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# Vision Quest

## Research to Save Sight

### Investing in Eye Research The Return? Saving and restoring vision for us and our loved ones



A Message from  
Dr. Bill Stell,  
Director of Research  
Programs, FFB

Sight-saving research is being conducted by scientists funded by the FFB-Canada. This research is continuing to attract attention around the world for its quality, impact, and strong potential for understanding and

treating inherited retinal causes of blindness.

This is a time of explosive growth in uncovering the genetic and biomedical causes of inherited retinal disease. We are discovering methods for preventing or slowing the progression of blinding eye disease and for restoring vision to those who have already lost their sight. Just in the past year, clinical tests have proven that gene therapy can be safe

and effective – restoring sight by delivering normal genes to the retina, to replace the patient’s non-functioning genes.

**This is a fantastic time to be supporting research. Canada is a world leader in this enterprise, largely thanks to your generous funding of research through the Foundation Fighting Blindness (FFB).**

We understand that many people are going through difficult economic times. This makes us especially grateful for your ongoing financial support. The global economic downturn has affected the eye research community and the FFB in particular, making it difficult to raise funds.

But we can’t afford not to invest in new research projects that lead to new sight-saving discoveries! **We need to fuel the research momentum, not slow it down.** People around us, people we know and love, are continuing to lose their sight to retinitis pigmentosa (RP),

Usher syndrome, Leber congenital amaurosis, macular degeneration, and other devastating retinal conditions. Your continued financial support gives them the hope and promise of receiving the gift of sight.

Beginning July 1, 2009, the FFB has committed funds to five exciting new research projects, led by world-class Canadian researchers. This year, the FFB also partnered in funding two major research partnerships with the Canadian Institutes of Health Research, to test genetic and stem cell therapies for various retinal diseases. These involve teams of researchers at universities and hospitals across Canada, with some collaborators in the U.S.

**Please consider giving a NEW gift today to say ‘Yes, I’m committed to NEW research, NEW discoveries.**

Your donation makes all the difference to patients and their families, to our researchers who are making important discoveries despite funding challenges, and to the world of medical discovery!

As you read about the remarkable research advances highlighted in this newsletter, you should feel proud of our accomplishments and optimistic about the outlook for treatments and cures. We hope that this will persuade you to reaffirm your commitment today to advance world-class vision research through the FFB.

These projects have undergone critical review by the FFB’s Scientific Advisory Board (SAB), made up of some of North America’s top retinal experts. These SAB scientists volunteer their time and expertise to ensure that only the very best and most promising projects are recommended for funding.

You should support these outstanding new research projects because retinal research is an excellent investment. The return on this investment is in saving and restoring vision, for us and our loved ones. Enclosed is a donation card and return stamped envelope for your convenience.

## **We can’t do it without you!**

The FFB needs your support in fulfilling its ongoing commitments.

In total, current commitments to 30 research projects over the next two years total \$2.4 million.

For a complete listing of research commitments and summaries, please visit: [www.ffb.ca](http://www.ffb.ca), Research.

**Please also sign-up for e-news at [www.ffb.ca](http://www.ffb.ca).**

## Read about the research you funded!

On March 4, 2009, Forbes.com, MSN Health.com, CanWest and more than 30 media outlets in North America, reported on a new gene discovery, involving our FFB funded researcher, Dr. Robert Koenekoop. Read the news excerpt below.

**Forbes.com** **Retinal Gene is Linked to Childhood Blindness:**  
**Discovery might someday yield therapies to restore sight, experts suggest.**

THURSDAY, March 5 (Health Day News) -- A gene that plays a major role in two forms of childhood blindness has been identified by an international team of researchers. The discovery of the link between the retinal gene SPATA7 and Leber congenital amaurosis (LCA) and retinitis pigmentosa is important because it pinpoints a new retinal metabolic disease pathway that might be crucial for many patients, according to the researchers. The finding could help lead to gene-based treatments, they say. The study was published March 5 in *The American Journal of Human Genetics*.

