

Alliance For Eye
And Vision Research

AEVR

Educating about the Value of Vision Research

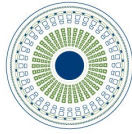
Seventh Annual Emerging Vision Scientists

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Research to Prevent Blindness



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FEDERAL FUNDING FOR VISION RESEARCH IS VITAL

The National Eye Institute (NEI) within the National Institutes of Health (NIH) is responsible for funding sight-saving and sight-restoring vision research. Congressional action in Fiscal Years (FY) 2016 to 2021 has increased NEI's enacted budget to \$835.7 million—19 percent more than its pre-sequester FY2012 funding level of \$702 million—meaning that over nine fiscal years it has averaged a 2.1 percent increase as compared to the average biomedical inflation rate of 2.7 percent, resulting in a loss of purchasing power. In fact, NEI's FY2021 purchasing power is less than that in FY2012.

The annual cost of vision disorders in the U.S. is \$177 billion and is projected to grow to \$373 billion by year 2050—or \$717 billion in inflation-adjusted dollars. The direct medical costs of vision disorders are the fifth highest—only less than heart disease, cancers, emotional disorders, and pulmonary conditions. Adequately funding vision research is vital since:

- NEI's \$835.7 million budget is less than 0.5 percent of the \$177 billion annual cost of vision disorders. The U.S. spends only \$2.53 per-person, per-year for vision research, while the cost of treating low vision and blindness is \$6,680 per-person, per-year.
- The first wave of the 78 million Baby Boomers—also called the “Silver Tsunami”—started turning age 65 in 2010. Each day, for the next 18 years afterward, 10,000 Americans will turn age 65 and be at greatest risk for age-related eye disease.
- Vision loss can be a co-morbid condition of chronic diseases, such as diabetes, which is at epidemic levels due to the increased incidence of obesity.
- The African American and Hispanic communities, which increasingly account for a larger share of the population, experience a disproportionately greater risk of eye disease.
- A 2016 *JAMA Ophthalmology* article reported that a majority of Americans across racial and ethnic lines describe losing vision as potentially having the greatest impact on their day-to-day life, more so than loss of limb, memory, hearing, and speech.
- Vision research is a cost-effective investment since it leads to therapies that can delay or avoid vision loss and associated healthcare expenditures. Vision loss is associated with increased depression and accelerated mortality.
- The U.S. is the world leader in vision research. Without adequate funding, the NEI may not be able to pursue its primary “audacious goal” of regenerating neurons and neural connections in the eye and visual system, thereby restoring vision and returning individuals to productive, independent, and quality lives.
- The U.S. is also a leader in scientific training. Not adequately funding the NEI threatens the development of the next generation of vision scientists.

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Alliance for Eye and Vision Research (AEVR) is a 501(c)3 non-profit foundation which serves as the privately funded “Friends of the National Eye Institute (NEI)” and is dedicated to education about the importance of federal funding for eye and vision research. In 2021, AEVR launched the *Research Saving Sight, Restoring Vision Initiative* to provide sustained education about the impact of eye disease and vision impairment and the enormous strides that past federally-funded vision research has made in terms of new diagnostics and therapies to treat vision conditions, and the potential these new approaches hold for even more dramatic scientific and quality-of-life advances. Visit its Web site at www.eyereseach.org

Research to Prevent Blindness (RPB) is the leading nonprofit organization supporting eye research directed at the prevention, treatment or eradication of all diseases that damage and destroy sight. As part of this purview, RPB also supports efforts to grow and sustain a robust and diverse vision research community. Since it was founded in 1960 by Dr. Jules Stein, RPB has awarded more than \$383 million in research grants to the most talented vision scientists at the nation’s leading medical schools. As a result, RPB has been associated with nearly every major breakthrough in the understanding and treatment of vision loss in the past 61 years. Learn more at www.rpbusa.org.



