



Glaucoma Research
Society of Canada

We Support New Ideas

2018 RESEARCH GRANT PROJECTS

THANKS TO OUR DONORS RESEARCHERS RECEIVE \$374,931 IN GRANTS

Dr. Graham Trope, founder of the GRSC and chair of its Scientific Advisory Committee, recently announced the Society's 2018 research grants for the following twenty projects:

Cost-related non-adherence with topical glaucoma medications

This study aims to determine the frequency of cost-related reasons for non-adherence with topical glaucoma eye drops among glaucoma patients aged 25-64. Factors such as lack of insurance coverage for glaucoma medications, employment status and marital status will be examined.

The study results will provide important information to health administrators, governments and hospital charities regarding the problem of non-adherence with eye drops due to cost. Our data should help policy makers design effective programs to help glaucoma patients in financial need.

*- Dr. Yaping Jin, Dr. Yvonne Buys, Dov Kagan,
University of Toronto, Toronto ON*

NSAID drops for trabeculectomy wound management

Topical steroidal anti-inflammatory drugs are used to control inflammation in glaucoma surgery patients. These drugs are associated with adverse effects such as steroid-associated spikes in intraocular pressure and inhibition of wound healing.

In a clinical trial, we will assess the merits of non-steroidal anti-inflammatory (NSAID) treatment compared to steroid for trabeculectomy wound management. If NSAID treatment can be shown to be as effective as using a steroid, patients could be offered lower risk treatment options with fewer adverse side effects.

- Dr. Cindy M. L. Hutnik, James J. Armstrong (MD/PhD Candidate), Lawson Health Research Institute, London ON

Identification of the genetic basis of pigmentary glaucoma

In research supported by the GRSC, we discovered the first causative gene for pigmentary glaucoma (PG) in humans, revealing that mutations of the premelanosome protein (PMEL) cause PG. But PMEL mutations are not the sole genetic cause of PG. Our new research will determine if CNIH mutations cause PG in our patients.

Our studies will allow the presymptomatic detection of at-risk individuals and set the stage for additional experiments directed at developing optimal treatment for PG patients.

- Dr. Michael Walter, University of Alberta, Edmonton AB

Risk of angle closure glaucoma in migraine patients using triptans

We hypothesize that migraine patients using serotonin receptor agonists (triptans) are at a higher risk of developing acute angle closure glaucoma (ACG). Our study will quantify the risk of ACG with triptans using an epidemiologic study and a large health claims database from the U.S.

Since millions of people around the world are using triptans for migraine relief, a potential risk of ACG with these drugs will have profound public health implications. Conversely, a negative association between triptans and ACG will put patients and clinicians at ease with respect to the risk of ACG with triptans.

*- Dr. Mahyar Etminan, Mohit Sodhi (BSc Candidate),
Dr. Frederick Mikelberg, University of British Columbia,
Vancouver BC*

Evaluating the ability of optical coherence tomography to distinguish glaucomatous optic neuropathy

It can be difficult to distinguish glaucomatous optic neuropathy (GON) from other forms of less common, non-glaucomatous optic neuropathies such as ischemic optic neuropathies (ION).

Our research will determine the structural parameter(s) of the optic nerve head and retina that best distinguish GON from ION through a variety of optical coherence tomography (OCT) imaging tests.

We hope to reveal the unique OCT structural signature for GON and ION. This data will improve the clinician's ability to accurately diagnose glaucomatous optic neuropathy .
- Dr. Brennan Eadie, Dr. Marcelo Nicoleta, Dalhousie University, Halifax NS

Enhancing retinal ganglion cell production for cell replacement therapy

Humans have no capacity to regenerate retinal ganglion cell (RGC) neurons.

Recent work has demonstrated that RGCs can be successfully transplanted, and can integrate into the recipient circuitry. But a pipeline for efficient generation of RGCs needs to be developed to bring cell replacement therapy to the clinic.

My project will lay the groundwork for developing an efficient pipeline for RGC production.

