



Glaucoma Research
Society of Canada

We Support New Ideas

2016 RESEARCH GRANT PROJECTS

THANKS TO OUR DONORS RESEARCHERS RECEIVE \$300,000 IN GRANTS

Dr. Graham Trope, founder of the GRSC and chair of its Scientific Advisory Committee, recently announced the Society's 2016 research grants for the following sixteen projects:

Comparing the effect of oral glucose tolerance tests in diabetic and glaucoma patients

One of the risk factors identified for the development and progression of primary open angle glaucoma (OAG) is diabetes. However, there is conflicting evidence as to whether diabetes increases or decreases the risk of OAG.

This study will compare the effect of oral glucose tolerance tests on intraocular pressure, visual fields, anterior segment and choroidal changes in patients with glaucoma and diabetes. The results will help clinicians stratify risk and possibly determine treatment and management options to prevent complications from glaucoma and diabetes.

– Dr. Enitan Sogbesan, McMaster University, Hamilton, ON

Determining the effectiveness of retrobulbar injection versus IV analgesia for transscleral diode (TSD) laser treatment

TSD laser is used to reduce intraocular pressure by ablating the ciliary body. The procedure is painful and traditionally done with retrobulbar anesthesia. The retrobulbar injection itself has a complicated side effect profile that includes brain stem anaesthesia; retrobulbar hemorrhage; and penetration of the globe.

This randomized control trial will investigate if adequate anesthesia can be achieved with a method that avoids the side effect profile of retrobulbar injection.

– Dr. Delan Jinapriya, Dr. Isabella Irrcher, Dr. Dale Engen, Queen's University, Kingston, ON

Comparing the protein deposits in the eyes of dementia patients with those found in glaucoma

Glaucoma and dementia are both age-related disorders characterized by progressive neural degeneration. Abnormal protein accumulation is implicated in both diseases.

This study will compare the abnormal protein deposits observed in the eyes of dementia patients with those seen in glaucoma eyes.

Exploring the pathology and characteristics of circulating eye proteins in each of these major debilitating diseases will provide new insights into possible underlying shared and different disease pathways and may point to new approaches to preventing blindness from glaucoma.

– Dr. Neeru Gupta, Dr. Yeni Yücel, St. Michael's Hospital, Toronto, ON

Establishing a zebrafish model for Axenfeld-Rieger Syndrome

In this study we will generate *foxc1* mutant fish and examine the effects on retinal ganglion cell (RGC) survival. We will determine if oxidative stress is responsible for RGC death and assess whether the *platelet derived growth factor alpha* (*pdgfra*) signaling pathway is responsible for the phenotype.

This novel approach will identify compounds that can affect *foxc1* and *pdgfra* function and potentially offer new treatment options to slow or halt glaucoma progression in Axenfeld-Rieger patients.

– Dr. Curtis R. French, Memorial University of Newfoundland, St. John's, NL

Developing a tool that links quality of life to utility values and health economic measures

No instrument currently exists to obtain utility values from glaucoma patients in clinical trials. This complicates the comparison of glaucoma treatment options using economic evaluations, specifically, cost-effective analysis. Hence, public and hospital administrators are faced with challenges when making selection decisions.

The objective of this study is to develop a preference-based tool that is capable of capturing important impacts of treatment and disease on health-related quality of life among patients with glaucoma.

– Dr. Iqbal Ike Ahmed, Dr. Dominik Podbielski, University of Toronto, Toronto, ON; Dr. Feng Xie, Sergei Muratov, McMaster University, Hamilton, ON

Studying the biometric properties of patients with narrow-angle glaucoma and determining the angle opening after iridotomy

Narrow-angle glaucoma has a lower prevalence rate than open-angle glaucoma in North America, but accounts for the majority of blindness from glaucoma world-wide.

This study will characterize the biometric properties and refractive status of a Canadian narrow-angle glaucoma population and determine the extent of angle opening post treatment for narrow angles with a peripheral iridotomy.