"This is a very important step that opens up a number of new research avenues, particularly in our understanding of the specific cellular

processes involved in blindness," said Dr. Robert Koenekoop, director of pediatric ophthalmology and the McGill Ocular Genetics Laboratory at the Montreal Children's Hospital of McGill University Health Centre. "This finding also increases the number of potential therapeutic targets and, therefore, the chances of finding a treatment."

Sharon Colle, President & CEO of The Foundation, said "this is an incredible discovery that gives great hope to patients and their families, that gene based therapies can and will be developed to restore sight." The Foundation funded the research.

**Kylie and her little sister, Livya, who has LCA, will benefit from the research you support.**



**The girls' grandparents support research through Ride for Sight ([www.rideforsight.com](http://www.rideforsight.com)), the FFB's signature motorcycle fundraiser.**

## New Gene Discovery for Retinitis Pigmentosa

Funded in part by the FFB, Dr. Koenekoop, in collaboration with a team of Dutch researchers, discovered a new gene, RP25, for retinitis pigmentosa (RP). It is thought to be a major cause of autosomal recessive RP. The gene was discovered with a new method for gene identification, called single nucleotide polymorphism (SNP) micro-array genotyping, developed with funding from the FFB. This finding was published in the *American Journal of Human Genetics* (Nov. 2008).

## Protein to Protein Interaction Explains Vision Loss in Genetic Diseases

An international consortium of researchers, including FFB-funded researcher Dr. Koenekoop, explained why vision loss varies in people with a host of disorders associated with defective cilia within the cells. They also developed a blueprint for unraveling similar variations of disease severity among people with other genetic conditions. Every new discovery concerning genes and proteins related to cilia (minute, hair-like sensory structures) has implications for understanding and treating Usher syndrome, LCA, RP, and related conditions. Published in *Nature Genetics* (May 2009).

## Age-Related Macular Degeneration and Brain Aging Breakthrough

**Reported by 25 news journals worldwide, including CBC News Radio and Radio-Canada TV.**

Dr. Gilbert Bernier and his research team at the Maisonneuve-Rosemont Hospital have taken a giant step in the fight against diseases related to brain aging. They identified a gene that controls the normal and pathological aging of neurons in the central nervous system. This knowledge could one day help scientists slow the aging of the brain and prevent diseases, such as age-related macular degeneration (AMD), Alzheimer's disease, and Parkinson's disease. The finding was funded in part by the Foundation Fighting Blindness, and was published in the prestigious *Journal of Neuroscience* on January 14, 2009.

By working with a genetically engineered strain of mice, Dr. Bernier and his team have identified a mutation (genetic variation) that dramatically accelerates the process of aging in the brain and the eye. This study revealed that neurons in the retina and cerebral cortex require a gene called *Bmi1* to prevent the accumulation of free radicals, which are widely believed to play a role in AMD.

“Since aging is a major risk factor in

AMD, understanding the aging process of the eye is important for understanding the disease,” explains Dr. Bernier. “Overall, we have now established that *Bmi1* controls cellular aging through its role in regulating free radical concentrations.”

Although many researchers have tried to better understand the genetics and pathophysiology (disease process) of these age-related diseases, few studies have focused on the basic molecular mechanisms that control neuronal aging. Thus, this work in Dr. Bernier’s lab is truly ground-breaking.

## Identifying Modifier Genes Uncovers Clues about Vision Loss and Potential Treatments

Researchers have been working for several decades to understand why people with the same disease and underlying genetic mutation can have dramatic differences in the rate of progression and extent of vision loss. While experts speculate that light exposure and diet may play a role in this variation, they have also been looking for additional genes — modifier genes — that may affect the magnitude and time course of vision loss.

