• Review Article •

Critical role of lipid metabolism in axial myopia development

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Abstract

● The global prevalence of myopia is becoming increasingly severe, with epidemiological models predicting that by 2050, approximately 50% of the world's population will be affected by myopia, and about 10% will suffer from high myopia. The incidence of high myopia is projected to increase fivefold, making it the leading cause of irreversible vision impairment. Myopia often leads to various complications and has been associated with other ocular diseases, including early-onset cataracts, age-related macular degeneration, and primary open angle glaucoma. As a result, the control and management of myopia have become ongoing and long-term research priorities. The pathogenesis of myopia involves complex multisystem interactions. Current mainstream theories focus primarily on choroidal hypoxia-induced scleral remodeling, with neurotransmitters such as acetylcholine and dopamine playing regulatory roles. However, recent studies have increasingly suggested that changes in nutritional intake, including proteins, fats, and cholesterol, may also be related to myopia development. The role of lipid metabolism in the onset and progression of myopia has gradually attracted growing attention. Therefore, this review aims to systematically elucidate the molecular mechanisms of lipid metabolism regulatory networks in axial myopia, integrating multidimensional factors to provide a theoretical foundation for precision intervention strategies.

● **KEYWORDS:** axial myopia; lipid metabolism; scleral remodeling; choroidal hypoxia; precision intervention strategies

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INTRODUCTION

Myopia, the most common refractive disorder worldwide, is pathologically classified based on etiology into axial myopia (caused by an elongated axial length, AL), refractive myopia (resulting from structural or positional changes in the eye's optical components), and secondary myopia (caused by specific conditions not typically associated with conventional myopia risk factors)[1-2]. As a global public health issue, the epidemiological trends of myopia have drawn widespread attention. According to WHO epidemiological data, by 2000, the number of people affected by myopia worldwide had reached 1.4 billion (22.9% of the global population), among whom 163 million (2.7%) suffered from high myopia[3]. The latest predictive models suggest that by 2050, the prevalence of myopia could rise to 5 billion people (50% of the global population), with 1 billion (10%) developing high myopia[4]. Refractive errors are expected to become the most common ophthalmic disorder among adolescents. According to the quantitative classification standard based on diopter measurements, myopia is clinically divided into low myopia (-0.5 to -3.0 D), moderate myopia (-3.0 to -6.0 D), and high myopia (<-6.0 D)[2-4]. Although genetic factors undoubtedly play an important role in the development of myopia[5], the impact of environmental factors appears to be even greater[6-8]. Recent studies have revealed that in the signaling pathways related to myopia onset, the retina often acts as a signal receptor, regulated by multiple factors such as hormones [dopamine, insulin, insulin-like growth factor 1 (IGF-1], glucagon, prostaglandins, *etc*.)[9-12], neurotransmitters [acetylcholine, nitric oxide (NO), gamma-aminobutyric acid (GABA), *etc*.][13-16], and hypoxia-induced stress pathways mediated by hypoxia-inducible factor-1α (HIF-1α)[17-18]. These signals are transmitted downstream to the choroid, where choroidal thinning and hemodynamic changes affect the scleral tissue, triggering scleral fibroblast phenotypic transformation and extracellular matrix remodeling [mainly characterized by decreased collagen type I synthesis and increased matrix metalloproteinase (MMP) activity], ultimately leading to

posterior eye elongation and refractive error development[19-21]. Currently, the estimated global productivity loss caused by uncorrected myopia-related vision impairment exceeds $30 billion[22]. Meanwhile, myopia is often accompanied by various complications, including open angle glaucoma, macular degeneration, and retinal detachment, which can severely reduce vision or even lead to blindness[7,23-26], thus imposing additional social and economic burdens on healthcare systems[27-29]. Further analysis indicates that the mechanisms underlying myopia progression are significantly associated with dietary nutrients. Multiple cohort studies have confirmed that dietary components can regulate intraocular metabolic pathways and alter metabolic demands, contributing to the onset of diseases such as cataracts, age-related macular degeneration, and diabetic retinopathy[30-31].

