Annual RESEARCH Report

DALHOUSIE UNIVERSITY 2016
A message from the Department Head and Chief

I would like to congratulate our research teams for a very successful year in research for our Department. For a small department, where the majority of members are busy clinicians, our research productivity and ability to attract research funding are very impressive.

It gives me particular pleasure to witness the calibre of research being conducted by our trainees, from undergraduate, graduate to post-graduate levels. We are certainly fulfilling one of our main mandates, which is to train the future researchers who will advance our specialty.

Finally, I would like to welcome Dr. Jayme Vianna, the newest member of our research group, joining our faculty as the QEII Foundation Scholar in Glaucoma Research. Dr. Vianna completed his medical and ophthalmological training at the Sao Paulo University in Brazil, before joining our glaucoma research group for a post-doctoral fellowship. We are very pleased to welcome Dr. Vianna to our department.

A message from the Research Director

We are very proud to present the Annual Research Report for 2016. The Department of Ophthalmology and Visual Sciences has a rich tradition in departmental and collaborative research within various faculties and departments at Dalhousie. Our national and international collaborations are resulting in research output of the highest calibre.

There are numerous achievements we can be proud of. In the current difficult funding climate, I am pleased to say that a department of our size is punching well above its weight. Specific highlights are two new awards from the Canadian Institutes of Health Research and one from the Atlantic Innovation Fund on orphan drug development. Our annual research funding for new and ongoing projects is an impressive $4.6 million. Our research productivity is equally impressive with a total of 64 publications for the year.

I invite you to explore our achievements in the various research areas, those of our trainees and the facts and figures for this year. I want to thank Leah Wood, our research manager for compiling this document. Do not hesitate to contact me with any questions, queries or comments (contact information is on the back page). Our objective as always is to improve.
Glaucoma

Glaucoma is a common eye disease causing irreversible visual loss. We are at the forefront of measuring progressive changes in glaucoma and developing clinically valuable visual field testing and imaging tools to allow ophthalmologists to provide the best care by tracking the disease accurately. We develop and assess new diagnostic tools and therapeutic interventions.

We strive to advance our current knowledge in the following areas:

- root causes
- associated risk factors
- imaging techniques
- disease progression
- non-surgical treatments
- surgical treatments

Pediatric Ophthalmology

Pediatric ophthalmology encompasses a variety of ocular problems ranging from infections of the external eye to serious diseases that can affect ocular structures. Our researchers, and projects, span the range from basic science to clinical research so that we can take the information we learn about the fundamentals of vision function and apply it to providing better care to children at the Izaak Walton Killam Health Centre and around the world.

The Pediatric Vision Science Research Group (PVSRG) collectively has expertise in:

- genetic disorders affecting vision
- cutting edge diagnostic techniques to detect deficiencies in vision function
- the treatment of common pediatric vision problems like amblyopia (lazy eye) and exploring the ways vision is interpreted by the brain to guide movement.
Research Strengths

Retina and Optic Nerve

Research on the basic processes of the retina in health and disease are vital for understanding and treating significant sight-threatening eye diseases. The primary aim of the Retina and Optic Nerve Research Laboratory is to investigate the function of the retina to aid in the discovery of the physiological, pharmacological and anatomical properties of synaptic circuits and receptive fields in the retina. These discoveries also lead to the identification of therapeutic strategies that could reduce, eliminate or slow damage to retinal neurons in diseases such as glaucoma caused by pathological synaptic and ion channel activity.

Clinical Retina

Retinal degenerative diseases such as diabetic retinopathy and age-related macular degeneration are leading causes of blindness. Our clinical retina research team is involved in world-leading clinical trials that aim to develop new treatment approaches that have the potential to halt the disease process and possibly stop vision loss or restore vision. Our researchers use unique and powerful imaging tools such as optical coherence tomography to track the success of novel treatments.

