



Glaucoma Research  
Society of Canada

*We Support New Ideas*

# 2012 RESEARCH GRANT PROJECTS

## THANKS TO OUR DONORS RESEARCHERS RECEIVE \$122,000 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 2012 research grants for the following projects:

### **Determining the Biomechanic Response of Optic Nerve Head Glial Cells to Combined Stretch and Compression**

The cells of the lamina cribrosa in glaucomatous eyes experience high levels of compression and stretch as the tissue becomes deformed. We have developed a novel model that allows neural cells from the lamina cribrosa region of human optic nerves to be grown on a flexible surface enabling us to stretch and compress the cells. This causes the cells to respond and become active.

We can harvest the resulting proteins and RNA and analyze them to determine how the cells respond. By understanding their response, we will better understand how the deformation that occurs within the human optic nerve at the earliest stages in the development of glaucoma, may contribute to developing the disease.

– *Kenneth Olsen, PhD Candidate, Dr. John G. Flanagan, Toronto Western Hospital, Toronto, Ontario*

*Kenneth Olsen is a PhD student in the Institute of Medical Sciences at the University of Toronto.*

*Dr. Flanagan holds three research grants from the Canadian Institutes of Health Research.*

### **Studying the Potential Mechanism of Intraocular Pressure Modulation by Selective Laser Trabeculoplasty**

Glaucoma is a common disease resulting in irreversible blindness. In patients with glaucoma the pressure in the eye is too high. This causes damage to the parts of the eye that are important for normal vision. A laser treatment is available that can be used to lower the eye pressure. It is known as selective laser trabeculoplasty (SLT).

Lack of understanding of how this laser works has caused uncertainty as to how it should fit in the individual treatment plans for patients.

We have designed some experiments that can be done safely on the isolated part of the eye involved in pressure control. We will test to see if the laser causes mild stress that is beneficial by causing this part of the eye to produce certain chemicals that lower the pressure. Understanding how SLT works may help ophthalmologists to use this treatment in managing glaucoma.

– *Dr. Cindy Hutnik, Dr. Sunil K. Parapuram, St. Joseph's Health Centre, London, Ontario*

*Dr. Hutnik is Professor, Depts of Ophthalmology & Pathology, University of Western Ontario; Adjunct Professor, Dept of Chemistry & Biochemistry, University of Windsor; Associate Scientist, Centre for Clinical Investigation and Therapeutics, Lawson Health Research Institute, London.*

*Dr. Parapuram received the prestigious Cambridge-Nehru scholarship for his PhD at the University of Cambridge, UK. After moving to Canada in 2008, he was appointed an independent research associate with the department of Ophthalmology at the University of Western Ontario and has recently been promoted as a faculty member.*

## Studying the Use of a Scleral Mounting Device for the Continuous Monitoring of Intraocular Pressure (IOP)

IOP is the leading risk factor for glaucoma. It is measured clinically by depressing the cornea, the clear tissue at the front of the eye. There is great interest in measuring IOP throughout the full diurnal period, including sleep.

The sclera, the white part of the eye, is a fibrous, elastic tissue that extends from the cornea, front of the eye, to the optic nerve. It is the principle load-bearing tissue of the eye, constantly being subjected to IOP and external environmental pressure changes. Unlike the cornea, its stress versus strain capability in terms of elasticity is much higher. In particular, IOP elevations may alter the curvature of the sclera but not that of the cornea.

We have presented an approach to monitoring IOP, allowing for measurements to be taken throughout a 24-hour period with minimal invasiveness by using a strain gauge sensor attached to the sclera. Our goal is to embed the strain gauge in a hydrogel material, such as a contact lens, that can be worn on the conjunctiva overlying the sclera. Yet, we need to further our understanding of the impact that a contact lens material would have on the sclera especially during sleep.

We would like to examine the inflammatory response, if any, at the cellular level in humans when wearing a contact lens overnight on the sclera. By washing out the eye after overnight contact lens wear, the eye wash fluid will then be collected and the cells will be stained with a fluorescent dye showing cells that are only damaged or dead. Since IOP during sleep is an important part of knowing an individual's true IOP, it is beneficial to examine what these responses would be.

These experiments will be a stepping-stone to a device that can be able to measure IOP for the entire day and night, changing the way all forms of glaucoma are identified and managed.

– *Aphrodite Dracopoulos, PhD Candidate, Dr. John G. Flanagan, Toronto Western Hospital, Toronto, Ontario*

*Aphrodite Dracopoulos is a PhD Candidate in the Glaucoma lab at the Toronto Western Hospital, University Health Network in Toronto.*

*Dr. Flanagan holds three research grants from the Canadian Institutes of Health Research.*

## Investigating Mesenchymal Stem Cell Transplantation as a Treatment for Glaucoma

We have recently shown that mesenchymal stem cells help regenerate the cellular components of the eye's drainage system, thereby lowering the intraocular pressure in a rodent model of glaucoma.

The objective of the current study is to understand the mechanism by which these stem cells exert this effect.

Our hypothesis is that the stem cells secrete factors that activate native ocular progenitor cells, leading to regeneration of the eye's drainage system.

We have proposed a series of experiments that will test this hypothesis. This work could lead to a novel treatment for glaucoma.

– *Dr. Mark Lesk, Maisonneuve-Rosemont Hospital Research Centre, Montreal, Quebec*

*Dr. Lesk is a leading Canadian researcher into the effects on glaucoma of blood flow to the eye.*

## Studying the Influence of Retinal Astrocytes on Retinal Ganglion Cell Survival

Glaucoma has remained a challenge to treat due to a complex combination of risk factors, which ultimately damage specialized neurons in the eye, called retinal ganglion cells. This retinal damage is accompanied by a response from local astrocytes, which are important support cells that normally help to maintain neural function. In response to injury or disease, astrocytes ‘activate’ secreting signals and enzymes to influence neuronal survival, coordinate remodeling of retinal tissues, and producing antioxidants.

