Glaucoma Research Society of Canada

We Support New Ideas

2010 RESEARCH GRANT PROJECTS

Investigating a New Procedure for Treating Plateau Iris Syndrome

Often multiple mechanisms, including plateau iris syndrome, contribute to angle closure glaucoma. In plateau iris, the peripheral iris bunches up in the drainage angle and does not allow drainage of the eyes' internal fluid despite medical and laser treatment.

Treatments that aim to halt the progression of glaucoma and decrease the risk of acute angle closure episodes, do not address the underlying cause of plateau iris. And imaging studies show that cataract surgery does not treat the underlying problem in plateau iris syndrome.

In our project, we present endocycloplasty, a new technique where a laser applied behind the iris attempts to open the drainage system in the eye. This procedure is combined with cataract surgery so patients with a cataract and plateau iris syndrome will be enrolled. We feel that this new procedure will be safe and effective in managing plateau iris syndrome.

– Dr. Dominik W. Podbielski, Dr. Iqbal I. Ahmed, University of Toronto, Toronto, Ontario

Determining if Regulating Endocannabinoid Levels Provides Retinal Protection after Ischemia and Optic Nerve Injury

Abnormal ocular blood flow may contribute to the development and progression of vision loss in glaucoma. Local alterations in endocannabinoid levels are critical in regulating vascular tone and blood flow.

We are examining whether manipulating the endocannabinoid system using enzyme inhibitors can decrease vascular and neuronal damage in experimental models of retinal blood vessel occlusion and optic nerve injury.

This research has relevance to the discovery of novel therapeutics for the treatment of glaucoma and retinal diseases involving vascular dysregulation.

– Dr. Melanie E.M. Kelly, Dalhousie University, Halifax, Nova Scotia

Comparing the Cost Effectiveness of Telemedicine versus In-Person Consultation in the Detection and Treatment of Glaucoma

Our study will determine and compare the cost effectiveness of a collaborative remote model of consultation versus the traditional in hospital/in person consultations from health system, practitioners' and patients' perspectives using various outcome measures including quality of life and functional assessments.

We will also explore the level of use needed for telemedicine services to compare favorably with traditionally organized health care.

– Dr. Enitan A. Sogbesan, Dr. Karim F. Damji, University of Alberta, Edmonton, Alberta

Comparing the Ahmed-FP7 Valve and the Baerveld-350 Implant in Treating Refractory Glaucoma

Our study will continue to compare these devices in a multi-centre, randomized controlled trial.

In 2005, we recruited 238 patients with refractory glaucoma from seven international clinical centres. Patients received an Ahmed-FP7 valve implant or a Baerveldt-350 implant and were followed for five years. Outcome measures include intraocular pressure, glaucoma medication use, visual acuity, complications and treatments required.

After one year, the Baerveldt group had a lower mean intraocular pressure, required fewer medications and had better overall survival. But they also had a higher incidence of hypotony-related devastating complications and required more post-operative interventions than the Ahmed group.

Our study will continue to follow patients for five years post operation and we hope that our results will offer insight into the treatment of refractory glaucoma.

– Dr. Ike Ahmed & Panos Christakis, University of Toronto, Toronto, Ontario

Studying Vascular Reactivity in Primary Open Angle Glaucoma

In earlier studies, we have shown that patients with untreated primary open angle glaucoma exhibit a reduced capacity for vascular regulation compared to age-matched controls. We have also shown that the regulation capacity of the blood vessels returns to normal following eye pressure lowering treatment using eye drops.

Our new study will determine if the recovery in vascular regulation of the blood vessels at the back of the eye is due to the reduction of eye pressure, or a direct response of the blood vessels to the eye drops, or a combination of the two.

We will recruit patients undergoing surgical laser treatment to reduce their eye pressure and assess the regulatory response of the blood vessels at the back of the eye by non-invasively measuring the blood flow in these vessels before and during carbon dioxide breathing.

– Dr. Chris Hudson, Dr. John G. Flanagan, Toronto Western Research Institute, Toronto, Ontario

Studying Real-Time Imaging of Intraocular Pressure Increases

High pressure inside the eye is a significant risk factor for developing glaucoma. It has been difficult to understand how the eye responds to high IOP because the tissues and regions of the optic nerve head are at the back of the eye.