Oculogenetics

Our oculogenetics team is working to characterize genetic eye diseases in Maritime families and to identify the genes that cause these diseases. They are using this information to test new treatments for hereditary blinding conditions and associated, nonhereditary eye diseases. By making these kinds of discoveries, we will develop new treatments, and offer appropriate counseling and new detection methods.
Awards and Accolades

Finding a Cure for Familial Exudative Vitreoretinopathy (FEVR)

Dr. Johane Robitaille in collaboration with Dr. Chris McMaster and her research team were awarded a $2.75 million award from the Atlantic Canada Opportunities Agency, part of a $4.5 million investment to enable the development of drugs for orphan genetic diseases. Dr. Robitaille and her team discovered a gene causing Familial Exudative Vitreoretinopathy (FEVR) in 2002. Using this information, the researchers believe that they have discovered a drug that will hopefully be a cure for FEVR. Their current research focus is to test the toxicity and efficacy of a drug to combat FEVR, and then move it into clinical use.

Dr. R. Evatt and Rita Mathers Trainee Awards in Ophthalmology and Visual Sciences

Lianne Esmore and Richard (Ross) Porter were the recipients of the 2016 Dr. Evatt and Rita Mathers Trainee Awards in Ophthalmology and Visual Sciences.

Lianne, under the supervision of Dr. Francois Tremblay, is investigating the mechanism responsible for long-term retinal toxicity caused by vigabatrin, a very potent antiepileptic drug using Multi-Electrode Array technology.

Ross and his supervisor Dr. Melanie Kelly are aiming to identify non-steroidal pharmacological targets to treat ocular inflammation. An emerging target is the endocannabinoid system, specifically the cannabinoid 2 receptor (CB2) which has been shown to be anti-inflammatory in a number of experimental models of disease including ocular inflammation. His research will identify the cell targets (i.e neutrophils, monocytes, endothelium) and associated signalling pathways responsible for CB2-mediated anti-inflammatory actions in the eye.
Awards and Accolades

Awards

**Dr. Francois Tremblay:** Dr. Ruth Goldbloom, IWK Auxiliary Award - IWK Health Centre

**Dr. Darrell Lewis:** Global Health Photography Contest, First Prize - Dalhousie University

**Dr. Mark Seamone:** Award for Excellence in Ophthalmic Research - Canadian Ophthalmological Society

**Dr. Jayme Vianna:** Annual Translational Science Research Award for Best Paper Published in 2015 for Translational Research in Glaucoma - Canadian Glaucoma Society

**Dr. Anuradha Mishra:** Royal College Professional Development Grant - Royal College of Physicians and Surgeons of Canada

Ist Place Dalhousie University Global Health Photography Contest - Pediatric Shy-Eye Exam Photo taken in Accra Ghana in 2010 by Darrell Lewis.
Resident Research

Resident Research Project Fund Recipients

Dr. Darrell Lewis, PGY5 was a recipient of a Dalhousie Department of Ophthalmology and Visual Sciences Resident Research Project Grant for his research project titled: “UV-A Cross-Linking of Cryopreserved Donor Corneas”. Darryl’s research examines whether UV-A corneal cross-linking confers resistance to keratolysis (corneal enzymatic degradation) in fresh donor corneas.

Dr. Mark Seamone, PGY4 received a Dalhousie Department of Ophthalmology and Visual Sciences Resident Research Project Grant for his research project titled: “Anti-VEGF Therapy Reduces Ocular Inflammation in Peptidoglycan and Endotoxin-Induced Uveitis”. Mark’s research sets out to determine if targeted VEGF-A blockade with intravitreal Bevacizumab (Avastin®) decreases leukocyte-endothelial interactions in Endotoxin-induced uveitis (EIU) and Peptidoglycan-induced uveitis (PIU) as measured by intravital microscopy in BALB/c mice and if the administration of intravitreal Bevacizumab (Avastin®) decreases pro-inflammatory cytokine expression induced by EIU and PIU in eyes of BALB/c mice.