Astrocyte activation is a prominent early feature during glaucoma pathogenesis. However, the role of this response in the disease process remains unclear.

We have developed and established a system to isolate and activate retinal astrocytes in order to explore their direct influence on the injured retina, and characterize the molecular signals mediating this effect.

Further experiments will manipulate these pathways, with a goal towards introducing new treatment strategies aimed at moderating retinal astrocyte function.

– Dr. Jeremy Sivak, Toronto Western Hospital, Toronto, Ontario

*Dr. Sivak was recently appointed to the Glaucoma Research Chair at the Toronto Western Hospital Research Institute, and is Assistant Professor at the University of Toronto.*

*He received his graduate training at the New England Medical Center/Tufts University in Boston, MA, followed by postdoctoral research at the Wellcome Trust funded Gurdon Institute, at the University of Cambridge, UK.*

## Determining if Prostaglandin Glaucoma Drugs Increase Lymphatic Drainage from the Eye

Glaucoma most often occurs when the eye is unable to clear fluid, leading to a build-up of pressure in the eye and, eventually, degeneration of the optic nerve connecting the eye to the brain.

All current treatment is based on drugs lowering pressure in the eye. Multiple drugs are often needed to control pressure in patients with glaucoma, and one third of the patients on maximum therapy have still uncontrolled pressure. These restrictions are due to limited drug choices and frequent side effects.

In the face of uncontrolled pressure, surgery with potential serious complications is often required. There is a compelling need for new glaucoma drugs with novel targets and minimal side effects.

Our team has recently discovered lymphatic vessels in the eye that pump fluid out of tissues. We are investigating the role of lymphatic drainage in the glaucoma eye, and the study of drug classes that can manipulate the lymphatic drainage to lower pressure in the eye and prevent blindness.

– Dr. Neeru Gupta, Dr. Yeni Yücel, St. Michael’s Hospital, Toronto, Ontario

*Dr. Gupta is Professor, Ophthalmology & Vision Sciences Laboratory Medicine & Pathobiology, University of Toronto; Director, Glaucoma & Nerve Protection Unit, The Keenan Research Centre, Li Ka Shing Knowledge Institute, St. Michael’s Hospital.*

*Dr. Yücel, a neuropathologist, is a leading multidisciplinary researcher into the effects of glaucoma on the brain.*

## Determining if Sirtuin 3 Prevents Cell Death in Glaucoma

Glaucoma is caused by loss of specific cells in the eye, known as retinal ganglion cells and ultimately results in blindness. Currently, there are no therapies that are able to prevent the inevitable progression of retinal ganglion cell loss once glaucoma has been diagnosed. If such an effective therapy were available, loss of vision might be preventable.

While the cause of glaucoma is unknown, increased age is the most commonly associated risk factor. Retinal ganglion cells have higher energy demands than most cells, which makes them particularly reliant on mitochondria – the energy-generating compartments of cells. Since mitochondrial health declines with age, retinal ganglion cells are particularly vulnerable to impaired mitochondrial health, which is thought to be central to glaucoma pathogenesis.

The Sirtuin family is a group of proteins that enhance energetic processes within cells, which results in protective effects within the cells, and leads to enhanced cellular and organismal longevity.

We hypothesize that in a cell model of glaucoma, elevating levels of cellular Sirtuin 3 – the most predominant Sirtuin present in mitochondria – will enhance mitochondrial health, reducing cell death and preventing the progression of glaucoma. These Sirtuin 3 levels will be enhanced using genetic engineering techniques. A successful outcome could potentially result in a cure for glaucoma. – *Dr. Joanne E. Nash, University of Toronto, Scarborough, Ontario*

*Dr. Nash is Associate Professor of Neurobiology at the University of Toronto where she began her independent research career in 2005.*

## The Nova Scotia Discus Study: Evaluating Clinician Performance in Assessing Optic Disc Images

Visual inspection of the optic disc, the site where the optic nerve exits the eye, is one of the most important procedures carried out by eye doctors diagnosing glaucoma. This task is difficult – healthy optic discs come in a large range of sizes and shapes, and early signs of optic disc damage are often quite subtle.

We have developed a freely available computer program (Discus) which eye doctors and trainees can use to self-assess their skills in interpreting photographs of healthy and damaged optic discs.

The Nova Scotia Discus study aims to gather a large dataset from ophthalmologists and optometrists across Nova Scotia to pinpoint specific strengths and weaknesses in optic disc assessment. This will help in the design of glaucoma-related medical education programs. – *Dr. Paul Artes, Dr. Neil O’Leary, Dalhousie University, Halifax, Nova Scotia*

*Dr. Artes trained as an optometrist at the University of Bradford (UK) and the Manchester Royal Eye Hospital. After finishing a PhD, he completed a two year postdoctoral fellow with Balwantray Chauhan at Dalhousie University. Since 2007, he is Associate Professor and Foundation Scholar in Glaucoma Research in the Department of Ophthalmology and Visual Sciences in Halifax.*

*Dr. O’Leary has an MSc. in Modern Methods of Mathematics from the University of Bath, UK and a PhD in Optics and Vision Science from City University London, UK. His current post-doctoral fellowship at the Ophthalmology Department at Dalhousie University has involved devising statistical methods for clinical data analysis and interpreting these for non-technically trained clinicians.*