showing frost-like degeneration in the right eye and cystic retinal degeneration with vitreous traction and pigmentary changes in the left eye. Corneal topography suggested the presence of keratoconus in the right eye, along with concurrent night blindness symptoms. Pedigree analysis revealed that their maternal aunt (III2) reported nyctalopia symptoms; however, clinical examination showed normal visual acuity and a non-myopic refractive status, likely due to a history of corneal laser refractive surgery.

In this study, ophthalmic examination data were collected from eight family members, and based on the observed maternal inheritance pattern, the proband's father (III6) was excluded from genetic sequencing. DNA samples were obtained from seven affected relatives for analysis (Figure 1).

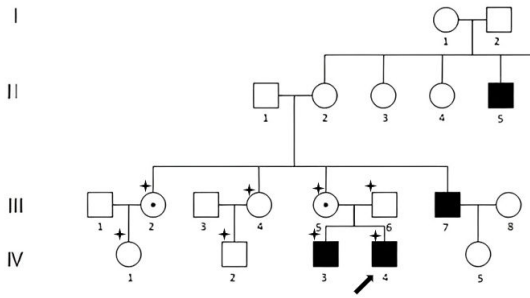

Figure 1: Pedigree of the family with high myopia and night blindness. **Note:** ○ Normal female, □ Normal male, ⊙ Female carrier, □ Male carrier, ● Affected female, ■ Affected male, ✦ Participating researcher, ↗ Proband

Analysis of WES sequencing results

A de novo mutation in the NYX gene was identified in the proband (Figure 2), with whole-genome sequencing localizing the variant to chromosome Xp11.4 (chrX:41,332,970). The specific mutation was designated as NM_001378477.1:exon3:c.264dup (p.Arg89Alafs*26), representing a single-nucleotide duplication that causes a frameshift. This mutation alters the codon for arginine (Arg/R) at position 89 to Alanine (Ala/A) and introduces a premature stop codon 26 amino acids downstream, leading to the production of a truncated and likely non-functional protein.

Segregation analysis confirmed that the mutation was maternally inherited, consistent with an X-linked recessive pattern of transmission. Targeted sequencing of additional family members identified individuals III:2 and III:5 as heterozygous carriers of the variant (Figure 2). Notably, the mutation was absent from major public variant databases, including the 1000 Genomes

Project and gnomAD, thereby supporting its classification as a novel pathogenic variant.

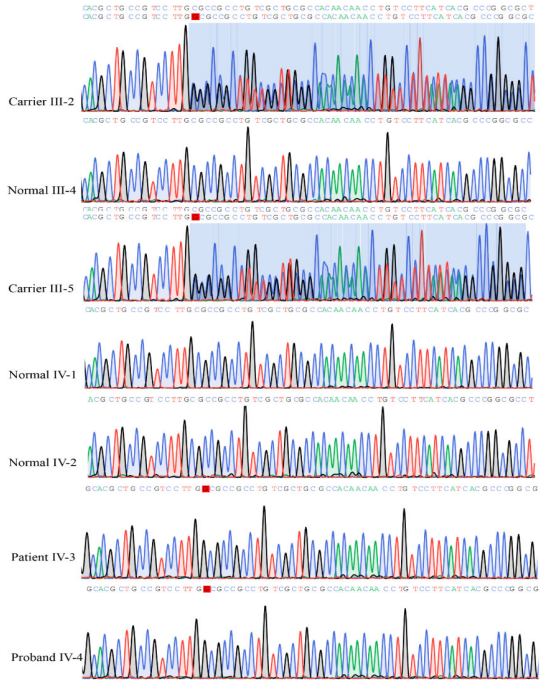

Figure 2: Sequencing chromatograms of the proband and selected family members.

Evolutionary conservation analysis of NYX gene

During the cross-species homology analysis of the NYX-encoded protein sequence, a remarkable pattern of evolutionary conservation was identified, with the amino acid residues surrounding the mutation site exhibiting an exceptionally high degree of sequence preservation across a wide range of species (Figure 3), highlighting the potential functional significance of this region and suggesting that alterations at this site may have critical biological implications.

