Glaucoma Research Society of Canada

We Support New Ideas

2015 Research Grant Projects

Thanks to Our Donors Researchers Receive $260,000 in Grants

Dr. Graham Trope, founder of the GRSC and chair of its Scientific Advisory Committee, recently announced the Society's 2015 research grants for the following fifteen projects:

Studying the relationship between *gaze behaviour* and mobility deficits in individuals

People with visual field loss from glaucoma often bump into objects and fall while walking because they have difficulty seeing their surroundings. Vision normally provides essential information to plan and control safe foot placement to specific locations through *gaze behaviour* - appropriate eye and/or head movements. This is integral for navigating in the cluttered and complex environment in which we live.

How glaucoma changes *gaze behaviour* and how this relates to the spatio-temporal eye-foot coordination needed for safe mobility is unclear. The goal of our project is to establish the relationship between *gaze behaviour* and mobility in order to design a training program that teaches people where and when to look when walking in cluttered environments. This would lead to safe and improved walking, resulting in better quality of life for people with glaucoma.– *Dr. Dan Marigold, Simon Fraser University, Burnaby, BC*

Developing portable visual field testing (perimetry)

Currently visual fields are tested by specialized and expensive instruments in controlled environments under the supervision of trained technical staff.

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.

We hypothesize that the many sensors and the computing power available on standard mobile devices (tablets and cell phones) can support the development of a portable perimeter that will not require any specialized hardware. A series of studies will characterize and test different aspects of the novel portable perimeter.

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*

Evaluating the effect of sleep apnea treatments on IOP in people with glaucoma

People with glaucoma are reported to have a higher prevalence of obstructive sleep apnea (OSA) compared to the general population and treatment of OSA may increase intraocular pressure (IOP).

This study will compare the effect of two treatments currently used for sleep apnea on IOP in patients with both obstructive sleep apnea and open angle glaucoma.

Measuring the IOP on patients using a standard continuous positive airway pressure device (cPAP) with those using a mandibular advancement oral appliance (OAm) will help determine if patients with glaucoma are more suitable for one device over the other. It will also allow doctors to recommend a particular kind of treatment for OSA in patients with glaucoma.– *Dr. Yvonne M. Buys, Dr. Mariana Cabrera Perez, Toronto Western Hospital, Toronto, ON*

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

PGC-1α (peroxisome proliferator-activated receptorγ co-activator-1α) is induced in the adult retina in response to metabolic and oxidative challenge, age, and in a model of chronic optic neuropathy. Deleting PGC-1α dramatically increases RGC loss from metabolic challenge. Pharmacologic and genetic methods to increase PGC-1α pathway activity induces protective and detoxifying responses to hypoxic and oxidative stresses in cultured cells.

We hypothesize that inducing this pathway will prove efficacious when tested in animal models. Our study will provide critical data to establish methods to induce this pathway, and generate proof of principle before expanding to more intensive models of chronic optic neuropathy and glaucoma.– *Dr. Jeremy Sivak, Toronto Western Research Institute, Toronto, Ontario*

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. We will develop *in vitro* and *in vivo* assays to test this hypothesis.

We have previously shown that the X-linked inhibitor of apoptosis (XIAP) can protect RGCs in an acute model of retinal ischemia. Here, we will combine XIAP gene therapy with a novel small molecule compound that has previously 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 *in vitro* and *in vivo* models of RGC cell death and glaucoma.– *Dr. Catherine Tsilfidis, Ottawa Hospital Research Institute, Ottawa, ON*

Designing a new delivery system for glaucoma drugs

Our research project deals with developing a new nanoparticle-based drug delivery system that will improve the efficiency of glaucoma treatments.

Travoprost and timolol are two drugs used to lower IOP in patients with glaucoma. However their topical application on the cornea results in low absorption and short-lasting effects in the eye. This project will use gold nanoparticles to encapsulate travoprost and timolol and to enhance their action in the eye.