Moreover, recent epidemiological research shows that differences in dietary habits, such as variations in the intake of sugars, fats, or proteins, are also linked to the development and progression of myopia[32-33]. Research into the relationship between nutrition metabolism and myopia can be traced back to the mid-20th century. As early as 1956, Gardiner[34] first proposed that changes in nutrition, including protein, fat, and cholesterol intake, might be associated with myopia. In a case-control study (active myopia group n=33, stationary myopia group n=251), using dietary recall methods, it was found that the stationary myopia group had significantly higher daily protein intake and lower fat and carbohydrate intake compared to the active group. Subsequent longitudinal intervention studies confirmed that increasing protein intake in patients with active myopia could reduce the rate of myopic progression, providing early clinical evidence that dietary protein might regulate refractive development[32,35-36].

However, the underlying mechanisms by which nutrient metabolism influences myopia development remain unclear. With the advancement of metabolomics technologies, the role of lipid metabolism in myopia has gradually been elucidated. A study conducted in Singapore found that higher intake of saturated fats and cholesterol was associated with faster axial elongation in myopic Chinese schoolchildren[33]. In recent years, further research has indicated that lipid metabolism may influence myopia progression through multiple pathways, including changes in scleral structure, retinal signal regulation, and oxidative stress responses[37-38].

Additionally, epidemiological surveys in various regions have suggested that dietary factors, especially lipid intake, might influence the progression of myopia through specific metabolic pathways[39], and a large number of lipid metabolites have even been detected in the aqueous humor of myopic patients[40]. Based on these cumulative findings, lipid metabolism is anticipated to remain a highly active area of research in the field of myopia development. This review aims to systematically summarize the current understanding of the potential mechanisms by which lipid metabolism contributes to rapid axial myopia progression. It seeks to deepen our comprehension of the relationship between metabolic issues and myopia development, providing a translational medicine perspective for developing myopia prevention and control strategies targeting lipid metabolism.

FOUNDATION OF MYOPIA DEVELOPMENT: SCLERAL REMODELING

The development of myopia is closely associated with scleral remodeling. Research into its pathological mechanisms can be traced back to 1977, when Wiesel and Raviola[41] first established a pathological model of axial elongation using a monocular deprivation paradigm in primates. Multiple studies have shown that myopia progression is characterized by excessive axial elongation and refractive errors, both of which are tightly linked to scleral remodeling[42-43]. Scleral fibroblasts regulate the synthesis and degradation of type I collagen and elastic fibers [*e.g.*, through an imbalance in the MMP-2/tissue inhibitors of matrix metalloproteinase-1 (TIMP-1) ratio], leading to a significant reduction in scleral stiffness (with elastic modulus decreasing by 37%–52%) and tensile strength[44-45].

Using single-cell RNA sequencing, Wu *et al*[18] identified activated pathways in the sclera during myopia development, discovering that hypoxia-related eukaryotic initiation factor 2 (eIF2) signaling and mammalian target of rapamycin (mTOR) signaling pathways were upregulated in myopic mouse sclera. Supporting these findings, human genome-wide association studies (GWAS) have shown that 32.6% of myopia risk loci are genetically associated with collagen metabolism genes regulated by HIF-1α. Numerous animal model studies have demonstrated that form deprivation or optical defocus can induce scleral thinning and axial elongation through retinal signaling pathways (such as dopamine and retinoic acid)[12,46-47], by upregulating α-smooth muscle actin (α-SMA) expression in scleral fibroblasts and accelerating extracellular matrix (ECM) degradaticonsenon. In addition, recent research suggests that systemic metabolism may influence scleral remodeling through mechanisms such as energy supply and oxidative stress, thereby contributing to the development of myopia[10,48-50]. The process of scleral remodeling in myopic eyes is further detailed in Figure 1.