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Focus of Vision Research and its Economic/Societal Impact:

My work focuses on glaucoma pathogenesis. Glaucoma is the world's leading cause of irreversible blindness, affecting more than 70 million individuals globally and 4 million individuals in the United States. The annual economic burden caused by glaucoma is \$5.8 billion and is expected to double by 2050. Despite its increasing impact on the quality of life and economy, glaucoma pathogenesis remains largely unknown. Current therapies are focused on lowering the eye pressure. However, eye pressure is the only clinically modifiable risk factor, and glaucoma may continue to progress in some patients after controlling eye pressure. Therefore, a clearer picture of other major factors involved in glaucoma will lead to more effective treatments beyond controlling eye pressure, thereby benefiting millions of people and reducing the economic burdens incurred by individuals and the U.S.

Specific Project Described in the Video:

A study involving more than 6,700 people demonstrated that glaucoma patients have a higher prevalence of sleep disorders. While such connection implies common mechanisms shared by glaucoma and sleep disorders, it is not yet clear whether and how they are directly connected. New knowledge addressing this connection is critical because it will deepen our understanding of glaucoma and may eventually lead to therapeutic advancements.

In the 5-minute personal research video, I will discuss how we attempted to understand the mechanisms of brain degeneration in glaucoma that may lead to sleep disorders. In particular, we focused on a major sleep-inducing system in human subcortical structures called the ventrolateral preoptic nucleus (VLPO), because VLPO receives input from intrinsically photosensitive retinal ganglion cells (ipRGCs) that are shown to be impaired in glaucoma. Considering such an anatomical link between ipRGCs and VLPO, it is likely that the function of VLPO is compromised as well in glaucoma. Therefore, we investigated whether the sleep-regulating subcortical systems involving VLPO and their inhibitory projections to the cortex are impaired in glaucoma. Our results show that glaucoma patients present functional alterations in the sleep-regulating subcortical systems involving VLPO and their inhibitory connections to the cortex. This finding suggests that glaucomatous pathogenesis involves changes in the sleep-regulating systems and that such changes may underlie high prevalence of sleep disorders in glaucoma.



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Focus of Vision Research and its Economic/Societal Impact:

My group focuses on Inherited Retinal Diseases (IRD). These are a group of diseases that lead to blindness due to a genetic mutation. The economic burden associated with IRD is up to \$31.8 billion in the United States in 2019. This includes costs associated with the health system and productivity, as well as loss of well-being and deadweight loss (loss of economic efficiency). Patients with IRD are 28.8 percent less likely to be employed than the normal-sighted population, which leads to society-wide efficiency losses from reduced taxation revenue due to decreased workforce participation and higher government expenditures. Thus, our research serves these patients by determining the genetic basis for their IRD, researching how the genetic mutations cause retinal degeneration, and by seeking ways to prevent or reverse blindness.

Specific Project Described in the Video:

The discipline of genomic medicine has been rapidly progressing since the sequencing of the human genome. There have been more than 500 mutations linked to eye disease. Since the FDA approval of gene therapy to treat RPE65-related retinal degeneration, there has been a rapid upsurge in the planning and initiation of clinical trials using gene-targeted therapeutics to treat IRD. However, our understanding of disease progression and the cellular or genetic mechanisms underpinning IRD remains underdeveloped. To address these shortcomings, our laboratory studies genetic variations in IRD, clinical outcomes in disease progression, clinical diversity in IRD, and the molecular mechanisms that lead to retinal degeneration. We use in-depth clinical assessments as well as laboratory assays to determine if genetic variants are pathogenic. Additionally, we use patient stem cells and develop their “retinas-in-a-dish” to evaluate the molecular consequences of the genetic mutations that cause IRD. By understanding how genetic mutations cause blindness, we can start to develop treatments against these mutations or the detrimental cellular effects resulting from the mutations.



