École D'ÉTÉ 2022 SUMMER school

RESTAURATION DE LA VISION

VISION RESTORATION

RÉSEAU DE RECHERCHE EN SANTÉ DE LA VISION

VISION HEALTH RESEARCH NETWORK

Réseau thématique soutenu par le

Fonds de recherche Santé Québec

25 au 28 juillet 2022
July 25 to 28 2022

Le Baluchon – Éco-villégiature
3550 Chemin des Trembles
Saint-Paulin, Québec
J0K 3G0

Programme / *Program*

Site internet : https://reseauvision.ca/ecole-dete/ecole-dete-2022/
Web site: https://visionnetwork.ca/ecole-dete/ecole-dete-2022/

Le RRSV est soutenu par le Fonds de recherche du Québec – Santé (FRQS) et la Fondation Antoine-Turmel. /
The VHRN is supported by the Fonds de recherche du Québec – Santé (FRQS) and la Fondation Antoine Turmel

Table des matières / *Summary*

MOT DE BIENVENUE

C'est avec un immense plaisir que nous vous accueillons à la première **École d'été sur la restauration de la vision** parrainée par le Réseau de recherche en santé de la vision (RRSV). Nous sommes particulièrement heureux que la situation du Covid-19 ait évolué pour nous permettre de tenir une réunion en personne, ce qui, selon nous, est essentiel pour favoriser le meilleur environnement interactif pour l'apprentissage et les échanges scientifiques productifs. Notre objectif est de réunir des étudiants diplômés et des stagiaires postdoctoraux de divers horizons, des chercheurs et des cliniciens scientifiques établis dans le domaine de la vision, des partenaires patients et des dirigeants d'organisations à but non lucratif afin de créer un environnement immersif, dynamique et collégial.

L'**École d'été 2022** se concentre sur la recherche de pointe dans tous les aspects de la restauration de la vision. Le programme comprend des conférences complètes, chacune donnée par un scientifique de renommée mondiale dans son domaine respectif, des séances d'affichage et des exposés éclair présentés par des étudiants. Les conférences couvrent un large éventail de sujets, notamment la restauration de la cornée humaine, la biologie et la régénération de la rétine, le glaucome et le dysfonctionnement neurovasculaire, la thérapie rétinienne optogénétique, les modifications cérébrales associés à la perte de vision, les avancées translationnelles dans le domaine de la myopie et les stratégies de réadaptation.

Cette école n'aurait pas été possible sans les généreux soutiens du RRSV et du Département d'ophtalmologie de l'Université de Montréal qui ont rendu cette initiative possible. Merci !

Notre objectif ultime avec cette **École d'été** est de fournir aux étudiants un environnement invitant et stimulant pour apprendre les dernières avancées en matière de recherche sur la vision, et de présenter une plateforme d'échange ouverte et stimulante qui favorisera des collaborations fructueuses entre les participants.

Nous vous souhaitons une **École d'été 2022** productive et agréable!

Adriana Di Polo, PhD

Stuart Trenholm, PhD

WELCOME REMARKS

It is with tremendous pleasure that we welcome you to the first **Vision Restoration Summer School** sponsored by the Vision Health Research Network (VHRN). We are particularly pleased that the Covid-19 situation has evolved to allow us to hold an in-person meeting, which we believe is essential to foster the best interactive environment for learning and productive scientific exchange. Our goal is to bring together graduate students and postdoctoral fellows from diverse backgrounds, established vision researchers and clinician scientists, patient partners, and non-profit organization leaders to provide an immersive, high energy, and collegial environment.

The **2022 Summer School** focuses on cutting edge research in all aspects of vision restoration. The program features comprehensive lectures, each given by a world-class scientist in their respective field, poster sessions, and lightning talks by students. The lectures cover a wide range of topics including human cornea restoration, retinal biology and regeneration, glaucoma and neurovascular dysfunction, optogenetic retinal therapy, brain changes associated with vision loss, translational advances in myopia, and strategies for rehabilitation.

This school would not have been possible without the generous support from the VHRN and our institutional sponsor, Department of Ophthalmology, University of Montreal, who have made this initiative possible. Thank you!

Our ultimate goal with this summer school is to provide students with an inviting and nurturing environment to learn about the latest advances in vision research, and to present a platform for open and stimulating exchange that will foster successful collaborations among participants.

We wish you a productive and enjoyable **Summer School 2022**!

Adriana Di Polo, PhD

Stuart Trenholm, PhD

COMITÉ ORGANISATEUR / *ORGANIZING COMMITTEE*

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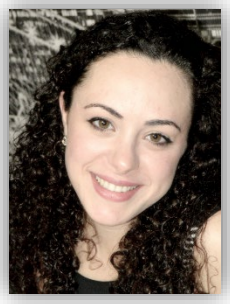

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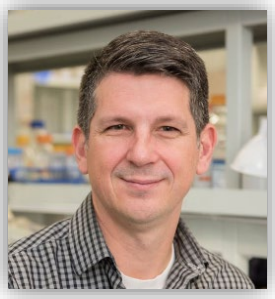

Michel Cayouette, PhD
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Montreal, Quebec, Canada

Conférenciers / Speakers

May Griffith, PhD

Tuesday, July 26th 2022 – 8:45 – 9:45 AM

Biography

Canada Research Chair in Biomaterials and Stem Cells in Ophthalmology, Caroline Durand Foundation Research Chair in Cellular Therapy of the Eye and Director of the Cornea and Anterior Segment Axis of the Quebec Vision Health Research Network. To combat severe world shortage of donor corneas for transplantation, MG and her international team developed the world's first biosynthetic corneal implants that regenerated human corneal tissue and nerves as an alternative to donor tissues. More recently, her LiQD Cornea that is applied as a liquid but gels within corneal tissue defects is aimed at promoting corneal regeneration without the need for transplantation, targeting the unmet medical needs of millions of corneal blind patients particularly in developing regions of the world.

Title: ***Restoring function to the human cornea: bench to bedside and back***

Abstract: The most common treatment for corneal blindness is corneal transplantation, which involves replacing the damaged or diseased cornea with a donor cornea. While this treatment has been proven effective, due to a severe worldwide shortage of donor corneas, an estimated 12.7 million patients are still awaiting treatment. Only one out of 70 patients is being treated, necessitating an alternative to human donor corneal transplantation. In order to bring a therapy from concept to clinical application, many factors must be considered. At the outset, the regulatory pathway is an important consideration. Different bioengineered corneas or corneal implants will have separate pathways according to whether they contain cells or are cell-free and any drugs or bioactives that confer pharmacologic properties. Hence, clinical use must factor into the project's start, right from the design of the biomaterials. For a medical device such as a cell-free, pro-regeneration corneal implant, right from the development of new biomaterials, the design must consider patient safety and the desired time to clinical application. Manufacturing methods, e.g., moulding versus additive manufacturing, should also be considered, as the ultimate goal is scale-up. Here, the development of a biosynthetic cornea from bench to bedside will be discussed. In addition, changes in the design to adapt to the needs of different groups of patients are considered. Finally, the change from a solid implant to a liquid formulation, the LiQD Cornea, designed for allowing clinical application in outpatient clinics instead of operating theaters to maximize practicality for use, particularly in low to middle-income countries and under austere conditions, will be discussed.

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Conférenciers / Speakers

Adriana Di Polo, PhD

Tuesday, July 26th 2022 – 9:45 – 10:35 AM

Biography

Dr. Di Polo is a Professor in the Departments of Neuroscience and Ophthalmology at the University of Montreal (Quebec, Canada) and currently holds a Canada Research Chair in glaucoma and age-related neurodegeneration. She completed her Bachelor of Science in biology from the Universidad Central de Venezuela (Caracas, Venezuela) and her PhD in physiology from the University of California (Los Angeles, USA; Supervisor: Dr. Deborah Farber). Dr. Di Polo then pursued postdoctoral training at the Center for Research in Neuroscience at McGill University (Quebec, Canada; Supervisor: Dr. Albert Aguayo). Dr. Di Polo's research program focuses on understanding mechanisms of neuronal, glial, and vascular deficits in glaucoma. The ultimate goal of her laboratory is to develop regenerative therapies to restore retinal ganglion cell function and, ultimately, vision in patients affected by glaucoma. She has received continuous research funding throughout her career and is presently Principal Investigator on grants from the Canadian Institutes of Health Research, National Institutes of Health, Department of Defense USA, and other competitive grants and awards from non-profit organizations as well as industry. Dr. Di Polo serves on numerous national and international committees. She is the current Director of the Retina and Posterior Segment Group of the Quebec Vision Health Research Network and will serve as the Canadian Association for Neuroscience (CAN) President in 2023-2024. She is an ARVO Gold Fellow since 2015. Recent accomplishments include the 2019 Shaffer Prize from the Glaucoma Research Foundation and the Lewis Rudin Glaucoma Research Prize awarded in 2020.

Title: ***The neurovascular unit: a new therapeutic target for glaucoma***

Abstract: Glaucoma is the leading cause of irreversible blindness worldwide, affecting 80 million people globally in 2020. There is no cure for glaucoma and current therapies rely solely on controlling high intraocular pressure, the major risk factor for developing the disease, albeit with limited success. A crucial element in the pathophysiology of glaucoma is the gradual loss of retinal ganglion cells (RGC), neurons with long projecting axons that form the optic nerve and establish terminals in the brain. Despite decades of clinical and basic research, we still do not understand the factors that cause or contribute to retinal neuron death and loss of vision in glaucoma patients. The vascular theory of glaucoma proposes that insufficient blood flow contributes to RGC neurodegeneration. Glaucoma patients suffer from vascular deficits that include decreased blood flow in the retina and optic nerve, reduced vessel caliber, and capillary defects. The current lack of understanding of the mechanisms leading to neurovascular deficits in glaucoma is a major knowledge gap in the field. Retinal pericytes regulate microcirculatory blood flow and coordinate neurovascular coupling through inter-pericyte tunneling nanotubes (IP-TNTs). Our laboratory demonstrated that pericytes constrict capillaries in a calcium-dependent manner during glaucomatous stress, decreasing blood supply and compromising neuronal function. Moreover, we showed that ocular hypertension damaged IP-TNTs and impaired light-evoked neurovascular responses. The reestablishment of calcium homeostasis in pericytes restored vascular and neuronal function and prevented retinal ganglion cell death in glaucomatous eyes. Our study provides important insights into the therapeutic potential of pericytes to counter vascular dysregulation in glaucoma.

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Conférenciers / Speakers

Isabelle Hardy, MD, FRCSC

Tuesday, July 26th 2022 – 10:35 – 10:45

Biography

Cumulating 28 years as an ophthalmologist specialized in oculoplastic, Dr. Hardy graduated from the University of Montreal, where she had completed her medical school studies and her residency in ophthalmology, which was followed by 2 years of specialized training in oculoplastic and orbital surgery at McGill University and at the Fondation Ophtalmologique Adolphe de Rothschild in Paris, France.

Upon her return to the University Montreal, Dr. Hardy actively participates in the development and the promotion of the oculoplastic division. Under her leadership, the University of Montreal has trained more than 19 international fellows in oculoplastic and the surgical team has grown from 3 to more than 10 internationally renowned surgeon-professors.

As Chief of the Ophthalmology Department at the Maisonneuve-Rosemont Hospital (HMR), Dr. Hardy gathers teams of professionals to achieve numerous projects. Among them, the designation of the Ophthalmology Department at HMR as a University Center for Ophthalmology (CUO-HMR) by the Quebec Ministry of Health and Social Services in 2016 is a great example.

As Department Chair, Dr. Hardy demonstrates great support in the development of research and to the researchers. Her contribution by a judicious administration of philanthropic funds allows the creation of a diseased cornea bank as well as a vitreous and intraocular fluid bank, the development of a program in artificial intelligence and collaborative research with NASA through the Canadian Space Agency. She also establishes a postdoctoral fellowship grant program and more recently, she orchestrates the creation of a new departmental research Chair of 3,5 million of dollars.

Dr. Hardy is as well involved in different research projects and has a particular interest for dysthyroid orbitopathy. Since 2015, she joined a team of investigator at University of British Columbia in an international multicenter randomized controlled trial for treating patients with early progressive thyroid orbitopathy. Greatly appreciated by students, residents and fellows for her passionate and dynamic teaching, Dr. Hardy cumulates until now, more than thirty publications and numerous presentations at local, national and international scientific events.

Title: ***La fondation Dre Suzanne Véronneau-Troutman – a pioneer in many ways***

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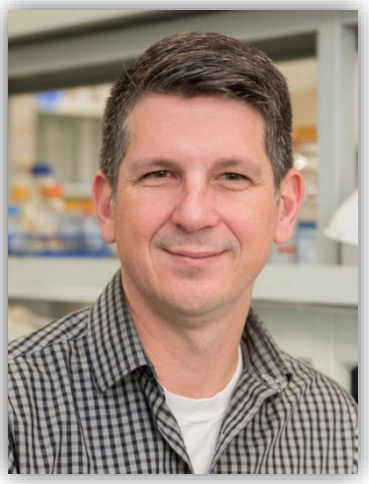
Conférenciers / Speakers

Michel Cayouette, PhD

Tuesday, July 26th 2022 – 11:15 AM – 12:15 PM

Biography



Michel Cayouette (Ph.D.) is Director of the Cellular Neurobiology Research Unit and Vice- President, Research and Academic Affairs at the Montreal Clinical Research Institute (IRCM). He is also a Full Research Professor in the Department of Medicine at Université de Montréal, and Adjunct Professor in the Department of Anatomy and Cell Biology at McGill University. He is Director of the FRQS Vision Health Research Network, a provincial initiative dedicated to promoting research capacity and international visibility for more than 100 vision scientists in Quebec by funding collaborative projects and various infrastructures. He is also Chair of the Scientific Advisory Board of Fighting Blindness Canada. His research focuses on the cellular and molecular mechanisms regulating neural development and regeneration.

Title: ***Regenerating the retina via cell reprogramming***

Abstract: Retinal dystrophies are incurable diseases caused by the degeneration of light-sensing rod and cone photoreceptor cells. While cell transplantation to replace lost photoreceptors has received much attention in recent years, it remains unclear whether the transplanted cells can actually integrate the retinal circuitry. One alternative to circumvent the need for transplant is to use a resident cell population as a potential source of stem cells. Müller glia, which are the main glial cell type of the retina, were shown to function as a source of stem cells in adult lower vertebrates, but it remains unknown whether mammalian Müller glia can generate clinically-relevant cone photoreceptor cells. Interestingly, the transcriptome of Müller glia is very similar to that of late-stage retinal progenitors, suggesting that the retinal glial cells might have retained some neurogenic capacity. In this lecture, I will discuss recent work providing proof of concept that this is indeed the case. More specifically, I will talk about a small-scale screen carried out in our lab to identify factor(s) that might promote cone photoreceptor production by Müller glia. We used the Cre/loxP system to specifically express 25 different combinations of transcription factors into adult mouse Müller glia and used genetic lineage tracing to identify potential progeny. Of the different factors tested, we identified one combination sufficient to reprogram adult Müller glia into cone-like and bipolar-like cells. This work provides proof of concept that adult retinal glia could potentially be used as an endogenous source of retinal stem cells for retinal regeneration.

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Conférenciers / Speakers

Darlene Dartt, PhD

Tuesday, July 26th 2022 – 2:00 – 3:00 PM

Biography

Dr. Dartt was also a Professor II (non-voting) at the University of Oslo School of Dentistry. Dr. Dartt received her A.B. degree from Barnard College of Columbia University in New York City and her Ph.D. from the Department of Physiology at the University of Pennsylvania. She joined the Schepens Eye Research Institute in 1985. Her primary research interests are the signaling pathways used by neurotransmitters in the lacrimal gland and conjunctival goblet cells to induce secretion and proliferation and how dysregulation of these pathways can lead to dry eye syndromes in mouse models and humans. Currently her lab is investigating the effect of allergic inflammation and its resolution on conjunctival goblet cell secretion and the effect of bacterial infection on goblet cell function. She has been continuously funded by NIH since 1980 for her work. Dr. Dartt directed the Institute's Department of Defense Research Program and chaired six Military Vision Research Symposia. She chaired the ARVO Cornea Program Planning Committee. She is a Vice-President for the International Society for Contact Lens Research. She chaired the 2016 Cornea, Biology and Pathobiology, Gordon Research Conference. She served on the NIH Study Section Diseases and Pathology of the Visual System (DPVS). Dr. Dartt Has additionally trained about fifty students and postdoctoral fellows.

Title: ***Ocular surface nerves: structure, function, and protection of Vision***

Abstract: The front of the eye is in contact with the environment and needs to respond to its changes to protect itself and the remainder of the eye to ensure clear vision. The changes include thermal, chemical, mechanical, infectious, and evaporative. The front of the eye has multiple structures, tissues and fluids that are protective and include the lids, tear film, lacrimal gland, Meibomian gland, cornea, and conjunctiva. Together this system is known as the lacrimal gland functional unit. This system is regulated by a complex neural reflex and well as hormones and growth factors. The presentation today will focus on the neural regulation of the lacrimal gland functional unit to produce tears and protect vision. The afferent part of the complex neural pathway is the sensory nerves in the cornea and conjunctiva. These nerves travel to the trigeminal ganglion, trigeminal nucleus and other central areas of the brain that encode secretion and pain. The efferent part of the pathway are the sympathetic and parasympathetic nerves that travel through the superior cervical and pterygopalatine ganglia, respectively, to the tissues that produce tears. These tissues include the Meibomian gland (lipid layer) and lacrimal gland and conjunctiva (electrolyte and water layer and mucous layer). The elements of this complex neural pathway will be discussed in detail.