EPIDEMIOLOGICAL ASSOCIATION OF ABNORMAL LIPID METABOLISM WITH MYOPIA

Association Between Lipid Metabolism and Myopia

Lipids, due to their chemical structural diversity, perform multiple biological functions within living systems. They not only contribute to maintaining the dynamic structure of cell membranes (such as lipid raft formation and membrane fluidity

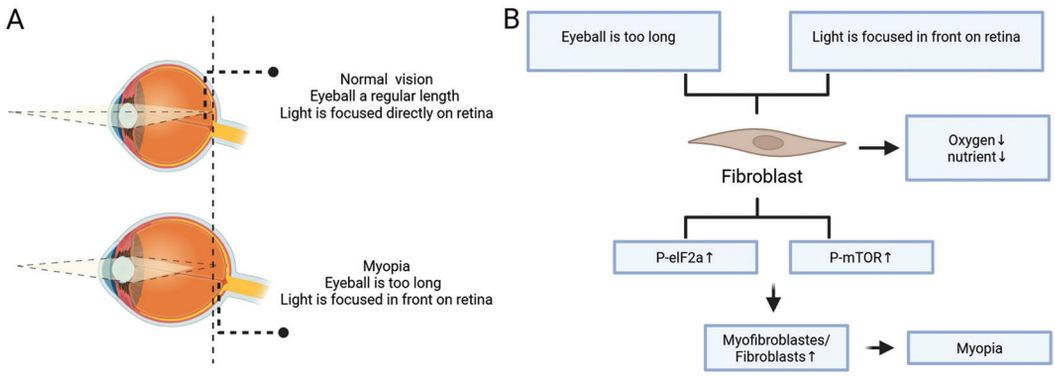

Figure 1 Scleral remodeling in myopic eyes A: The difference eye axial length between normal vision and myopia (light is focused directly on retina in normal vision, but in front on retina in myopia); B: The process of scleral remodeling in myopic eyes (scleral fibroblasts regulate the synthesis and degradation of type I collagen and metabolism influence a significant change in scleral stiffness and tensile strength).

regulation) but also play crucial roles in energy homeostasis (through the β-oxidation pathway) and G-protein-coupled receptor (GPCR) signal transduction[51].

However, excessive lipid accumulation in the body is often associated with systemic diseases such as cardiovascular diseases, obesity, and diabetes, which in turn are linked to a range of ocular disorders[30-31,51-53]. Data from large multicenter studies, such as the UK Biobank, indicate that several biomarkers show a significant positive correlation with spherical equivalent refraction (SER), including ω-3 fatty acids, ω-3 to total fatty acid ratio, docosahexaenoic acid (DHA), DHA to total fatty acid ratio, polyunsaturated fatty acid (PUFA) to total fatty acid ratio, and overall unsaturation degree. Higher levels of these biomarkers are associated with higher SER values and a lower risk of developing myopia. Furthermore, higher levels of ω-3 fatty acids, DHA, and their related ratios are significantly correlated with increased choroidal thickness[30,38].

This finding aligns with the mechanism revealed by Mori *et al*'s[54] team using optical coherence tomography angiography (OCTA), showing that n-3 PUFAs affect choroidal blood flow and thickness, which may influence myopia progression. Meanwhile, research by Bersuker and Olzmann[55] identified fatty acid oxidation as a key metabolic pathway controlling fibroblast behavior and maintaining ECM dynamic balance. Vertebrate model studies have provided further mechanistic evidence. In fish models that possess cone-rich retinas and color vision like humans, clustered regularly interspaced short palindromic repeats-CRISPR-associated protein 9 (CRISPR-Cas9) was used to generate lumican gene knockouts (with sgRNA efficiency >85%). Through optomotor response (OMR) and optokinetic response (OKR) testing, researchers observed aggravated scleral ECM degradation (with a 2.3-fold increase in MMP-2 activity), resulting in abnormal axial elongation (+14.7%, P<0.001)[54,56].

These findings echo mechanisms observed in human studies: lipid metabolism disorders may drive myopia progression through three pathways, dysregulation of retinal signaling pathways, impairment of choroidal microcirculation, and abnormal remodeling of the ECM.