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Focus of Vision Research and its Economic/Societal Impact:

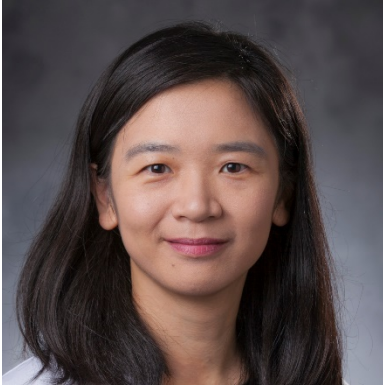
My research focuses on vision loss from diabetic retinal diseases. The global prevalence of diabetes has more than quadrupled over the last four decades. An estimated 34 million (about 1 in 10) Americans currently have diabetes and 88 million (about 1 in 3) have pre-diabetes. Diabetic retinopathy (DR), a complication of diabetes, is the leading cause of vision loss among working-age adults in the United States. It costs the country an estimated \$500 million annually and its prevalence is estimated to almost double from 7.6 million in 2010 to 14.6 million in 2050. Over the past few decades, researchers have identified effective treatments that can prevent vision loss. However, two problems persist which continue to make DR a leading cause of vision loss: poor compliance with screening eye exams; and that about a third of our patients continue to have poor vision despite receiving standard-of-care treatments.

Specific Project Described in the Video:

My research program focuses on addressing the two problems mentioned above by: studying implementation of point-of-care artificial intelligence (AI) based techniques to improve access to screening for diabetic retinopathy; and identifying novel pathways of vision loss in diabetes by leveraging advances in retinal imaging, AI-based tools, and genetic data.

AI-based screening for DR: Point-of-care screening can significantly improve the number of people who get screened and diagnosed in a timely fashion. Our recent study showed that implementation of AI based detection of DR improved compliance with screening exams from 46 percent to over 90 percent. Our ongoing work is focused on cost-effectiveness of AI-based screening of DR and leveraging AI to decrease disparities in access to care.

Identifying novel disease pathways in DR: Current evaluation of DR is primarily based on human grading of fundus photos. In the past decade there have been advances in retinal imaging, improved AI-based image analysis techniques, and availability of big data including genetic data. These advances allow us to study disease in much more detail than was previously possible. My team is studying how to incorporate data from Optical Coherence Tomography (OCT) images to evaluate retinal neurodegenerative damage from diabetes. We are also using AI-based techniques to extract features from retinal images, called “endophenotypes” that may not be readily visible to the human eye. We are correlating these endophenotypes with genetic data to identify novel disease pathways that can ultimately lead to more effective treatments.



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Focus of Vision Research and its Economic/Societal Impact:

My area of vision research is to use advanced bedside imaging tools to study the development of preterm infant retina and Retinopathy of Prematurity (ROP). One out of every ten infants is born premature. Premature birth is associated with neurological, vision, and hearing disabilities, with vision impairment being among those with most cost. ROP, caused by immature retinal blood vessel growth associated with preterm birth, affects 15,000 infants in the United States per year. Even in the absence of ROP or neurological disability, children born preterm still exhibit subtle impairments in vision. Vision disabilities associated with preterm birth and retinopathy of prematurity affects the child for a lifetime, with attendant quality of life and economic issues.

A better understanding of the development of the infant retina and how it changes in disease conditions such as ROP will not only expand our knowledge of the development of vision, but also can identify early imaging markers of retinopathy of prematurity and inform early detection and intervention of visual impairments.

Specific Project Described in the Video:

Bedside Imaging of Pre-term Infant Retinal Development and ROP

The fovea is located in the central retina, where the field of vision is focused, and is the most critical region determining visual acuity and visual function. In collaboration with our colleagues in biomedical engineering, we utilized investigational bedside Optical Coherence Tomography (OCT) and OCT angiography imaging to image the development of preterm fovea and multiple stages of pathological blood vessel growth (neovascularization) in infants with ROP. We found that retinal vascularization of the superficial retinal vessels correlates with the foveal formation of the inner retina, while the development of the deeper retinal vessels correlates with the outer retina development. We also imaged and categorized multiple stages of retinal neovascularization in infants with ROP. Our studies further our understanding of infant retinal development and the disease process in infants with ROP.

Dr. Chen is a 2017 recipient of a Research to Prevent Blindness Career Development Award.



