



Glaucoma Research
Society of Canada

We Support New Ideas

2019 RESEARCH GRANT PROJECTS

THANKS TO OUR DONORS RESEARCHERS RECEIVE \$180,000 IN GRANTS

Dr. Graham Trope, founder of the Glaucoma Research Society of Canada and chair of its Scientific Advisory Committee, recently announced the Society's 2019 research grants for the following 14 projects:

Measuring the IOP of patients using the Water Drinking Test or the iCare Home Tonometer before and after glaucoma surgery

Since intraocular pressure (IOP) is known to change throughout the day, single measurements are not accurate in detecting fluctuations or potential spikes in IOP over time.

Monitoring IOP for 24 hours provides a much better way of understanding how IOP is being controlled but it is cumbersome to do.

The Water Drinking Test, where patients drink one litre of water in clinic and have their IOP measured before and after drinking, is a faster way of measuring patients' highest IOP and how stable their IOP can remain, than 24 hour monitoring.

The iCare Home Tonometer is a device that patients can use to measure their IOP themselves, in the convenience of their home, at scheduled times throughout the day.

Our study will allow surgeons to better understand how patients' IOP is being managed, rather than making clinical decisions based on single in-office measurements.

It would also allow us to understand how effective micro-invasive glaucoma surgeries are in managing IOP stability throughout the day.

- Dr. Iqbal Ike K. Ahmed, Nick Andrew, Taylor Lukasik, University of Toronto, Toronto ON

Studying the adverse effects of oral carbonic anhydrase inhibitor treatment for elevated intraocular pressure

Oral carbonic anhydrase inhibitor medications are used in clinical practice to reduce intraocular pressure (IOP).

Clinicians sometimes hesitate to prescribe these medications because of the potential risks of serious complications including a severe allergic reaction, a significant drop in blood counts, or acute kidney failure.

We hypothesize that the risks of a serious adverse reaction associated with an oral carbonic anhydrase inhibitor are low, particularly among patients who do not have risk factors.

Our study will track patients 65 and older in Ontario who are prescribed an oral carbonic anhydrase inhibitor medication over a ten-year period to determine the incidence of complications.

We will compare the incidence of these complications to a control group of patients.

We will also investigate risk factors for developing these complications to better understand who is at highest risk.

- Dr. Don Redelmeier, Dr. Matthew Schlenker, Dr. Vinay Kansai, Sunnybrook Research Institute, Toronto ON

Establishing a new model in the causality of a late-onset disease such as glaucoma

Our research aims to determine if changes resulting from aberrant ocular development may predispose people to developing disease late in life.

We hypothesize that intercellular signaling plays a critical role in the migration, proliferation, and survival of cells that give rise to components of the anterior segment in the eye.

Our research will determine the sites of active signaling during ocular development and determine which ligands are active in this region. We will subsequently generate animal models that lack such signaling proteins and determine their functions in eye development as well as mature eye function.

- Dr. Andrew J. Waskiewicz, University of Alberta, Edmonton AB

Measuring blood flow changes in the retina of glaucoma patients and healthy subjects

Currently, imaging of blood flow in the retina is measured by calculating a single value for the whole image. This results in throwing away valuable information, since blood flow can vary throughout the retina.

Our approach is to include regional differences of blood flow in our measures.

We will use non-invasive optical coherence tomography angiography images of the retina to measure how much blood flow changes over time between glaucoma patients and control subjects.

We expect that this research will help us better understand when changes in blood flow are occurring in glaucoma patients.

- Dr. Corey Smith, Nova Scotia Health Authority, NS

Using zebrafish to understand glaucoma and discover new therapies

Mutations of two genes located on chromosome 6 (*FOXC1* and *GMD5*) have been previously demonstrated to increase the risk of developing glaucoma.

In our research, we use the zebrafish as a model to try and determine why changes in the sequences of these genes increase glaucoma risk. The zebrafish genome is highly similar to humans, and the structure of the eye is well conserved.

Our new research will determine if these fish lose retinal ganglion cells over time, and display defects in the structure of the optic nerve as seen in glaucoma patients with the same gene mutations.

This will provide us with an animal model that closely mimics the disease found in glaucoma patients, allowing us to learn more about how the disease progresses and to screen for new drugs that may help to slow or even halt vision loss.

