Glaucoma Research Society of Canada

We Support New Ideas

2014 Research Grant Projects

Thanks to Our Donors Researchers Receive $200,000 in Grants

Dr. Graham Trope, founder of the GRSC and chair of its Scientific Advisory Committee, recently announced the Society's 2014 research grants for the following thirteen projects:

Studying self-induced motion in people with glaucoma

A powerful illusion of self-motion, called vection, occurs when large parts of the peripheral field are filled with moving stimuli. The most common experience many people have of vection occurs when they watch a large-screen movie of the view from the cockpit of a banking airplane. The audience tilts in the opposite direction to the tilting field because they feel themselves to be tilting and they try to compensate for this induced feeling of self-motion. In an earlier study, we have shown how this effect is weakened in people with peripheral field loss from glaucoma.

Our current project aims at identifying the amount of damage to the neurons that make up the optic nerve by using modern imaging techniques and meticulous visual field measures. We can estimate the numbers of neurons lost and correlate that with the strength of the vection response to a large moving visual field. This can be done before there is direct visual loss and the hope is that we can 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*

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

RGCs are particularly vulnerable to metabolic and oxidative injury associated with the development of glaucoma. We have recently shown that 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, in association with disregulated expression of its target genes, and glial reactivity. We also have evidence that pharmacologic and genetic methods to increase PGC-1α pathway activity induces protective and detoxifying responses to hypoxic and oxidative stresses cultured cells.

We hypothesize that inducing this pathway will prove efficacious when tested in animal models of RGC damage as well. Our goal is to induce PGC-1α signaling in combination with acute rodent models of metabolic and ischemic optic neuropathy. This work will provide critical pilot data to establish methods to induce this pathway, and generate proof of principle before expanding this strategy to more intensive models of chronic optic neuropathy and glaucoma. *– Dr. Jeremy Sivak, Toronto Western Research Institute, Toronto, Ontario*

Use of paracrine factors secreted by mesenchymal stem cells (MSCs) as a treatment of glaucoma

Our objective is to harness the regenerative effect of factors secreted by MSCs to develop a curative treatment for open angle glaucoma. We hypothesize that this regenerative effect is achieved through the activation and proliferation of endogenous ocular progenitor cells by specific factors which are secreted by MSCs and that the MSCs induce native ocular cells to secrete factors that promote regeneration.

To achieve our goals, we will attempt to identify the paracrine factors responsible for the trabecular meshwork regeneration. This could result in making new molecules clinically accessible to regenerate the TM and lower IOP in glaucoma treatment. *– Dr. Mark R. Lesk, Dr. Denis-Claude Roy, University of Montreal, Montreal, Quebec*

The mechanisms underlying excess matrix deposition in the trabecular meshwork

In glaucoma, excess accumulation of matrix molecules, such as collagen, in the trabecular meshwork reduces the size of the pores, preventing proper drainage of aqueous humor. Reversing the excess deposition could allow normal drainage of aqueous humor and maintain normal pressure in the eye.

Recently, researchers have found that the protein, phosphatase and tensin homolog (PTEN), can control the deposition of matrix molecules. Increasing the amounts of PTEN prevented the excess deposition of collagen by skin cells. But the role of PTEN in the trabecular meshwork in normal or in glaucomatous eyes remains unknown.

We will investigate the function of PTEN in the trabecular meshwork. Because of its ability to prevent excess collagen deposition, PTEN has the potential to be used as a treatment for preventing loss of vision in glaucoma. – *Dr. Sunil Parapuram, University of Western Ontario, Lawson Health Research Institute London, Ontario*

Studying the interaction of trabecular meshwork cells with metal stents for micro-invasive glaucoma surgery

In patients with glaucoma, aqueous humor (AH) accumulates due to a blockage of the trabecular meshwork (TM) and results in elevated pressure. As a novel therapy, the first generation of small metallic stents has started to be used in glaucoma management. This micro-invasive glaucoma surgery (MIGS) is being developed in parallel with other surgical procedures that are looking to increase the safety profile in patient care.

In ophthalmology, these microscopic stents are inserted into the TM to increase drainage of AH by creating a bypass of the dysfunctional tissue. It has been predicted that MIGS may become the first line therapy in glaucoma management due to its potential effectiveness and safety.