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Focus of Vision Research and its Economic/Societal Impact:

My work focuses on the design of evidence-based decision support interventions that bridge the gap between clinical research and patient care. It takes, on average, nearly 20 years for high-quality research to make its way from clinical trials to routine patient care. In eye care, this delay results in not only suboptimal care for patients, but preventable vision loss and disability.

I am currently using acute demyelinating optic neuritis (often associated with multiple sclerosis) as a model for this work, a condition that affects approximately 20,000 people annually. Although it is not a common condition, it is the ideal model for understanding how to best implement the highest level of evidence to guide care into routine clinical care as the trial demonstrating limited value for corticosteroid treatment was first published more than 20 years ago. This project will provide a framework for designing similar interventions aimed at dissemination of clinical trial evidence and adherence to best clinical practices for other eye-related diseases.

Specific Project Described in the Video:

We have developed personalized, quantitative prediction models of long- and short-term benefits of corticosteroid treatment for patients with optic neuritis built on clinical trial data. Our prediction models can be used by clinicians and patients together to discuss the short-term and long-term visual prognosis both with and without corticosteroid treatment. We are also currently working on quantifying and personalizing harms from corticosteroid treatment using a large, national observational dataset. By integrating personalized information on corticosteroid treatment benefits *and harms* for patients with optic neuritis, we aim to overcome the hurdles of translating clinical trial evidence into best evidence-based practices for patients with optic neuritis.



Kimberly Gokoffski, MD, PhD

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Focus of Vision Research and its Economic/Societal Impact:

The goal of my research is to develop a technology to regenerate the optic nerve, a collection of retinal ganglion cell (RGC) communicating fibers or axons whose function is to relay visual information from the eye to the brain. Blinding diseases such as glaucoma and optic neuritis are triggered by damage to the RGC axon from mechanical or inflammatory forces, respectively. RGCs, however, have a poor intrinsic capacity for self-repair—rather than regenerating their axon, RGCs undergo programmed cell death. To date, no therapy exists to restore vision in the more than 64 million people worldwide who are legally blind as a result of such diseases, and this number is expected to increase to over 100 million by 2040. The annual economic burden of vision loss, eye diseases and vision disorders in the United States is estimated to be \$177 billion, a striking figure in that it represents nearly 0.5 percent of the world's gross domestic product. Glaucoma is the leading cause of blindness in the U.S. and the second leading cause of blindness worldwide, although these are only estimates since a significant number of individuals affected by glaucoma are not aware of it. These diseases also present with inequity in distribution and consequences, as African Americans are 6-times more likely to develop glaucoma and 15-times more likely to be blinded by it compared to Caucasians. Glaucoma also disproportionately affects women. Morbidity associated with optic nerve disease ranges from increased rates of falls to driver's license revocation.

Specific Project Described in the Video:

The approach we are taking to address this clinical need is to use electric fields (EFs) to promote RGC survival and direct RGC axon regeneration. This hypothesis is based on previous findings that immediate application of EFs after optic nerve injury increased RGC survival 1.5-fold over untreated controls, and that EFs directed regeneration of RGC axons in tissue culture experiments. We have collected compelling data that indicate that EF stimulation directs 3-fold more RGC survival and axon regeneration after crush injury in rat optic nerves compared to untreated controls; EF stimulation directed full-length optic nerve regeneration; and EF stimulation led to partial restoration of visual function. This work has the potential to make large strides towards solving one of the greatest challenges in ophthalmology—restoring vision to patients blinded by optic nerve disease.



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Focus of Vision Research and its Economic/Societal Impact:

Glaucoma is a progressive, neurodegenerative disease of the optic nerve. If not diagnosed early, it can lead to irreversible blindness, and it disproportionately affects racial minorities such as African Americans and Latinos. My research has been looking for ways to expand access to eye care for vulnerable patients by utilizing portable, home-use devices. It thus expands the reach of eye doctors into home-bound, rural, and other vulnerable populations.