Our work will use a new imaging technology, spectral domain optical coherence tomography (SD-OCT), to image the eye's response to a brief increase in IOP in real-time.

By directly observing the changes the eye undergoes, we hope to gain a better understanding of the mechanical behavior of the eye. This may help us understand how glaucomatous damage develops and whether some individuals are at greater risk of disease.

– Dr. John G. Flanagan, Richard Norman, Toronto Western Research Institute, Toronto, Ontario

Searching for Markers and Studying the Influence of Peptides and Preservatives in Ocular Cell Injury

It has been recently recognized that many patients with glaucoma also have "ocular surface disease". In these patients, the surface of the eye is already compromised before glaucoma treatment. These patients may be at higher risk of not tolerating conventional anti-glaucoma eye drop treatment.

In our research, we will take specimens from the surface of the eye in patients with glaucoma and ocular surface disease. We will test these specimens for indicators of cell injury.

We also plan on exposing elements from the eye surface to a common preservative found in eye drops to determine if, and how, it may be leading to ocular surface problems. Finally, we will be determining whether a novel peptide known as lacritin contributes to the health of the eye surface in our laboratory models.

–Dr. Cindy Hutnik, Dr. Negin Ashki, Dr. Gordon Laurie, Dr. Robert McKown, Dr. Julia Baryla, St. Joseph's Health Centre, London, Ontario

Evaluating if RGMa Proteins Promote Retinal Ganglion Cell Survival in Glaucoma

Our study will build on our earlier research, supported by GRSC, and recently published in the journal "Neuroscience".

Our earlier research demonstrated that RGMa, a protein that can be found at the surface of retinal cells, can be used to promote retinal cell survival. Direct injection of RGMa induced a strong protection, which resulted in a strong increase of retinal cells survival in our models for glaucoma.

The extent of protection was among the best published so far and clearly indicates that RGMa is an invaluable target for glaucoma treatment.

– Dr. Philippe Monnier, Toronto Western Research Institute, Toronto, Ontario

Determining Cost-Effectiveness of Various Glaucoma Screening Tests in High-Risk Populations

No national program for screening for glaucoma exists in Canada. Public health consultants have not recommended such a program partially because of lack of evidence that screening is cost-effective.

We hypothesize that screening high-risk populations may be cost-effective using newer testing technologies. We will simulate screening sessions using different screening tests in a virtual population of 10,000 high-risk subjects.

The cost-effectiveness ratio will be evaluated using specialized software. The models will help determine the appropriate combination of tests in a screening program for high-risk populations.
– Dr. Alvine A. Kamdeu Fansi, Dr. Gisèle Li, Dr. Paul Harasymowycz, Dr. Jacques LeLorier, Maisonneuve-Rosemont Hospital Research Centre, Montreal, Quebec

Using Bevacizumab in Trabeculectomy Surgery

The most common form of glaucoma surgery is trabeculectomy with an anti-scarring agent, Mitomycin C.

This surgery involves cutting a channel into the eye so eye fluid can drain into the surrounding tissue. The surgery and fluid flow cause inflammation and scarring which can lead over time to narrowing or closing of the channel causing the surgery to fail and IOP to rise again.

Vascular endothelial growth factor (VEGF) is involved in healing and scarring of surgical wounds.

Using Bevacizumab, an anti-VEGF agent, in glaucoma filtering surgery can reduce post-operative blood vessel formation and scarring with wound healing and has the potential to improve outcomes for patients.
–Dr. Catherine Birt, Dr. Christoph Kranemann, Dr. Deepan Selvadurai, Sunnybrook Health Sciences Centre, Toronto, Ontario

Studying Proliferating Cells in the Adult Human Optic Nerve

Stem cells can renew themselves and become a variety of cell types. This means that they have the capacity to replace and/or restore diseased tissue, as in optic nerve damage from glaucoma.

It is not known whether stem cells exist within the human optic nerve head. We have recently found populations of proliferating cells in the adult human optic nerve head. As some of these may have stem cell potential, we will be performing detailed studies to characterize these cells based on criteria for their identification.