I will identify combinations of transcription factors that can enhance RGC production from retinal progenitors, characterize these "induced RGCs" (iRGCs) to ensure that they express appropriate gene expression profiles and neurite projection patterns, and determine whether iRGCs can be successfully transplanted.
- Dr. Pierre Mattar, Ottawa Hospital Research Institute, Ottawa ON

Is cerebrospinal fluid entry into the optic nerve impaired in glaucoma?

Preventing damage to dying nerve cells of the optic nerve in glaucoma is critical. We have recently discovered a glymphatic circulation in the optic nerve that functions as a waste removal system.

This project will allow us to determine whether there is a problem with clearing toxins by way of the glymphatic system in glaucoma. This work may contribute to new understandings of the disease and strategies to protect sight.
- Dr. Neeru Gupta, Dr. Yeni Yücel, Providence St. Joseph's & St. Michael's Healthcare, Toronto ON

Is lymphatic drainage from the eye altered in glaucoma?

All glaucoma treatments aim to reduce eye pressure, many by improving fluid drainage from the eye. There are two known pathways by which fluid leaves the eye, and we have recently described a third lymphatic pathway.

This project will study whether in glaucoma, there is a problem with the third pathway and may lead to new insights into the disease and novel targets to prevent blindness.
- Dr. Neeru Gupta, Dr. Yeni Yücel, Providence St. Joseph's & St. Michael's Healthcare, Toronto ON

The relationship between beta atrophy and ocular rigidity

We hypothesize that biomechanical stress and strain in the peripapillary area contribute to the development of beta atrophy.

Recent biomechanical models suggest that scleral rigidity would play a major role in determining stress and strain in both the optic nerve head and the peripapillary retina, even a greater role than intraocular pressure. Ocular rigidity is determined primarily by scleral rigidity.
- Dr. Mark R. Lesk, Maisonneuve Rosemont Hospital Research Centre, Montreal QC

Assessing RGMa antibodies that promote optic nerve regeneration

Glaucoma induces optic nerve degeneration, which leads to vision impairment. The optic nerve itself contains molecules that will prevent any kind of regeneration.

We propose to develop a compound that will neutralize one major inhibitor of optic nerve regeneration. We aim to show that this compound can promote optic nerve regeneration, a critical step towards vision restoration.

- Dr. Philippe Monnier, Krembil Research Institute, University Health Network, Toronto, ON

Comparing corneal endothelial cell loss after different surgeries

Our study will compare corneal endothelial cell count and health status after trabeculectomy vs combined trabeculectomy, phacoemulsification and IOL implantation.

The outcomes will increase knowledge about preserving corneal health and clarity. If our study shows a significant decrease of endothelial cell count, surgeons might have to reconsider applying different or new techniques in performing trabeculectomy or combined surgery in patients with compromised endothelial function such as Fuchs endothelial dystrophy.

- Dr. Ali Ahadian, Dr. Hall Chew, Dr. Catherine Birt, Sunnybrook Research Institute, Toronto ON

MNK1 - a novel neuroprotective target in RGC injury

MNK1 is a protein that regulates the production of other proteins in response to external signals, such as stress and inflammation. The objective of this study is to examine the role and mechanism of MNK1 signaling in models of glaucomatous retinal injury. Understanding this mechanism could offer novel treatment strategies for glaucoma and other neurodegenerative diseases.

- Dr. Jeremy Sivak, Alessandra Tuccitto (Student), Krembil Research Institute, University Health Network, Toronto ON

Dendritic retraction and physiological responses in RGCs

The main thrust of our research is to correlate the structural dendritic retraction of retinal ganglion cells (RGCs), evaluated by serial *in vivo* confocal scanning laser ophthalmoscopy in Thy1-YFP mice, with electrophysiological RGC responses, evaluated by *ex-vivo* multi-electrode array whole-retina recordings, in a model of moderate chronic intraocular pressure elevation by microbeads injection in the anterior chamber.

- Dr. François Tremblay, Dr. Balwantray Chauhan, Dalhousie University, Halifax NS

Mechanisms underlying excess matrix deposition in the TM

We have found that signaling by the protein phosphatase and tensin homolog (PTEN) has a role in balancing the production and degradation of matrix molecules in the trabecular meshwork (TM). We will study the role of PTEN signaling and determine the mechanisms by which PTEN protein control the production and degradation of matrix molecules in the trabecular meshwork.