We will use an innovative chemical assembly of gold nanoparticles to build drug vehicles with strong adhesion properties to the cornea. We expect that the retention of nanoparticles on the cornea will considerably improve both the action time and the concentration of drugs in the eye.

Cutting-edge chemistry methods and *in vivo* experiments will be carried out to test the effects of drug-containing nanoparticles in a mouse model of glaucoma. An optimized nanoparticle system will then be subjected to clinical trials. *– Dr. Elodie Boisselier, Dr. Vincent Pernet, Dr. Beatrice Des Marchais, Laval University, Laval, Quebec*

Novel LAP-based ligand traps in the treatment of glaucoma

Our study will investigate the possible therapeutic use of the latency-associated peptide (LAP) as a competitive inhibitor. LAP naturally binds with high affinity to TGFβ2 (transforming growth factor) and prevents it from binding to its receptors. We hypothesize that high-affinity decoy receptors for TGFβ2 using the LAP peptide will abrogate TGFβ2 receptor binding and signaling.

We anticipate that our higher affinity decoy receptor will prove to be highly effective and result in a novel approach to the treatment of glaucoma.– *Dr. Sanjoy K. Gupta, Dr. Neelam Khaper, Northern Ontario School of Medicine, Lakehead University, Thunder Bay, ON*

Identifying the genetic basis of pigmentary glaucoma (PG)

PG is the most common secondary glaucoma in North America, but to date, no causative gene for PG has been found in humans. Our objective is to discover the genetic basis of PG.

PG appears to segregate as a simple Mendelian trait in rare families. To discover the genetic basis of PG in families, we plan to conduct whole exome sequencing on individuals from two Mennonite families in which PG is segregating as an autosomal dominant trait.

We expect that genetic variants underlying PG in isolated communities will allow us to detect the pre-symptomatic at-risk individuals in the Mennonite community and set the stage for more experiments to understand the root cause of PG and the best treatment and management strategies for patients.– *Dr. Michael A. Walter, Dr. Ordan Lehmann, University of Alberta, Edmonton, AB*

Studying the role of Neogenin on TNF-α expression and neurodegeneration

We have developed and published a peptide based approach to promote neuronal survival and regeneration in optic nerve and spinal cord injury models. This study will use a similar approach to reduce inflammation and TNF-α levels, a major factor in the apoptotic death of retinal ganglion cells (RGCs) in glaucoma.

Preliminary data from our lab indicates that blocking RGMa-Neogenin interaction leads to lower TNF-α expression after stimulation of immune cells. Given the critical role of TNF-α in the pathogenesis of glaucoma and RGC death, we hypothesize that RGMa-Neogenin pathway mediates neurodegeneration in glaucoma. In this study, we hope to unravel a new role for Neogenin in regulating microglial secretion of TNF-α and neurodegeneration with the aim of developing novel approaches for the treatment of glaucoma.– *Dr. Nardos Tassew, Dr. Philippe Monnier, Toronto Western Research Institute, Toronto, ON*

Comparing the effectiveness of treatments to prevent scarring after glaucoma surgery

Our study will compare the use of two drugs in conjunction with bleb needling for the rescue of failing blebs. During a trabeculectomy, an opening is made in the wall of the eye so that fluid from the eye can exit and collect in the space created (bleb) which decreases the pressure. Failure of this to adequately decrease eye pressure is most often due to excessive scarring which closes the bleb off.

Treatment usually involves a needling procedure which breaks the scar tissue followed by injection of 5-fluorouracil (5FU) which helps to prevent further scarring.

But 5FU could lead to complications such as a very thin bleb, bleb leak, very low pressure and infections. Another drug (Bevacizumab or Avastin) may also help rescue these scarring blebs. Our study aims to determine whether Avastin is as effective as 5FU in reducing the eye pressure and whether it has less side-effects. *– Dr. Catherine Birt, Dr. Christoph Krannemann, Sunnybrook Health Science Centre, Toronto, ON*

Mapping the outflow pathways from the eye with photoacoustic technology

This study will measure fluid drainage out of the eye via 3 routes: conventional, unconventional and the "uveolymphatic" pathway.

