Glaucoma Research Society *of* Canada

SPECIAL REPORT

2008 RESEARCH GRANTS

THANKS TO OUR DONORS RESEARCHERS RECEIVE MORE THAN $170,000

Dr. Graham Trope, founder of the Glaucoma Research Society and chair of its Scientific Advisory Committee, recently announced the Society's 2008/2009 research grants for the following projects:

- Studying the Function of Lymphatic Channels in the Eye to Improve Fluid Drainage
- Inhaling Carbon Dioxide and Its Effect on Blood Vessels in the Eye
- Comparing the Precision of Two Instruments in Mapping Visual Field Defects in Patients with Advanced Glaucoma
- Studying the Link between Elevated Anticardiolipin Antibodies and Glaucomatous Visual Field Progression
- Conducting a Study to Assess the Validity of Self-reported Glaucoma in Canadians
- Detecting Glaucomatous Optic Nerve Damage by Comparing Rim and Disc Area Asymmetry Ratios
- Studying a Clinical Application for Flicker Defined Form
- Studying the Role of a Peptide in Protecting the Eye from the Outside World
- Using A Molecular Approach to Understand the Cause of Glaucoma
- Studying the Response of Human Optic Nerve Cells to Different Modes of Mechanical Strain
- Studying the Role of Immune Cells in Retinal Cell Survival.

STUDYING THE FUNCTION OF LYMPHATIC CHANNELS IN THE EYE TO IMPROVE FLUID DRAINAGE

Current approaches in treating glaucoma are designed to lower pressure in the eye, either by reducing fluid formation and/or improving fluid drainage out of the eye.

Lymphatic vessels are specialized channels throughout the body that carry body fluids out of tissues. These channels do not exist in the hair or nails, and it is also well accepted that they do not exist in the eye.

However, we have recently identified a rich network of lymphatic channels in the human ciliary body, a structure in the eye involved in helping fluid leave the eye. We will study the mouse eye to understand the function of these specialized channels. If lymphatic vessels help fluid to exit the eye, they could be manipulated to lower eye pressure, and would represent a breakthrough strategy to treat glaucoma and prevent vision loss.

– Dr. Neeru Gupta, Dr. Yeni Yücel, Toronto, ON

INHALING CARBON DIOXIDE AND ITS EFFECT ON BLOOD VESSELS IN THE EYE

Some glaucoma patients have unstable or inadequate blood supply to the nerves at the back of the eye. Non-invasive, laser-based optical instruments are used with various stimuli to assess blood flow in the eye.

One of the ways to assess the response of the retinal blood vessels is by inhaling safe amounts of carbon dioxide. Carbon dioxide normally results in widening the blood vessels, increasing blood flow to the eye.

Our study will determine the effect of inhaling carbon dioxide on blood vessels of patients with glaucoma and of age-matched subjects without glaucoma. Preliminary results suggest that the response of the retinal blood vessels in the two groups is distinctly different.

– Dr. Chris Hudson, Dr. John Flanagan, Waterloo, ON

Comparing the Precision of Two Instruments in Mapping Visual Field Defects in Patients with Advanced Glaucoma

Patients with advanced glaucoma often have constricted visual field. To detect the disease's progression and to preserve the compromised field of vision, we often need to do advanced visual field tests that are accurate, reliable and reproducible. In most cases, if there is confirmed progression, prompt intervention is needed.

Unfortunately, patients with central visual field loss are difficult to assess with standardized static automatic perimetry (SAP) due to inability to maintain stable fixation. Using newer tests – SLO microperimetry (SLO-MP) and Ocular Coherence Tomography (OCT) – helps give an unbiased assessment of the visual field.

Our research compares the precision of the two instruments (SAP and SLO-OCT) in mapping central visual field defects in patients with advanced glaucoma. Our postulation is that SLO-MP is more accurate than SAP in these patients because it is better at maintaining fixation.