Regulation of Retinal Signaling Pathways and Lipid Metabolism In recent years, research on the molecular mechanisms by which lipid signaling molecules released by retinal photoreceptors and retinal pigment epithelial (RPE) cells, through paracrine and endocrine pathways, regulate axial eye development and scleral tissue remodeling has become a major focus in molecular biology and ophthalmic disease studies. Lipid signaling molecules secreted by photoreceptors and RPE cells, such as arachidonic acid derivatives[57], retinoid-related orphan receptors (RORs)[58], and cholesterol metabolism products[59], are believed to influence axial elongation by regulating choroidal thickness or modulating scleral fibroblast activity. Through a two-stage genome-wide association study (GWAS), Jiang *et al*'s[60] team identified the leukocyte immunoglobulin-like receptor B (*LILRB2*) gene at the 19q13.42 locus (rs12976445, $P=4.2\times10^{-9}$) as a key regulator. LILRB2 was found to activate the ERK-P38-JNK signaling pathways (increasing phosphorylation levels by 2.8 times), thereby regulating the expression of lipid metabolism core proteins such as apolipoprotein E (APOEε4), leading to a reduction in choroidal thickness by 38.7±5.2 μm (measured by SS-OCT). Validation in animal models demonstrated that CRISPR-Cas9-mediated knockout of Pirb (the murine homolog of human LILRB2, with an editing efficiency of 92.3%) could reverse axial elongation induced by form deprivation myopia (FDM).

At the mechanistic level, Jin and Stjernschantz[61] reported that intravitreal injection of endogenous lipid signaling molecules, such as prostaglandin receptor agonists (*e.g.*, prostaglandin F2α), significantly inhibited axial elongation in myopia models. Recent mechanistic studies further revealed that the release of such lipid signaling molecules enhances the activity of MMPs, thereby mitigating hypoxia-induced scleral changes, including

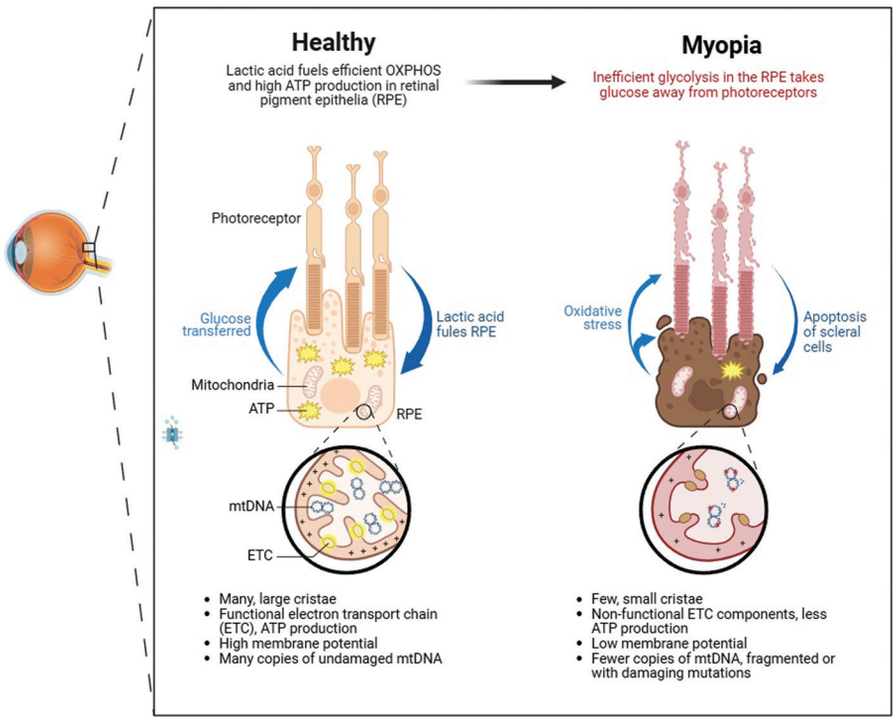

Figure 2 The involvement of lipid-derived signals in mediating retinal-scleral interactions and promoting axial elongation Various lipid-derived signals from the retina act on the sclera inducing changes in scleral fibroblasts; lipid signals trigger inflammation and oxidative stress, leading to scleral cell apoptosis and promoting axial elongation.

collagen loss, increased collagen turnover, myofibroblast transdifferentiation, and ECM remodeling[62]. Notably, clinical sample analyses suggest that some lipid signaling molecules, such as phosphatidylglycerol (PG) and phosphatidylserine (PS), may trigger a cascade of pro-inflammatory responses within the vitreous cavity[63].