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Conférenciers / Speakers

Krystel Huxlin, PhD

Tuesday, July 26th 2022 – 5:30 – 6:30 PM

Biography

Dr. Krystel Huxlin is the James V. Aquavella Professor and Associate Chair for Research in the Department of Ophthalmology and Flaum Eye Institute at the University of Rochester. She also serves as the Associate Director of the Center for Visual Science and co-Director of its Training program. She holds secondary appointments in the Institute of Optics, the Departments of Neuroscience and Brain & Cognitive Sciences at the University of Rochester. Dr. Huxlin earned her bachelor's (1991) and doctorate (1994) degrees in Neuroscience at the University of Sydney, Australia, before joining the Ophthalmology faculty at the University of Rochester (1999). Her work seeks to understand how visual functions can be restored after damage to the adult visual system. She holds 9 patents and divides her attention between developing perceptual training strategies to induce vision restoration in stroke patients, and manipulating molecular substrates of corneal wound healing to prevent and treat scarring, and to restore optical quality following insults to the ocular surface. She is also part of the team that developed LIRIC, a novel, non-surgical paradigm for laser refractive error correction. She was the inaugural President of the Rochester SFN Chapter, is a reviewing editor for eLife and was just elected to the Board of Directors of VSS.

Title: ***A vision for the future: How to recruit neural plasticity for sight restoration after stroke***

Abstract: In humans, damage to the primary visual cortex (V1) causes a large loss of vision referred to as cortically-induced blindness (CB). Currently, this affects up to half a million new cases per year in the US from stroke alone, with rates rising worldwide. A major barrier these patients encounter is that in contrast with early-onset physical therapies prescribed to rehabilitate motor cortex damage, there are no accepted vision restoration therapies for CB. Over the last 15 years, the assumption that damaged, adult visual systems cannot recover functionally has been challenged by research in both humans and animal models. Human studies, which have been largely restricted to chronic CB patients whose deficits are deemed stable and permanent, point to one method consistently able to recover vision after V1 damage: visual training to detect or discriminate stimuli in the blind field. Our group was responsible for key developments in this approach, leading to mechanistic insights, but also uncovering key barriers to implementation. Among them is the fact that recovery in chronic CB requires months of daily training and the vision restored is low-contrast, coarse and restricted to the blind field perimeter, limiting its usefulness in everyday life. Evidence suggests that some of these limitations may arise because some chronic patients lose neurons that contribute to vision fundamentals not only in V1, but also – through trans-synaptic, retrograde degeneration - in the thalamus and retina. In contrast, there is little evidence of such degeneration in subacute CB patients (<3 months post-stroke). Moreover, when trained, subacute patients recover the same discrimination abilities as chronic patients, but do so 6 times faster, and with recovery extending deeper into their blind field. These data form a strong premise for refocusing investigative efforts on the substantial differences in plastic potential between subacute and chronic stroke-affected visual systems, and on defining how they can best be exploited to maximize visual restoration in CB.

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Conférenciers / Speakers

Arjun Krishnaswamy, PhD

Wednesday, July 27th 2022 – 8:30 – 9:30 AM

Biography

I joined the Department of Physiology at McGill University in 2017 after finsihing a postdoctoral fellowship at Harvard University under the supervision of Dr. Joshua Sanes. My laboratory has two research themes: 1) to understand the molecular mechanisms that establish specific wiring patterns among neurons; and 2) to understand how specific wiring patterns endow circuits with computational abilities. We study this phenomenon by observing the assembly and function of neural circuits the retina and the retinorecipient visual thalamus (LGN). Our goal is draw links among wiring genes, wiring patterns, and circuit function and leverage these links to develop a better understanding of how circuits miswire in disease conditions, such as blindness, and potentially, develop interventions that could restore normal function.

Title: ***The assembly and function of motion-selective retinal circuits***

Abstract : Nearly 50 different mouse retinal ganglion cell (RGC) types sample the visual scene for distinct features. RGC feature selectivity arises from their synapses with a specific subset of amacrine (AC) and bipolar cell (BC) types, but how RGC dendrites arborize and collect input from these specific subsets remains poorly understood. In this talk, I will present our current work on this phenomenon which employs two-photon imaging and optogenetics, electrophysiology, and type-specific genetic labelling. We have discovered that recognition molecules from the immunoglobulin (IgSF) and Cadherin (Cdh) superfamilies play distinct roles in specifying RGC connections with ACs and BCs, which suggests members of these two families could act as an adhesive blueprint for retinal circuit connectivity.

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Conférenciers / Speakers

SPEAKER – Stuart Trenholm, PhD

Wednesday, July 27th 2022 – 9:30 – 10:30 AM

Biography

Dr. Trenholm is an Assistant Professor at the Montreal Neurological Institute where his lab examines the neuronal circuitry underlying visual perception, the changes that occur in the brain following vision loss and vision rehabilitation strategies.

Title: ***Effects of vision loss on the brain's internal compass***

Abstract: Vision plays an important role in instructing the brain's spatial navigation systems. Still, little is known about how vision loss affects the neuronal encoding of spatial information. Here, recording from head direction (HD) cells in the anterior dorsal nucleus of the thalamus in mice, we examine HD tuning in blind animals compared to sighted animals placed in darkness.

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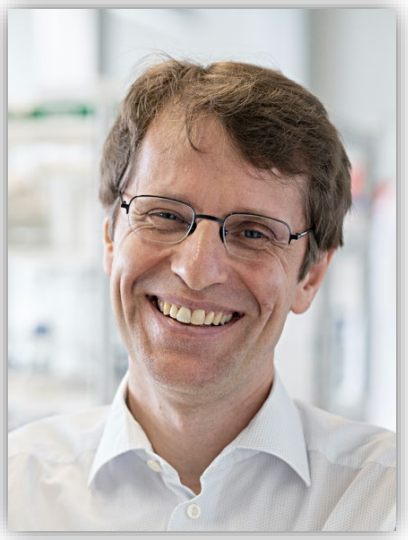
Conférenciers / Speakers

Botond Roska, MD, PhD

Wednesday, July 27th 2022 – 2:00 – 3:00 PM

Biography



Botond Roska obtained his M.D. at the Semmelweis Medical School, a Ph.D. in neurobiology from the University of California, Berkeley and studied genetics and virology as a Harvard Society Fellow at Harvard University and the Harvard Medical School. He then led a research group at the Friedrich Miescher Institute in Basel from 2005-2018. In 2010 he became Professor at the Medical Faculty and in 2019 Professor at the Science Faculty of the University of Basel. Since 2018 he is a founding director of the Institute of Molecular and Clinical Ophthalmology Basel (IOB). At IOB he leads a research group focusing on the understanding of vision and its diseases and the development of gene therapies to restore vision.

Botond Roska was elected as a member of the European Molecular Biology Organization (EMBO) in 2011 and the Academia Europaea in 2020. He has received several awards, including the Viva Award in 2010, the Alcon Award in 2011, the Alfred Vogt Award in 2013, the Cogan Award in 2016, the Bressler Prize and the W. Alden Spencer Award in 2018, the Louis-Jeantet Prize for Medicine, the Cloëtta Prize, the Semmelweis Budapest Award in 2019, the Körber European Science Prize and the Greenberg End Blindness Visionary Prize in 2020.

Title: ***Restoring Vision***

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Conférenciers / Speakers

Maureen Neitz, PhD

Wednesday, July 27th 2022 – 5:30 – 6:30 PM

Biography

Maureen Neitz's research includes work on color vision, gene therapy, and the prevention of nearsightedness. She earned a Ph.D. in biochemistry and molecular biology from the University of California, Santa Barbara in 1986. She did a post-doctoral fellowship studying color vision also at UC Santa Barbara. She joined the faculty at the Medical College of Wisconsin in 1991, where she moved through the ranks from Assistant Professor to Professor with Tenure and held the Richard O. Schultz and Ruth A. Works Endowed Professorship in ophthalmology. In 2009, she and Jay Neitz, her husband and long-time collaborator, moved to the University of Washington. Her "claims to fame" include starting a company to translate discoveries at the bench to therapeutic interventions for nearsightedness and using gene therapy to "cure" color blindness in a non-human primate.

Title: ***A solution to the worldwide myopia epidemic: A tale of translation from bench to clinic***

Abstract : ***Purpose****: New therapies are urgently needed to slow or stop myopia progression in children and therefore reduce the risk of long-term, sight-threatening complications from myopia. The discovery that polymorphisms at the myopia genetic locus, MYP1, are associated with splicing defective cone opsin genes (OPN1LW and OPN1MW) led to the hypothesis that contrast signaling in the retina plays an important role in myopia development and progression. This hypothesis predicted that reducing the contrast of images on the retina could slow myopia progression. Novel spectacle lenses, Diffusion Optics Technology (DOT) lenses were developed to evaluate this hypothesis, and a multi-center, double-masked, randomized, controlled clinical trial was initiated. The trial was designed in collaboration with the U.S. FDA, and included pre-planned interim analyses at 12- and 24- months.* ***Methods:*** *CYPRESS (NCT03623074) evaluated two investigational spectacle lenses (Test 1, Test 2) designed to slightly reduce contrast compared to control spectacle lenses for the ability to reduce myopia progression in children 6-10 years of age over a period of 3 years. Two hundred and fifty-six (256) eligible myopic subjects were randomized and dispensed spectacles at 14 clinical sites in North America. Subjects were asked to wear the study spectacles constantly, except for activities in which standard spectacle wear would be inappropriate, such as contact sports and swimming. "Full time wearers" were defined as those subjects whose parents reported that they did not remove the study spectacles for near vision activities. Axial length (AL) and cycloplegic autorefraction (SER) were measured at baseline and annual follow-up visits, now through 24-months.* ***Results:*** *Approximately two-thirds of study subjects (61, 45, and 66 in Test 1, Test 2, and Control respectively) met criteria for "full-time wearers". After 24-months, the mean (± SD) change from baseline in AL was 0.33 ±0.23, 0.34 ± 0.39, and 0.53 ± 0.33 mm for Test 1, Test 2, and Control respectively. The mean change from baseline in SER after 24-months of usage was -0.36 ± 0.54, -0.48 ± 0.85, and -0.88 ± 0.77 D for Test 1, Test 2, and Control, respectively. The difference in means (Test 1 minus Control) for change from baseline of AL (-0.21 mm) and SER (0.52 D) were statistically significant ($p<0.0001$).* ***Conclusions:*** *DOT spectacle lenses were designed to reduce retinal contrast to slow the progression of myopia. After 24-months of usage, subjects who wore DOT lenses full-time had less myopia progression than control subjects.*

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Conférenciers / Speakers

Walter Wittich, PhD, FAAO, CLVT

Thursday, July 28th 2022 – 8 :45 – 9 :45 AM

Biography

Walter Wittich is an Associate Professor at the School of Optometry at the University of Montreal, in Quebec, Canada. His research focuses on the rehabilitation of older adults with combined vision and hearing loss. Following his Master's in Psychology (Concordia University) and PhD in Visual Neuroscience (McGill University), he completed a postdoctoral fellowship in audiology at the University of Montreal. Coming from a background in age-related vision loss, he now conducts research in dual sensory impairment and acquired deafblindness. His research domains include basic sensory science, as well as medical, psychosocial, and rehabilitation approaches to sensory loss, where he has published over 130 peer-reviewed articles. He is the inaugural chair of the Deafblind International Research Network, is a Fellow of the American Academy of Optometry and is Quebec's first Certified Low Vision Therapist.

Title: **An overview of vision rehabilitation: what we can do now while we wait for the 'cure'?**

Abstract: It is a common patient experience in eye care to be told at some point by a vision care provider that 'nothing more can be done' in their treatment regimen. This professional sentiment applies to advanced levels of almost all eye diseases and has been the cause of desperation for numerous individuals living with 'untreatable' vision impairment. However, nothing could be more from the truth, given that the sentence should really read 'nothing more can be done MEDICALLY to restore your vision'. Vision rehabilitation often begins where the treatment experience of patients ends – in case a referral is made, or the patients discover vision rehabilitation themselves, often through word of mouth. In this presentation I will first provide an overview of visual impairment (meaning low vision and blindness), and then provide the professional context and scope of practice of vision rehabilitation therapy (sight substitution), low vision therapy (sight enhancement) and orientation & mobility (independent travel for persons living with a visual impairment). Thereafter, I will highlight current research topics and challenges, as well as the breadth of research opportunities that exist in vision impairment and its rehabilitation, and how they are linked to the improvement of independence, participation, and quality of life of persons living with visual impairment.

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Conférenciers / Speakers

Robert Koenekoop, MD, PhD

Thursday, July 28th 2022 – 9:45 – 10:45 AM

Biography

RESEARCH PROFILE: Dr. Robert Koenekoop (Rob) was born in Stockholm, Sweden but went to High school and the University of Utrecht in The Netherlands. After Bachelor's and Master's degrees in Biology, Vegetation Science and Population Biology, a Fulbright fellowship from Amsterdam brought him to the USA for a PhD in Molecular Biology. His wife then brought him to Quebec, Canada and Medical school studies at the University of Toronto and McGill University followed. He saw the light in the retina clinic and finished his residency in Ophthalmology at McGill and his Ocular Genetics and Paediatric Ophthalmology Fellowships at Johns Hopkins University. For the past 25 years he has devoted his research career to discovering new retinal genes for childhood blindness due to retinal degenerations, and more recently in testing the safety and efficacy of new therapies for these same diseases, with some very important early successes. He has a broad background in human clinical trials and drug development, molecular genetics, clinical and paediatric ophthalmology, retinal degenerations, childhood blindness research and data analyses. In the past few years, in international collaborations, he has been able to discover 15+ new genes for childhood blindness due to retinal degenerations. This work was supported by grants from NIH (NEI), CIHR, Fighting Blindness Canada, The MCH foundation, Telethon of stars, the FRSQ and Reseau de Vision. This led to the publication of 150+ peer-reviewed papers. He is now the principal investigator (PI) at McGill, the Montreal Children's Hospital and the MUHC Center for Innovative Medicine (CIM) for human clinical trials to test new drugs, new genes, gene editing, new genetic methods and other modalities to combat blindness due to photoreceptor diseases. In his free time, he bikes 365 days per year and keeps a healthy diet.

CLINICAL PROFILE: In Canada, Dr. Koenekoop sees Paediatric and Inherited Retinal Degeneration patients 5 days per week, at the new Glen Eye clinic (MUHC), at the new Children's Clinic and at the new Mohawk Eye clinic. IRD patients in these clinics receive extensive workups, deep genetic testing and genetic and treatment counselling.

Title: **How to discover a new retinal gene for retinal degeneration, build a human data base and perform a human therapeutic trial for blindness**

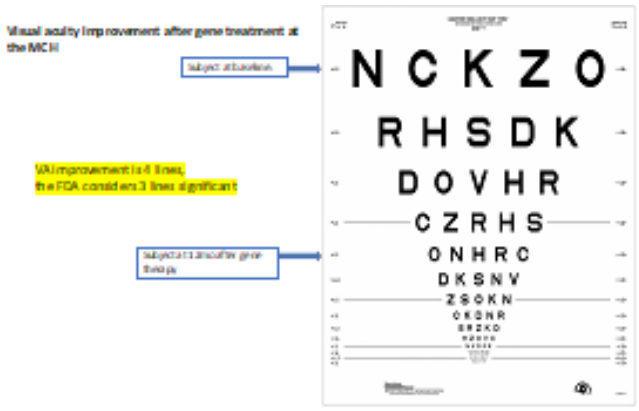
Abstract: Inherited Retinal Degenerations (IRDs) are devastating retinal photoreceptor degenerations, leading to complete blindness. Almost 6 million people around the world have IRDs and carry mutations in one of over 300 retinal genes. Twenty genes are commonly mutated. It took over 20 years to identify all these genes, and we will illustrate in this talk how to discover new retinal genes. In IRDs, the retinal-photoreceptor neurons die, the inner retinal layers remain intact for a long time. Rods die first due to the mutation in a crucial retinal gene, followed by apoptosis which leads to nightblindness. Cone death occurs later, through a different mechanism, likely not due to the mutation, but due to oxidative stress, which leads to progressive tunnel vision followed by visual acuity and color loss and complete blindness. The most common form of IRDs are retinitis pigmentosa (RP) in adults and Leber Congenital amaurosis (LCA) in childhood.

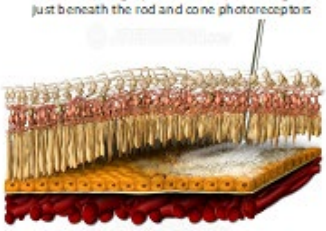
Many research questions remain for the new generation of vision scientists, including which patient and which genotype gets what treatment? When is the best time for intervention? and in combination or alone? For example, gene augmentation is a sub-retinal surgical therapy and is confined to local areas of living cells and is of course gene specific but mutation independent. Gene editing is given intra-vitreally and reaches all retinal

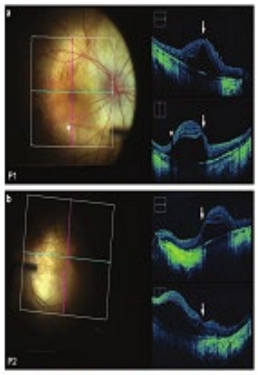
cells but is mutation dependent. Atrophic regions need to be treated by stem cells, and/or optogenetic treatments which may be possible in remaining inner retinal cells, when rods and cones have died, while drugs may be efficacious and gene agnostic. Strikingly, it is currently possible to replace at least 5 retinal genes in human studies (i.e. RPE65 in juvenile RP and LCA, CHM in Choroideremia, RPGR in x-linked RP and CNGA3 and CNGB3 in complete achromatopsia, while others are coming). Gene editing is now studied by ASO and CRISPR in CEP290-related LCA and USH2a- related RP and Usher patients (with exon 13 mutations). Optogenetic, stem cell and several drug trials are gene agnostic and have started in humans.

My talk will focus three related endeavors: 1. How to find retinal genes that cause IRDs, my example will be the "candidate gene approach" and how we discovered NMNAT1. 2. Next will be a discussion about how to perform a clinical trial, with the help of novel endpoints, genotyped patients, a whole team of experts and 3. The new registries and data bases containing genotype and phenotype data.