Photoacoustic technology is the next generation in biomedical imaging and combines laser technology with ultrasound technology for deeper tissue penetration and high resolution optics.

Using the first *in vivo* photoacoustic tomography system in Canada, we will evaluate nano-infrared tracers injected into the mouse eye. This unique platform will allow testing of novel glaucoma drugs that aim to lower IOP in order to prevent blindness from glaucoma.– *Dr. Yeni Yucel, Dr. Neeru Gupta, St. Michael's Hospital, Toronto, ON*

Testing the neuroprotective potential of TCAP-1

Currently there are no effective neuroprotective agents for preventing further retinal ganglion cell (RGC) loss once glaucoma has been diagnosed. If such a treatment were available, further neurodegeneration might be halted, preventing complete loss of vision.

Due to their structural and energetic constraints, RGCs are susceptible to hypoxia, oxidative stress, mitochrondrial dysfunction and loss of homeostasis. This is the main cause for the development of glaucoma.

We have identified TCAP-1, a peptide which has the ability to protect cells against these metabolic stressors. Our study will test the neuroprotective potential of this peptide in a model of glaucoma. We hypothesize that TCAP-1 will provide neuroprotection in glaucoma by protecting against metabolic stress through maintaining homeostasis, specifically by enhancing mitochrondrial function and reducing oxidative stress.– *Dr. Joanne E. Nash, Dr. David Lovejoy, University of Toronto, Scarborough, ON*

Determining if tetracyclines reduce the ability of PGAs to lower eye pressure

Many people with glaucoma take medications for other health conditions. Tetracyclines are often prescribed to treat dry eyes or ocular rosacea. There is always a risk that unrelated drugs might interact with each other, altering their efficacy.

Prostaglandin analogues (PGAs) lower IOP in part by activating matrix metalloproteinases (MMPs), a group of proteins, found within the eye. Tetracyclines are known to strongly inhibit MMPs. Our research aims to determine whether tetracyclines reduce the ability of PGAs to lower eye pressure. If so, a patient with glaucoma who was prescribed a tetracycline for their dry eyes might find it more difficult to control their eye pressure.– *Dr. Gdih A. M. Gdih Dr. Raageen Kanjee, Dr. Stephen Brodovsky, Dr. Tenley N. Bower, University of Manitoba, Winnipeg, MB*

Studying neuroprotective strategies in glaucoma

While current therapies for glaucoma involve decreasing IOP, this is not always sufficient to halt progression of the disease. Complementary neuroprotective therapies directly targeting retinal ganglion cells may also be beneficial. Our study will investigate the potential of therapies that target tumor necrosis factor alpha-induced changes in cpAMPAR expression.

We hypothesize that preventing pathologic TNFα levels and resultant increases in cpAMPARs will increase RGC survival in glaucoma. Results from this work will be applicable to understanding mechanisms giving rise to glaucomatous pathology and to identifying novel therapeutics to prevent RGC apoptosis and vision loss.
– Dr. William H. Baldridge, Dr. Melanie E. M. Kelly, Elizabeth Cairns, BSc, PhD Candidate, Dalhousie University, Halifax, NS

Studying self-induced motion in people with glaucoma

Vection, a powerful illusion of self-motion, occurs when large parts of the peripheral field are filled with moving stimuli. The most common experience of vection occurs when people watch a large-screen movie of the view from the cock-pit of a banking airplane. The audience tilts in the opposite direction to the tilting field because they feel themselves to be tilting and try to compen-sate for this feeling of self-motion. This effect is weakened in people with peripheral field loss from glaucoma.

Our project aims to estimate the amount of damage to neurons that make up the optic nerve and correlate that with the strength of the vection response to a large moving visual field.

Because this can be done before there is direct visual loss, we hope to identify patients at risk using the amount of vection as a biomarker. Aggressive treatment begun earlier may lessen the damage that glaucoma produces.– *Dr. Martin J. Steinbach, Toronto Western Research Institute, Toronto, Ontario*