This cascade results in elevated inflammatory cytokine levels and suppressed antioxidant enzyme system function in highly myopic eyes, ultimately inducing oxidative stress. At the scleral level, oxidative stress can promote scleral cell apoptosis, thereby accelerating scleral growth and contributing to the progression of myopia[64-67]. The involvement of lipid-derived signals in mediating retinal-scleral interactions and promoting axial elongation is depicted in Figure 2.

CHANGES IN CHOROIDAL BLOOD FLOW AND LIPID METABOLISM

Key Role of Choroidal Blood Flow in Myopia Lipid Metabolism There is a notable relationship between changes in choroidal blood flow and lipid metabolism. As the tissue with the highest blood flow in the eye (accounting for 85% of total ocular blood flow), the choroid maintains the oxygen pressure gradient of the outer retina and sclera through its unique lobular vascular structure, playing a vital role in ocular health[68]. Lipid metabolism, which involves the synthesis, degradation, and transformation of fats and lipids within the body, is closely linked to various ocular diseases[69]. As a highly oxygen-demanding organ, the structural integrity and normal function of the eye depend heavily on adequate blood supply. Insufficient blood perfusion may lead to abnormalities in lipid metabolism, whereas good blood flow promotes the even distribution of nutrients and oxygen, supporting normal cellular function and lipid metabolism. Blood oxygen supply is the only pathway to enhance visual sensitivity; increased choroidal blood flow provides the retina with abundant nutrients essential for biochemical reactions, helping restore and enhance the photoreceptor functions[68,70].

Multiple studies have shown a reduction in choroidal blood supply in myopic eyes. For instance, laser Doppler velocimetry revealed that choroidal blood flow declined after form deprivation-induced myopia in chicks[71]. Similarly, reduced choroidal perfusion is observed in myopic patients, likely due to vascular narrowing and stiffening[72]. Recent studies have discovered that decreased choroidal blood flow and tissue hypoxia activate the HIF-1α signaling pathway, inducing scleral fibroblasts to secrete MMPs such as MMP-2 and MMP-9, leading to collagen degradation, scleral hypoxia, subsequent scleral remodeling, and axial elongation[73].

Advancements in choroidal hemodynamics assessment, such as OCTA, now provide effective tools to observe choroidal blood flow changes in myopic and highly myopic patients[74-76], establishing choroidal hemodynamic changes as potential indicators for myopia monitoring. In some ocular diseases, such as macular degeneration, changes in choroidal blood flow are closely associated with lipid metabolism abnormalities.