Dr. Robert Koenekoop (McGill University) and his colleagues identified the gene RPGRIP1L as

having a significant modifying impact on vision in people with syndromes and diseases caused by RPGR, including individuals affected with a form of Leber congenital amaurosis.

Finding modifier genes such as RPGRIP1L not only helps retinal scientists to understand better the cause of variations in vision loss for some diseases; it also gives them promising targets for designing new, vision-saving treatments.

## Chemical Signaling Research Provides Critical Information for Stem Cell Treatments

The development of stem cell therapies to treat retinal diseases requires scientists to understand how to create retinal cells from stem cells. FFB researcher, Dr. Valerie Wallace, of the Ottawa Health Research Institute, has learned how the gene *Shh* regulates the activation of two other genes *Gli2* and *Hes1* in the development of retinal cells. This new knowledge about chemical signaling among these three genes, will help researchers to understand better, how to coax stem cells to become mature cells such as rods and cones, to replace lost retinal photoreceptors.

This knowledge may also enable scientists to create sight-saving drugs that mimic this chemical-signaling process.

## Retinal Degeneration in Zebrafish and Fruit Flies Gives Targets for Treatments in Humans

Dr. Ulrich Tepass, of the University of Toronto, has found that mutations in *crumbs* and *prominin* genes in fruit flies can lead to photoreceptor degeneration. (Photoreceptors are the cells in the retina that enable us to see. They convert images into signals that are sent back to the brain.)

Dr. Tepass has also learned that mutations in *yurt* and *crumbs* genes can lead to retinal degeneration in zebrafish.

Because the genes that control eye development and function in flies and fish are very similar to those in mammals, this knowledge helps investigators to identify genes that might cause retinal disorders (such as RP) in humans, as well as to discover potential targets for therapies to prevent or cure those disorders.

## Usher 2 Genetic Link Found in Canadians of French Origin

Usher syndrome is a leading cause of deaf-blindness in Canadians and people around the world. There are three main types of Ushers, with type 1 and type 2 being characterized by congenital hearing loss.

While the genetic basis of Usher syndrome type 1 in French Canadians has been known, the genetic cause of Usher syndrome type 2 in this population has been hard to uncover.

Dr. Robert Koenekoop (McGill University) and his colleagues were recently able to identify the genetic basis of Usher syndrome type 2 in French-Canadian families from Quebec and New Brunswick.

These findings will help doctors diagnose Usher syndrome in more children of French-Canadian descent born with congenital hearing loss. Also, with earlier diagnosis, families can better prepare for the onset of their children's vision loss, and potentially take advantage of future clinical trials of new treatments for Usher syndrome type 2.

Molly has retinitis pigmentosa (RP).



"One of the biggest challenges with vision loss, unlike cancer or heart disease, is that it's difficult to find people to fund research," said Molly's dad, Peter.

"On the day Molly was diagnosed, doctors were convinced that within her lifetime they'd find a cure."

Your support gives her and her family hope for a cure.

# New Grants Approved for Funding!

## Partnerships with Canadian Institutes of Health Research

### 1. Eye Stem Cells: Biology and Therapeutic Applications

Funded in part by Sun Life Insurance

Primary Investigator:

Dr. Valerie Wallace, Ottawa Health Research Institute.

Collaborators: Dr. Per Fagerholm, Linköping University, Sweden; Dr. May Griffith, Ottawa Health Research Institute, University of Ottawa; Dr. Bernard Hurley, Ottawa Hospital; Dr. Derek van der Kooy, University of Toronto; Dr. Carol Schuurmans, University of Calgary; Dr. Vincent Tropepe, University of Toronto.