Previously, IRDs were deemed untreatable, based on the non-detectable ERGs, the severe loss of acuity, the loss of visual fields and the retinal thinning on OCT. Remarkably, recent human research has shown that this is not true and IRDs respond to a wide variety of treatments, ranging from cell, drug, gene augmentation, gene editing (ASO and CRISPR), to optogenetic interventions. These novel therapies are in various stages of human therapeutic development, ranging from pre-clinical studies to phase I to phase III human trials to FDA approval (e.g. Luxturna, RPE65 gene therapy, 2019). It is important to realize how three major, converging advances in Genetics and Genomics, novel retinal and brain functional testing and imaging, plus animal model therapies have revolutionized this field. Also, how there are multiple treatment avenues in study and in development, increasing the chance of commercial successes and the possibilities of combination treatments.







Intra operative video lifting the retina to deliver the normal gene

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Horaires / *programs*

HORAIRE - Lundi, 25 juillet 2022

15 h 45 -16 h 00	Embarquement – Navette « Symphony Bus International » Montréal-St-Paulin **Station de métro Berri-UQAM (coin Berri & de Maisonneuve), Montréal, QC** **Groupe IRCM – École d'été**
16 h 00	**DÉPART (durée : 2h00)**
17 h 00 -18 h 30	**ARRIVÉE ET ENREGISTREMENT** **Le Baluchon Éco-Villégiature** 3550, Chemin des Trembles, St-Paulin, Québec, J0K 3G0
18 h 30 -19 h 30	**Mot de bienvenue du directeur du RRSV** **Michel Cayouette, PhD** Institut de recherches cliniques de Montréal, Montréal, Québec, Canada
19 h 30	Diner de bienvenue

PROGRAM – Monday, July 25th 2022

3 h 45 -4 h 00 PM	Boarding – Shuttle « Symphony Bus International » Montreal-St-Paulin **Metro station Berri-UQAM (corner Berri & de Maisonneuve), Montreal, QC** **IRCM Group – Summer School**
4 h 00 PM	**DEPARTURE (duration: 2h00)**
5 h 00 -6 h 30 PM	**ARRIVAL AT VENUE AND CHECK-IN** **Le Baluchon Éco-Villégiature** 3550, Chemin des Trembles, St-Paulin, Quebec, J0K 3G0
6 h 30 -7 h 30 PM	**Reception and welcoming remarks by the VHRN Director** **Michel Cayouette, PhD** Institut de recherches cliniques de Montréal, Montreal, Quebec, Canada
7 h 30 PM	Welcome dinner

HORAIRE - Mardi, 26 juillet 2022

7 h 00 – 8 h 30	Petit-déjeuner
8 h 30 – 8 h 45	**Mot d'ouverture** **Adriana Di Polo, PhD**, Université de Montréal, Montreal, Québec, Canada **Stuart Trenholm, PhD**, Université McGill, Montréal, Québec, Canada
	Modérateur : **Adriana Di Polo, PhD**
8 h 45 – 9 h 45	*Restoring function to the human cornea: bench to bedside and back* **May Griffith, PhD**, Université de Montréal, Montréal, Québec, Canada
9 h 45 – 10 h 35	*The neurovascular unit: a new therapeutic target for glaucoma* **Adriana Di Polo, PhD**, Université de Montréal, Montréal, Québec, Canada
10 h 35 – 10 h 45	*Dr Suzanne Véronneau-Troutman, a pioneer in many ways* **Isabelle Hardy, MD, FRCSC**, Université de Montréal, Montréal, Québec, Canada
10 h 45 – 11 h 15	Pause
11 h 15 – 12 h 15	*Regenerating the retina via cell reprogramming* **Michel Cayouette, PhD** Institut de recherches cliniques de Montréal, Montréal, Québec, Canada
12 h 15 – 14 h 00	Lunch
	Modérateur : **May Griffith, PhD**
14 h 00 – 15 h 00	*Ocular surface nerves: structure, function, and protection of Vision* **Darlene Dartt, PhD,** Harvard University, Cambridge, Massachusetts, États-Unis
	Modérateur: **Stuart Trenholm, PhD**
15 h 00 – 15 h 30	*Groupe de discussion avec les patients partenaires* **Intervenants** **Mary-Kate Fraser** et **Conrad Eder** Représentante de la VCC (**Larissa Moniz**/**Morgan Ineson**, *Vaincre la cécité Canada* (VCC), Ontario, Canada **Stuart Trenholm**, Université McGill, Montréal, Québec, Canada **Michel Cayouette**, PhD, IRCM, Montréal, Québec, Canada
15 h 30 – 17 h 30	*Temps libre (activités plein air ou autre)*
17 h 30 – 18 h 30	*A vision for the future: How to recruit neural plasticity for sight restoration after stroke* **Krystel Huxlin, PhD,** University of Rochester, Rochester, New York, États-Unis
18h 30 – 19 h 30	**Session 1 : Présentation des affiches (chiffres impairs)**
19 h 30	Dîner BBQ

PROGRAM – Tuesday, July 26th 2022

7 h 00 – 8 h 30 AM	Breakfast
8 h 30 – 8 h 45 AM	**Opening remarks** **Adriana Di Polo, PhD**, University of Montreal, Montreal, Quebec, Canada **Stuart Trenholm, PhD**, McGill University, Montreal, Quebec, Canada
	***Moderator*: Adriana Di Polo, PhD**
8 h 45 – 9 h 45 AM	*Restoring function to the human cornea: bench to bedside and back* **May Griffith, PhD**, University of Montreal, Montreal, Québec, Canada
9 h 45 – 10 h 35 AM	*The neurovascular unit: a new therapeutic target for glaucoma* **Adriana Di Polo, PhD**, University of Montreal, Montreal, Quebec, Canada
10 h 35 – 10 h 45 AM	*Dr Suzanne Véronneau-Troutman, a pioneer in many ways* **Isabelle Hardy, MD, FRCSC**, University of Montreal, Montreal, Quebec, Canada
10 h 45 –11 h 15 AM	Coffee break
11 h 15 AM – 12 h 15 PM	*Regenerating the retina via cell reprogramming* **Michel Cayouette, PhD** Institut de recherches cliniques de Montréal, Montreal, Quebec, Canada
12 h 15 – 2 h 00 PM	Lunch
	***Moderator*: May Griffith, PhD**
2 h 00 – 3 h 00 PM	*Ocular surface nerves: structure, function, and protection of Vision* **Darlene Dartt, PhD,** Harvard University, Cambridge, Massachusetts, USA
	***Moderator*: Stuart Trenholm, PhD**
3 h 00 – 3 h 30 PM	*Group discussion with patient partners* **Panel Session** **Mary-Kate Fraser** and **Conrad Eder** FBC representative (**Larissa Moniz**/**Morgan Ineson**, *Fighting Blindness Canada* (FBC), Ontario, Canada **Stuart Trenholm**, Université McGill, Montréal, Québec, Canada **Michel Cayouette**, PhD, IRCM, Montréal, Québec, Canada
3 h 30 – 5 h 30 PM	*Free time (outdor activities or other)*
5 h 30 – 6 h 30 PM	*A vision for the future: How to recruit neural plasticity for sight restoration after stroke* **Krystel Huxlin, PhD,** University of Rochester, Rochester, New York, USA
6h 30 – 7 h 30 PM	**Session 1: Poster presentations (odd numbers)**
19 h 30	Dinner BBQ

HORAIRE - Mercredi, 27 juillet 2022

7 h 00 – 8 h 30	Petit-déjeuner
	Modératrice: **May Griffith, PhD**
8 h 30 – 9 h 30	*The assembly and function of motion-selective retinal circuits* **Arjun Krishnaswamy, PhD** Université McGill, Montréal, Québec, Canada
8 h 45 – 9 h 45	*Effects of vision loss on the brain's internal compass* **Stuart Trenholm, PhD** Université McGill, Montréal, Québec, Canada
10 h 30 – 11 h 00	Pause **Visualisation des affiches**
11h 00 – 12 h 00	**Session 2: Présentations orales étudiantes "éclairs" (2.1 à 2.6)**
12 h 00 – 14 h 00	Lunch
	Modérateur: **Stuart Trenholm, PhD**
14 h 00 – 15 h 00	*Restoring Vision* **Botond Roska, MD, PhD** Institute for Molecular and Clinical Ophthalmology, Bâle, Suisse
15 h 00 – 15 h 30	**Session photo** et *temps libre*
15 h 30 – 15 h 45	Pause **Visualisation des affiches**
15 h 45 – 17 h 30	*Temps libre (activités plein air ou autre)*
	Modératrice : **Adriana Di Polo, PhD**
17 h 30 – 18 h 30	*A solution to the worldwide myopia epidemic: A tale of translation from bench to clinic* **Maureen Neitz, PhD** University of Washington, Seatle, Washington, États-Unis
18h 30 – 19 h 30	**Session 3 : Présentation des affiches (chiffres pairs)**
19 h 30	Dîner et gala

PROGRAM – *Wednesday, July 27th 2022*

7 h 00 – 8 h 30 AM	Breakfast

	***Moderator*: May Griffith, PhD**
8 h 30 – 9 h 30 AM	*The assembly and function of motion-selective retinal circuits* **Arjun Krishnaswamy, PhD** McGill University, Montreal, Quebec, Canada
8 h 45 – 9 h 45 AM	*Effects of vision loss on the brain's internal compass* **Stuart Trenholm, PhD** McGill University, Montreal, Quebec, Canada
10 h 30 – 11 h 00 AM	Coffee break **Poster viewing**
11h 00 AM – 12 h 00 PM	**Session 2: Flash talks by students (2.1 to 2.6)**
12 h 00 – 2h 00 PM	Lunch
	***Moderator*: Stuart Trenholm, PhD**
2 h 00 – 3 h 00 PM	*Restoring Vision* **Botond Roska, MD, PhD** Institute for Molecular and Clinical Ophthalmology, Basel, Switzerland
3 h 00 – 3 h 30 PM	***Photobooth** and Free time*
3 h 30 – 4 h 45 PM	Coffee break **Poster viewing**
3 h 45 – 5 h 30 PM	*Free time (outdoor activities or other)*
	***Moderator*: Adriana Di Polo, PhD**
5 h 30 – 6 h 30 PM	*A solution to the worldwide myopia epidemic: A tale of translation from bench to clinic* **Maureen Neitz, PhD** University of Washington, Seatle, Washington, USA
6 h 30 – 7 h 30 PM	**Session 3: Poster presentations (even numbers)**
7 h 30 PM	Gala Dinner

HORAIRE - Jeudi, 28 juillet 2022

7 h 00 – 8 h 45	Petit-déjeuner
8 h 45 – 9 h 45	*An overview of vision rehabilitation: what we can do now while we wait for the 'cure'?* **Walter Wittich, PhD, FAAO, CLVT** École d'optométrie - Université de Montréal, Montréal, Québec, Canada
	Modérateur : **Walter Wittich, PhD**
9 h 45 – 10 h 45	*How to discover a new retinal gene for retinal degeneration, build a human data base and perform a human therapeutic trial for blindness* **Robert Koenekoop, MD, PhD** Université McGill, Montréal, Québec, Canada
10 h 45 – 11 h 00	Pause **Visualisation des affiches**
11h 00 – 12 h 00	**Session 4: Présentations orales étudiantes "éclairs" (4.1 à 4.6)**
12 h 00 – 12 h 15	**Mot de clôture et remerciements** **Adriana Di Polo, PhD** Université de Montréal, Montréal, Québec, Canada **Stuart Trenholm, PhD** Université McGill, Montréal, Québec, Canada
12 h 30 – 14 h 00	Lunch
14 h 00 -14 h 15	Embarquement – Navette « Symphony Bus International » St-Paulin-Montréal **Le Baluchon Éco-Villégiature**
14 h 15	**DÉPART (durée : 2h00)**
16 h 30	**ARRIVÉE À MONTRÉAL** **Station de métro Berri-UQAM (coin Berri & de Maisonneuve), Montréal, QC**

PROGRAM – Thursday, July 28th 2022

7 h 00 – 8 h 45 AM	Breakfast
8 h 45 – 9 h 45 AM	*An overview of vision rehabilitation: what we can do now while we wait for the 'cure'?* **Walter Wittich, PhD, FAAO, CLVT** École d'optométrie, University of Montreal, Montreal, Quebec, Canada
	***Moderator*: Walter Wittich, PhD, FAAO, CLVT**
9 h 45 – 10 h 45 AM	*How to discover a new retinal gene for retinal degeneration, build a human data base and perform a human therapeutic trial for blindness* **Robert Koenekoop, MD, PhD** McGill University, Montreal, Québec, Canada
10 h 45 – 11 h 00 AM	Break **Poster viewing**
11h 00 AM – 12 h 00 PM	**Session 4: Flash talks by students (4.1 to 4.6)**
12 h 00 – 12 h 15 PM	**Closing comments and wrap-up** **Adriana Di Polo, PhD** University of Montreal, Montreal, Quebec, Canada **Stuart Trenholm, PhD** McGill University, Montreal, Quebec, Canada
12 h 30 – 2 h 00 PM	Lunch
2 h 00 - 2 h 15 PM	Boarding – Shuttle « Symphony Bus International » St-Paulin-Montréal **Le Baluchon Éco-Villégiature**
2 h 15 PM	**DEPARTURE (duration: 2h00)**
4 h 30 PM	**ARRIVAL at MONTREAL** **Station de métro Berri-UQAM (corner Berri & de Maisonneuve), Montreal, QC**

PRÉSENTATIONS ÉTUDIANTS

Horaires détaillés

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STUDENT PRESENTATIONS

Detailed programs

Horaires détaillés / *Detailed programs*

Présentations par affiche – chiffres impairs / *Poster Presentations – odd numbers*

Résumé / *Abstract*

Session 1	**Mardi 26 juillet - 18h30-19h30** ***Tuesday, July 26 2022 6:30 PM - 7:30 PM***
1	Uncovering the role of Podxl in cone photoreceptor cell development and survival **Samantha Boudreau**, Michael Housset, Michel Cayouette
3	Assessing the interocular delay in amblyopia and its link to visual acuity **Daniel Gurman**, Alexandre Reynaud
5	Formation de contacts synaptiques : contribution du récepteur GPR55 **Lucile Lacomme,** Philippe Germain, Aurélie Stil, Jean-François Bouchard
7	Mesure fonctionnelle de la quantité de lumière détectée par les bâtonnets **Geneviève Rodrigue,** Laurine Paris, Judith Renaud, Rémy Allard
9	Nanoparticles for Drug Delivery to Treat Ocular Melanoma **Mozhgan Aghajanzadeh**, Thai Hien Tu, Christopher E Rudd, May Griffith
11	La synthèse de corps cétoniques par l'endothélium ischémique favorise l'angiogenèse pathologique dans la rétinopathie proliférante **Charlotte Betus**, Candace Yang, Gael Cagnone, Emilie Heckel, Tapan Agnihotri, Sheetal Pundir, Jose Carlos Rivera, Grant Mitchell, Jean-Sébastien Joyal
13	Pten Regulates the Development of Starburst Amacrine Cell Dendrites **Teva Bracha**, Kevin Wright
15	Mast cell activation contributes to experimental choroidal neovascularization **Rabah Dabouz**, Pénélope Abram, Carlos José Rivera, Sylvain Chemtob
17	Évoquer la vision par stimulation optogénétique du cortex visuel chez la souris **Ismaël Djerourou,** Emma Morgan, Véronique Chouinard, Valérie Daigneault, Maurice Ptito, Matthieu Vanni.