Worldwide, fewer than 24 reports have published beyond 6-12 month surgical data. Because devices can be approved without the rigor of Phase I-III trials seen with medications, virtually no reports exist that examine the cellular impact of these metallic foreign bodies on the human trabecular meshwork.

We propose to examine the morphological and functional reaction of human trabecular meshwork cells to candidate surgical metal alloys. Our goal is to provide information that may be of use in the understanding and optimization of how stents may be used in the management of glaucoma. – *Cindy M.L. Hutnik, Kelsey Watson, S. Jeffrey Dixon, Amin Rizkalla, Schulich School of Dentistry and Medicine, University of Western Ontario, London, Ontario*

Investigating diurnal intraocular pressure fluctuation in treated glaucoma patients

Fluctuations in eye pressure can occur over a 24-hour period. One explanation for this is body posture. To date, there are no studies directly comparing the effects of different glaucoma treatments (drops, laser, and surgery) on eye pressure control in the daytime sitting upright versus the nighttime lying position. Our research will compare the control of eye pressure - in the two positions and according to the method of treatment - in patients being treated for glaucoma.

The results of our study may provide insight as to why some patients with reasonably controlled daytime IOP on glaucoma drops still develop progressive glaucoma. The results will also help explain why we recommend surgery or laser, even when eye pressure appears to be reasonably well controlled during patients' clinic visits.

In addition, if our results indicate that laser trabeculoplasty provides a better 24-hour IOP control, this procedure may be advocated as an earlier and preferential treatment modality instead of glaucoma drops thus altering our current standard of care. – *Dr Lesya Shuba, Dr. Paul Artes, Dr. J. Murphy, Dr. M. Nicolela, Dr. Paul Rafuse, Dalhousie University, Halifax, Nova Scotia*

The tele-glaucoma validation (TGV) study

Tele-ophthalmology uses advanced technologies to detect eye disease and deliver eye care without seeing the patient in-person. Our team has been using these technologies to remotely diagnose and manage patients with glaucoma in Northern Alberta and Sub-Saharan Africa.

This tele-glaucoma system has the potential to save time and costs. It is however, critical to prove that the virtual assessment is as accurate in diagnosing glaucoma as an in-person visit.

Our study will compare in-person clinical assessment with a tele-ophthalmology virtual assessment for patients with, or at risk for, glaucoma. Initially, we will assess and diagnose 225 patients for their potential glaucoma status in a clinical setting. Three months later, to make a diagnosis, the same ophthalmologist will review the patients' history, exam, and diagnostic imaging which will have been uploaded through the tele-glaucoma system.
– Dr. Karim Damji, Dr. Chris Rudnisky, Dr. Sourabh Arora, University of Albert, Edmonton, Alberta

Investigating the role of lipid synthesis on RGC regeneration

Glaucoma is a neurodegenerative disease in which retinal ganglion cell (RGC) axons degenerate and eventually die. Over the last few years, researchers have made considerable progress in developing strategies to promote RGC survival. Our study will focus on assessing new strategies that promote reconnection between RGCs and their target cells in the brain.

Our preliminary data suggest that blocking late cholesterol synthesis promotes RGC regeneration and we aim to confirm that hypothesis. Inhibiting cholesterol synthesis with Lovastatin (early cholesterol inhibition) did not have the same pro-regenerative capacity. We believe that the difference between late and early cholesterol inhibition is based on the fact that early cholesterol inhibition abolishes synthesis of metabolites required for prenylation.
– Dr. Philippe Monnier, Dr. Nardos Tassew, Toronto Western Research Institute, Toronto, Ontario

Does VEGF-C stimulate lymphatic outflow from the eye?

Our study aims to determine whether VEGF-C treatment enhances lymphatic drainage of aqueous humour in mice and if that decreases IOP. We will use quantum dot tracers in the mouse eye along with in vivo hyperspectral imaging to determine whether VEGF-C stimulates lymphatic drainage.

This work may provide novel evidence that VEGF-C acts on the lymphatic outflow pathway. This finding would stimulate the development of novel compounds to manipulate the lymphatic outflow pathway, to lower IOP and to prevent blindness from glaucoma.