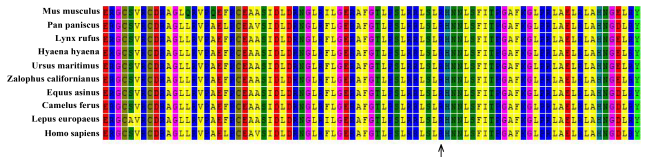

Figure 3: Multiple sequence alignment of NYX protein orthologs.

Phylogenetic analysis of NYX gene

The maximum-likelihood phylogenetic reconstruction produced a tree with a total branch length of 0.43948689, indicating strong evolutionary conservation of the NYX gene across diverse taxa (Figure 4); furthermore, bootstrap analysis based on 1,000 replicates provided robust nodal support exceeding 70% for all major clades, thereby reinforcing the reliability and stability of the inferred phylogenetic topology.

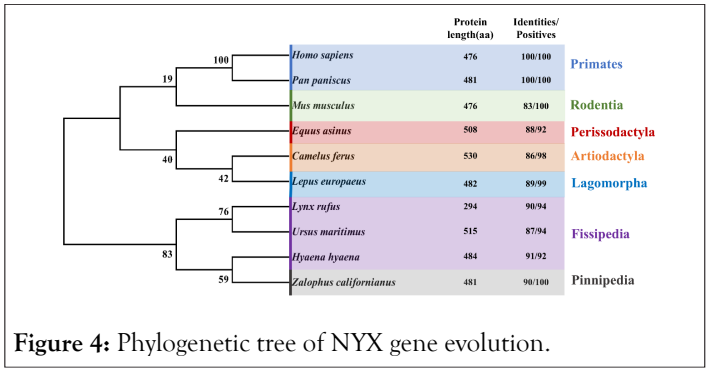

Figure 4: Phylogenetic tree of NYX gene evolution.

Structural comparison between wild-type and mutant NYX proteins

The three-dimensional structures of the wild-type NYX protein and its mutant variant, predicted using the AlphaFold3 platform, are shown in Figures 5.1,5.2; for this analysis, the model with the highest confidence score was selected to ensure maximum accuracy and structural reliability. Comparative analysis revealed that the mutant protein preserved an identical N-terminal sequence (residues 1-88) to that of the wild-type, as confirmed by a low Root Mean Square Deviation (RMSD) value of 0.286, indicating minimal structural deviation in this region. However, beginning at codon 89, a frameshift mutation led to significant sequence alterations that introduced a Premature Termination Codon (PTC) at position 115, resulting in a truncated protein lacking 361 amino acids (residues 89-476) when compared to the full-length wild-type counterpart (Figure 6).

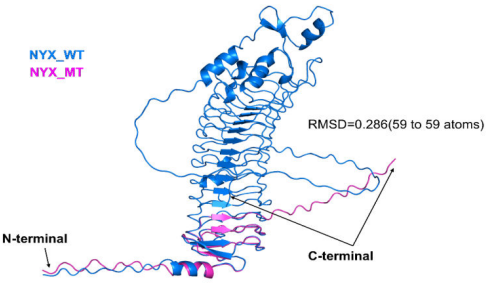

Figure 5: Structural comparison between wild-type and mutant NYX proteins.

Comparative analysis of wild-type and mutant protein amino acid sequences

Alignment of the mutant and wild-type NYX protein sequences revealed a series of consecutive amino acid substitutions beginning precisely at the mutation site, with notable changes including Arginine (Arg) to Alanine (Ala), Histidine (His) to Proline (Pro), Asparagine (Asn) to Glutamine (Gln), Leucine (Leu) to Proline (Pro), Serine (Ser) to Valine (Val), Phenylalanine (Phe) to Leucine (Leu), Isoleucine (Ile) to Histidine (His), Threonine (Thr) to Histidine (His), Proline (Pro) to Alanine (Ala), Glycine (Gly) to Arginine (Arg), Alanine (Ala) to Arginine (Arg), Lysine (Lys) to Glutamine (Gln), and Alanine (Ala) to Glycine (Gly), collectively illustrating the disruptive impact of

the frameshift mutation on the downstream amino acid sequence and reinforcing its structural and functional implications (Figure 7).

The most functionally significant substitutions involved: Arg →Ala, Asn →Gln, Leu →Pro, Phe →Leu, Pro →Ala.