Résumé / *Abstract*

Session 1	Mardi 26 juillet - 18h30-19h30 *Tuesday, July 26 2022 6:30 PM - 7:30 PM*
19	Cellular signals corresponding to structural alterations to single retinal ganglion cells in glaucoma with in vivo imaging **Aliénor Jamet**, Balwantray Chauhan
21	Morphology and Characteristics of MafB+ Retinal Ganglion Cells and Amacrine Cells **Nina Luong**, Kevin Wright, Benjamin Sivyer
23	The cell adhesion molecule Sdk1 shapes the assembly of a retinal circuit that detects visual orientation **Pierre-Luc Rochon**, Catherine Theriault, Aline G. Rangel Olgin, Arjun Krishnaswamy.
25	Wound healing response of the alkali burnt cornea after treatment with novel anti-inflammatory drugs **Neethi Thathapudi**, Marc Groleau, Naoufal Akla, Marie-Claude Robert, May Griffith
27	The anti-uveal melanoma effect of miR-181a and combinational therapies **Rui Wang**, Houda Tahiri, Chun Yang, Pierre Hardy
29	Restoration of mitochondrial axonal transport prevents neurodegeneration and rescues visual function in glaucoma **Heberto Quintero**, Yukihiro Shiga, Nicolas Belforte, Luis Alarcon-Martinez, Sana El Hajji, Deborah Villafranca-Baughman, Florence Dotigny, Adriana Di Polo
31	Asymmetries in Connections Between Wide-Field Amacrine Cells and Starburst Amacrine Cells in the Mouse Dorsal Retina **Ilia Capralov**

Horaires détaillés / *Detailed programs*

Présentations orales – chiffres impairs / *Oral Presentations – odd numbers*

Résumé / *Abstract*

Session 2	**Mercredi 27 juillet - 11h00-12h00** ***Wednesday July 27 – 11:00 AM – 12:00 PM***

Modérateur / ***Moderator***: **May Griffith, PhD**

7	**11h00**	Mesure fonctionnelle de la quantité de lumière détectée par les bâtonnets **Geneviève Rodrigue,** Laurine Paris, Judith Renaud, Rémy Allard
11	**11h10**	La synthèse de corps cétoniques par l'endothélium ischémique favorise l'angiogenèse pathologique dans la rétinopathie proliférante **Charlotte Betus**, Candace Yang, Gael Cagnone, Emilie Heckel, Tapan Agnihotri, Sheetal Pundir, Jose Carlos Rivera, Grant Mitchell, Jean-Sébastien Joyal
13	**11h20**	Pten Regulates the Development of Starburst Amacrine Cell Dendrites **Teva Bracha**, Kevin Wright
15	**11h30**	Mast cell activation contributes to experimental choroidal neovascularization **Rabah Dabouz**, Pénélope Abram, Carlos José Rivera, Sylvain Chemtob
25	**11h40**	Wound healing response of the alkali burnt cornea after treatment with novel anti-inflammatory drugs **Neethi Thathapudi**, Marc Groleau, Naoufal Akla, Marie-Claude Robert, May Griffith
31	**11h50**	Asymmetries in Connections Between Wide-Field Amacrine Cells and Starburst Amacrine Cells in the Mouse Dorsal Retina **Ilia Capralov**

Présentations par affiche – chiffres pairs / *Poster Presentations – even numbers*

Résumé / *Abstract*

Session 3	Mercredi 27 juillet - 18h30-19h30 *Wednesday, July 27 2022 - 6:30 PM – 7:30 PM*
2	Assessment of Visual Function in a Snf2h Knockout Mouse Model of Retinal Degeneration **Skyra Cheng,** Pamela Lagali, Adam Baker, Catherine Tsilfidis
4	Evaluation and Adaptation of the FACE-Q | Craniofacial Patient-Reported Outcome Measure for Ophthalmology Patients **Farheen Khan**, Roxanne Noronha, Sara Williams, Karen Wong-Riff, Asim Ali, Helen Dimaras
6	Tear evaporation rate and influential factors measuring with the Waterloo Evaporimeter **Naeimeh Monfared**, Paul J. Murphy
8	An ideal observer analysis of letter identification in wavelet noise mimicking spatial scrambling in amblyopia **Xingqi Raffles Zhu**, Alex Baldwin, Robert Hess
10	Comparing normal and optogenetically restored vision **Nicole Arnold**, Rudi Tong, Aude Villemain, Stuart Trenholm
12	3D Printed Tactile Maps to Improve Spatial Learning of Blind Individuals **Maxime Bleau**, Natalina Martieniello, Joseph Paul Nemargut, Maurice Ptito
14	The role of neuron-glia communication in retinal maturation **Thomas Brown**, Shashank Srikanta, Nicolas Cemarkian, Michel Cayouette
16	Novel approaches to stimulate regeneration in the mammalian retina **David Luke Ajay**, Michel Cayouette
18	Insulin promotes RGC dendrite regeneration through ribosomal protein S6 kinase activation leading to restoration of neuronal function in glaucoma **Sana El Hajji**, Yukihiro Shiga, Nicolas Belforte, Yves Carpentier Solorio, Philippe D'Onofrio, Florence Dotigny, Nathalie Arbour, Adriana Di Polo
20	The role of the dorsal raphe in visually guided behavior **Jonas Lehnert**, Kerry Yang, Kuwook Cha, Anmar Khadra, Erik Cook, Arjun Krishnaswamy

Résumé / *Abstract*

Session 3	Mercredi 27 juillet - 18h30-19h30 *Wednesday, July 27 2022 - 6:30 PM – 7:30 PM*
22	The role of cadherin 4 in the assembly of off retinal circuits **Aline Giselle Rangel Olguin**, Pierre-Luc Rochon, Catherine Theriault, Arjun Krishnaswamy
24	Time-course analysis of human trabecular meshwork single cell contraction after a 5-day dexamethasone treatment **Luis Sanchez**, Jie J. Zheng
26	A novel femtomolar hemodynamic modulation strategy reveals major microvascular defects in glaucoma at single-pericyte scale **Deborah Villafranca-Baughman,** Luis Alarcon-Martinez, Jorge L. Cueva Vargas, Nicolas Belforte, Florence Dotigny, Adriana Di Polo
28	Designing Injectable Liquid Corneas for Patients at High Risk for Rejecting Corneal Transplantation: synthesis, characterization, in vitro biocompatibility study **Mostafa Zamani**, Mozhgan Aghajanzadeh, May Griffith
30	Light-evoked RGC calcium dynamics are altered in glaucoma: live imaging evidence of abnormal calcium clearance **Yukihiro Shiga**, Aline Giselle Rangel Olguin, Luis Alarcon-Martinez, Nicolas Belforte, Heberto Quintero, Deborah Villafranca-Baughman, Florence Dotigny, Arjun Krishnaswamy, Adriana Di Polo

Horaires détaillés / *Detailed programs*

Présentations orales – chiffres pairs / *Oral Presentations – even numbers*

Résumé / *Abstract*

Session 4

Jeudi 28 juillet - 11h00-12h00
Thursday July 28 – 11:00 AM – 12:00 PM

Modérateur / ***Moderator***: **Walter Wittich, PhD, FAAO, CLVT**

2	**11h00**	Assessment of Visual Function in a Snf2h Knockout Mouse Model of Retinal Degeneration **Skyra Cheng,** Pamela Lagali, Adam Baker, Catherine Tsilfidis
8	**11h10**	An ideal observer analysis of letter identification in wavelet noise mimicking spatial scrambling in amblyopia **Xinggi Raffles Zhu**, Alex Baldwin, Robert Hess
12	**11h20**	3D Printed Tactile Maps to Improve Spatial Learning of Blind Individuals **Maxime Bleau**, Natalina Martieniello, Joseph Paul Nemargut, Maurice Ptito
16	**11h30**	Novel approaches to stimulate regeneration in the mammalian retina **David Luke Ajay**, Michel Cayouette
22	**11h40**	The role of cadherin 4 in the assembly of off retinal circuits **Aline Giselle Rangel Olguin**, Pierre-Luc Rochon, Catherine Theriault, Arjun Krishnaswamy
26	**11h50**	A novel femtomolar hemodynamic modulation strategy reveals major microvascular defects in glaucoma at single-pericyte scale **Deborah Villafranca-Baughman,** Luis Alarcon-Martinez, Jorge L. Cueva Vargas, Nicolas Belforte, Florence Dotigny, Adriana Di Polo

HISTORIQUE

Le Réseau de recherche en santé de la vision œuvre, depuis 1995, sous l'égide du Fonds de la recherche du Québec - Santé (FRQS). Cet organisme gouvernemental a favorisé la création de réseaux de recherche au début des années 1990 afin de permettre aux chercheurs du Québec d'accroître leur collaboration et de participer davantage et collectivement à l'avancement des connaissances et à l'accroissement de la compétitivité du Québec dans des domaines ciblés par la politique de santé du Québec.

L'objectif du Réseau est d'accroître la capacité de recherche et la compétitivité du Québec en recherche en santé de la vision sur la scène internationale avec comme but ultime d'améliorer la santé visuelle des patients et de la société. À cette fin, le Réseau subventionne des infrastructures communes et des plateformes (telles que des banques de cellules ou de tissus, des banques de données, ressources à utilisateurs multiples). Le programme de bourses de recrutement du Réseau a pour but de stimuler l'intérêt des étudiants pour la recherche en vision, afin qu'ils continuent dans cette voie. Enfin, le Réseau participe à la préparation des étudiants en vue des concours de bourses des grands organismes subventionnaires. Le Réseau stimule également l'émergence des chercheurs de demain en offrant un support financier à l'aide du programme « Projet-Pilote pour chercheur en début de carrière ». Enfin, le réseau promouvoit les collaborations internationales entre les chercheurs du Réseau et les chercheurs à travers le monde grâce à son programme de Réseautage national et international.

Le Réseau de recherche en santé de la vision regroupe aujourd'hui plus de 130 chercheurs cliniciens et chercheurs fondamentalistes du Québec. Les chercheurs et cliniciens du Réseau œuvrent au sein ou en collaboration avec les huit universités du Québec: Concordia, INRS, McGill, Laval, Montréal, Sherbrooke, Université du Québec à Montréal et Université du Québec à Trois-Rivières. Les membres du Réseau sont rattachés aux quatre départements universitaires d'ophtalmologie de la province, à l'École d'optométrie de l'Université de Montréal, à plus d'une douzaine de départements universitaires de sciences fondamentales (psychologie, biologie, pharmacologie, biophysique) et à plus d'une douzaine de départements hospitaliers et centres de recherche clinique (Centre Hospitalier Universitaire de Montréal, Centre Hospitalier Universitaire de Québec, Centre de recherche Côte des Neiges, Centre de recherche Lucie-Bruneau, Centre Universitaire en Santé de l'Estrie, Centre Universitaire en Santé McGill, Centre de recherche de l'Hôpital Maisonneuve-Rosemont, Centre de recherche de l'Hôpital Sainte Justine, Centre de recherche de l'Hôpital juif de Montréal, Laboratoire d'organogenèse expérimentale, Centre de recherche de l'Hôpital pour enfants de Montréal, l'Institut neurologique de Montréal).

HISTORY

The Vision Health Research Network is funded by the Fonds de la recherche du Québec en santé (FRQS). This governmental agency instigated the creation of research networks in the early 1990's in order to promote collaboration within the research community in Quebec and to give Quebec a competitive edge in matters targeted by our health policy.

The Network's aim is to increase research capacity and competitiveness of Quebec in vision health research on the international scene with the ultimate goal of improving visual health of the patients and community. Therefore, the Network subsidizes common infrastructures and platforms (such as cells or tissues banks, databases, resources to multiple users). As part of the "Recruitment Scholarship" program, the Network intends to stimulate students' interests in vision research and to encourage them pursuing their studies in this direction. Finally, the Network helps students to outperform at competitions for awards from important granting agencies with the "Graduate Student Excellence Award" program. The Network is also stimulating the emergence of tomorrow's researchers by providing financial support through the "Pilot Project for Early Career Researcher" program. Finally, the network promotes international collaborations between Network researchers and researchers around the world through its "National and International Networking" program.

Today, the Network includes more than 130 clinical and fundamental researchers. The researchers and clinicians work or collaborate with the eight universities in Quebec: Concordia, INRS, McGill, Laval, Montreal, Sherbrooke, Université du Québec à Montréal, Université du Québec à Trois-Rivières. Members are affiliated with the four departments of ophthalmology in Quebec and a dozen fundamental science departments (psychology, biology, pharmacology, biophysics) and clinical research centers (Centre Hospitalier Universitaire de Montréal, Centre Hospitalier Universitaire de Québec, Centre de recherche Côte des Neiges, Centre de recherche Lucie-Bruneau, Centre Universitaire en Santé de l'Estrie, Centre Universitaire en Santé McGill, Centre de recherche de l'Hôpital Maisonneuve-Rosemont, Centre de recherche de l'Hôpital Sainte Justine, Centre de recherche de l'Hôpital juif de Montréal, Laboratoire d'organogenèse expérimentale, Centre de recherche de l'Hôpital pour enfants de Montréal, l'Institut neurologique de Montréal).

LA FONDATION ANTOINE-TURMEL

La fondation en bref

Depuis 2013, la Fondation Antoine-Turmel et le Réseau de recherche en santé de la vision (RRSV) ont développé un partenariat fructueux. Depuis cette collaboration, le RRSV a pu investir plusieurs années des milliers de dollars à la recherche sur la dégénérescence maculaire liée à l'âge (DMLA) sous toutes ses formes (fondamentale, clinique translationnelle, épidémiologie/santé publique, réadaptation). Elle mobilise l'ensemble des ressources disponibles dans le milieu de la DMLA et implique l'ensemble des intervenants (chercheurs, cliniciens, décideurs, organismes à but non lucratif, partenaires et patients) susceptibles de faciliter la recherche sur la DMLA et l'implantation de ses résultats.

Objectifs spécifiques

Les sujets atteints de DMLA ou à risque de le devenir sont au cœur de cette collaboration.

Le but est de favoriser le développement de connaissances nouvelles afin de:

- Développer de meilleures traitements pour les sujets atteints de DMLA;
- Ralentir significativement le cours de cette maladie;
- Retarder de début, et même d'en prévenir l'apparition;
- Développer des programmes de réadaptation pour les patients atteints d'une DMLA avancée afin de leur permettre de mieux vivre avec leur maladie.

Cette collaboration vise également à contribuer au développement d'une masse critique de chercheurs québécois en DMLA et à positionner le Québec dans ce domaine de recherche au Canada et sur la scène internationale.

Les projets de recherche ayant un lien avec la DMLA sont identifiés avec ce logo et sont les suivants :

DMLA

26 juillet 2022	27 juillet 2022	28 juillet 2022
Présentations par affiche # 7, 15	Présentations orales # 7 et 15 Présentations par affiche # 2, 10	Présentations orales # 2

THE FONDATION ANTOINE-TURMEL

The Fondation at a glance

Since 2013, the Antoine-Turmel Foundation and the Vision Health Research Network (RRSV) have developed a fruitful partnership. Since this collaboration, the VHRN has been able to invest thousands of dollars in research on age-related macular degeneration (AMD) in all its forms (discovery research, translational clinical, epidemiology / public health, rehabilitation) for several years. It mobilizes all the resources available in the AMD community and involves all stakeholders (researchers, clinicians, decision-makers, non-profit organizations, partners and patients) who can facilitate research on AMD and the implantation of its results.

Specific objectives

Patients suffering from AMD or who are at risk are at the center of this partnership.

The goal is to promote the development of new knowledge in order to:

- *Develop better treatments for patients with AMD;*
- *Significantly slow the course of this disease;*
- *Delay the onset and even to prevent its onset;*
- *Develop rehabilitation programs for patients with advanced AMD to enable them to live better with their disease.*

The partnership also aims to contribute to the development of a critical mass of AMD researchers in the province of Quebec and to position the province in this research area in Canada and internationally.

All presentations related to AMD presented during the virtual meetings are identified by this logo and are listed below:

DMLA

July 26 2022	**July 27 2022**	**July 28 2021**
Poster presentations # 7, 15	*Oral presentations* # 7 et 15 *Poster presentations* # 2, 10	*Oral presentations* # 2

MEMBRES DU JURY / *MEMBERS OF THE JURY*

Thomas Brown
Rabah Dabouz
Michel Cayouette
May Griffith
Morgan Ineson
Robert Koenekoop
Arjun Krishnaswamy
Valérie Lavastre
Larissa Moniz
Heberto Quintero
Pierre-Luc Rochon
Luis Sanchez
Yukihiro Shiga
Stuart Trenholm

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Le comité d'organisateur de l'École d'été du Réseau de recherche en santé de la vision tient à remercier les personnes suivantes pour leur aide (logistique au transport):

The Organizing Committee of the 2022 Summer School of the Vision Health Research Network would like to thank the following people for their help (transportation logistics):

Rabah Dabouz
Lucile Lacomme

COMITÉ ÉTUDITANT DU RRSV / *VHRN STUDENT COMMITTEE*

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Sergio Crespo-Garcia (UdM) – VP Logistique / *Logistic*

Jiaru Liu (UdM) – VP Sensibilisation communautaire / *Community outreach*

Sheetal Pundir (U McGill) – VP Sensibilisation communautaire / *Community outreach*

RÉSUMÉS DES PRÉSENTATIONS –

PRESENTATIONS ABSTRACTS

1 - Uncovering the role of Podxl in cone photoreceptor cell development and survival

Samantha Boudreau[1], Michael Housset[2], Michel Cayouette[3]

[1]McGill University, Institut de recherches cliniques de Montréal (IRCM), Montréal, Québec, Canada; [2]Institut de recherches cliniques de Montréal (IRCM), Montréal, Québec, Canada; [3]McGill University, University of Montreal, Institut de recherches cliniques de Montréal (IRCM), Montréal, Québec, Canada.

But / *Background*: Rod and cone photoreceptors are specialized cells of the mammalian retina that exhibit a high degree of compartmentalization. Their apical domain consists of two distinct parts: an outer segment that houses the photosensitive proteins, and an inner segment responsible for their production. While critical for photoreceptor function and survival, it remains unknown how this polarity is established and maintained molecularly. In this perspective, Podocalyxin-like protein (Podxl) poses as an interesting candidate. First identified in the kidney where it acts to regulate protein localization and epithelial cell polarization, Podxl has recently been discovered to locate at the inner-segment of cones. We now aim to elucidate whether 1) Podxl is required for the development and maintenance of cone polarity; and 2) Podxl absence in cones affects vision.

Méthode / *Methods:* To address the aims above, we use a conditional Podxl knockout mouse (cKO) line in which exons 3-7 are flanked by loxP sites, allowing cre-dependent in activation of the Podxl gene in the retina. For aim 1, we cross the cKO line with a retinal progenitor-specific Cre line, conferring Podxl deletion in rods and cones beginning at E12.5, then analyze retinal cell composition and histology via immunostaining. For aim 2, we cross the cKO line with a cone-specific cre line, conferring Podxl deletion in all mature cones beginning at P10, and analyze cone cellular polarity and survival via immunostaining for inner- and outer-segment markers. Significance of Podxl activity in cones for vision is assessed using electroretinogram (ERG) recordings to evaluate electrical activity of cones in response to light.

Résultats / *Results:* Our results indicate that Podxl localizes to the inner-segment of both rods and cones, as well as retinal vasculature. Our preliminary results show that in the retinal progenitor-specific and cone-specific mouse models there is a reduced b-wave amplitude measured by ERG recordings in scotopic (rod-driven) and photopic (cone-driven) conditions, respectively. These results suggest that Podxl contributes to the response of rods and cones to light stimulation, and/or to its transmission to interneurons. In order to understand how Podxl mediates this effect, we aimed at identifying its interacting partners in the mouse retina. To this end, we purified Podxl partners by an in vivo immunoprecipitation followed by mass spectrometry. Thanks to this approach, we could identify novel Podxl interacting candidates which could account for the observed Podxl cKO phenotypes if validated functionally in our models.