Resident Research Projects

<table>
<thead>
<tr>
<th>Name</th>
<th>Year</th>
<th>Supervisor</th>
<th>Project Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Darrell Lewis</td>
<td>PGY 5</td>
<td>Dr. Christopher Seamone</td>
<td>UV-A cross-linking of cryopreserved donor corneas</td>
</tr>
<tr>
<td>Dr. Mark Seamone</td>
<td>PGY 4</td>
<td>Dr. Alan Cruess</td>
<td>Intravitreal anti-VEGF therapy reduces ocular inflammation in peptidoglycan and endotoxin induced uveits</td>
</tr>
<tr>
<td>Dr. Amr Zaki</td>
<td>PGY 4</td>
<td>Dr. Rishi Gupta</td>
<td>Assessment of anxiety and pain associated with intravitreal injections</td>
</tr>
<tr>
<td>Dr. Claire Hamilton</td>
<td>PGY 4</td>
<td>Dr. Lesya Shuba</td>
<td>Comparison of outcomes of trabeculectomy with subconjunctival injection of mitomycin C versus topical application with cellulose sponge</td>
</tr>
<tr>
<td>Dr. William Best</td>
<td>PGY 3</td>
<td>Dr. Daniel Belliveau</td>
<td>Dalhousie medicine undergraduate ophthalmology education: Targeted needs assessment</td>
</tr>
<tr>
<td>Dr. Aaron Winter</td>
<td>PGY 3</td>
<td>Dr. Alon Friedman</td>
<td>Traumatic brain injury and retinal vascular pathology</td>
</tr>
<tr>
<td>Dr. Wesley Chan</td>
<td>PGY 2</td>
<td>Dr. Jai Shankar</td>
<td>Transverse venous sinusous stenosis on magnetic resonance imaging in patients with idiopathic intracranial hypertension– A pilot study</td>
</tr>
<tr>
<td>Dr. Harald Gerde</td>
<td>PGY 2</td>
<td>Dr. Johane Robitaille &amp; Dr. Jason Bergman</td>
<td>The utility of a FZD4 knockdown zebrafish model for an efficacious drug screen</td>
</tr>
<tr>
<td>Dr. Tom Zhao</td>
<td>PGY 2</td>
<td>Dr. Steve Barnes &amp; Dr. Francois Tremblay</td>
<td>DENAQ photoswitch as a chemical visual prosthesis in a model of acquired retinal degeneration</td>
</tr>
</tbody>
</table>
### Glaucoma Research Society of Canada Research Grant

**Dr. Jayme Vianna**, a Glaucoma Research Fellow in the Department of Ophthalmology and Visual Sciences, was a 2016 recipient of a Glaucoma Research Society of Canada Research Grant for his research project entitled “Changes in Lamina cribrosa Depth as an Early Marker of Glaucoma Progression”. Dr. Vianna’s research uses Optical Coherence Tomography and newly developed software to analyze changes in the lamina cribrosa depth. His study aims to test if changes in the lamina cribrosa depth can be detected earlier in glaucoma progression than other previously known markers of glaucoma damage such as retinal nerve fiber layer and Bruch’s membrane opening-minimal rim width.