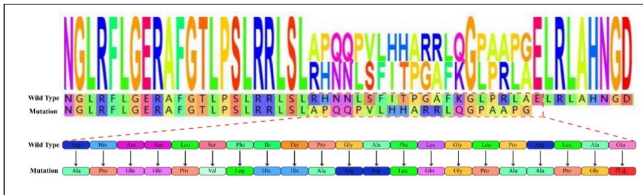

Figure 6: Sequence alignment of wild-type versus mutant NYX proteins.

Discussion

The Through whole-exome sequencing of a Northeastern Chinese pedigree exhibiting high myopia and congenital night blindness, a de novo frameshift mutation in the NYX gene (c. 264dup, p.Arg89Alafs*26) was identified; this finding not only broadens the known mutational spectrum of NYX but also offers novel insights into the overlapping pathophysiological mechanisms underlying high myopia and CSNB, highlighting the gene's critical role in retinal function and visual development.

The NYX gene encodes nyctalopin, a 481-amino-acid protein classified within the Small Leucine-Rich Proteoglycan (SLRP) family, which plays a critical role in visual signal transduction by facilitating communication between photoreceptors and retinal ON bipolar cells; our phylogenetic analysis revealed exceptionally high sequence conservation of NYX among primates, reinforcing its essential role in visual function and possibly other fundamental biological processes, a conclusion that aligns with prior studies and underscores its central importance in retinal signaling [15]. Functionally, NYX contributes to glutamate-mediated postsynaptic signaling from photoreceptors to bipolar cells, where the mGluR6 receptor (encoded by GRM6) modulates the closure of TRPM1-formed ion channels, a mechanism that relies on the proper localization of NYX to the bipolar cell membrane. The c.264dup mutation identified in this study introduces a premature stop codon, truncating the C-terminal functional domain of nyctalopin and potentially impairing its ability to anchor or stabilize TRPM1 channels at the synapse, thereby disrupting normal signal transduction. This mechanistic insight is consistent with prior findings linking nyctalopin dysfunction to impaired ON bipolar cell signaling [16]. Clinically, both the proband (IV4) and his monozygotic twin brother (IV3) presented with early-onset high myopia (Spherical Equivalent [SE]<-6.00 D before age 4) accompanied by classic nyctalopia; however, unlike typical NYX-related myopia cases, which exhibit SE values between -10.00 D and -15.00 D, our patients displayed an extreme "ultra-high myopia" phenotype (SE <-23.00 D), suggesting that NYX may influence axial elongation through previously unrecognized molecular pathways beyond its established role in retinal signal transduction.

Sequence alignment between the wild-type and mutant NYX proteins revealed several key amino acid substitutions, Arginine (Arg) to Alanine (Ala), Asparagine (Asn) to Glutamine (Gln), Leucine (Leu) to Proline (Pro), Phenylalanine (Phe) to Leucine (Leu), and Proline (Pro) to Alanine (Ala), which are likely to influence ocular physiology through a variety of molecular mechanisms. The deletion of residues 89-476 in the mutant form eliminates ten critical Leucine-Rich Repeat (LRR) domains, resulting in a substantial structural loss that, when considered in the context of the patients' clinical presentations, strongly suggests a significant impairment of the protein's biological function. Particularly, the substitution of Arg with Ala at position 89 disrupts the local salt-bridge network, while the complete alteration of the downstream amino acid sequence leads to the replacement of multiple functionally important residues. Among these, Leu-to-Pro substitutions may destabilize β-sheet secondary structures, and Phe-to-Leu changes could perturb the hydrophobic core, both contributing to conformational instability. Additionally, the Arg-to-Ala substitution may impact Nitric Oxide (NO)-mediated smooth muscle relaxation, as arginine serves as a precursor for NO synthesis, and NO donors have been shown to enhance the efficacy of atropine in suppressing myopia progression [17,18]. Disruptions in Phe metabolism may affect dopamine synthesis pathways, with dopamine playing a well-established role as a protective retinal neurotransmitter against axial elongation [19]. Furthermore, altered proline levels may be linked to dysregulated collagen metabolism, potentially affecting corneal biomechanics in high myopia, while disturbances in Glutamine (Gln) metabolism may influence retinal neurotransmitter balance [20,21]. Interestingly, these amino acid changes parallel metabolic pathway abnormalities found in other myopia-associated genes such as FLRT3 and TGIF1, suggesting that high myopia pathogenesis may involve broader dysregulation of interconnected amino acid metabolic networks [22,23]. Although the precise molecular mechanisms linking these specific amino acid alterations to the observed myopic phenotypes remain to be fully elucidated, these findings offer valuable insights into potential pathways and open new directions for research into high myopia, laying a theoretical foundation for developing targeted metabolic interventions.