Conclusion (s): This project will make a substantial contribution to the field of cellular neurobiology and retinal biology, as the role of Podxl has never been investigated in the retina. Uncovering the role of Podxl in photoreceptor development and survival will contribute to a better understanding of the etiology of cone photoreceptor degenerative diseases that lead to visual impairment, affecting millions of people around the world.

2 - Assessment of Visual Function in a Snf2h Knockout Mouse Model of Retinal Degeneration

Skyra Cheng[1,2], Pamela Lagali[2], Adam Baker[2], Catherine Tsilfidis[2,3]

[1]Department of Cellular and Molecular Medicine, University of Ottawa, Ontario, Canada; [2]Neuroscience Program, Ottawa Hospital Research Institute, Ontario, Canada; [3]Department of Ophthalmology, University of Ottawa, Ontario, Canada.

But / *Background*: Retinal degenerative diseases are a leading cause of visual impairment worldwide and primarily arise from progressive loss of neurosensory retinal cells. However, animal models still do not exist for many retinal diseases. Preliminary studies from our lab show that over 100 human retinal disease genes are dysregulated when the chromatin remodelling protein Snf2h is ablated in cerebellar neurons. Our goal is to elucidate the role of the chromatin remodeling protein Snf2h in the visual system by examining the functional and morphological changes in a Snf2h cKO mouse model of retinal degeneration. We propose that the Snf2h retinal conditional knockout (cKO) mouse has the potential to serve as a promising model for studying multiple ocular diseases.

Méthode / *Methods:* Snf2h retinal cKO mice were generated using Snf2h floxed mice and a Chx10-Cre retina-specific Cre driver line. An optomotor response (OMR) assay and full-field scotopic electroretinography (ERG) were performed on Snf2h cKO mice to assess visual function. Mouse retinal cryosections were immunostained and various retinal cell populations were quantified via cell counting. Mice were analyzed at 1, 2, 3, and 6 months of age to track progression of visual dysfunction and changes in retinal histology.

Résultats / *Results:* Visual acuity (p<0.05) and ERG a-wave and b-wave peak amplitudes (p<0.0001) show a significant decline in Snf2h cKO mice compared to wild-type mice. These functional changes correlate with retinal histological analyses, which display thinning of the inner and outer nuclear cell layers and a reduction in the number of various retinal neurons in the Snf2h cKO mice compared to control littermates. No significant decline in visual acuity or ERG amplitudes was observed in Snf2h heterozygotes.

Conclusion (s): Ablation of the Snf2h gene in mice results in decreased visual performance and retinal cell loss. Subsequent steps following the phenotypic characterization of the Snf2h cKO mouse model include identifying potential therapeutic targets to induce retinal neuroprotection and recovery of visual function.

3 - Assessing the interocular delay in amblyopia and its link to visual acuity

Daniel Gurman[1], Alexandre Reynaud[1]

[1]McGill University, Montréal, Québec, Canada.

But / *Background*: Research on interocular synchronicity in amblyopia has demonstrated a deficit in synchronization (i.e. a neural processing delay) between the two eyes. Current methods for assessing interocular delay are either costly or only effective for assessments in mild amblyopia. In this study, we adapted a novel protocol developed by Burge & Cormack (2020) based on continuous psychophysics to measure the interocular delay on a wide range of amblyopes. The purpose of the current study is to assess the efficacy and accessibility of this protocol and determine whether the measurements of interocular synchronicity it produces are correlated with visual acuity

Méthode / *Methods:* This protocol is performed in both binocular and monocular viewing conditions and consists of following a target undergoing lateral Brownian motion as closely as possible with the mouse curser. The lag between the target and cursor is computed for each eye by determining the offset between the stimulus and mouse sequence at which the cross-correlation coefficient is maximal. This lag reflects the processing delay for a given eye. Additionally, assessment of the quality of the correlation indicates the accuracy at which the target was tracked.

Résultats / *Results:* Our results show that all but the most severe amblyopes successfully performed this task and exhibited interocular delay ranging from 1.6ms to 125.3ms. For the majority of amblyopes, this delay was attributed to the amblyopic eye. The correlations used to determine delays were generally high in quality but were lower in quality for the amblyopic eye. The magnitude of the delay was positively correlated with larger differences in interocular visual acuity.

Conclusion (s): These results demonstrate the efficacy of this new protocol and further support the link between interocular synchronicity and amblyopia. These results could lead to the development of a universal interocular assessment procedure for diagnostic purposes.

4 - Evaluation and Adaptation of the FACE-Q | Craniofacial Patient-Reported Outcome Measure for Ophthalmology Patients

Farheen Khan[1,2], Roxanne Noronha[1], Sara Williams[1], Karen Wong-Riff[3,4], Asim Ali[1,5], Helen Dimaras[1,5,6,7,8]

[1]The Hospital for Sick Children, Ophthalmology and Vision Sciences, Toronto, Ontario, Canada; [2]University of Toronto, Institute of Medical Science, Toronto, Ontario, Canada; [3]The Hospital for Sick Children, Division of Plastic and Reconstructive Surgery, Surgery, Toronto, Ontario, Canada; [4]University of Toronto, Division of Plastic and Reconstructive Surgery, Surgery, Toronto, Ontario, Canada; [5]University of Toronto, Ophthalmology & Vision Sciences, Toronto, Ontario, Canada; [6]SickKids Research Institute, Child Health Evaluative Sciences Program, Toronto, Ontario, Canada; [7]SickKids Research Institute, The Centre for Global Child Health, Toronto, Ontario, Canada; [8]University of Toronto, Division of Clinical Public Health, Dalla Lana School of Public Health, Toronto, Ontario, Canada.

But / *Background*: This study aims to assess the content validity of questions in the FACE-Q patient-reported outcome measure (PROM) among patients/survivors and parents/legal guardians of patients/survivors treated for corneal anesthesia (CA), retinoblastoma (RB), or strabismus (SB).

Méthode / *Methods:* This is a cross-sectional qualitative study that will be performed in two rounds. Eligible participants are identified in the medical record and recruited in-person during clinic visits at The Hospital for Sick Children, or by a mailed introduction letter, followed by a phone call. Individuals are eligible if they are (i) CA, RB, or SB patients/survivors ≥8 years old, or (ii) parents/legal guardians of CA, RB, or SB patients/survivors <8 years old, developmentally delayed, or hard of hearing. The target sample size is n = 7 per participant type, and condition, per round.

Résultats / *Results:* Participants complete cognitive debriefing interviews where they review seven FACE-Q sections measuring eye-related, appearance-based, and psychosocial outcomes. The first round will ascertain the relevance of, identify problems with, and solicit modifications to the FACE-Q. Input from round 1 will inform the modification of applicable FACE-Q questions, which will then be evaluated in round 2, upon further discussion with partner partners and relevant clinical and scientific stakeholders. The interviews are transcribed, coded, and analyzed via thematic analysis to identify confirmatory and non-confirmatory feedback, and new concepts. The number of participants offering confirmatory, non-confirmatory, and new-concept feedback are tallied; a minimum of 3 instances of non-confirmatory and new-concept feedback is required for modifications to be made to the FACE-Q for round 2.

Participant recruitment, data collection, and analysis are ongoing. Based on the 24 interviews completed thus far, to improve FACE-Q's comprehensibility, a common consensus among all participants has been that certain words and instructions should be altered to enhance clarity and appropriateness in relation to the three conditions, visual impairment, and enucleation. To further improve FACE-Q's relevance and comprehensiveness, RB participants have suggested additional concepts, including those related to prosthetic eyes and visual impairment. While RB survivors have also suggested adding the concept of interpersonal relationships among a few others, parents of survivors have indicated that survivors <8 years old are not yet concerned about their appearance. In the case of CA and SB participants, additional concepts for eye function and adverse effects sections have been suggested only

Conclusion (s): The study results will be used to adapt the FACE-Q to ensure that it is comprehensible, comprehensive, and relevant to CA, RB, and SB patients/survivors. The adapted FACE-Q will then undergo field testing for assessment of validity and reliability as part of a future study.

5 - Formation de contacts synaptiques : contribution du récepteur GPR55

Lucile Lacomme[1], Philippe Germain[1], Aurélie Stil[1], Jean-François Bouchard[1]

[1]École d'optométrie, Université de Montréal, Montréal, Québec, Canada.

But / *Background*: Recent experimental studies have demonstrated an important role of the endocannabinoid system in the development of the visual system through the presence of the GPR55 receptor and its involvement in the modulation of the guidance and growth of axons during the fetal and perinatal periods notably. Considering some molecules and cellular mechanisms involved in these processes may also play a role in synaptogenesis, the objective of this study is to determine the contribution of GPR55 in the formation of synaptic contacts.

Méthode / *Methods:* To do this, mouse embryo cortex from wild type and gpr55-/- were isolated. The dissociated pyramidal neurons were cultured up to the 9th day of in vitro culture and then exposed for 24 hours to a GPR55 (O-1602) agonist or GPR55 antagonists (ML-193, CBD). The effect of the treatments were studied in immunocytochemistry, by quantification of the fluorescence of the co-localizations of pre and post-synaptic markers using software using artificial intelligence to optimize the detection of the region of interest, and immunoblotting.

Résultats / *Results:* The results demonstrate that treatment with GPR55 agonist would increase synaptic contacts. Conversely treatments with GPR55 antagonists would seem to decrease synaptic contacts. All in a GPR55 dependent way.

Conclusion (s): Understanding the mechanisms of synaptic formation and their actors will ultimately improve our knowledge in the fields related to the normal or pathological development of the nervous system. These results will also allow us to develop new pharmacological agents that can increase or decrease the formation of synapses, which is a relevant pharmacological target in the context of vision restoration following trauma for example. From a public health perspective, understanding the impact of GPR55 modulation by CBD on the formation of synaptic contacts will lead to a better awareness of the effects of perinatal CBD use.

6 - Tear evaporation rate and influential factors measuring with the Waterloo Evaporimeter

Naeimeh Monfared[1], Paul J. Murphy[1]

[1]School of Optometry and Vision Sciences, University of Waterloo, Waterloo, Ontario, Canada.

But / *Background*: Tear evaporation is a normal physiological process that regulates blink activity and tear production. The measurement of tear evaporation rate (TER) is useful for diagnosing evaporative dry eye. The reported values for normal TER vary widely, possibly due to variation in the instrument used to measure it, as well as other factors. To address this issue, this presentation reviews the effect of the different factors and uses the Waterloo Evaporimeter as a test instrument for practical investigations.

A literature search for articles on tear evaporation and factors that influence evaporation were identified from more than 200 articles and books using search items of tear evaporation, tear evaporation rate/TER, factors affecting tear evaporation rate/TER, tear film structure, tear evaporation rate/TER measurement measurement, normal tear evaporation rate/TER. Several in vitro studies were completed to evaluate the instrument's accuracy and repeatability: the effect of salt concentration composition on TER, and the effect of lipid composition on TER.

Méthode / *Methods:* TER is influenced by ocular (tear film quality and stability, exposed ocular surface area, ocular surface temperature (OST) and the rate of cooling of the ocular surface, blinking), environmental (relative humidity, ambient temperature, airflow), and systemic factors (diurnal, age, sex and sex hormones). No significant difference was found in evaporation rate between distilled water and TheraTears (p<0.05).

Résultats / *Results:* suggesting that both can be used as a simulated tear film in future in vitro tests. Also, TER in a model eye containing lipid layer and distilled water was significantly lower than in the model eye which only distilled water (p<0.05).

Conclusion (s): TER is very susceptible to influencing factors, and these factors may be a key factor in the normal TER variability reported in the literature. Differences in the design and modality of use of measurement instruments may also be contributing to the variability. Also, an increase in lipid layer thickness can decrease the TER.

7 - Mesure fonctionnelle de la quantité de lumière détectée par les bâtonnets

Geneviève Rodrigue[1], Laurine Paris[1], Judith Renaud[1], Rémy Allard[1]

[1]École d'optométrie, Université de Montréal, Montréal, Québec, Canada.

But / *Background*: Des études antérieures ont montré que la quantité de lumière détectée par les cônes de la rétine peut être estimée à partir de deux seuils de contraste (avec et sans bruit visuel) mesurés dans des conditions spécifiques : lorsque le seuil de contraste en absence de bruit est inversement proportionnel à la racine carrée de la luminance. De plus, les différentes sensibilités spectrales des cônes et bâtonnets (ex : insensibilité des bâtonnets aux longues longueurs d'onde, c.-à-d., au rouge) permettent d'utiliser la chromaticité du stimulus afin de déterminer si la perception résulte du traitement des cônes ou des bâtonnets. La présente étude visait à déterminer les conditions visuelles permettant d'évaluer la quantité de lumière détectée par les bâtonnets à l'aide d'un test fonctionnel.

Méthode / *Methods:* Les seuils de contraste d'une tâche de discrimination de la direction du mouvement ont été mesurés dans la région rétinienne parafovéale avec et sans bruit visuel sur une large gamme de luminance à l'aide d'un affichage monochromatique rouge ou bleu.

Résultats / *Results:* À des luminances élevées, les seuils de contraste étaient similaires sur fond rouge et bleu à luminance égale suggérant l'implication des cônes. À des luminances faibles, les seuils de contraste étaient considérablement meilleurs sur fond bleu suggérant l'implication des bâtonnets pour le stimulus bleu. Également, les seuils de contraste en absence de bruit étaient inversement proportionnels à la racine carrée de la luminance suggérant que, dans ces conditions particulières, nous pouvons mesurer la quantité de lumière détectée par les photorécepteurs.

Conclusion (s): Ces résultats suggèrent que la quantité de lumière détectée par les bâtonnets peut être évaluée en mesurant les seuils de contraste de mouvement à de faibles luminances avec un stimulus bleu. Sachant que notre test fonctionnel permet de mesurer l'efficacité des bâtonnets et des cônes, nous le mettons actuellement en application dans un second projet de recherche auprès de participants atteints de dégénérescence maculaire liée à l'âge (DMLA). Bien que la DMLA atteigne la macula où les cônes sont très denses, à ce jour, il n'y a pas de consensus dans la littérature à savoir si ce sont les bâtonnets ou les cônes qui sont affectés en premier et ce projet de recherche permettra de déterminer si la DMLA affecte plus les bâtonnets que les cônes, et ce, en comparant les taux de détection des photons par les photorécepteurs.

8 - An ideal observer analysis of letter identification in wavelet noise mimicking spatial scrambling in amblyopia

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But / *Background*: Spatial scrambling refers to disruptions in topological mappings in the visual system and previous studies have found elevated spatial scrambling in amblyopic patients. Past studies suggest it could occur at the input to V1 simple cells from LGN, or the simple cell output to higher visual cortices. To test the site of the spatial scrambling using psychophysics, we aim to develop forms of noise that resemble the effect of spatial scrambling at the subunit or the V1 level and compare their effects on an objective scale for a template-matching ideal observer using a letter identification task.

Méthode / *Methods:* Four letters (D, E, C, F) that are commonly found in vision testing optotype were each decomposed by convolving the stimulus with log-Gabor wavelets with a spatial frequency determined by the optimal frequency channel used for letter identification and a fixed bandwidth at five orientations. The wavelet letter was resynthesized by convolving this map with the log-Gabor wavelets. This decomposition and resynthesis procedure simulates the receptive field responses of V1 neurons and how they are combined by higher-order visual centers. Subunit noise was made by applying pixel swapping to the wiring diagram that convolves with LGN receptive fields to form log-Gabor wavelets. V1 noise was simulated by swapping the map positions for resynthesizing the wavelet letters. These two forms of noise were applied to a letter identification task for an ideal template-matching observer at noise levels six log units apart.

Résultats / *Results:* The Modulation Transfer Function (MTF) of the subunit noise was characterized as globally reducing the gain across spatial frequencies and orientations, thereby preserving the tuning of log-Gabor wavelets. Increasing levels of both forms of noise induce noise in the ideal observer in a non-linear fashion with a fast increase and then saturation. The ideal observer performance, determined by the ratio of the same letter-template match over the mean of all letter-template matches, decreases to chance levels in the high noise regime for all target letters. In the low noise regime, there are considerable variations in performance between target letters. A comparison between subunit and V1 forms of noise shows similar trends.

Conclusion (s): Transfer properties of the subunit scrambling (that they preserve the tuning of spatial channels) are compatible with previous results obtained from amblyopic participants. It is a promising model of the spatial scrambling that may occur in their visual system. This paves the way for future studies that will investigate spatial scrambling using model-driven spatial metamers that individuals experiencing scrambling cannot distinguish.

9- Nanoparticles for Drug Delivery to Treat Ocular Melanoma

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But / *Background*: Melanoma is a cancer that involves the pigment cells of the body, including those in the eye. Melanoma in the eye can cause vision loss and can spread to other parts of the body, as these cells are extremely motile. Glycogen synthase kinase 3 (GSK3) is an inhibitory kinase in T-cells. We showed that its inhibition in immunotherapy against B16 melanoma cells can activate T-cells to limit tumor growth similar to that seen with anti-PD1 therapy (Taylor et al., Immunity 2016 PMID: 26885856; Rudd et al., Cell Reports 2020 PMID: 32075731). Inhibitors of glycogen synthase kinase 3 (GSK3) have been reported to inhibit the motile behaviour of T-cells (Taylor A, Rudd CE. 2020 PMID: 32188506) and melanoma cells (John et al. PMID: 22810307). In this study, SB415286, an inhibitor of GSK3 is tested for its ability to reduce the size of melanomas in mice. It is critical for drugs to reach the target tissue from the site of administration in appropriate concentration, and a sufficient period of time. As such, a delivery system that allows for sustained drug release is an efficpolyvinyln. Poly lactic-co-glycolic-acid nanoparticles (PLGA NPs) are usually prepared using the emulsion solvent evaporation method. In most cases poly vinyl alcohol is used to stabilize the emulsion. Our objective is to develop PLGA NPs that can be loaded with SB415286 (GSK3 inhibitor), administered intraperitoneally to target tumour cells that have been established in mouse models.