A better understanding of proliferating cell types in the human optic nerve is a first step toward identifying endogenous stem cells with the potential to treat glaucoma.
– Dr. Yeni H. Yücel, Dr. Neeru Gupta, St. Michael's Hospital, Toronto, Ontario

Analysing Cortical Cell Loss in Normal IOP Glaucoma Models

The mechanisms that cause some types of glaucoma to progress, despite consistently normal intraocular pressures, are largely undefined. The involvement of the part of the brain that receives and interprets visual information from the eye is one such potential factor.

Demonstrating involvement of visual pathway components beyond optic nerve cells may substantially advance understanding of the mechanisms underlying disease.

Our research has shown cortical changes associated with mutation of one glaucoma-causing gene, in patients as well as a mouse model. We hypothesize that through a process called trans-synaptic degeneration, loss of cerebral cortical cells may contribute to death of optic nerve cells.

We will investigate the timing of these changes to see if cortical loss precedes optic nerve changes. We will also determine if synaptic degradation results in loss of retinal ganglion cells.
– Dr. Ordan J. Lehmann, University of Alberta, Edmonton, Alberta

Investigating the Cellular Response of Human Optic Nerve Heads to Mechanical Strain

We have developed a cellular human model where optic nerve head cells are grown on stretchable membranes which are then deformed, mimicking the deformation occurring in patients with glaucoma.

The resulting proteins from these cells are then collected and analyzed to determine if any bio-markers are present indicating the presence or development of glaucoma.

The goal of these studies is to better understand the progression of glaucoma and specify bio-markers that are present at this early stage of the disease. This research is significant, as it will improve the understanding of how biomechanical factors affect the initiation and progression of glaucomatous optic neuropathy.

– Ronan Rogers, Dr. Suzanne Ackloo, Dr. John G. Flanagan, Toronto Western Research Institute, Toronto, Ontario

Determining the Effect of Compressive Strain on Human Optic Nerve Astrocytes and Lamina Cribrosa Cells

Many risk-factors are known to be associated with glaucoma including elevated IOP. Lowering the IOP remains the only evidence-based method for managing the disease. The biological mechanisms involved are poorly understood.

We developed highly advanced computer models to determine the anatomical and biomechanical effects of elevated IOP on the optic nerve head.

Based on these models, we propose a novel method for simulating the levels of compression experienced by cells in the lamina cribrosa during elevated IOP. Proteins will then be isolated and analysed in collaboration with the Ontario Cancer Biomarker Network. These data will be used to identify the pathways and mechanisms associated with early glaucoma.

– Kenneth Olsen, Dr. Suzanne Ackloo, Dr. John G. Flanagan, Toronto Western Research Institute, Toronto, Ontario

Studying Mechanisms Responsible for Normal Tension Glaucoma

Mutations in two identified glaucoma genes, MYOC and OPTN, and a congenital glaucoma gene, CYP1B1, can lead to glaucoma. These account for only a small percentage of patients with normal tension glaucoma suggesting that there are other genes and factors yet to be identified.

We have previously shown that a protein encoded by the OPTN gene, optineurin, is essential for the transport of stress reducing growth factors to the eye. Retinal ganglion cells are dependent on the growth factor BDNF for survival. Deficiencies in BDNF transport along the optic nerve have been implicated as a potential cause of both normal and high tension glaucoma.

We have already shown that reducing optineurin levels in cultured retinal cells increases their sensitivity to stress by interfering with BDNF signalling.

In the current GRSC project, we will use the same technique, called micro RNA based gene silencing, to change the protein levels in retinal ganglion cells. This technology will help identify the ways that BDNF reduces stress and the resulting cell death associated with glaucoma.

We hope that identifying these factors will not only increase our understanding of the different causes of glaucoma, but lead to new strategies to prevent the progression of the disease.

– Dr. Alexander K. Ball, McMaster University, Hamilton, Ontario

Evaluating Mesenchymal Stem Cell Transplantation as a Treatment for Glaucoma

A summary of this research project by Dr. Mark Lesk and Dr. Denis Claude Roy of the Maisonneuve-Rosemont Hospital Research Centre, Montreal, Quebec, was not available at the time of publication.