### Trainee Research Projects

<table>
<thead>
<tr>
<th>Name</th>
<th>Program</th>
<th>Supervisor</th>
<th>Project Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stephanie Blandford</td>
<td>MSc Medical Neuroscience</td>
<td>Dr. William Baldridge &amp; Dr. Spring Farrell</td>
<td>Retinal characterization of the THY1-GCAMP3 mouse after optic nerve transection</td>
</tr>
<tr>
<td>Philip Bobbie-Ansah</td>
<td>MSc Clinical Vision Science</td>
<td>Prof. Emeritus Donald Mitchell &amp; Dr. Kevin Duffy</td>
<td>Is the rapid visual recovery in the amblyopic eye of kittens following a short period of darkness guided by vision in the non-deprived eye?</td>
</tr>
<tr>
<td>Elizabeth Cairns</td>
<td>PhD Pharmacology</td>
<td>Dr. Melanie Kelly &amp; Dr. William Baldridge</td>
<td>Neuroprotective therapies for glaucoma</td>
</tr>
<tr>
<td>Dr. Vishva Danthurebandara</td>
<td>Research Fellow</td>
<td>Dr. Balwantray Chauhan</td>
<td>Cost-effectiveness analysis of following patients with glaucoma</td>
</tr>
<tr>
<td>Lianne Ophel Esmores</td>
<td>MSc Clinical Vision Sciences</td>
<td>Dr. Francois Tremblay</td>
<td>Short- vs long-term changes in retinal activity induced by vigabatrin, a potent anti-epileptic drug.</td>
</tr>
<tr>
<td>Tenille Fleischhaker</td>
<td>MSc Clinical Vision Science</td>
<td>Dr. Johane Robitaille &amp; Dr. Jason Bergman</td>
<td>Utilizing zebrafish to characterize a novel childhood blinding disorder familial exudative vitreoretinopathy (FEVR) gene and test novel therapeutics</td>
</tr>
<tr>
<td>Heather Gerrie</td>
<td>BSc Neuroscience</td>
<td>Dr. Steven Barnes</td>
<td>Restoration of damaged retinal visual responsivity with an optochemical channel activator</td>
</tr>
<tr>
<td>John Gobran</td>
<td>BSc Pharmacy</td>
<td>Dr. Balwantray Chauhan &amp; Dr. Spring Farrell</td>
<td>Effects of 3D Stratification of Retinal Ganglion Cells in Sholl Analysis</td>
</tr>
<tr>
<td>Delaney Henderson</td>
<td>BSc Medical Sciences</td>
<td>Dr. Balwantray Chauhan &amp; Dr. Spring Farrell</td>
<td>Characterizing longitudinal in vivo changes of RGC dendrites after retinal injury</td>
</tr>
<tr>
<td>Annie Li</td>
<td>BSc Medical Sciences</td>
<td>Dr. Steven Barnes</td>
<td>Calcium influx in retinal ganglion cells mediated by calcium-permeable AMPA receptors</td>
</tr>
<tr>
<td>Skye McIntosh</td>
<td>BSc Neuroscience</td>
<td>Dr. William Baldridge</td>
<td>Retinomotor movements in flat fish</td>
</tr>
<tr>
<td>Syed Mohammad</td>
<td>BSc Medicine</td>
<td>Dr. Balwantray Chauhan &amp; Dr. Spring Farrell</td>
<td>In vivo labelling and imaging of retinal ganglion cells</td>
</tr>
<tr>
<td>Dr. Michael Hung Ngo</td>
<td>Postdoctoral Fellow Pharmacology and Visual Sciences</td>
<td>Dr. Johane Robitaille</td>
<td>Familiale exudative vitreoretinopathy</td>
</tr>
<tr>
<td>Andrea Nuschke</td>
<td>PhD Physiology and Biophysics</td>
<td>Dr. Balwantray Chauhan</td>
<td>Spatiotemporal assessment of axonal transport and cytoskeletal structure in retinal ganglion cells following acute elevated intraocular pressure in the rat</td>
</tr>
</tbody>
</table>

Department of Ophthalmology and Visual Sciences

Annual Research Report 2016
### Trainee Research Projects (continued)

<table>
<thead>
<tr>
<th>Name</th>
<th>Program</th>
<th>Supervisor</th>
<th>Project Title</th>
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<tbody>
<tr>
<td>Ross Porter</td>
<td>MSc Pharmacology</td>
<td>Dr. Melanie Kelly</td>
<td>Cannabinoid 2 receptor signalling during ocular inflammation</td>
</tr>
<tr>
<td>Benjamin J. Smith</td>
<td>PhD. Biological Sciences</td>
<td>Dr. Francois Tremblay</td>
<td>Implication of voltage-gated sodium channels in inner retina processing</td>
</tr>
<tr>
<td>Corey Smith</td>
<td>PhD Physiology and Biophysics</td>
<td>Dr. Balwantray Chauhan</td>
<td>In vivo labeling and imaging of retinal ganglion cells</td>
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<tr>
<td>Jin Soo Andy Song</td>
<td>MedII Student, Queen’s University</td>
<td>Dr. Marcelo Nicolela</td>
<td>Efficacy of selective laser trabeculoplasty versus argon laser trabeculoplasty in patients with pseudoexfoliative glaucoma</td>
</tr>
<tr>
<td>Justine Sy</td>
<td>MSc Clinical Vision Sciences</td>
<td>Dr. Balwantray Chauhan &amp; Dr. Spring Farrell</td>
<td>Retinal ganglion cell counting: Comparing sampling vs entire retina</td>
</tr>
<tr>
<td>Dinesh Thapa</td>
<td>MSc Pharmacology</td>
<td>Dr. Melanie Kelly</td>
<td>Cannabinoid therapeutics for ocular pain and inflammation</td>
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<tr>
<td>Sophie Thapa</td>
<td>MSc. Anatomy and Neurobiology</td>
<td>Dr. William Baldridge</td>
<td>The role of tyrosinase in the time course of light-induced cone movements in the goldfish retina</td>
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<tr>
<td>Dr. J. Thomas Toguri</td>
<td>Postdoctoral Fellow Pharmacology</td>
<td>Dr. Melanie Kelly &amp; Dr. Eileen Denovan-Wright</td>
<td>Cannabinoid receptor modulation for the treatment of ocular pain and inflammation</td>
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<tr>
<td>Dr. Lucas Torres</td>
<td>Glaucoma Research Fellow</td>
<td>Dr. Balwantray Chauhan</td>
<td>Non-retinal nerve fibre layers within the optic nerve head neuroretinal rim</td>
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<tr>
<td>Dr. Jayme Vianna</td>
<td>Glaucoma Research Fellow</td>
<td>Dr. Balwantray Chauhan</td>
<td>Serial changes in lamina cribrosa depth and neuroretinal parameters in glaucoma. Impact of choroidal thickness</td>
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<tr>
<td>Tareq Yousef</td>
<td>MSc Medical Neuroscience</td>
<td>Dr. William Baldridge</td>
<td>Dopaminergic signalling and ipRGCs</td>
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<tr>
<td>Adel Zrein</td>
<td>MSc Pharmacology</td>
<td>Dr. Melanie Kelly</td>
<td>Endothelin receptor heterodimerization inhibit β-arrestin function</td>
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</table>

