Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

Tight Junction Proteins For Glaucoma Treatment

Overview

Glaucoma is one of the most prevalent causes of global visual handicap. Researcher at Trinity College Dublin have developed a novel technology for reducing intra-ocular pressure by down-regulation of a number of 'tight-junctions' joining the endothelial cells running around the circumference of the Iris, allowing fluid to leave the eye. Efficacy of this approach has been demonstrated in mice, to be extended into primates.

The Technology

- Endothelial cells of Schlemm's canal (SCEC) are the main barrier to fluid drainage from the eye
- Down-regulation of selected tight junction components results in an increase in the permeability of the Canal and thus decrease intraocular pressure in glaucoma.
- The invention employs RNAi inducing agents, whose presence within a cell results in production of an siRNA or shRNA, targeting tight junction proteins expressed in the tight junction complex joining Schlemm's canal endothelial cells (SCEC) in the eye, for the transient, reversible and controlled opening of these tight junctions.
- Specifically,siRNA-mediated synergistic suppression of tight junction transcripts encoding **Claudin-11, Tricellulin and Zo-**1 in human Schelmm's canal cells in vitro increases the paracellular permeability to 70kDa dextran and a decrease in transendothelial electrical resistance

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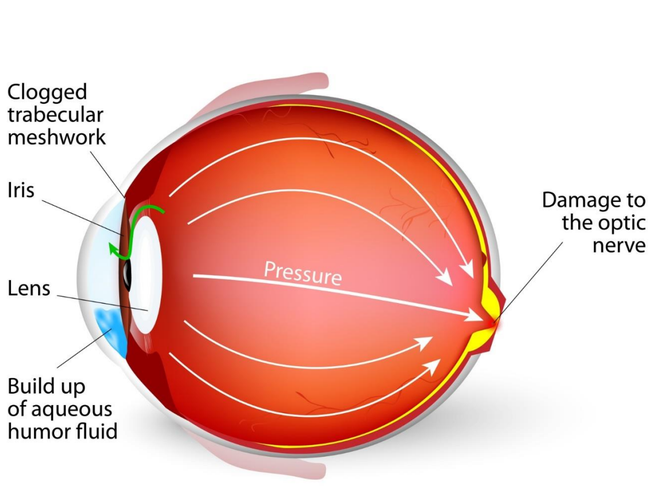
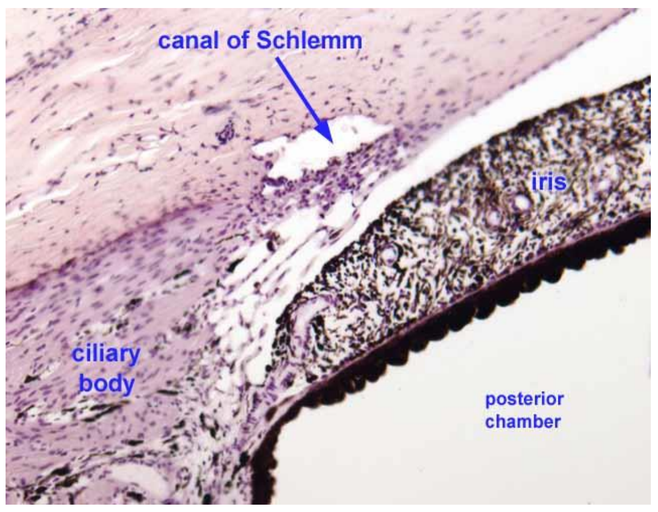


Clinical need and potential market

- Open angle glaucoma (OAG) currently affects over 2 million people in the USA, a figure which is estimated to increase to approximately 3.4 million by 2020.
- There is a similar prevalence in Europe and other developed parts of the World, with the primary risk factor being elevated intra-ocular pressure (IOP). World prevalence is approximately 65m people.
- Up to 5% of cases of OAG do not respond to conventional pressure-reducing eye drops or can become resistant to them.
- While surgical intervention is possible, there are significant complications.
- The present invention would allow a novel , non-invasive means of controlling aqueous outflow in cases of OAG that are resistant or non-responsive to conventional pressure-reducing medications.
- Administration: introduction of siRNA into the eye, either in unmodified form, or in combination with other modes of delivery or via viral vector comprising the RNAi inducing agent. could then be activated periodically by using an activating agent, for example, doxycycline, as an eye drop

Technology Status:

- Intracameral injection in mice of siRNAs validated against ZO-1 and tricellulin increased outflow facility, and reduced IOP.
- Characterisation of expression of tight junction and tight junction associated components in mouse and non-human primate outflow tissues - showing that SCECs in non-human primates and mice possess a similar TJ barrier composition to those found in humans



Market
Therapeutics, siRNA , Glaucoma

IP Status
PCT/EP2017/060301 has been filed

The opportunity

Trinity College is seeking to collaborate and/or licence the technology for development and commercialisation.

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