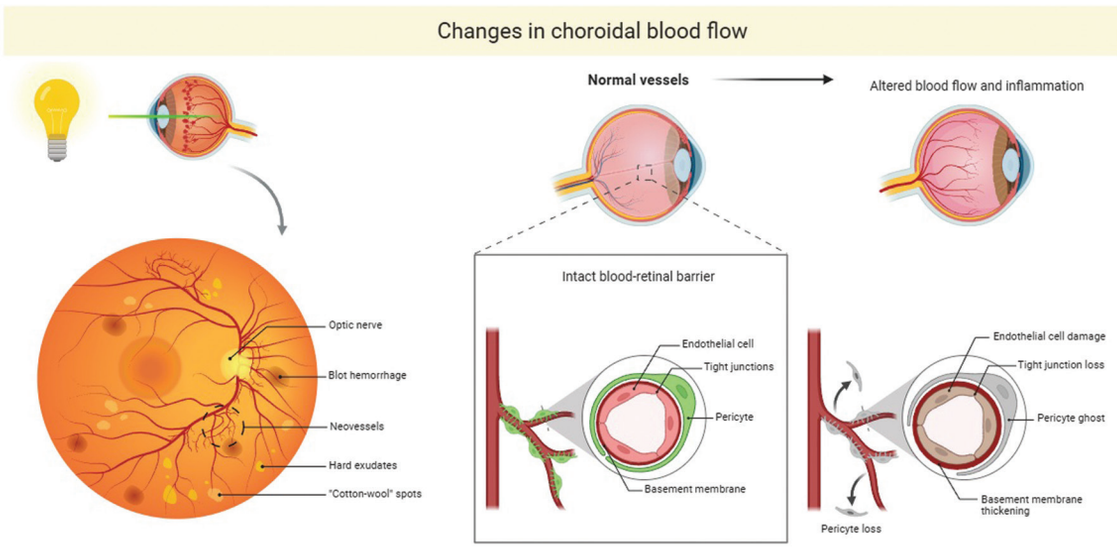

Figure 3 Choroidal blood flow changes causing alterations in the sclera Changes in choroidal blood flow leading to retinal vascular alterations and breakdown of the blood-retinal barrier.

Macular degeneration involves degeneration of parts of the retina, impairing vision, and is characterized by reduced choroidal blood flow and lipid accumulation[69,77]. Research by Geng *et al*[78] explored choroidal features before and after the onset of myopia, finding that changes in choroidal thickness during myopia progression were primarily due to vascular changes rather than alterations in the stromal matrix.

Mechanism of Lipid Metabolism Affecting Choroidal Blood Flow A study by Yang *et al*[79] "Immediate effects of 650 nm low-intensity red light therapy on children's retina and choroid", measured the short-term changes in retinal and choroidal thickness and blood flow characteristics after low-level red-light therapy (LLRLT) in children. The results showed that while 3min of LLRLT did not affect choroidal blood flow, it temporarily increased retinal blood flow perfusion density (RFPD), which normalized within approximately one hour, providing theoretical support for the role of LLRLT in myopia control.

Mori *et al*[54] found that n-3 PUFAs significantly upregulated endothelial nitric oxide synthase (eNOS) activity in myopia model rodents, improving choroidal microcirculation perfusion. This enhanced blood flow-mediated mechanical signal transmission and helped suppress choroidal thinning. On another front, Pan *et al*[80-81] described the nuclear receptor-dependent mechanism by which fatty acids regulate myopia. ω-3 PUFAs can bind to and activate peroxisome proliferator-activated receptors (PPARs), proteins closely associated with lipid metabolism. Activation of PPARα by agonists in experimental guinea pigs altered HIF-1α expression levels in the choroid, influencing scleral fibroblast differentiation and significantly inhibiting pathological myopia progression. Simultaneously, ω-3 PUFAs can also function as lipid signaling molecules secreted by retinal photoreceptors and RPE cells, modulating choroidal thickness and scleral fibroblast activity to influence ocular axial growth[38].

Furthermore, a study based on the National Health and Nutrition Examination Survey (NHANES) database found that high intake of eicosapentaenoic acid (EPA) from PUFAs in adolescents was associated with a reduced risk of developing high myopia[82]. Changes in choroidal blood flow leading to retinal vascular alterations and breakdown of the blood-retinal barrier are shown in Figure 3.

POTENTIAL INTERVENTION DIRECTIONS

Dietary Regulation Previous studies have shown that reduced choroidal blood perfusion can lead to scleral hypoxia, activating the HIF-1α signaling pathway. This activation promotes the transdifferentiation of scleral fibroblasts into myofibroblasts and extracellular matrix remodeling, ultimately contributing to the onset and progression of myopia. Meanwhile, ω-3 PUFAs are known for their cardiovascular benefits and play an important role in neuronal development at various stages of human growth, drawing increasing attention to their potential role in myopia control. Reducing the intake of cholesterol-rich low-density lipoproteins and increasing the intake of ω-3 PUFAs, such as α-linolenic acid (ALA), EPA, and DHA, may improve local ocular anti-inflammatory and antioxidant responses, enhance choroidal blood flow, alleviate choroidal hypoxia, and thereby inhibit myopia progression.

