Regulation of intraocular pressure by microRNA cluster miR-143/145

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Glaucoma is a major cause of irreversible blindness worldwide. Elevated intraocular pressure (IOP) , which causes optic nerve damage and retinal ganglion cell death, is the primary risk factor for blindness in glaucoma patients. IOP is controlled by the balance between aqueous humor secretion from the ciliary body (CB) and its drainage through the trabecular meshwork (TM) . How microRNAs (miRs) regulate IOP and glaucoma in vivo is largely unknown. Here we show that miR-143 and miR-145 expression is enriched in the smooth muscle and trabecular meshwork in the eye.

Targeted deletion of miR-143/145 in mice results in significantly reduced IOP, consistent with an ~2-fold increase in outflow facilities. However, aqueous humor production in the same mice appears to be normal based on a microbeads-induced glaucoma model. Mechanistically, we found that miR-143/145 regulates actin dynamics and the contractility of TM cells, consistent with its regulation of actin-related protein complex (ARPC) subunit 2, 3, and 5, as well as myosin light chain kinase (MLCK) in these cells. Our data establish miR-143/145 as important regulators of IOP, which may have important therapeutic implications in glaucoma.

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