Of particular interest, one proband in this study exhibited vitiligo, a pigmentary disorder characterized by progressive melanocyte loss and the development of sharply demarcated hypopigmented macules; the pathogenesis of vitiligo is multifactorial, involving genetic predisposition, autoimmune dysregulation, oxidative stress, and metabolic disturbances [24]. Metabolic profiling revealed significantly elevated levels of glutamate and proline in the affected individual compared to healthy controls, suggesting that these abnormalities may contribute to disease progression. Specifically, proline dysregulation could impair collagen synthesis and disrupt the cutaneous extracellular matrix, while increased glutamate may induce oxidative stress and further damage melanocytes [25]. Although phenylalanine, a key precursor in the melanin biosynthesis pathway via its conversion to tyrosine, was also affected by the mutation, its concentration remained substantially lower than that of glutamate and proline,

indicating that the imbalance in amino acid metabolism, particularly involving glutamate and proline, may offer a partial explanation for the vitiligo phenotype observed [26]. This metabolic profile raises the possibility of a novel link between NYX-related mutations and cutaneous pigmentary disorders; however, several limitations must be considered: (1) the vitiligo phenotype was documented in only a single individual, requiring validation in larger cohorts to determine clinical relevance; (2) NYX expression in skin tissue has not been directly investigated, leaving uncertainty about its potential role outside the retina; and (3) the exact molecular mechanisms by which the altered amino acid profile may intersect with immune pathways to drive melanocyte destruction remain unclear, highlighting the need for further mechanistic studies to substantiate these preliminary observations.

The current findings introduce a novel diagnostic marker for complete Congenital Stationary Night Blindness (cCSNB), emphasizing the clinical relevance of NYX gene mutations in patients presenting with both high myopia and nyctalopia, where genetic testing not only facilitates accurate diagnosis but also supports informed genetic counseling. To advance the clinical and biological understanding of NYX-associated visual disorders, future research should prioritize (1) detailed mechanistic studies to elucidate the pathogenic pathways linking NYX mutations to high myopia, (2) comprehensive retinal expression profiling and subcellular localization analyses of mutant NYX proteins to clarify their impact on cellular function, and (3) the development of targeted therapeutic strategies aimed at correcting or compensating for NYX-related dysfunction in retinal signal transmission.

CONCLUSION

In conclusion, The novel NYX mutation identified in this study broadens the known mutational spectrum of CSNB and offers valuable insights into the complex interplay between retinal signal transduction and refractive development, thereby deepening our understanding of the molecular mechanisms underlying visual dysfunction; these findings lay a critical foundation for improving diagnostic precision and guiding the development of targeted therapeutic interventions for NYX-associated ocular disorders, underscoring their substantial clinical relevance.

ACKNOWLEDGMENT

We sincerely thank the participating family members for their invaluable contribution to this study; this work was supported by the Natural Science Foundation of Heilongjiang Province (Grant No. LH2023H042) and the Medical Development Foundation of Heilongjiang Province (Grant No. YSWL002), whose support made this research possible.