Méthode / *Methods:* SB415286-loaded PLGA NPs were prepared through a single emulsion evaporation method. The size and zeta potential of NPs were measured by ZetaView (Z-NTA) instrument. Encapsulation efficiency was measured on aTecan plate reader at 396 nm and its release profile at two different pH was determined.

Résultats / *Results:* The average PLGA NPs' size was 81 nm with a zeta potential of -26/mV. Encapsulation efficiency was calculated as approximately 80 %. The release profile at pH 6.4 and 7.2 over one week showed that the release of SB415286 was significantly greater in the more acidic pH after 48 hours. Aspects of the immune landscape is similar for NP and soluble delivery of SB415286.

Conclusion (s): Since NPs have a size up to 200 nm, we observed that they tend to accumulate in tumor tissues much more than in normal tissues. PLGA NPs are therefore expected to collect within cancer tissue. Tumor tissue has acidic pH, possibly enhancing the drug release from the PLGA NPs. Results to date show that targeting of ocular melanoma may be possible in the future using GSK3 inhibitor released from PLGA nanoparticles. The use of a PLGA system will help to increase the therapeutic index of the drug.

10 - Comparing normal and optogenetically restored vision

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But / *Background*: A promising therapeutic strategy for treating vision loss is optogenetics, which involves driving the expression of light-activated channels in surviving retinal neurons following rod and cone degeneration. However, current optogenetic treatments do not restore normal retinal light responses and it is unclear to what extent abnormal retinal light responses will restore normal visual perception. To address this question, we will use adeno-associated viruses to drive optogenetic channels in retinal neurons in blind mice. To examine how restored retinal light responses are processed outside the retina, we will perform in vivo 2-photon calcium imaging in visual cortex. Afterwards, to assess the efficacy of optogenetic vision therapy on visual perception, we will examine visual acuity and pattern recognition with behavioral testing. Together, our results will indicate to what extent restoring abnormal retinal light-responsivity limits effective vision therapy.

Méthode / *Methods:* To test to what extent normal visual perception can be restored following optogenetic therapy in blind mice, we will use intravitreal injection of an AAV driving expression of the medium-cone opsin (MW-Opsin) in retinal ganglion cells of rd1 mice (a mouse model of retinitis pigmentosa) under control of a ganglion cell-specific promoter. 2-3 weeks after AAV injection, we will examine retinal fluorescence in vivo using a Micron-IV fluorescent retina microscope. Mice with good retinal expression of MW-Opsin will then be used to install a head bar and cranial window over primary visual cortex (V1) and we will perform 2-photon microscopy while we present mice with a series of different visual stimuli, and we will compare response properties of individual cells in V1 between wild type and rd1-mice expressing MW-Opsin in their ganglion cells. Finally, we will assess visual perception in rd1 optogenetically treated mice by performing behavioral tests to examine visual acuity and pattern recognition skills.

Résultats / *Results:* To date, we have set up the pipelines for all procedures. We have collected the wild type datasets for the 2-photon imaging experiments in V1 and the behavioral data for acuity and pattern recognition tests. Behavioral tests were performed in head-fixed animals, but we are currently working to transition these to freely moving behavioral tests using touchscreen operant reward chambers. Furthermore, we are now performing intravitreal injections of AAV_pRGC_MW-Opsin into the retina of rd1 mice, and I am just starting 2-photon imaging experiments from these animals.

Conclusion (s): The outcomes from this study will help us understand to what extent the current version of optogenetic vision therapy, which is currently in clinical trials, can be a useful for restoring normal visual cortical responses and visual activity. While optogenetic vision therapy has incredible potential, results from our study will help elucidate possible limitations and will help guide development of more efficacious version of this therapy.

11 – La synthèse de corps cétoniques par l'endothélium ischénique favorise l'angiogenèse pathologique dans la rétinopathie proliférante

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But / *Background*: La rétinopathie proliférante (RP), associée tant à la prématurité qu'au diabète, engendre une néovascularisation pathologique qui peut provoquer la cécité des patients. Les cellules endothéliales (CE) s'adaptent métaboliquement à l'hypoxie. Parmi ces métabolites utilisés, les corps cétoniques participent à la prolifération des CE. L'enzyme limitante de la cétogenèse est HMG-CoA Lyase (Hmgcl). Le rôle des corps cétoniques dans la rétine reste inexploré. Nous supposons que la synthèse locale des corps cétoniques par les cellules endothéliales de la rétine alimente l'angiogenèse pathologique.

Nous proposons les objectifs suivants :

1. Définir chez l'Homme et la souris atteints de rétinopathie proliférante la source des corps cétoniques ;
2. Caractériser le phénotype vasculaire de souris déficientes pour Hmgcl dans l'endothélium;
3. Explorer les mécanismes engendrant une cétogenèse endothéliale.

Méthode / *Methods:* Objectif 1 A l'aide des expériences de métabolomique et transcriptomique unicellulaire, nous explorerons le profil des patients diabétiques atteints de RP et l'expression génique des enzymes impliquées dans la cétogenèse dans la rétine de souris. Objectif 2 Grâce au système Cre/Lox (Hmgclfl/fl; Tie2-Cre), nous avons généré des souris transgéniques conditionnelles pour supprimer Hmgcl dans les vaisseaux. Nous étudierons l'impact de la cétogenèse in situ en utilisant un modèle murin de rétinopathie induite par l'oxygène (OIR). Les souris sont exposées à 75% d'oxygène du 7ème jour post-natal (P7) à P12 provoquant une vaso-oblitération puis retournées à l'air ambiant pour induire une néovascularisation (NV) jusqu'à P17. Objectif 3 Des CE microvasculaires rétiniennes humaines (HRMEC) seront cultivées en hypoxie et en carence nutritionnelle, et l'expression de l'HMGCL par qPCR et Western blot, ainsi que la synthèse des corps cétoniques (test colorimétrique), seront mesurées.

Résultats / *Results:* Les métabolites cétoniques étaient augmentés dans le vitré des patients par rapport aux contrôles. L'expression des gènes du métabolisme des cétones était dérégulée dans l'endothélium en OIR. La privation de nourriture des CE pendant 12h augmente significativement (p<0,01) l'expression de l'HMGCL. La perte conditionnelle de Hmgcl dans les CE de la rétine réduit significativement (p<0,01) la néovascularisation pathologique par rapport aux contrôles, mais n'affecte pas la zone avasculaire.

Conclusion (s): La cétogenèse in situ dans les rétines des souris mises en OIR semble jouer un rôle important dans le métabolisme de ce phénomène angiogénique pathologique. Nous observons une diminution de la NV pathologique dans la rétine en cas de délétion de Hmgcl dans l'endothélium vasculaire et une augmentation de l'expression de HMGCL en cas de carence nutritionnelle. La découverte de la cétogenèse in situ est une avancée significative qui nous permettra de mieux comprendre l'impact du métabolisme énergétique de l'endothélium vasculaire associé aux rétinopathies proliférantes. En fonction des découvertes de ce projet, un rôle bénéfique potentiel de l'intervention diététique ou d'un traitement pharmacologique régulant la production de corps cétoniques pourrait aider à prévenir le développement de rétinopathies proliférantes.

12 - 3D Printed Tactile Maps to Improve Spatial Learning of Blind Individuals

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But / *Background*: For individuals with visual impairments, tactile maps are useful tools to stay oriented in new environments as they offer essential spatial information through touch. However, tactile maps are rarely available outside of rehabilitation services and highly differ in their production and presentation, thus delaying spatial learning. 3D printing has the potential to provide standardized tactile maps by taking advantage of computer-aided design to convey a wider range of spatial information. We investigated the use of 3D printed tactile maps to assist individuals with total blindness in generating cognitive maps of mazes. Our goal is to determine if 3D printing has an advantage over traditional production methods (i.e. swell paper) in order to promote its implementation in rehabilitation services.

Méthode / *Methods:* Participants with early (EB) and late (LB) onset blindness (n=24) were tasked to learn the layouts of tactile mazes containing different items (symbols and points of interest, or POIs) and varying in terms of production method (swell paper vs 3D printing) and complexity (simple vs complex mazes). After a limited period of tactile exploration, participants were asked to recall all POIs and formulate routes between them. All participants were given eight mazes.

Résultats / *Results:* No differences in recalling abilities between 2D and 3D mazes were observed. While LB participants performed equally well in the route condition when presented with 2D and 3D mazes, EB manifested stronger cognitive maps (more accurate routes) with 3D mazes (simple=69.77%, complex=63.31%) than with 2D mazes (simple=53.71%, complex=47.4%).

Conclusion (s): 3D printed tactile maps have the potential to improve spatial learning of people with visual impairments and to promote independent travel in unfamiliar environments, especially for those with little to no visual experience. However, the effect of 3D printing on navigation within a real environment remains to be tested.

13 - Pten Regulates the Development of Starburst Amacrine Cell Dendrites

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But / *Background*: Characteristic cell morphologies, which are crucial for synaptic formation and information processing in the central nervous system, require tightly regulated growth during development. Our goal is to investigate the role growth signaling pathways play in determining the adoption of cell-type specific morphologies. As the primary negative regulator of the PI3K-Akt-mTOR pathway, Phosphatase and tensin homolog (Pten) constrains growth during development. Mutations in Pten have been implicated in several neurodevelopmental disorders. However, few studies have examined how Pten regulates the development of highly stereotyped neurons whose form critically underlie their function. The mammalian retina is an excellent model to address this question as many different amacrine cell (AC) subtypes must adopt unique dendritic morphologies in the Inner Plexiform Layer (IPL) to produce the full dynamic range of visual processing within the retina. Specifically, Starburst Amacrine Cells (SACs) are the primary inhibitory neuron involved in generating retinal direction-selectivity, and their highly conserved radially symmetric dendritic morphology serves a critical role in this computation.

Méthode / *Methods:* We utilize a genetic approach via the Cre-Lox system to delete Pten in the retina exclusively in SACs. Specifically, we employ a ChAT Cre mouse line combined with a Pten flox allele. We intravitreally inject mice at P2 with a FLEX-tdTomato AAV to sparsely label SACs. We then perform immunohistochemistry to visualize sparsely labeled SACs and determine the effect loss of Pten has on their morphology. Images are then analyzed in Imaris for quantification.

Résultats / *Results:* We imaged the entire SAC population, as well as individual SACs at P21 and P28 to determine whether conditionally deleting Pten affected developmental processes such as specification, migration, and dendrite development. SACs showed no changes in cell density or mosaic spacing, indicating no clear defects in specification or migration. This was an important control to confirm our mutation does not affect developmental processes prior to dendrite formation. Sparsely labeled SACs lacking Pten showed dramatic increases in branching, but no change in their total dendritic field area. This suggests that Pten plays a large role in regulating dendritic branching during development, but other pathways in the cell are responsible for controlling SAC dendritic field area.

Conclusion (s): Our current findings suggest that Pten regulates SAC dendritic branching, but not dendritic field area, cell autonomously during development. There are still open questions as to whether Pten plays a role in branch maintenance, and whether its regulation is through its canonical activity in the PI3K pathway.

14 - The role of neuron-glia communication in retinal maturation

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But / *Background*: Intrinsically photosensitive retinal ganglion cells (ipRGCs) are light-responsive cells that transduce environmental light cues into nerve signals controlling the sleep-wake cycle and pupillary light reflex. In addition to these roles during adulthood, recent work has shown that ipRGCs modulate several key steps of retinal development and maturation, including photoreceptor lamination and the propagation of spontaneous waves of activity across the retina, which are essential to refine retina-brain connections. Although these developmental roles of ipRGCs are well established, how exactly this is achieved remains unclear. We hypothesized that cell-cell signaling may be involved to modulate ipRGC function.

Méthode / *Methods:* Using a trans-synaptic rabies viral vectors, we traced pre-synaptic partners of ipRGCs during the first two postnatal weeks in mice. After expression of Cre-inducible tetanus toxin in mice, we stained for various proteins associated with retinal cell types, to determine if there were changes in number, morphology or localization and also carried out circadian photoentrainment assays.

Résultats / *Results:* We found a large number of glial cells labelled by rabies tracer, indicating possible associations between glial cells and ipRGCs during the first two weeks of life in mice. In addition, after silencing retinal glial cells during fist two postnatal weeks we found defects in cone lamination and circadian photoentrainment, taking much longer to adapt their sleep-wake cycle in response to changes in light. Further studies will seek to determine if this silencing will leads to a disruption in electrical signaling within the retina, as well as of retina-brain connections.

Conclusion (s): This work suggests for the first time that neuron-glia signaling through classical chemical synapses plays a role in retinal maturation and in the function and/or development of the circadian system. Furthermore, as the circadian system is associated with many diseases, both as a risk and aggravating factor, understanding the development of this system is of importance.

15 - Mast cell activation contributes to experimental choroidal neovascularization

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But / *Background*: Accumulation and degranulation of mast cells has been reported in the compromised choroid of patients with wet age-related macular degeneration (AMD). Nevertheless, the precise role of mast cells in the pathogenesis of wet AMD remains largely unknown. The purpose of this study is to determine the role of mast cells in pathological CNV.

Méthode / *Methods:* Choroidal CNV was induced using laser photocoagulation. Mast cell infiltration was assessed by avidin and tryptase staining. CNV area was determined using lectin staining on RPE/choroid flat mounts. Gene expression patterns of RPE/choroid complex was determine by high-throughput RNA-sequencing The angiogenic effect of mast cells was examined using mast cell-deficient Kitwsh/wsh mice and a mast cell stabilizer, ketotifen fumarate.

Résultats / *Results:* Avidin- and tryptase-positive mast cells were found at the injury site three days post-laser burn. RNA-seq data on RPE/choroid complex at this timepoint revealed an enrichment in genes involved in extracellular matrix organization and integrin pathways, suggesting a potential involvement of choroidal mast cells in this process. CNV was attenuated in ketotifen fumarate-treated mice and in mast cell-deficient Kitwsh/wsh mice. Likewise, inhibition of tryptase, the main mast cell-derived protease, using nafamostate fumarate was effective in decreasing the CNV area. Tryptase and conditioned media from activated peritoneal mast cells exerted proangiogenic effects ex vivo on choroidal vascular sprouting, and in vitro on choroidal endothelial migration and tube formation.

Conclusion (s): This study shows that mast cells confer proangiogenic properties in the choroid and are a potential target for the treatment of CNV and the preservation of photoreceptor survival.

16 - Novel approaches to stimulate regeneration in the mammalian retina

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But / ***Background*:** Currently, there are no treatments available to cure retinal neurodegeneration, so that vision loss does not progress to legal blindness. In Canada alone, 1.5 million Canadians suffer from vision impairment, with a further 5.5 million having an eye disease that could lead to blindness (from the Canadian Survey on Disabilities 2017 report). In fish and frogs, adult Müller glia mediate natural retinal regeneration by responding to retinal insult and replacing any lost cell types. Unfortunately, for us and other mammals, mammalian Müller have lost this ability to self-heal, instead activating a cytotoxic process known as reactive gliosis. Our goal is to understand why mammalian Müller glia have lost this regenerative ability and subsequently activate them to regenerate lost neurons.

Méthode / ***Methods:*** We have identified the expression of the late-stage temporal identity factor Casz1, the mammalian ortholog of Drosophila castor, as an injury-specific and mammalian specific response of Müller glia. Previous work has demonstrated that Casz1 plays a role in chromatin remodelling in maintaining the inverted chromatin in rods and in recruiting the nucleosome remodeling and deacetylase (NuRD) complex in retinal progenitor cells. We performed experiments looking at chromatin remodelling events, proliferation assays and lineage tracing in wild-type Müller glia. We are in the process of generating a Müller glia specific knock-out (KO) of Casz1 and a Caz1 over-expression model to further decipher the role this transcription factor following injury.

Résultats / ***Results:*** We have identified that Casz1 is expressed at both the RNA and protein level in mammalian Müller glia following injury. We have confirmed that this expression is not limited to one type of injury but present even in the genetic ablation of photoreceptors such as in Rd1 mice. Being a transcription factor, Casz1 is found in the nucleus, and given its previous role in chromatin remodelling, we show a decrease in the number of chromocenters, decrease in laminar chromocenters and increase in total heterochromatin area in Casz1 expressing Müller glia. These data posits that Muller glia-specific expression of Casz1 results in chromatin remodelling events that abrogate the accessibility of regenerative cues such as proneural genes, and thus aborts the regenerative response in mammals.

Conclusion (s): Our work may be translated to targeting Müller glia for gene therapy which may allow us to combat all forms of retinal diseases mediated by loss of any retinal cell.

17 - Évoquer la vision par stimulation optogénétique du cortex visuel chez la souris

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But / *Background*: L'optogénétique semble être une alternative prometteuse à la stimulation électrique dans les approches de neuroprothèses visuelles corticales. Déjà révolutionnaire dans le domaine de la recherche en neuroscience, l'optogénétique permet une haute spécificité spatiale, temporelle et neuronale. Pour la première fois en 2019, deux études ont montré que l'optogénétique permettait d'évoquer une perception visuelle fonctionnelle chez la souris, en utilisant une stratégie de stimulation holographique à résolution neuronale. Bien que très efficace pour étudier les circuits neuronaux, cette stratégie n'est pas adaptée pour les neuroprothèses corticales par sa complexité et sa taille. C'est pourquoi l'objectif de ce projet est d'explorer la stimulation optogénétique de patrons à large champ plus adaptée aux neuroprothèses, dans le but d'évoquer une vision fonctionnelle chez la souris.