This research has the potential to shed light on new drugs that may stimulate the lymphatic pathway with the potential to reduce intraocular pressure in the treatment of glaucoma. Scientific interest in studying novel drug classes that specifically target the lymphatic outflow pathway may increase the glaucoma drug class options for patients with glaucoma - a key step toward blindness prevention. *– Dr. Yeni Yücel, Dr. Neeru Gupta, St. Michael's Hospital, Toronto, Ontario*

Using the Markov model to evaluate selective laser trabeculoplasty (SLT)

We will perform an economic review and cost effectiveness analysis of SLT for patients with glaucoma using the Markov model approach. This study will compare the cost and effectiveness of two treatment strategies: medication only and SLT in patients with primary OAG to assess the value of using SLT treatment in hospitals.

The study's results may have a major impact on preserving vision and significantly reducing healthcare costs since clinicians, scientists, health economists, hospital administrators, researchers, and government policy and decision-makers can use the results to make cost-effective decisions.
– Dr. Monali Malvankar and Dr. Cindy Hutnik, University of Western Ontario, London, Ontario

Investigating the role of PEA15 in glial cell activation

Biomechanical strain generated by increased intra-ocular pressure (IOP) is a major risk factor for primary open angle glaucoma (POAG). The mechanisms associating elevated IOP with retinal ganglion cell death are poorly understood, but involve activation of associated glia of the optic nerve head (ONH) and nerve fiber layer (NFL).

This study will characterize the function of the astrocytic phosphoprotein (PEA15) in regulating glial cell responses to biomechanical insult. We hypothesize that the lamina cribrosa is exposed to physiologically significant, IOP-dependent biomechanical strain that causes ONH and NFL glia to transform to reactive phenotypes characterized by specific biomarkers, including PEA15. These reactive glia contribute to ONH remodeling and RGC apoptosis, and hence the development of glaucomatous optic neuropathy. We also hypothesize that PEA15 is involved in mediating the astrocyte stress responses that lead to RGC death and glaucomatous optic neuropathy.

However, availability and quality of human primary tissue for these studies is limited. We have therefore developed a model to rapidly isolate and culture primary NFL and ONH astrocytes from adult rats. We propose to use this model to investigate the molecular mechanisms by which PEA15 regulates glial cell responses to pathologically relevant biomechanical strain. *– Dr. John G. Flanagan, Dr. Jeremy Sivak, Toronto Western Research Institute, Toronto, Ontario*

Studying far peripheral visual fields in patients with glaucoma

Peripheral vision is important for mobility, balance, and driving. However, standard tests examine only the central 30° of the visual field, less than 20% of the entire field of vision. Our study will examine the relationship between central and peripheral visual fields in patients with glaucoma, and establish the performance (retest variability, dynamic range) of a novel peripheral visual field test based on kinetic automated perimetry.

Our hypotheses are that standard central fields do not correlate closely with far peripheral vision, and that automated kinetic perimetry of a single isopter (III1e) provides repeatable data of the peripheral visual field, under both monocular and binocular conditions.

For this study, we will recruit sixty patients with open-angle glaucoma to attend two sessions approximately one week apart. During each session, both eyes will be examined with a novel fully automated kinetic visual field test, under monocular and binocular conditions. Statistical analyses will be performed to investigate the relationship between central and peripheral visual fields, and to quantify the retest variability of the test.*– Dr. Paul H Artes, Dalhousie University, Halifax, Nova Scotia*

Randomized control trial of trabeculectomy versus iStent

To our knowledge, iStent, which is becoming an increasingly popular surgical alternative to antimetabolite trabeculectomy in early-moderate stage glaucoma, has not been directly compared to trabeculectomy in terms of efficacy and safety. Nonetheless, many clinicians and policy makers consider trabeculectomy to be the first line surgical treatment for glaucoma.

Our study will investigate the efficacy and safety of Trabeculectomy with Mitomycin C versus Phaco-iStent X2 for control of intraocular pressure (IOP) in 112 early to moderate stage open angle glaucoma (OAG) patients undergoing cataract surgery. We hypothesize that Phaco-Trab MMC is superior to Phaco-iStent X2 in terms of IOP lowering effect and that Phaco-iStent X2 results in fewer complications than Phaco-Trab MMC.

The results of our study may guide future practice and help to distinguish the type of patients most likely to benefit from either procedure. *– Dr. Michael Dorey, Dr. Sourabh Arora, Dr. Chris Rudnisky, Dr.Karim Damji, University of Alberta, Edmonton, Alberta*