Granted: \$2.4 million over 5 years, January 2009 - December 2013

Stem cell therapies have the potential to benefit more than one million Canadians affected by degenerative eye diseases, such as retinitis pigmentosa, age-related macular degeneration and corneal diseases; all of which cause blindness. By replacing cells that have been lost through disease or injury, stem cell therapies could potentially benefit anyone, at any stage of eye disease. Together this research team hopes to

develop better methods for controlling the kinds of cells that can be derived from stem cells, so that they can coax the stem cells into producing different kinds of eye tissues, such as retina and cornea. This is currently the greatest challenge to developing effective stem cell therapies. The team will also develop more efficient transplantation methods that help new eye cells integrate with existing tissue to restore lost vision. A further goal is to combine cells, genes, biomaterials and pharmaceuticals in a way to create an improved artificial cornea.

### 2. Novel Gene Therapy Approaches for the Treatment of Retinal Degenerative Diseases

Primary Investigator: Dr. Robert Molday, University of British Columbia

Collaborators: Dr. Jim Hu, University of Toronto; Dr. Bill Hauswirth, University of Florida; Dr. Robert Koenekoop, McGill University; Dr. Marinko Sarunic, Simon Fraser University.

Granted: \$3 million over 5 years, January 2009 - December 2013

The application of gene therapy for retinal degenerative diseases will be investigated in Stargardt disease, cone-rod dystrophy, Leber congenital amaurosis, and retinitis pigmentosa. The strategy is to replace the defective gene with a new “healthy” gene in specific animal models for

retinal degenerative diseases, with the aim of slowing photoreceptor loss and partially restoring vision. Success in these animal models would lead to future human clinical trials. Recent successes in clinical trials of gene therapy for the RPE65 form of LCA have opened the door to using gene therapy to treat a variety of inherited human retinal disorders.

## Operating Grants

### **Dr. Gautam Awatramani**

Dalhousie University

*Probing and Repairing Circuits During Retinal Degeneration*

Granted: \$90,000

July 2009 - June 2010

Dr. Awatramani will test restorative biological strategies for restoring vision in people already blind from retinal degeneration. His focus is on probing and repairing retinal circuits that have been compromised as a result of photoreceptor degeneration. He was part of a team that partially restored vision in animals that were otherwise completely blind from inherited retinal degeneration (Lagali et al., 2008). This breakthrough revealed the therapeutic potential of reprogramming surviving, non-photoreceptive retinal neurons to be light-responsive.

The outcomes of the research will give researchers a better understanding of the bipolar cells

(neurons that relay signals from rods and cones across the retina) and what is the most effective way to make them respond to visual images.

### **Dr. Michel Cayouette**

Institut de recherches cliniques de Montréal

*Specification of Temporal Identity in Retinal Progenitor Cells*

Granted: \$80,000

July 2009 - June 2010

The investigators will work towards a better understanding of *Ikaros*, a newly discovered gene expressed in early retinal progenitor cells. Understanding why the *Ikaros* gene is critical for generating early-born neurons, especially photoreceptors, may assist researchers in developing more effective ways to produce new rod and cone photoreceptors for therapeutic replacement to restore eyesight.

### **Dr. Catherine Tsifidis**

Ottawa Health Research Institutes

*XIAP Gene Therapy for the Treatment of Retinal Degeneration*

Granted: \$80,000

July 2009 - June 2010

Mutant genes cause degeneration by triggering the death of retinal cells (apoptosis). Making the retinal cells less susceptible to this process may be an effective way to treat many different types of retinal degeneration, regardless of the underlying genetic

basis and pathology. The goal here is to conclude the preclinical studies and thus position XIAP therapy for clinical (human) trials.

**Dr. Gilbert Bernier**

Maisonneuve Rosemont Hospital  
*Stem Cell Transplantation for the Treatment of Retinal Degenerative Disease*

Granted: \$50,000  
July 2009 - June 2010

In retinitis pigmentosa and age-related macular degeneration, replacing lost photoreceptors is one potential way to stop disease progression and restore visual function. Human embryonic stem cells (hES cells) can be expanded (multiplied) and manipulated in the lab to produce specific cell types, such as photoreceptors. Recent work revealed developing photoreceptors from newborn mice could functionally integrate into the retinas of adult mice. The goal here is to differentiate hES cells into photoreceptors in the test tube and test their therapeutic potential in animal models with retinal degeneration.