Identifying those with narrow angles will allow preventive measures to be taken to avoid blindness. Understanding what the ocular characteristics of narrow-angle patients are in Canadians will help practitioners identify narrow angles.

– Dr. Delan Jinapriya, Dr. Eddie Moss, Dr. Harman Singh, Dr. Isabella Irrcher, Queen's University, Kingston, ON

Establishing a genetic database in open-angle glaucoma

The influence of inherited genetic elements in glaucoma remains incompletely characterized, with many genes yet to be discovered.

Identifying underlying genetic defects requires large-scale collections of glaucoma cases and appropriate controls via multi-centered collaborations like the NEIGHBOR consortium, an American effort to identify genetic variants associated with primary open-angle glaucoma (POAG) and to elucidate the molecular pathogenesis of POAG.

We intend to gather DNA samples from about 400 individuals affected with perimetric open-angle glaucoma and a corresponding reference population drawn from clinical labs. These will be submitted for inclusion in the NEIGHBOR study, increasing its statistical power to detect glaucoma risk alleles.

– Dr. Andrew C. Orr, Dr. Paul E. Rafuse, Dalhousie University, Halifax, NS

Studying changes in lamina cribrosa depth (LCD) as an early marker of glaucoma progression

Advances in optical coherence tomography (OCT) have enabled more detailed visualization of the optic nerve head. However no longitudinal studies in humans evaluate the advantages of LCD over other parameters of glaucoma damage.

We recently developed new software that allows practical measurement of LCD with OCT. Using these tools, we will analyze OCT images from glaucoma patients and normal controls followed for up to six years. Our study will confirm the value of LCD analyses as a new tool to assist in glaucoma management and enable clinicians to detect glaucoma progression at an earlier stage, potentially reducing the disability caused by the disease.

– Dr. Jayme R. Vianna, Dr. Balwantray C. Chauhan, Dalhousie University, Halifax, NS

Seeing if anti-inflammatory drug injections hasten the resolution of post-operative swelling

During glaucoma surgery, a new opening is created that allows fluid to drain out of the eye. In some patients too much fluid flows out, causing swelling at the back of the eye. This choroidal effusion often makes the eye pressure stay too low, resulting in decreased vision.

To treat a choroidal effusion, we try to raise the eye pressure somewhat so that the swelling subsides. We have found that an injection with an anti-inflammatory drug (triamcinolone) appears to help speed up healing.

Our study will compare the length of time it takes the choroidal effusions to disappear in a group of patients treated with triamcinolone and in a group with no drug injection.

– Dr. Catherine Birt, Dr. Kenneth Eng, Dr. Chrisoph Kranemann, Dr. Alberto Bonniard, Sunnybrook Health Sciences, Toronto, ON

Combination therapies for the treatment of glaucoma

Therapies that will prove effective in treating glaucoma must be able to target multiple cell death triggers in order to protect ganglion cells and their axons.

We hypothesize that a therapeutic strategy that targets both apoptosis and oxidative stress will provide optimal therapeutic benefit in animal models of glaucoma.

In this study we will combine X-linked inhibitor of apoptosis gene therapy with a novel small molecule compound that has been shown to potently suppress oxidative-stress induced cell death and neuronal inflammation in two mouse models of ALS. We will test this combination therapy in both *in vitro* and *in vivo* models of retinal ganglion cell death and glaucoma.

– Dr. Catherine Tsilfidis, Ottawa Hospital Research Institute, Ottawa, ON

Studying the cost effectiveness of treatment strategies for patients with glaucoma

This study will use a Markov model to perform a cost-effectiveness analysis to evaluate three treatment strategies for patients with glaucoma and cataract: iStent with phacoemulsification, phacoemulsification alone, and medical therapy.

Results of this study may have a major impact on significantly reducing healthcare costs and preserving vision since a broad range of groups, including clinicians, researchers, government policy-makers and hospital administrators can make use of the results to make efficient and economical decisions.

– Dr. Monali Malvankar, Dr. Cindy Hutnik, Lawson Health Research Institute, Ivey Eye Institute, London, ON

The relationship between gaze behaviour and mobility deficits

We have identified changes in gaze metrics and eye-foot coupling caused by glaucoma and their relationship to mobility deficits.