We intend to use OCT as a benchmark to confirm if the field loss corresponds to damage to the nerves on the retina. Subsequently, we will study if exact mapping of residual islands of vision can assist in developing appropriate low vision devices to aid in daily living.

– Dr.Sadhana V. Kulkarni, Dr. Karim F. Damji, Dr. Stuart G. Coupland, Ottawa, ON

Studying the Link between Elevated Anticardiolipin Antibodies and Glaucomatous Visual Field Progression

Recent studies have shown an association between the presence of antibodies in circulation and glaucoma. When comparing patients with glaucoma to those without glaucoma, more glaucoma patients tested positive for anticardiolipin antibody in their blood.

Anticardiolipin antibody is found in various diseases. In some people, this antibody is associated with a higher risk of forming certain types of harmful blood clots.

This study will check if glaucoma patients who test positive for anticardiolipin antibody have a higher probability of visual field worsening.

We will be identifying patients who have experienced worsening visual fields and checking their blood for elevated levels of anticardiolipin antibody. If there is an association between elevated anticardiolipin antibody and worsening of glaucoma, it may be possible to better identify patients requiring closer follow-up and more aggressive treatment in the future.

– Dr. Gisele Li, Dr. Ellen Freeman, Dr. Daniel Desjardins, Dr. Mark Lesk, Dr. Paul Harasymowycz, Montreal, QC

Conducting a Study to Assess the Validity of Self-Reported Glaucoma in Canadians

Glaucoma poses a considerable health burden to Canada. Nation-wide phone surveys have provided the only source of data on the prevalence of this major cause of blindness. However, the interpretation of such surveys is suspect due to the uncertainties inherent in self-reported diagnosis.

The primary objective of this study is to obtain data to determine if it is feasible and practical to perform a population-based clinical study to validate self-reported glaucoma in this country.

We will randomly invite a number of people to participate in a phone survey and then invite them to attend a clinical eye examination. We will then compare the results of questionnaire-based phone calls with the results of clinical examination. If the data provides evidence that a full validation study is feasible, we will then consider conducting Canada's first major validation study to determine the usefulness of questionnaires as a basis for the epidemiological study of glaucoma.

– Dr. Yaping Jin, Toronto, ON

Detecting Glaucomatous Optic Nerve Damage by Comparing Rim and Disc Area Asymmetry Ratios

Neuroretinal rim and optic disc asymmetry are an important component in diagnosing and managing glaucoma. Recently, another parameter has been described – Rim Area to Disc Area Asymmetry Ratio (RADAAR). The RADAAR seems to be useful in describing normality with consistency and it correlates significantly with intraocular pressure and the degree of the severity of glaucomatous optic nerve damage in patients with glaucoma.

Our goal is to determine and analyze inter-eye asymmetry of rim and disc areas among subjects classified as *normal*, *glaucoma suspect*, and *glaucoma*. We will use different formulas to calculate RADAAR.

Our hypothesis is that rim area to disc area asymmetry ratio (RADAAR) may be a strong parameter to describe and detect early glaucomatous optic nerve damage. This may be useful for screening and will permit early treatment of glaucoma in asymptomatic patients.
– Dr. Alvine A. Kamdeu Fansi, PhD candidate, Dr. Hélène Boisjoly, Director, Dr. Paul Harasymowycz, Co-Director, Montreal QC

Studying a Clinical Application for Flicker Defined Form

Flicker defined form (FDF) has been shown to be useful for detecting early glaucoma. Preliminary results show test-retest characteristics that are superior to existing perimetry tests. This suggests that the approach may be useful for monitoring disease progression.

Our research aims to:

- continue investigating the mechanisms responsible for the FDF illusion,
- identify the cortical regions responsible for the FDF illusion using functional MRI,
- instigate a prospective clinical trial of FDF perimetry in patients with glaucoma, and
- continue investigating manipulations of FDF stimulus configurations to optimize monitoring of moderate to late stage glaucomatous visual function loss.