REFERENCES

1. Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology. 2016;123(5):1036-42.
2. Chen J, Lian P, Zhao X, Li J, Yu X, Huang X, et al. PSMD3 gene mutations cause pathological myopia. J Med Genet. 2023;60(9): 918-924.
3. Li YJ, Guggenheim JA, Bulusu A. An international collaborative family-based whole-genome linkage scan for high-grade myopia. Invest Ophthalmol Vis Sci. 2009;50:3116-3127.
4. Lin Z, Gao TY, Vasudevan B. Near work, outdoor activity, and myopia in children in rural China: The Handan offspring myopia study. BMC Ophthalmol. 2017;17:203.
5. Rose KA, Morgan IG, Ip J. Outdoor activity reduces the prevalence of myopia in children. Ophthal mology. 2008;115:1279-1285.
6. Hua WJ, Jin JX, Wu XY. Elevated light levels in schools have a protective effect on myopia. Ophthalmic Physiol Opt. 2015;35:252-262.
7. Hawthorne FA, Young TL. Genetic contributions to myopic refractive error: Insights from human studies and supporting evidence from animal models. Exp Eye Res. 2013;114:141-149.
8. Cai XB, Shen SR, Chen DF, Zhang Q, Jin ZB. An overview of myopia genetics. Exp Eye Res. 2019;188.
9. Flitcroft DI, Loughman J, Wildsoet CF, Williams C, Guggenheim JA, CREAM Consortium. Novel myopia genes and pathways identified from syndromic forms of myopia. Invest Ophthalmol Vis Sci. 2018;59(1):338-348.
10. Li J, Zhang Q. Insight into the molecular genetics of myopia. Mol Vis. 2017;23:1048-1080.
11. Varin J, Bouzidi N, Gauvain G, Joffrois C, Desrosiers M, Robert C. Substantial restoration of night vision in adult mice with congenital stationary night blindness. Mol Ther Methods Clin Dev. 2021;22:15-25.
12. Kim HM, Joo K, Han J, Woo SJ. clinical and genetic characteristics of korean congenital stationary night blindness patients. Genes (Basel). 2021;12(6):789.
13. Zeitz C, Labs S, Lorenz B, Forster U, Uksti J, Kroes HY, et al. Genotyping microarray for CSNB-associated genes. Invest Ophthalmol Vis Sci. 2009;50(12):5919-26.
14. Malaichamy S, Sen P, Sachidanandam R, Arokiasamy T, Lancelot ME, Audo I. Molecular profiling of complete congenital stationary night blindness: A pilot study on an Indian cohort. Mol Vis. 2014;20:341-51. Erratum in: Mol Vis. 2014;20:780.
15. De Silva SR, Arno G, Robson AG, Fakin A, Pontikos N, Mohamed MD, et al. The X-linked retinopathies: Physiological insights, pathogenic mechanisms, phenotypic features and novel therapies. Prog Retin Eye Res. 2021.
16. Zeitz C, Robson AG, Audo I. Congenital stationary night blindness: an analysis and update of genotype-phenotype correlations and pathogenic mechanisms. Prog Retin Eye Res. 2015;45: 58-110.
17. Lee S, Park CY. Nitric oxide: An old drug but with new horizons in ophthalmology-a narrative review. Ann Transl Med. 2023;11(10): 352.
18. Carr BJ, Stell WK. Nitric Oxide (NO) Mediates the Inhibition of Form-Deprivation Myopia by Atropine in Chicks. Sci Rep 2016;6:9.
19. Chakraborty R, Landis EG, Mazade R, Yang V, Strickland R, Hattar S. Melanopsin modulates refractive development and myopia. Exp Eye Res. 2022;214:108866.
20. Wu W, Song Y, Sun M, Li Y, Xu Y, Xu M, et al. Corneal metabolic biomarkers for moderate and high myopia in human. Exp Eye Res. 2023;237:109689.
21. Guoping L, Xiang Y, Jianfeng W, Dadong G, Jie H, Wenjun J. Alterations of glutamate and γ-aminobutyric acid expressions in normal and myopic eye development in guinea pigs. Invest Ophthalmol Vis Sci. 2017;58(2):1256-1265.
22. Swierkowska J, Karolak JA, Gambin T, Rydzanicz M, Frajdenberg A, Mrugacz M, et al. Variants in FLRT3 and SLC35E2B identified

using exome sequencing in seven high myopia families from Central Europe. Adv Med Sci. 2021;66(1):192-198.

23. Rasool S, Dar R, Bhat AA, Ayub SG, Rehman MU, Rashid S, et al. A novel G26A variation in 5' half of TGIF1 gene associates with high myopia in ethnic Kashmiri population from India. Taiwan J Ophthalmol. 2019;10(4):294-297.
24. Picardo M, Dell'Anna ML, Ezzedine K, Hamzavi I, Harris JE, Parsad D, et al. Vitiligo. Nat Rev Dis Primers. 2015;1:15011.
25. Marzabani R, Rezadoost H, Choopanian P, Kolahdooz S, Mozafari N, Mirzaie M, et al. Metabolomic signature of amino acids in plasma of patients with non-segmental Vitiligo. Metabolomics. 2021;17(10): 92.
26. Dutta RR, Kumar T, Ingole N. Diet and Vitiligo: The Story So Far. Cureus. 2022 Aug 28;14(8):e28516.