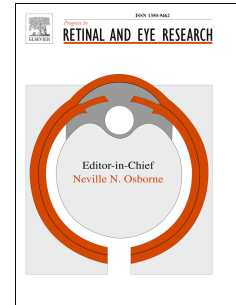


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Manipulating ocular endothelial tight junctions: applications in treatment of retinal disease pathology and ocular hypertension

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Abstract

Protein levels of endothelial tight-junctions of the inner retinal microvasculature, together with those of Schlemm's canal, can be readily manipulated by RNA interference (RNAi), resulting in the paracellular clefts between such cells to be reversibly modulated. This facilitates access to the retina of systemically-deliverable low molecular weight, potentially therapeutic compounds, while also allowing potentially toxic material, for example, soluble Amyloid- β 1-40, to be removed from the retina into the peripheral circulation. The technique has also been shown to be highly effective in alleviation of pathological cerebral oedema and we speculate that it may therefore have similar utility in the oedematous retina. Additionally, by manipulating endothelial tight-junctions of Schlemm's canal, inflow of aqueous humour from the trabecular meshwork into the Canal can be radically enhanced, suggesting a novel avenue for control of intraocular pressure. Here, we review the technology underlying this approach together with specific examples of clinical targets that are, or could be, amenable to this novel form of genetic intervention.

Key words; Tight junctions, RNAi, blood-retina barrier (BRB), Schlemm's canal, endothelium. Retinal degeneration.

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