- Dr. Curtis R. French, Memorial University, St. John's NL

Frequent visual field tests at home for robust detection of changes in visual fields of glaucoma patients

Our study will determine if more frequent visual field (VF) tests using automated perimeters in a home setting can support earlier detection of patients who lose vision rapidly and require surgical intervention. The Toronto Portable Perimeter (TPP) uses a personal smartphone and a virtual reality viewer to allow VF testing anywhere. Since the TPP is affordable and can be used by patients at home, it can support procedures that require more frequent VF tests.

- Dr. Moshe Eizenman, University of Toronto, Toronto ON

Investigating the cause of mutations in genes in patients with ocular dysgenesis and developmental glaucoma

Inherited forms of childhood glaucoma, including the rare condition Axenfeld-Rieger Syndrome (ARS), are devastating, difficult to manage forms of blindness.

While research has identified the mutations in genes that cause ARS in about 40% of patients, discovery of the underlying cause of glaucoma and ARS in the remaining patients is an unmet need.

Our research will identify regions that regulate the expression of the genes known to be mutated in some ARS patients, and then search these regions for mutations that cause ARS and glaucoma.

Research into the discovery and analyses of the regulatory regions of the human genome is the new frontier of human biology and disease, thus our study may have a broad impact on the field of genomic medicine.

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

Studying the role of a water channel on cerebrospinal fluid flow into the optic nerve

We have described a new waste clearing pathway called the glymphatic system in the optic nerve that communicates with the fluid surrounding the brain.

It is lined by aquaporin water channels that control fluid movement.

Our research will look closely at this channel (Aquaporin-4) to better understanding its possible role in glaucoma and possible new approaches to prevent blindness from the disease.

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

Dendritic retraction and physiological responses in retinal ganglion cells

We have developed state of the art expertise to record simultaneously the activity of hundreds of retinal ganglion cells (RGCs) through multielectrode array. Our work focusses on determining how increased IOP in a bead IOP mouse model influences the size of the RGC dendritic tree and the size of the RGC physiological receptive fields.

In our model, we found that it takes up to one month to see measurable damage at this level. To demonstrate that effect more reliably, we had to find a way to eliminate the contribution of the displaced amacrine cells that are also found in the ganglion cell layer but are not affected by the glaucomatous neuropathy. We used a specific voltage-gated sodium channel blocker (Nav1.6) to preferentially eliminate the activity of the amacrine cells.

This recording technique allowed us to be more specific in determining the type and importance of injury sustained by the RGCs in early and late disease process and to more realistically characterise the functional impact of the IOP glaucomatous neuropathy process.

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

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. Our study will 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

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

In this project, 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

Developing a novel combination treatment for robust regeneration after optic nerve injury

In glaucoma, optic nerve degeneration causes irreversible loss of visual functions.

In recent GRSC supported research, we developed two independent strategies that will allow for optic nerve repair.

Because each strategy taken on its own allows for limited repair, this new research combines both therapies in order to obtain robust optic nerve repair.

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

Do adrenergic glaucoma drugs affect lymphatic outflow from the eye?

We have recently discovered a new third pathway for fluid to leave the eye that depends on lymphatic drainage.

Using a novel imaging system that uses both light and sound, we will study commonly used glaucoma drugs to determine whether they work to lower intraocular pressure by acting on this new lymphatic outflow pathway.

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

Comparing the effectiveness of medications versus laser trabeculoplasty as initial glaucoma treatment

Initial glaucoma therapy consists of topical ophthalmic medications (prostaglandin analogue therapy) or laser trabeculoplasty.

Each year in Ontario alone, more than 180,000 seniors are prescribed glaucoma medications and more than 25,000 laser trabeculoplasty procedures are undertaken.

We hypothesize that patients who receive laser trabeculoplasty as initial glaucoma therapy are at lower risk of requiring additional glaucoma treatment than patients who receive medication as initial therapy.

Our research will be the first population-based study to investigate the comparative effectiveness of these initial glaucoma therapies in preventing the need for further glaucoma treatment.

- Dr. Robert Campbell, Dr. Sherif R. El-Dfrawy, Dr. Chaim M. Bell, Dr. Sudeep S. Gill, Dr. Michael A. McIsaac, Queen's University, Kingston ON