Dalhousie University Clinical Vision Science students.
On April 18, 2016, faculty and trainees attended the 27th Annual Department of Ophthalmology and Visual Sciences Research Day, a full-day symposium at the Lord Nelson Hotel & Suites. This event showcased the current basic science and clinical research that is being carried out in our department and beyond, and how it will impact eye care in our patient population.

The keynote speaker, Dr. Douglas Jabs, from The Mount Sinai Hospital, provided expert commentary and compelling presentations titled “Systemic Treatment of Uveitides” and “Approach to the Diagnosis of the Uveitides”.

Congratulations to the 2016 Research Day Award winners:

Resident Category

1st Prize: Dr. Mark Seamone “VEGF-A is increased in exogenous endophthalmitis: A potential target for immunomodulation”

2nd Prize: Dr. Darrell Lewis “Resistance to enzymatic dissolution of donor corneas cross-linked under variable UV-A fluence”

Non-Resident Category

1st Prize: Dr. Vishva Danthurebandara “Cost-effective analysis of following patients with glaucoma”

2nd Prize: Corey Smith “Fluorescence labeling of retinal ganglion cells with adeno-associated viral vectors for longitudinal imaging”
The Dalhousie University Department of Ophthalmology and Visual Sciences hosted the 7th Biennial Form & Function in Ocular Disease Symposium on October 28-29, 2016. This multi-disciplinary clinical and basic science symposium featured local and guest faculty who are world-class leaders in diverse areas of ophthalmology and vision research ranging from vision restoration in retinal disease to ocular surface health. This year’s guest faculty included:

Jose-Alain Sahel, M.D., UPMC-Sorbonne Universités  
*Vision restoration in retinal degenerations*

Steven Pflugfelder, M.D., Baylor College of Medicine  
*Conjunctival goblet cell - the least recognized but most important cell for ocular surface health*

Peter Tse, Ph.D., Dartmouth College  
*Where visual illusions come from*

Johane Robitaille, M.D., Dalhousie University  
*Genomics enhanced therapeutics for familial exudative vitreoretinopathy*

Emily Chew, M.D., National Eye Institute  
*Nutrition and age-related macular degeneration: You are what you eat!*

Claude Burgoyne, M.D., Devers Eye Institute  
*Why optic nerve head aging is our only normal tension glaucoma model*

Kwoon Wong, Ph.D., University of Michigan  
*Intrinsically photosensitive retinal ganglion cells and their relevance to health*

Michael Wall, M.D., University of Iowa  
*What have we learned from the Idiopathic Intracranial Hypertension Treatment Trial*

Congratulations to the 2016 trainee award winners:

Corey Smith, M.E.Sc., Dalhousie University  
*Quantitative analysis of fluorescently labelled RGCs in living retina*

