A radical approach for improved glaucoma treatment

**Objective**

Open angle glaucoma (OAG) is the second leading cause of world blindness. Treatments involving topically applied pressure-reducing medications or surgery targeting ocular drainage channels are effective, although significant complications exist. We propose to address the hypothesis that it is possible to develop a radical approach to management of intraocular pressure employing an AAV-mediated system for increasing the permeability of Schlemm's canal endothelial cells (SCEC), based on published supportive data from this laboratory showing that RNAi-mediated down regulation of mRNA encoding components of tight junctions of neuronal vascular endothelia induces increased cell permeability, a process which has been used to validate a procedure for acute treatment of neuronal edema. While tight junctions of neuronal vascular endothelial cells have been extensively studied and comprise of a series of up to 30 protein components, less is known of the organization of adherence mechanisms of SCEC, although electron- and immunofluorescence microscopy show the presence of tight junctions. We propose a comprehensive analysis of tight junction protein expression in SCEC in vitro. In vivo studies will involve introduction of AAV vectors into the anterior chamber of the eye in rodent models of elevated IOP. The vectors will be designed to express shRNAs targeting a variety of tight junction transcripts expressed in
SCEC using an inducible system. The effect of RNAi-mediated increase in the permeability of SCEC will be assessed using aqueous humour outflow measurement methods and we will also explore the utility of high resolution and diffusion-weighted MRI for this purpose, which may prove to be a simpler, non-invasive and clinically relevant method. This research will provide further fundamental insights into the mechanisms of ocular pressure maintenance and could provide benefit to those patients not responsive to conventional means of therapy.

Programme(s)

FP7-IDEAS-ERC - Specific programme: "Ideas" implementing the Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007 to 2013)

Topic(s)

ERC-AG-LS7 - ERC Advanced Grant - Diagnostic tools, therapies and public health

Call for proposal

ERC-2012-ADG_20120314

See other projects for this call

Funding Scheme

ERC-AG - ERC Advanced Grant

Principal Investigator

Peter Humphries (Prof.)

Host institution

THE PROVOST, FELLOWS, FOUNDATION SCHOLARS & THE OTHER MEMBERS OF BOARD OF THE COLLEGE OF THE HOLY & UNDIVIDED TRINITY OF QUEEN ELIZABETH NEAR DUBLIN

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Activity type

Higher or Secondary Education Establishments

EU Contribution

€ 2 439 232

Website

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