Scleral hypoxia is a target for myopia control

With the support by the National Natural Science Foundation of China, the research team directed by Prof. Zhou XiangTian (周翔天) and Prof. Qu Jia (瞿佳) at the School of Optometry and Ophthalmology and Eye Hospital, State Key Laboratory of Optometry, Ophthalmology and Vision Science, Wenzhou Medical University and Prof. Zeng ChangQing (曾长青) at the Key Laboratory of Genomic and Precision Medicine, Beijing Institute of Genomics, Chinese Academy of Sciences recently reported that Scleral hypoxia is a target for myopia control, which was published in *PNAS* (*2018*, *115*(*30*): *E7091—E7100*).

Myopia is the leading cause of visual impairment worldwide. Myopic eyes are characterized by scleral extracellular matrix (ECM) remodeling accompanied by ocular axial elongation. However, the initiators and signaling pathways underlying scleral ECM remodeling are largely unknown.

Their group addressed this question by performing single cell RNA-sequencing, which revealed a phenotypic shift from fibroblasts to myofibroblasts in sclera following myopia induction in mice. Gene-expression profiling indicated that HIF-1α, a hypoxia-induced transcription factor, might play an important role in mediating this phenotypic shift. Significant numbers of interactions were found between HIF-1α signaling pathway genes and myopia susceptibility genes, suggesting their involvement in human myopia. They found that localized scleral hypoxia is a common factor contributing to myopia development in both mice and guinea pigs. Since hypoxia exposure promoted myofibroblast transdifferentiation in cultured human scleral fibroblasts, this stress may account for how myopia is induced in these experimental animal models. This notion agrees with the fact that antihypoxia drugs inhibited myopia progression in an animal model.

These findings may provide new insight indicating that myopia-related visual signals decrease choroidal blood flow. Such declines lower oxygen delivery and nutrient availability to the neighboring avascular sclera. Scleral hypoxia thus ensues promoting myofibroblast transdifferentiation along with declines in collagen production mediated through rises in HIF-1α expression. These changes contribute to scleral thinning and declines in its stiffness accompanying excessive axial elongation. Their findings suggest that targeting modulators of scleral oxygenation levels may facilitate the development of novel approaches to improve myopia treatment.

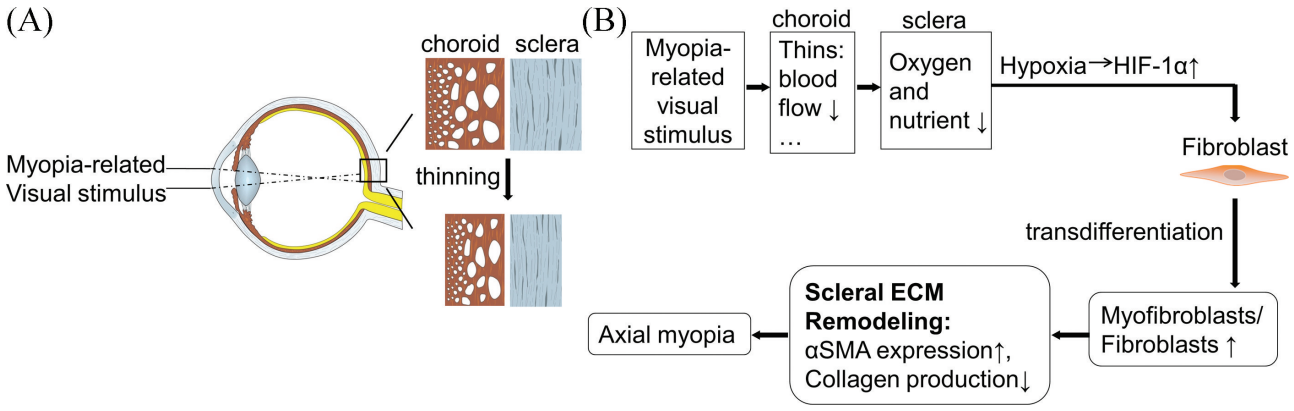

Figure Paradigm accounting for how scleral hypoxia affects scleral ECM remodeling and myopia progression.