– Dr. John G. Flanagan, Waterloo, ON

Studying the Role of a Peptide in Protecting the Eye from the Outside World

The surface of the eye plays a critical role in how we see and how our eyes feel. The clear window in the front of the eye, known as the cornea, is responsible for two thirds of the eye's focusing ability and for keeping noxious elements outside of the eye.

The outermost layer of the cornea is known as the epithelium. Many factors can overwhelm the epithelium to cause it to break down leading to pain, loss of vision, and potentially loss of the eye.

Chemicals in the environment, and even in the eye drops used to treat certain eye conditions, can threaten the epithelium. Chemicals that are generated when the eye is exposed to sunlight, as well as preservatives in eye drops can cause these epithelial cells to become dysfunctional leading to their ultimate death.

Because managing glaucoma with eye drops is still the mainstay of treatment, methods are required that minimize the negative effects of chronic use.

For this reason, we are studying a naturally occurring peptide known as lacritin. Lacritin is mainly secreted by the gland that produces tears. Preliminary studies have shown that its deficiency is associated with ocular surface breakdown. Other studies have shown that it has a protective effect on human corneal epithelial cells and can mitigate some of the negative effects that occur under situations of stress and inflammation.

Demonstrating a protective effect against two common sources of surface stress may be one step closer to potentially developing a new method for protecting the eye from surface insults.
– Dr. Cindy M.L. Hutnik, London, ON

Using A Molecular Approach to Understand the Cause of Glaucoma

Mutations in one of the genes associated with glaucoma has been implicated as a risk factor for glaucoma. This mutation in the protein *optineurin* is associated with cellular pathways that are known to be essential for retinal cell survival.

Our recent research used a new molecular approach to decrease *optineurin* levels in retinal cells. Continued research will determine why retinal cells are dependent on this protein for survival. We will reduce *optineurin* levels in retinal ganglion cells and then measure cell survival under stressful conditions that contribute to cell death in glaucoma.

Revealing the role that *optineurin* plays in retinal ganglion cell survival will lead to a better understanding of the cause of primary open angle glaucoma and new therapies for its treatment.
– Dr. Alexander K. Ball, Hamilton, ON

Studying the Response of Human Optic Nerve Cells to Different Modes of Mechanical Strain

Mechanisms proposed to explain the development of optic nerve damage in glaucoma include the effects of mechanical stress at the level of the lamina cribrosa (LC) and insufficient vascular perfusion of the LC.

We have developed a unique system, using post-mortem human eyes, that allows us to measure IOP-induced changes in optic nerve head (ONH) topography, and to then morphometrically analyze the underlying LC. We have used this system to investigate the biomechanical properties of the ONH using finite element modelling in order to better understand the mechanical environment experienced by astrocytes and nerve fibres at the level of the LC.

The specific aims of our research are focused towards developing models that will improve the understanding of how biomechanical factors affect the initiation and progression of glaucomatous optic neuropathy.
– Dr. John Flanagan , Toronto, ON

Studying The Role of Immune Cells in Retinal Cell Survival

Immune cells in the retina protect retinal cells from infection and disease. In animal models of glaucoma, immune cells become activated when retinal cells are lost and it is widely believed that the immune cells secrete toxic substances that worsen the disease.

Our recent research shows that immune cell activation is an early event in the animal model of glaucoma, and that retinal cell death continues even after the immune cells return to their resting state. We hypothesize that immune cells may become activated in an effort to increase retinal cell survival by removing cellular debris and by secreting survival factors.

Our research will determine if immune cell activation is beneficial, or detrimental, to retinal cell survival in glaucoma. We will use drugs to selectively inhibit or activate immune cells in animal models of glaucoma and measure retinal cell death. Our studies will lead to new glaucoma therapies aimed at controlling the activation of immune cells.
– Dr. Alexander K. Ball, Hamilton ON

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