Méthode / *Methods:* Dans le but de vérifier si cette stratégie de stimulation permet d'activer le réseau cortical de la même manière que la vision naturelle, nous allons présenter à des souris fixées et éveillées les stimuli utilisés pour la cartographie rétinotopique des aires visuelles et comparer les cartes obtenues lors d'une stimulation naturelle via un écran et artificielle par optogénétique. Ces souris exprimeront dans leurs neurones le senseur jrGECO1a pour mesurer l'activité neuronale par imagerie calcique et le canal ionique photosensible ChR2 pour l'optogénétique, et seront implantées avec une barre de tête et une chambre d'imagerie chronique couvrant l'ensemble du cortex dorsal incluant tout le cortex visuel. Après habituation, les souris seront fixées sur un système qui combine l'imagerie calcique à large champ et la stimulation optogénétique avec une matrice de micromiroirs permettant d'envoyer sur la surface du cortex un laser de forme voulue.

Résultats / *Results:* Sur chaque souris, nous avons obtenu une cartographie des aires visuelles. Les cartes de représentation du champ vertical et horizontal ont été extraites pour générer des patrons de photostimulation balayant V1, dans chacun des axes verticaux et horizontaux. Ces patrons de photostimulation ont ensuite été envoyés sur V1 et l'activité calcique évoquée a été mesurée dans tout le cortex visuel. L'activité calcique était diffuse et ne permettait pas de conclure. La cause principale était le faible signal calcique de nos souris.

Conclusion (s): Ce projet va explorer les bases de l'utilisation de la stimulation optogénétique très utilisée en neurosciences en vue d'une nouvelle génération de neuroprothèses corticales visuelles. Il permettra d'améliorer nos connaissances sur l'utilisation de cette nouvelle technologie avec pour objectif long terme de restaurer une vision fonctionnelle chez les personnes aveugles, améliorant ainsi leur autonomie et leur fournissant une meilleure inclusion dans la société.

18 - Insulin promotes RGC dendrite regeneration through ribosomal protein S6 kinase activation leading to restoration of neuronal function in glaucoma

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But / *Background*: We previously demonstrated that insulin promotes RGC dendrite regeneration through activation of the mTOR pathway. However, the precise mechanisms of insulin-mediated regeneration and the effect of insulin on vision restoration are not well understood. Here, we asked: 1) What are the mTOR downstream effectors responsible for insulin-induced dendritic regrowth? 2) Does insulin restore RGC function and visual responses in glaucoma?

Méthode / *Methods:* Ocular hypertension (OHT) was induced by injection of magnetic microbeads in Thy1-YFP mice. Daily insulin or saline eye drops started at 2-weeks after OHT induction, when there is marked dendritic retraction, and dendrites were imaged and reconstructed 1 or 4 weeks later. The role of the mTORC1 downstream effectors, S6K and 4EBP1, was assessed by loss of function using targeted siRNAs. RGC survival and function were evaluated using complementary methods: i) quantification of RBPMS-positive neurons, ii) single-RGC calcium dynamics using two-photon microscopy live imaging in transgenic mice carrying the calcium indicator GCaMP6f, and iii) optomotor reflex assays.

Résultats / *Results:* Insulin promoted a substantial increase in RGC dendritic length and complexity in glaucomatous eyes (n=6 mice/group, ANOVA, $p<0.001$). siRNA-based knockdown of S6K impaired insulin-mediated RGC dendrite regeneration, while 4EBP1 silencing had no effect. Intriguingly, S6K increased mTORC2 activity through phosphorylation of mSIN1 enhancing RGC dendrite regeneration. Insulin promoted robust RGC survival at 3 and 6 weeks of OHT induction relative to saline (OHT-3wks, insulin: 2057±34 RGC/mm2, vehicle: 1679±66 RGC/mm2, N=3-6 mice/group, ANOVA, $p<0.001$). Importantly, insulin restored light-evoked RGC calcium dynamics (n=6 mice/group, $p<0.01$) and improved visual acuity (N=5-8 mice/group, ANOVA, $p<0.01$) in glaucoma.

Conclusion (s): Our data show that S6K is a key signaling component required for insulin-mediated RGC dendrite regeneration, an effect that is enhanced by cross-talk with mTORC2 through mSIN1 activation. Importantly, insulin prevents RGC loss while restoring light-evoked responses and visual acuity. These findings support a critical role for insulin as a pro-regenerative therapy and identify downstream targets to restore RGC connectivity and function in glaucoma

Source de financement / *Funding:* NIH 1R01EY030838-01 (ADP), Canada Research Chair Tier 1 (ADP), Canadian Institutes of Health Research Postdoctoral Fellowship (YS).

19 - Cellular signals corresponding to structural alterations to single retinal ganglion cells in glaucoma with in vivo imaging

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But / *Background*: Glaucoma is an age-related eye disease that is characterized by the progressive degeneration of retinal ganglion cells (RGCs) leading to visual field loss and irreversible blindness. An interconnected network of numerous cell death signals, pathways and mechanisms cause structural alterations to RGCs leading to their degeneration and death. The aim of this research is to detect these alterations non-invasively by in vivo imaging. Furthermore, co-localising the in vivo imaging signatures to a specific immunohistochemistry (IHC) study of the primary cell death markers may be a more sensitive indicator for death signals in early glaucoma.

Méthode / *Methods:* Experimental glaucoma (EG) will be induced in adult and old mice with a novel hydrogel model which results in a constant and sustained elevation of intraocular pressure (IOP) leading to structural RGC loss. Unlike other EG models, this approach leaves the optical media clear allowing repeated in vivo imaging. In addition, using the Thy1-yellow florescence protein (YFP+) transgenic mouse strain will allow visualisation of the entire dendritic arbour, as it enables YFP to be expressed in only 0.2% of RGCs. After performing baseline in vivo imaging, the hydrogel model of EG will be induced in one eye and imaging will be repeated in 3 sets of Thy1-YFP-H mice survived to 14 days (with imaging at days 5, 10 and 14), 28 days (14, 21 and 28 days), and 56 days (28, 32, and 56 days). Following imaging, each imaged RGC at each time point will be submitted to Sholl analysis to derive indices of dendritic morphology. In addition, the retinas will be processed for IHC of the different cell death markers of the most important apoptotic pathways (MAPK, Bcl-2 family, Caspase family, etc.) as well as apoptotic assays for cytochrome-c release, Annexin V, and TUNEL. Changes in Sholl analysis parameters will be related to IHC analyses to see if they correlate to steps in cellular events during RGC degeneration. Furthermore, determination of how age and IOP alters susceptibility to these changes will be carried out.

Résultats / *Results:* I will gather in vivo imaging of visible structural alterations of single RGCs in Thy1-YFP+ mice with EG at multiple specific time points. Over time, I expect to see pruning of the RGC dendrites, soma shrinkage and synapse loss. I envisage the structural alterations will vary in both timing and magnitude depending on the subtype of RGC, contribution of other cell types and pathways, spatial location, severity of insults to the specific RGC, and more. This asynchronous degeneration of RGC generates an imprecise and highly challenging observation of the earliest cellular events in glaucoma. I am hoping to tackle this task by carrying out an in-depth IHC study of the different cell death markers of the most important apoptotic pathways, and monitor for cytochrome-c release, loss of membrane potential and DNA fragmentation, at the set time points. By co-localising the IHC study with the in vivo imaging, I hope to find a correlation that will enable a better understanding of the cellular signals governing early glaucoma.

Conclusion (s): If the proposed research is successful, it will give an accurate position of the activation of the apoptotic players and mechanisms, allow visualization of the detrimental effects on RGCs in vivo in an EG model, and moreover enable a therapeutic window to potential rescue RGCs in glaucoma.

20 - The role of the dorsal raphe in visually guided behavior

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But / *Background*: The visual perceptual process begins one synapse from the eye, in the primary visual thalamus (LGN) - the sole link between eye and cortex. Intriguingly, 90% of synaptic inputs to the LGN do not originate from the eye - most arise from brain regions encoding internal states. A major source of such input originates from the dorsal raphe (DR), a critical center for reward and satiety, suggesting that DR-LGN feedback may modulate responses to rewarding visual stimuli. However, the function, behavioral significance, and wiring of DR-LGN projections is uncharacterized. We aim to define how these feedback projections shape the visual perceptual process in awake and behaving animals.

Méthode / *Methods:* To learn more, we built several head-fixed virtual reality arenas where mice are presented with checkerboard noise from which a grating stimulus emerges: grating detection results in a juice reward. While animals perform this behavioral task, we collect fiber-photometric recordings from mice whose DR neurons express genetically encoded calcium indicators (gcamp6f) to search for neural correlates. To test the behavioral significance of these neural correlates we disrupt DR signals using optogenetic tools.

Résultats / *Results:* Mice learn to detect stimuli of varying saliency according to classical psychometric relationships. Our results show that DR activity is linked to both rewarding stimuli and the onset of rewards. Furthermore, DR activity profiles preceding stimulus presentation can enhance behavioral performance and track mouse attentional states. Preliminary results show that disrupting these activity profiles optogenetically decrease behavioral performance and reduce attention effects.

Conclusion (s): We show that DR responses encode both visual performance and attentional states in awake and behaving animals. These studies are the first to define how DR-LGN feedback regulates visual behavior.

21 - Morphology and Characteristics of MafB+ Retinal Ganglion Cells and Amacrine Cells

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But / *Background*: The mouse retina is a prime model for investigating the mechanisms that coordinate development and morphogenesis of diverse cell types. Early in development within the neural retina, progenitor cells give rise to fate-restricted cells that later segregate to the major 5 classes of neurons. Each class of neurons can be separated into subtypes, which can be defined by their morphology and molecular properties. However, how fate-restricted cells give rise to various subtypes is still unknown. The expression of transcription factors is instrumental in specifying the identity of retinal neurons and individual cell subtypes. Dr. Kevin Wright's lab at Oregon Health & Science University has sought to identify transcription factors that are involved in the development of AC and RGC subtypes by mining high-throughput single-cell RNA sequencing (scRNA-seq) databases. Dr. Wright identified a candidate transcription factor, MafB, with selective expression in a single AC subtype and 4 RGC subtypes in post development stages. To analyze MafB expression patterns, my preliminary analysis of mice at postnatal ages confirmed restricted expression of MafB in a subpopulation of ACs and RGCs. Surprisingly, I found that MafB labels all ACs and RGCs during embryonic development, which suggests that MafB has two waves of expression; first in postmitotic AC and RGC precursors and then sustained expression in selective subtypes. These results suggest that MafB is expressed in precursor cells and is required for the development of select AC and of RGCs subtypes and inspire the following question: What role does MafB play in determining and generating neuronal subtypes of retinal cells during development?

Méthode / *Methods:* I will be using a MafB-mcherry-cre mouse line, immunohistochemistry, and adeno-associated viruses to better understand the developmental timeline, morphology and stratification pattern of MafB+ AC and RGC subtypes, and if MafB is required for the development of these cells.

Résultats / *Results:* I anticipate that, in WT mice, the expression pattern of MafB will begin at E13. In the MafB-mCherry-Cre line, the expression of mCherry will be high during embryonic development where precursor cells are abundant and will experience a decline as AC and RGC adopt particular cell fates. I also anticipate that there will be a higher colabelling of GFP+/MafB+ cells at E13 and the colabeling will decline following AC and RGC specification. I anticipate that ACs and RGCs will not be maintained due to MafB being expressed in all AC and RGC precursors. I anticipate that the stratification and morphology of the 1 subtype of AC and 4 subtypes of RGCs will be distinct from one another. These unique profiles will aid in determining the morphological, physiological, and molecular properties of these neuronal subtypes.

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Conclusion (s): Classifying the morphology and stratification pattern of novel AC and RGC subtypes can be a valuable resource by providing a deeper understanding of the role MafB+ cells play in the visual system.

22 - THE ROLE OF CADHERIN 4 IN THE ASSEMBLY OF OFF RETINAL CIRCUITS

Aline Giselle Rangel Olguin[1], Pierre-Luc Rochon[1], Catherine Theriault[1], Arjun Krishnaswamy[1]

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But / *Background*: Neurons grow axons and dendrites into target regions where they face hundreds of proximate potential synaptic partners but connect with only a select few. This selectivity is critical for wiring patterns and circuit computations but how it arises is unclear. In the retina, a multilayered neuropil called the inner plexiform layer (IPL) organizes the processes of ~30 types of retinal ganglion cells (RGCs) to receive input from a subset of ~100 types of interneurons. Recent work suggests that such layered circuits assemble according to adhesive interactions among RGC and interneuron processes. Members of the Cadherin superfamily (Cdhs) are thought to mediate these adhesive interactions and bring eventual partners within close physical proximity. We focus on Cdh4, also known as retina Cdh, an attractive candidate given its high expression in the retina.

Méthode / *Methods:* Mice in which Cdh4 is replaced by a Cre-recombinase estrogen receptor fusion were used to study Cdh4 expressing neurons in the retina. As heterozygotes, they are driving lines and as homozygotes they are knockouts. Cell morphology and cell-type identification were done by coupling Cdh4Cre retinas with Cre-dependent markers and staining with immunohistochemistry. To study the functional responses of Cdh4 neurons, retinas from Cdh4Cre mice expressing Cre-dependent GCaMP6f were stimulated with a battery of visual stimuli, and their responses were recorded using a two-photon microscope. Ectopic Cdh4 expression in retinal neurons was achieved using herpes simplex viruses injected in the subretinal space of neonatal mouse pups.

Résultats / *Results:* Cdh4 was found to be expressed by RGCs and amacrine cells. These Cdh4 positive neurons target IPL layers where neurons sensitive to light offset (OFF) localize their processes. Loss of Cdh4 leads these neurons to target inappropriately and growth processes to ectopic lamina. This morphological deficit correlated with loss of OFF-responding RGCs, an increase in ON-responsive RGCs, and loss in the strength of OFF synaptic inputs. To assess the causal role of Cdh4 targeting, ectopic expression of Cdh4 in other retinal neurons has been achieved and will be further studied to ask if these cells target OFF IPL lamina.

Conclusion (s): Taken together, these results indicate that Cdh4 is required for a subset of RGCs to target OFF lamina and develop visual responses. Understanding how Cdh4 directs layer specific growth of retinal neurons establishes a system in which we can test how layer- and synaptic targeting mechanisms interact during circuit development.

23 - The cell adhesion molecule Sdk1 shapes the assembly of a retinal circuit that detects visual orientation

Pierre-Luc Rochon[1], Catherine Theriault[1], Aline G. Rangel Olgin[1], Arjun Krishnaswamy[1]

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But / *Background*: In the mouse retina, nearly 50 different retinal ganglion cell (RGC) types sample the visual scene for distinct features such as color, contrast, object motion or orientation. This feature selectivity arises from the synapses between each RGC and specific subsets of amacrine (AC) and bipolar cell (BC) types. How the dendrites of these cells arborize and coalesce into functional circuits remains poorly understood. We examined the hypothesis that RGCs employ molecular recognition systems to meet this challenge. We focused on the recognition molecule sidekick 1 (Sdk1) in the mouse retina.

Méthode / *Methods:* We leveraged published RNA sequencing data and used a combination of calcium imaging, type-specific histological stains, and electrophysiological recordings to define a family of retinal circuits that expresses Sdk1. Using mouse genetics, we subsequently investigated the effects of removing Sdk1 on the function of these circuits.

Résultats / *Results:* We found that Sdk1 is expressed in five types of RGCs: the ONα sustained cell, the intrinsically photosensitive M2 cell, two ON direction selective cells and a novel ON-OFF orientation selective cell we term the S1-RGC. Through genetic and electrophysiological experiments, we showed that Sdk1 loss disrupts the function of the S1-RGC without significantly affecting the other Sdk1 cell types. This disruption is defined by a loss in the cell's excitatory and inhibitory drive as well as a reduction in its orientation selectivity. In conjunction with these functional deficits, we found that the S1-RGC lost dendritic complexity, having a smaller harbor and fewer branches. We postulate that the resilience of the remaining Sdk1 RGCs to the knockout phenotype may be explained by their expression of a related molecule called sidekick 2 (Sdk2). Consistent with this idea, we found elevated expression of Sdk2 in Sdk1 knockout animals by quantitative PCR.

Conclusion (s): Studies of cell adhesion molecules in circuit development have thus far been sporadic across the brain, but findings have increasingly converged on their importance in circuit formation. This study further provides evidence for this, demonstrating how Sdk1 loss selectively impairs a retinal circuit that detects visual orientation. The remaining Sdk1 cells are largely unaffected by this loss and their co-expression of Sdk2 offers a great avenue to explore how similar adhesive signals can interact in the developing brain.

24 - Time-course analysis of human trabecular meshwork single cell contraction after a 5-day dexamethasone treatment

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But / *Background*: Glucocorticoids, such as dexamethasone, induce pathological changes in the human trabecular meshwork (HTM) akin to fibrosis. We and others have shown that dexamethasone treatment increases the expression of fibrotic markers in primary HTM cells. However, there are currently no definitive studies showing a contractile phenotype in HTM cells after dexamethasone treatment, another important functional marker of fibrosis. Because cellular contraction is a dynamic process, it is important to quantify contractile force generation over time. Additionally, observed heterogeneity in primary HTM cell cultures call for single cell contraction measurements.

Méthode / *Methods:* Primary HTM cells were isolated from human corneoscleral donor tissue, expanded, and cultured for 5 days in media containing vehicle (0.05% v/v DMSO), or 100 nM dexamethasone. Primary HTM cell strains used in this study were validated by the upregulation of myocilin after dexamethasone treatment via qRT-PCR and IHC. Screening of fibrotic markers was achieved via IHC. Primary HTM cells were harvested, dissociated to single cells, and seeded into the wells of the fluorescently labeled elastomeric contractible surfaces (FLECS) assay for single cell contraction measurements. Collagen IV at various stiffnesses was used as the attachment substrate for the cells in the FLECS assay. Cells were maintained under a 5% CO2 atmosphere at 37°C throughout the entire data collection period. Data were collected every hour over a period of 10 hours using an Image Xpress microXL fluorescence microscope. Data were analyzed using a computational algorithm.