Experimental studies by Zhang *et al*[83] demonstrated that daily oral gavage of ω-3 PUFAs significantly reduced the development of FDM in guinea pigs and mice, as well as lens-induced myopia in guinea pigs. Periocular injection of DHA also effectively suppressed FDM progression in guinea pigs. This suppression of myopia progression was accompanied

by the inhibition of the "choroidal blood perfusion (CHBP) reduction–scleral hypoxia cascade reaction"[52,57,82-83]. Furthermore, DHA or EPA was shown to antagonize hypoxia-induced transdifferentiation of human scleral fibroblasts.

In human subjects, oral supplementation with ω-3 PUFAs partially alleviated the reduction in blood pressure caused by prolonged near work. Additionally, a research by Pan *et al*[84] from the Eye Hospital, School of Ophthalmology and Optometry, Wenzhou Medical University, suggested that oral supplementation with fish oil rich in ω-3 PUFAs could serve as an effective myopia prevention and control strategy. Building on their earlier mechanistic breakthroughs—that choroidal hypoperfusion leads to scleral hypoxia and subsequent myopia—their team demonstrated in animal models that providing guinea pigs and mice with ω-3 PUFAs through oral fish oil gavage significantly inhibited both form deprivation-induced and lens-induced myopia progression and axial elongation. Their study further confirmed that the major components of ω-3 PUFAs, DHA and EPA, play key roles in suppressing myopia development. Although further research is needed to determine the optimal dosage and long-term effects, ω-3 PUFAs offer a promising new intervention approach for myopia prevention and control. They hold great potential to play a pivotal role in future global strategies to tackle the growing challenge of myopia.

Targeted Drug Therapy Due to the eye's unique anatomical structure, its enclosed physical space and the presence of the blood-ocular barrier render it an immune-privileged organ. This privilege limits immune responses to gene therapy but also makes effective drug delivery to the eye particularly challenging. For anterior segment drug administration, there are three major biological barriers that lead to excessive drug loss and extremely low ocular bioavailability, resulting in less-than-ideal therapeutic outcomes[85].

Current research focuses on improving drug formulations to prolong retention time and enhance drug permeability through the ocular surface. However, for posterior segment drug delivery, complex physiological barriers such as the blood-retinal barrier, choroid, and sclera further hinder treatment effectiveness; thus, topically administered drugs, despite better patient compliance, often fail to reach therapeutic concentrations at the target sites[85-86]. Studies have shown that these physiological characteristics result in ocular surface drug bioavailability of only 0.5%–5%, while systemic administration achieves retinal drug concentrations less than 1% of plasma levels due to the blood-ocular barrier. As core technologies in precision medicine and precision health, gene testing, targeted drugs, targeted vaccines, and targeted nutrition have become highly advanced globally. For example, *RPE65* gene enhancement techniques, gene-editing-driven conversion of neural cells into retinal cells, modulation of acetylcholine receptors (*e.g.*, low-dose atropine eye drops), targeting dopaminergic pathways (through specialized light spectra or microbial synthesis pathways), and regulation of glutamatergic signaling (through metabolic modulation) all represent types of targeted interventions aimed at myopia reversal[87].

Through gene sequencing, researchers can explore the relationship between the function of ocular tissues, photoreceptors, neuronal transmission cells, and micronutrient levels, thus opening new paths for targeted nutrition, biophotonic light supplementation, and the prevention and correction of myopia and other vision impairments. At the level of metabolic regulation, dual PPARα/γ agonists such as saroglitazar have shown promising effects in myopia animal models. They inhibit NF-κB nuclear translocation, reduce MMP-9 activity, upregulate superoxide dismutase 2 (SOD2) expression to alleviate scleral oxidative stress, and promote fatty acid β-oxidation to maintain ECM homeostasis, thereby protecting against pathological scleral remodeling[88]. Clinical translational studies have indicated that intravitreal injection of lipid signaling molecules in animal experiments has produced favorable outcomes, providing a promising basis for future clinical applications.