**Dr. Robert Koenekoop**

McGill University  
*Identifying Novel Leber Congenital Amaurosis Genes Using Novel Strategies*

Granted: \$50,000  
July 2009 - June 2010

This project will identify new genes and mutations responsible for Leber congenital amaurosis (LCA).

To identify new LCA-causing genes, Dr. Koenekoop will explore genes that encode proteins known to interact with *lebercilin*, the gene that is mutated in LCA type 5 (LCA5), as well as other genes (and related proteins) involved in the development and maintenance of the photoreceptors' ciliary backbones. Discoveries of new genes and understanding the effects of related mutations will enable researchers to develop therapies that are more efficiently targeted and more effective for these specific types of LCA.

**Your Support Makes a Difference!**

We hope that after reading this newsletter you will feel proud that your support is helping make vision research history! Treatments and cures really are in sight.

**Please reaffirm your commitment, TODAY, to advance world-class retinal research. Your gift today will say, 'Yes, I'm committed to NEW research, NEW discoveries, NEW ways to prevent blindness and restore sight'.**

Please return the enclosed donation card by mail, donate online at [www.ffb.ca](http://www.ffb.ca), or call 1-800-461-3331.

# Vision<sup>2009</sup> Quest

## Vision Quest Conferences – Register Today!

Our Foundation is committed to public education about vision research and the fight against blindness.

Each year, we bring patients, their families and friends together with some of North America's top retinal researchers to learn about the latest discoveries in retinal research and patient resources you won't hear anywhere else.

Due to popular demand, this year we are expanding the conference to three cities:

- Toronto - Sat. October 3 - Ryerson University
- Vancouver - Sat. October 24 - TELUS Auditorium
- Edmonton - Sat. November 7 - University of Alberta

Please visit [www.ffb.ca](http://www.ffb.ca), Vision Quest, for complete program, details and for simple and fast online registration. **Please act now, because seating is limited.**

No Internet access? Please call 1-800-461-3331 to register.



## ***Topics to be discussed at this year's conference, include:***

### **1) Who are You Seeing? The Right Eye Care Right Now**

When living with a degenerative eye disease, it's important to make sure you are seeing the right eye care specialists to get the best possible support and information you deserve. This talk explains who you should be seeing and why. As well, it will give guidelines on what ongoing care and referrals are available to you (i.e. genetic testing, counseling, low vision specialists, research trials).

### **2) Nutrition and Retinal Degeneration**

The media and the internet are inundated with reports on nutrition to prevent, slow down and treat various retinal degenerations. While nutritional therapies could benefit some patients, it could also harm others. This talk will separate fact from fiction, in terms of what nutritional therapies will benefit whom.

### **3) The Latest Discoveries in Retinal Research**

Discoveries in retinal research are happening each year, all around the world. This talk will give the latest update on: 1) gene therapy - LCA Phase II results; 2) pharmaceutical therapy (neurotrophic agents) – RP Phase II results; 3) stem cell research outlook; and 4) electronic prosthetic (artificial retina) trial results.

**Come out and enjoy a great discussion, ask the experts questions and network with others! For more information, please visit [www.ffb.ca](http://www.ffb.ca) or call 1-800-461-3331.**



# THANK YOU FOR YOUR SUPPORT!

Vision Quest is published by the Foundation Fighting Blindness to inform readers of research directed to finding the causes, treatments and cure of retinitis pigmentosa, macular and related retinal diseases, as well as providing Foundation News.

To contact the Foundation call 1-800-461-3331 or email: [info@ffb.ca](mailto:info@ffb.ca).

Share your comments about FFB's Vision Quest Newsletter.  
Write to FFB, Attn: Vision Quest Newsletter, or email: [info@ffb.ca](mailto:info@ffb.ca).

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