Résultats / *Results:* HTM cells in primary culture robustly upregulated myocilin after a 5-day 100 nM dexamethasone treatment, confirming their identity. In addition, dexamethasone treated HTM cells increased the expression of fibrotic markers such as α-SMA, F-actin, Fibronectin, Vimentin, & Col IV. The optimized single cell contractility assay, FLECS, was able to capture information of thousands of single cells at once over a period of 10 hours. Primary HTM cells displayed increased contractility in a time dependent manner & plateaued around 6-hrs post seeding regardless of the treatment. However, dexamethasone treated cells were clearly more contractile as evidenced by their higher mean contraction value when compared to the control. Equally interesting, HTM cells displayed a range of contractions previously unidentified by conventional contractile force measurement methods.

Conclusion (s): Here, we've shown that the glucocorticoid dexamethasone induces pathological changes in HTM cells which are reminiscent of fibrosis. More importantly, we've adapted and implemented a novel functional assay called FLECS for HTM single cell contraction measurements. The FLECS assay was able to capture information of thousands of single cells at once over a period of 10 hours. Primary HTM cells displayed increased contractility in a time dependent manner & plateaued around 6-hrs post seeding. Dexamethasone treated cells were clearly more contractile as evidenced by their higher mean contraction value when compared to control cells. Intriguingly, HTM cells displayed a range of contractions previously unidentified by conventional contractile force measurement methods. Future experiments aim to further characterize the contractility of HTM cells.

25 - Wound healing response of the alkali burnt cornea after treatment with novel anti-inflammatory drugs

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But / *Background*: There has been an increase in chemical injuries to the eye, during the pandemic, with the rise of usage of alkali-based cleansing agents. Despite immediate medical intervention with steroids and antibiotics, the cornea does not seem to recover its original state, with many patients developing complications such as corneal haze and vascularization. Our study aims to understand post-burn recovery and the ability of a novel drug to decrease corneal inflammation by targeting the cannabinoid 2 (CB2) receptor.

Méthode / *Methods:* Fifty mice were given corneal alkali burns in one eye with 0.25N NaOH. Ten animals were treated with the standard of care topical corticosteroid, Prednisolone, 10 animals for each of three doses of TA-A001 drug and 10 were given the drug vehicle only. The healing eyes were followed daily for 2 weeks with different tests. After 2 weeks, the mice were euthanized and corneas were processed for histopathology and immunohistochemistry to study their wound h ealing response as well as inflammation.

Résultats / *Results:* In acute corneal alkali burns, topical corticosteroids (e.g. Prednisolone) is used to decrease stromal inflammation even though there is evidence that steroids also inhibit epithelial healing, as the options are limited. TA-A001, unlike Prednisolone, promoted earlier wound closure as shown by a reduction in fluorescein staining of the epithelial-denuded surfaces. There was extracellular matrix remodeling of the stroma during recovery but the epithelium still showed recurrent erosion as previously reported for alkali burns. Macrophage markers such as F4-80, LYVE1 and CD63 had lower expression in samples treated with the new drug. Glaucoma after ocular burn has also been reported. Here, TA-A001 was able to lower intraocular pressure and may be effective for preventing glaucoma.

Conclusion (s): Our results suggest targeting the CB2 receptor does result in decreasing inflammation and a trend towards more rapid wound healing. In the future, drugs such as TA-A001 may be able to circumvent some of the issues such as glaucoma after burn. However, further studies on a larger group of mice and control, untreated corneas treated with the same compounds are needed to determine drug biocompatibility and cytotoxicity in normal corneas. Also, the mechanism of action and pathways involved will require further study.

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26 - A novel femtomolar hemodynamic modulation strategy reveals major microvascular defects in glaucoma at single-pericyte scale

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But / *Background*: Reduced blood flow and neurovascular deficits are recognized features of glaucoma, but the mechanisms underlying these alterations are poorly understood. Pericytes, the contractile cells that wrap around capillaries, regulate blood supply by modulating capillary diameter. Here, we developed a novel live imaging and femto-scale delivery system to study the role of single-pericyte hemodynamics in glaucoma.

Méthode / *Methods:* Ocular hypertension (OHT) was induced by intracameral injection of magnetic microbeads in NG2-DsRed mice, which allow visualization of retinal pericytes. Two-photon laser scanning microscopy (TPLSM) was combined with a femtomolar delivery system (FemtoJet Microinjector) to visualize and modulate single-pericyte longitudinal responses in living mice. A micromanipulator was used to place the microneedle adjacent to a pericyte-capillary pair, and vasomodulators (e.g. ET-1: endothelin-1, NO donors) were delivered at a femtomolar scale. Capillary diameter was measured by placing a linear probe perpendicular to the plane of the vessel, and blood flow was quantified by counting the number of red blood cells crossing a pre-fixed vessel location.

Résultats / *Results:* TPLSM adapted with a femto-microinjector provided high spatial-temporal resolution of single-pericyte-capillary responses without affecting neighboring vessels. Our data show decreased capillary diameter and blood flow at pericyte locations in glaucoma (sham: n=13 capillaries, OHT-2 wks: n=18 capillaries, N=5-7 mice/group, $p<0.01$). Femtomolar delivery of ET-1 in glaucomatous mice exacerbated the magnitude and duration of capillary constriction at pericyte locations and decreased blood flow relative to controls (vehicle: n=11 capillaries, ET-1: n=16 capillaries, N=3-5 mice/group, $p<0.001$). In contrast, NO donor administration rescued the ability of capillaries to dilate at pericyte locations enhancing blood flow despite OHT (vehicle: n=16 capillaries, NO donor: n=7 capillaries, N=3-5 mice/group, $p<0.01$), suggesting that microvascular defects in glaucoma are reversible.

Conclusion (s): We demonstrate the utility of combining TPLSM live longitudinal imaging and femtomolar delivery of vasoactive substances to study neurovascular defects caused by OHT. Our study identifies pericytes as critical regulators of capillary hemodynamics and unveils their potential as therapeutic targets to restore neurovascular function in glaucoma.

27 - The anti-uveal melanoma effect of miR-181a and combinational therapies

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But / *Background*: Somatic mutations in GNAQ/11 are oncogenic drivers in 85% of the uveal melanoma (UM). UM patients retain an approximately 50% risk of metastasis and die shortly after because of the lack of effective therapies for metastatic UM. The anti-cancer drug crizotinib has been shown to significantly reduce the development of distant metastases in a murine model of metastatic UM. Human microRNA-181a (miR-181a) is known to be involved in important cellular functions and is downregulated in both primary and high-risk UM and absent in metastatic UM. Here we hypothesize that miR-181a abrogates the dysregulated GPCR signaling in UM; miR-181a alone or in combination with crizotinib may be sufficient to inhibit metastatic UM.

Méthode / *Methods:* Human metastatic UM cells were transfected with miR-181a mimic, negative control or crizotinib and cell viability, migration ability, proliferation ability and apoptosis were measured. Western blot analysis was performed to find out whether miR-181a regulates GNAQ downstream events and interferes with the activated GPCR signaling in UM. GNAQ and Akt3 silencing as well as overexpression were also used to study the roles of GNAQ and Akt3 in anti-UM effects of miR-181a. Intratumoural injection of miR-181a was used to see its effect on UM tumor growth *in vivo*.

Résultats / *Results:* (a) miR-181a inhibited viability, migration and proliferation and increased apoptosis of UM cells; (b) miR-181a abrogates the dysregulated GPCR signaling in UM; (c) miR-181a suppressed GNAQ and Akt3 protein expression in UM cells. GNAQ and Akt3 siRNA mimics the anti-UM effect of miR-181a. GNAQ and Akt3 overexpression reversed the anti-UM effect of miR-181a; (d) Combinational use of miR-181a/crizotinib exhibited a complementary inhibitory effect on UM cell migration (e)miR-181a delayed the UM tumour growth in xenograft UM mouse model.

Conclusion (s): miR-181a exhibits strong anti-UM effect via targeting GNAQ and Akt3, and the combinational use of miR-181a/crizotinib exhibited a complementary inhibitory effect on UM cell migration.

28 - Designing Injectable Liquid Corneas for Patients at High Risk for Rejecting Corneal Transplantation: synthesis, characterization, in vitro biocompatibility study

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But / *Background*: Corneal perforations are emergency situations that require off-the shelf solutions to save the integrity of the eye. The Griffith Lab pioneered the use of bio-responsive materials to induce in situ tissue regeneration of the human cornea. Among them is an injectable Liquid Cornea comprising self-assembling collagen-like peptides (CLP) conjugated to a polyethylene glycol (PEG) backbone and fibrin glue that gels spontaneously within wounds. However, using fibrin glue for sealing necessitated use of a second syringe and an extra step that can be problematic in emergency situations. In addition, inflammation was not addressed by the formulation. My aim is to test the hypothesis that inflammation suppressing 2-methacryloyloxyethyl phosphorylcholine (MPC) can replace both the PEG backbone and fibrin glue. Here, I designed and synthesized novel tri-functional MPC-Acrylic acid (AA) co-polymers, S1AA and S3AA that will act as sealants modulate inflammation and attach to peptides such as CLP to promote regeneration.

Méthode / *Methods:* Linear (S1AA) and multi arms (S3AA) copolymers of MPC and AA were synthesized using RAFT polymerization. They were then characterized using proton nuclear magnetic resonance spectroscopy (1H NMR), differential scanning calorimeter (DSC), and Fourier-transform infrared spectroscopy (FTIR). To determine the biocompability, immortalized human corneal epithelial (HCE) cells were exposed to the polymers and evaluated using a Live/Dead Viability/Cytotoxicity Assay. Copolymers were then conjugated to CLP and mixed with DMTMM as cross linker to form hydrogels. This new formulation was also tested as an injectable liquid on excised pig corneas with surgical perforations to examine its efficacy to seal large perforations.

Résultats / *Results:* Characterization performed confirmed the successful synthesis of S1AA and S3AA polymers using RAFT. After 24 hours of exposure of human corneal epithelial cells to S1AA and S3AA polymer, more than 90% of cells were still alive, while exposure to monomeric MPC as a positive control resulted in cytotoxicity, decreasing cell viability to below 70%. Addition of AA increased the amounts of carbocyclic acid which consequently increased the amounts of crosslinking in hydrogel. Conjugation of both S1AA and S3AA to CLP form a hydrogel that remained stable up to 70 ^{o}C. When applied as a self-gelling sealant within a large perforation of 5 mm diameter at the epitelial surface tapering to 1.5 mm, bursting presssure tests showed that the both hydrogel can tolerate pressures up to almost 40 mm Hg.

Conclusion (s): MPC can be used to synthesize multifunctional polymers to form the basis for Liquid Cornea formulation that can be delivered in a single syringe for potential clinical use. These MPC-CLP polymers will be tested next in rodent models of córnea perforation and if successful, in a large animal model for future clinical translation.

29 - Restoration of mitochondrial axonal transport prevents neurodegeneration and rescues visual function in glaucoma

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But / *Background*: Mitochondria distribution in retinal ganglion cells (RGC) is crucial for energy homeostasis and neurotransmission. Here, we tested the hypotheses that: i) mitochondrial axonal transport deficits contribute to energetic imbalance and RGC damage in glaucoma, and ii) supplementation of the adaptor protein Disc1 (Disrupted in Schizophrenia 1) restores mitochondrial mobility, prevents energy decline, and rescues RGC function.

Méthode / *Methods:* Glaucoma was induced in the Thy1-CFP-MitoS mice. Disc1 levels in RGC were increased using a viral vector (AAV.Disc1). 2-photon microscopy was used to i) record mitochondrial movement in RGC axons followed by kymograph analysis, and ii) measure ATP levels using the sensor ATeam. Mitochondrial volume in single axons was quantified using Imaris software. RGC survival was quantified by immunostaining. RGC function was asses by positive scotopic threshold responses (pSTR) and the optomotor reflex assay for visual acuity.

Résultats / *Results:* In vivo, live imaging of mitochondrial axonal transport showed a reduction of anterograde transport in injured RGC. Transport deficits were accompanied by decreased mitochondrial volume in RGC axons, both in the retina and the optic nerve. AAV.Disc1 restored mitochondrial mobility and volume in damaged RGC axons. Remarkably, enhanced mitochondrial transport restored axonal ATP levels preventing energetic decline and promoting RGC survival. Furthermore, AAV.Disc1 preserved light-evoked pSTR responses and improved visual acuity.

Conclusion (s): In conclusion, disrupted anterograde mitochondrial transport along RGC axons leads to mitochondria depletion and energy decline. Disc1 supplementation improved mitochondrial anterograde transport, replenished axonal mitochondria, rescued energy homeostasis, and restored light-evoked responses and visual function in glaucoma.

30 - Light-evoked RGC calcium dynamics are altered in glaucoma: live imaging evidence of abnormal calcium clearance

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But / *Background*: The mechanisms underlying retinal ganglion cell (RGC) vulnerability and dysfunction in glaucoma are poorly understood. Here, we used two-photon laser scanning microscopy to investigate alterations in real-time light-evoked RGC calcium (Ca2+) responses during ocular hypertension (OHT) damage.

Méthode / *Methods:* Transgenic mice carrying the Ca2+ indicator GCaMP6f (Thy1.GCaMP6f) received an intracameral injection of magnetic microbeads to induce OHT. Two weeks following induction, prior to cell loss, retinae were two-photon imaged through the sclera of anesthetized mice or acutely dissected for ex vivo imaging. Next, ROIs were drawn on response movies using ImageJ or using suite2p to extract RGC signals and custom code (Rstudio/MATLAB) used to compute: i) rise time, ii) decay time, iii) amplitude, and iv) ON-OFF index, which indicates ON-OFF preference. For ex vivo recordings, computational methods (PCA/UMAP) were used to divide sham data into 7 functionally defined RGC types. Student's t-test or ANOVA methods were applied to detect significant differences (significance: $P<0.05$).

Résultats / *Results:* In vivo and ex vivo RGC Ca2+ transients were significantly altered and showed abnormalities consistent with a change in Ca2+ clearance. Specifically, trans-scleral imaging showed a several-fold increase in Ca2+ decay time in ON RGC (sham: 0.93 ± 0.09 sec, OHT: 3.53 ± 0.57 sec, N=7-8 mice/group, n=74-89 cells/group, $p<0.01$) and in OFF RGC (sham: 2.92± 0.42 sec, OHT: 6.60 ± 1.19 sec, N=4 mice/group, n=8-14 cells/group, $p<0.05$) leading to sustained Ca2+ accumulation. Data obtained with explant imaging were consistent and showed an increase in mean Ca2+ decay time for OHT RGC (sham: 0.97± 0.058 sec, OHT: 1.85± 0.197 sec, N>5 mice/group, n>400 RGC/group, $p<0.05$). We also observed a decrease in the proportion of OFF-RGCs as seen by a shift in the mean of the ON-OFF index (Sham: -0.05 ± .015 ON-OFF index, OHT: +0.03 ± .012 ON-OFF index).

Conclusion (s): Our study reveals major alterations in light-evoked RGC Ca2+ dynamics under OHT conditions, notably abnormal Ca2+ clearance. These findings suggest significant defects in the mechanisms that regulate Ca2+ efflux which can lead to RGC dysfunction and increased vulnerability in glaucoma.

31 - Asymmetries in connections between wide-Field amacrine cells and starburst amacrine cells in the mouse dorsal retina

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But / ***Background*:** It is often believed that the neural circuitry underlying vision is adapted to efficiently encode natural scenes, starting in the retina itself. One particular region of the retina where pronounced specializations have been observed in various species is the 'visual streak', a near-central part of the retina on which the horizon falls. Here, stark asymmetries in the luminance, size, and contrast gradients are likely to be experienced, due to asymmetries in the statistics of natural scenes (i.e., ground/sky statistics). Interestingly, recent studies carried out in mouse retina demonstrate that output ganglion cells located in the visual streak region just dorsal to the optic disk have asymmetric inhibitory receptive fields that are proposed to enable the efficient coding of objects near the horizon. Here we ask whether similar adaptations exist in the population of GABAergic/cholinergic starburst amacrine cells (SACs), which lie in the heart of the direction-selective circuit in the retina; and if so, what are the circuit mechanisms that underlie these specializations.

Méthode / ***Methods:*** In a whole-mount transgenic mouse retinal preparation, we recorded inhibitory post-synaptic currents (IPSCs) in genetically labeled SACs. The SAC's inhibitory receptive fields were mapped using a series of bars (7 orientations) that were flashed across the retina at pseudo-random positions. Receptive fields were then estimated based on the filtered back-projection (FBP) method. To test whether spiking wide-field amacrine cells (WACs) contribute to distant inhibition we applied a NaV channel blocker, tetrodotoxin (TTX). Two-photon Ca2+ imaging was used to measure light-evoked synaptic activity in SAC dendrites.

Résultats / ***Results:*** We observed large IPSCs in responses to light stimuli that were placed 700-1200 mm away from the center of the SAC's excitatory receptive field. Distant lateral inhibition was abolished by the bath application of TTX, indicating that it is mediated via spiking WACs. Importantly, the angular distribution of distant lateral inhibition to SACs was highly asymmetric. Inhibition tended to be most effectively evoked from the ventral retina, which would be a region that detects the bright sky. Surprisingly, mapping the inhibitory receptive field using the FBP method revealed that the lateral inhibition was offset by as much as 1200 µm. Notably, stimulation of the near-surrounding region (100-300 um away from the SAC soma) evoked little or no response, indicating that the WAC inputs may be sparse and rely on single WACs. We also observed that inhibition to neighboring SACs was not precisely aligned, indicating that inhibition may arise from distinct WAC sources.

Conclusion (s): SACs located in the dorsal mouse retina have asymmetric receptive field structures. These asymmetries arise from the asymmetric wiring of WAC processes to SACs. Thus, the adaptations for efficiently encoding natural scenes appear to be 'hard-wired' in the retina.