The objective of this new phase of our research is to provide proof-of-concept evidence that *gaze behaviour* is modifiable in people with glaucoma and leads to improved mobility.

We will test the hypothesis that task-specific gaze training leads to changes in the spatiotemporal pattern of gaze and temporal coordination of gaze with foot placement targets and obstacles, thereby reducing foot placement error and obstacle collisions.

This research will provide invaluable insight for orientation and mobility specialists on how to train *gaze behaviour* in everyday tasks, lead to larger-scale training studies and has the potential to greatly improve the mobility of people with glaucoma and their quality of life.

– Dr. Dan Marigold, Dr. Kim Zebehazy, Simon Fraser University, Burnaby, BC

Developing portable visual field testing (perimetry)

Our project will develop a portable visual field test that can be used by patients at home and also to screen for visual field defects in areas of the world in which access to expensive medical instrumentation and hospitals is limited.

In the next phase, we will integrate a fixation monitoring utility with an eye-tracking system into the visual field testing protocol and improve user interfaces. We will test glaucoma patients on the portable perimeter and on the Humphrey Field Analyzer (HFA). Ten patients will use the portable perimeter in their homes. The performance on the portable perimeter will be analyzed and compared with the results of the *gold standard* HFA.

Successful development of a portable perimeter can revolutionize the ability to detect and monitor visual field loss in patients with glaucoma.

– Dr. Moshe Eizenman, Dr. Jonathan Rose, University of Toronto, Toronto, ON

Identifying the genetic basis of pigmentary glaucoma (PG)

In our study so far, we collected DNA samples from two Mennonite families in which PDS/PG segregates as an autosomal dominant trait. Through whole exome sequencing, we identified variants present in affected individuals that are absent from unaffected siblings, ethnically matched controls and public databases. Now these candidate variants will be assayed in a panel of 113 PDS/PG patients to reveal whether they contribute to disease in the broader population.

We expect that these findings will allow the pre-symptomatic detection of at-risk individuals and set the stage for more experiments to understand the root cause of PG and develop optimal treatment for patients.

– Dr. Michael A. Walter, Dr. Ordan Lehmann, University of Alberta, Edmonton, AB

Mechanisms underlying excess matrix deposition in the trabecular meshwork

We hypothesize that cells in the trabecular meshwork (TM) can control the deposition of extracellular matrix (ECM) molecules by regulating the expression and activity of the protein phosphatase and tensin homolog (PTEN). Our study will investigate the effect of transforming growth factor beta (TGF- β) and mechanical strain, factors implicated in the pathogenesis of glaucoma, on the expression and function of PTEN using human TM cells in culture.

We have found that TGF- β can regulate ECM deposition by modulating the expression and activity of PTEN in TM cells. This novel finding indicates that maintaining normal activity of PTEN in the TM cells could prevent the excess accumulation of ECM and thus has the potential to be the therapeutic target for lowering the IOP in glaucoma.

– Dr. Sunil Parapuram, Lawson Health Research Institute, University of Western Ontario, London, ON

Efficacy of PGC-1 α induction on retinal ganglion cells (RGCs)

RGCs are particularly vulnerable to metabolic and oxidative injury associated with pathogenesis of glaucoma. However a molecular mechanism underlying this sensitivity has not been established *in vivo*.

PGC-1 α (peroxisome proliferator-activated receptor γ co-activator-1 α) is a master regulator of adaptive metabolism and oxidative stress responses in a tissue and cell-specific manner. Aberrant PGC-1 α signaling is implicated in neurodegeneration, but the mechanism underlying its role in neuronal injury remains unclear.

Our research will test whether increased and sustained PGC-1 α pathway activity will be neuroprotective to the inner retina by showing increased RGC protection and functional survival in acute and chronic models of optic neuropathy.

– Dr. Jeremy Sivak, Krembil Research Institute, Toronto Western Hospital, Toronto, ON