Metabolomics Screening The pathogenesis of myopia involves complex genetic–environmental interactions. Among them, epigenetic regulatory networks influence the expression of vitamin A/D-binding proteins and photoreceptor pigment genes, thereby modulating the efficiency of retinal phototransduction. This regulation affects the availability of essential micronutrients and molecular ligands (Ligands) required for normal gene expression during the development of ocular tissues. Subsequently, necessary exogenous biophotonic signals initiate and modulate these processes, improving cellular morphology and function, thereby enhancing the structure of ocular tissues, improving visual perception, and increasing light and color sensitivity.

From an epigenetic perspective, both biophotonic signals and nutrients can modulate or enhance gene expression, improve cellular metabolism, especially the absorption and utilization of nutrients, and in turn regulate the development of the sclera, corneal strength, lens, visual cells, neurons, and pigment epithelial cells. By improving the metabolic function of ocular tissues and even target cells, it becomes possible to prevent and treat myopia and other visual impairments. Through high-throughput lipidomics sequencing[89-90], the expression profiles of plasma lipids (such as phosphatidylcholine and sphingomyelin) can be obtained. By screening for lipid biomarkers associated with high myopia risk, it is possible to identify biological markers for myopia risk prediction. In combination with clinical OCTA imaging data and

other biological parameters[74-75,78], early optical regulation, pharmaceutical intervention, and nutritional strategies can be applied to high-risk individuals to control rapid axial elongation.

CONCLUSION AND FUTURE OUTLOOKS

Lipid signaling molecules derived from the retina and RPE act as "metabolic switches" during axial elongation by regulating the choroid–sclera signaling axis. Lipid metabolism itself can also influence the inflammatory and oxidative environment of the choroidal blood flow microenvironment. Aqueous humor metabolomic analyses have shown that prostaglandin E2 concentrations in patients with high myopia are elevated by 3.8 times compared to normal individuals and are positively correlated with the expression of choroidal vascular endothelial growth factor (VEGF), suggesting that a lipid-driven inflammatory microenvironment may aggravate scleral remodeling *via* paracrine mechanisms. However, current research has limitations, as most mechanistic insights rely heavily on correlational evidence. Establishing causal relationships will require Mendelian randomization analyses and conditional gene knockout models[15,40,63,66].

Single-cell transcriptomic sequencing has revealed the presence of a fatty acid-binding protein 4 ($FABP4^+$) metabolic subpopulation of scleral fibroblasts, which exhibit 2.4–3.1 times higher expression of lipid uptake-related genes (CD36, FATP1) compared to other subpopulations. This suggests that this group may serve as a critical target for lipid metabolism interventions[91]. Further metabolomics studies have found that sphingomyelin deposition is significantly higher in the posterior sclera compared to peripheral regions and is positively correlated with MMP-2 activity[92-93].

Future research should focus on integrating single-cell transcriptomics and lipidomics of scleral fibroblasts to further characterize lipid metabolism features in the sclera, providing precise targets for intervention. In addition, current clinical studies are mostly limited to correlational analyses and lack causal evidence. Future progress will require interdisciplinary technological integration to accelerate clinical translation. For example, combining high throughput lipidomics sequencing and spatial metabolomics technologies could allow prediction and assessment of scleral hypoxia severity in myopic patients, enabling timely intervention strategies[94].

Moreover, developing localized drug delivery systems targeting lipid metabolism pathways for conditions like high myopia and hereditary myopia may improve therapeutic specificity. The integration of lipid metabolism network analysis with new delivery systems holds promise to open new avenues for myopia prevention and control, enabling a paradigm shift from "population-wide" to "individualized precision" strategies[95]. Nonetheless, continued interdisciplinary collaboration will be crucial to drive successful translational applications.

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