Vasiliki Tellios, B.Sc., Western University  
*Nitric oxide, administered using novel copper-chitosan derivatives, accelerates corneal epithelial wound healing*

Delaney Henderson, Dalhousie University  
*The effects of IOP elevation on the structure of Thy-1 YFP retinal ganglion cells*

Alex Baldwin, Ph.D., McGill University  
*Using short-term patching to shift ocular dominance*
Facts and Figures

2016 Publications

<table>
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<tr>
<th>Peer Reviewed Articles</th>
<th>Book Chapters</th>
<th>Abstracts</th>
<th>Total</th>
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<tbody>
<tr>
<td>25</td>
<td>6</td>
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Number of peer-reviewed manuscripts, book chapters, and abstracts published in 2016.

Invited presentations by Department members: 37
Peer reviewed manuscripts published: 25
Peer reviewed abstracts published: 33

2016 Invited Presentations

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<th>International</th>
<th>National</th>
<th>Total</th>
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<tr>
<td>19</td>
<td>18</td>
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Number of international and national invited presentations by department members in 2016.
Peer Reviewed Journal Publications


Books and Chapters


Facts and Figures

2016 Grants and Contracts

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<tr>
<th>Number</th>
<th>Grant New</th>
<th>Contract</th>
<th>Grant Ongoing</th>
<th>Contract</th>
<th>Grant Total</th>
<th>Contract Total</th>
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<td>6</td>
<td>2</td>
<td>19</td>
<td>12</td>
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</table>

Number of newly acquired and continuing research grants and contracts in 2016. All research projects in which a

1.5 million in new and ongoing research contracts

3.1 million in ongoing and new research grants

4.6 million in research funding

2016 Research Funding

<table>
<thead>
<tr>
<th>Amount</th>
<th>Grants</th>
<th>Contracts</th>
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<tbody>
<tr>
<td>$3,150,034</td>
<td>$1,484,103</td>
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The value of research funding including revenue from all awards generating funds in that year (for multi-year awards, the revenue is reported the year it is budgeted).
Research Grants and Contracts

*Note: The amounts listed are the total value of the award whereby annual departmental amounts are provided in the figures.

New Research Grants and Contracts


Robitaille JM, Berman J (2016-2017). Familial exudative vitreoretinopathy zebrafish model development for gene discovery and therapeutics development - Canadian Rare Diseases Models and Mechanisms (RDMM) Network - $25,000

Shuba LM, Nicolela MT (2016-present). A prospective, double-masked, randomized, multi-center, active-controlled, parallel-group, 3-month study assessing the safety and ocular hypotensive efficacy of PG324 ophthalmic solution 0.02% and latanoprost ophthalmic solution 0.005% in subjects with elevated intraocular pressure - Aerie Pharmaceuticals Inc. - $118,475.


Continuing Research Grants and Contracts


Dickinson J, Cruess A, Gupta RR (2015 - 2017). Open-label phase-4 study to examine the change of vision-related quality of life in subjects with diabetic macular edema (DME) during treatment with intravitreal injections of 2 mg Aflibercept according to EU label for the first year of treatment (AQUA) - Bayer - $257,072.


Nicolela MT (2014 - present). A double-masked, randomized, multicentre, active-controlled, parallel, 12 month study assessing the safety of AR-13324 Ophthalmic Solution, 0.2% q.d. and b.i.d. compared to Timolol Maleate Ophthalmic Solution, 0.5% b.i.d. in patients with elevated intraocular pressure - Aerie Pharmaceuticals Inc. - $152,140.

Nicolela MT (2015 - present). Additive effect of twice-daily brinzolamide 1% /Brimonidine 0.2% fixed dose combination as adjunctive therapy to a prostaglandin analogue - Alcon Research Ltd. - $50,900.

Nicolela MT (2015 - present). The efficacy and safety of Bimatoprost SR in patients with open-angle glaucoma or ocular hypertension - Allergan Inc. - $404,862 (USD).

Robitaille JM, Berman J (2015 - 2016). Familial exudative vitreoretinopathy zebrafish model development for gene discovery and therapeutics development - Canadian Rare Diseases Models and Mechanisms Network - $25,000.