We believe that our study will lead to targets which can be manipulated to prevent fibrosis of the TM, with high potential to be used as a treatment for glaucoma in the future.

- Dr. Sunil Parapuram, Lawson Health Research Institute, London, ON

Changes in the TM with an IOL implant after cataract surgery

We hypothesize that there is an ideal intraocular lens (IOL) implantation site and model that results in the least amount of TM pathological changes, which can be optimized to help regulate IOP. The aim of our study is to examine the changes in TM and corneal endothelial changes between anterior chamber IOLs and posterior chamber IOLs. We will also compare the effects of the different types of posterior chamber IOLs on the trabecular meshwork.

- Christina Mastromonaco (PhD Candidate), Dr. Miguel N. Burnier Jr., Dr. Nabil Saheb, McGill University, Montreal QC

MRTF-A as a novel anti-fibrotic target in TM cells for OAG

We have identified a candidate regulator of stress fibre formation in trabecular meshwork (TM) cells, MRTF. MRTF is a transcription factor that activates expression of cytoskeletal genes, including α -smooth muscle actin (α -SMA), a major contractile actin isoform.

Our research will further characterize the role of MRTF in regulation of key cytoskeletal molecules responsible for TM cell contraction and stiffness, and to test novel MRTF inhibitors for efficacy in animal models of open angle glaucoma (OAG).

- Dr. Judith West-Mays, McMaster University, Hamilton ON

The relative value of health states as measured by HUG-5

From 2016 to 2018 we developed and validated a glaucoma quality of life tool (HUG-5) to obtain health utility values from glaucoma patients in clinical trials. The HUG-5 compares glaucoma treatment options in economic evaluations to determine cost-effectiveness.

To determine the relative value associated with health states as measured by the HUG-5, we will ask members of the general population which of these health states they prefer. This study will give researchers additional information needed for cost-effective analyses with the HUG-5.

- Dr. Feng Xie, Kevin Kennedy, McMaster University, Hamilton ON; Dr. Iqbal Ike Ahmed, Dr. Dominik Podbielski, University of Toronto, Toronto ON

Development of a customizable prototype low vision device

Our study will determine if an optimized, electronically controlled non-invasive optical device can improve mobility, navigation and certain tasks of daily living in patients with severely constricted visual fields.

- Dr. Yogesh Patodia, Dr. Alexander Mao, Dr. Cindy Hutnik, Lawson Health Research Institute, London, ON

Retinal ganglion cells neuroprotection in animal models of glaucoma

The degeneration of the retinal ganglion cells (RGCs) in glaucoma is preceded by defects in anterograde and retrograde axonal transport between retina and visually-related brain structures.

EphA4, a tyrosine kinase receptor widely expressed throughout the brain, exerts a pivotal role in neuronal degeneration following nerve injury and in multiple neurodegenerative diseases, hindering neuronal regeneration and axon regrowth.

Our goal is to characterize RGCs axons degeneration in EphA4-signaling deficient mice with induced-elevated IOP. We hypothesize that the lack of EphA4 signaling in glaucoma models will protect RGCs from dysfunction and slow down degeneration.

- Dr. Michael Reber, Dr. Jeremy Sivak, Krembil Research Institute, University Health Network, Toronto ON

Influence of Bruch's membrane opening area on the diagnostic performance of optical coherence tomography

This study will determine whether the diagnostic performance of optical coherence tomography accurately adjusts for Bruch's membrane opening area.

We will recruit healthy subjects and glaucoma patients from three centres and compare the sensitivity and specificity of the current normative classifications between the eyes with smaller, medium, and larger Bruch's membrane opening areas.

This knowledge will provide valuable information for clinical judgment of neuroretinal parameters on subjects with different Bruch's membrane opening area.

- Dr. Lucas A. Torres, Dr. Balwantray C. Chauhan, Nova Scotia Health Authority, Halifax NS