Specific Project Described in the Video:

During the COVID-19 pandemic, healthcare providers often found themselves unable to offer care to their patients. As a result, clinicians cancelled many appointments they deemed “non-urgent” and pivoted patients to telemedicine when feasible. Many patients with progressive eye disease were part of vulnerable populations (elderly, comorbid conditions) that were too high risk to bring into clinic. While our faculty conducted thousands of telemedicine visits, we found that many portions of the examination could not be performed via telemedicine. Specifically, intraocular pressure monitoring, ancillary testing, and imaging was not possible. We recognized the potential impact of being able to move some portions of regular ophthalmic care delivery away from densely populated clinics and into the home. In ophthalmology, we rely on several components of the exam to diagnose and monitor eye disease. At present, many parts of the eye exam require in-person evaluation (measuring the vision, intraocular pressure, visual field, macular function). However, the technology is available to perform these assessments remotely.

The purpose of this project is to develop a process whereby these assessments can be delivered to a patient’s home, used by the patient for a single self-assessment, and returned in a timely manner to the treating physician for interpretation and either confirmation or alteration of care. Implementation of a suitable delivery and monitoring system could revolutionize ophthalmic care at a time when our aging population could be greatly served by receiving much of their care in a home environment.



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Focus of Vision Research and its Economic/Societal Impact:

My work is focused on glaucoma and related ischemic retinopathies, such as Diabetic Retinopathy (DR). We are interested in leveraging adaptive epigenetics and multiple-modality non-invasive therapeutic options. Glaucoma and DR represent two of the greatest health and economic burdens on the United States economy when considering vision disorders and are leading causes of irreversible vision loss worldwide. Glaucoma currently costs the U.S. healthcare system about \$3 billion annually, while the Centers for Disease Control and Prevention (CDC) projects visual disorders to exceed \$700 billion by the year 2050. Currently, there are more than 3 million Americans and 75 million people globally living with glaucoma. As of 2021, over half a billion people are living with diabetes, and three-out-of-four of those individuals will develop ocular pathologies after fifteen years. Moreover, Latino Hispanic and African American populations are disproportionately affected by these diseases. Age, sex, genetic background, and comorbidities such as diabetes and hypertension are considered risk factors for these diseases. Early treatment modalities are focused on managing intraocular pressure or managing the metabolic dysregulation of diabetes, but efficacious therapies related to neuroprotection are still scarce.

Specific Project Described in the Video:

Along with my PhD mentor, Dr. Jeff Gidday, we have adopted a multi-faceted approach to investigating the retinal structure, function, metabolism, proteome, and epigenetic changes that occur in our adaptive models of preconditioning. We have focused on using both male and female inbred and outbred mouse models to explore further the biological roles that sex and genetic background play in ocular disease progression. Dr. Gidday's previous work has demonstrated that repetitive hypoxic conditioning can induce long-lasting neuroprotection in the brain and retina. The goal of my dissertation work was to test the hypothesis that by extending the duration of conditioning, we could also extend the duration of the therapeutic window. We were able to demonstrate resilience against retinal ischemia in the untreated next generation of offspring. The ongoing work is focused on identifying the specific molecules and molecular pathways involved to eventually develop pharmacological targets that may serve to translate this therapy clinically.



Patrice Marie Hicks, PhD

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Focus of Vision Research and its Economic/Societal Impact:

My research focuses on improving vision care for underserved populations and communities. It aims to address health disparities in vision care that disproportionately burden specific populations and communities such as racial and ethnic minority groups, women, and individuals from lower socioeconomic status. This research has implications for impacting the individual level through precision medicine and at a population health level through public health initiatives.

The rationale for my research focuses on highlighting that it is essential to understand who is most at risk for vision loss and blindness, what factors are associated/modifiable with vision loss, and how vision loss can be impacted through health policy and health care. Identifying individual community vision care needs is imperative to creating a population health approach to increase health equity within vision care. It is essential to work towards diversity, equity, and inclusion within this research which can have lasting implications by working towards representation within studies that impact vision care outcomes to address risk factors and implement both interventions and policy.

Specific Project Described in the Video:

During my doctoral studies with Dr. Meg DeAngelis, our laboratory focused on vision-threatening eye conditions in three distinct geographically isolated, underserved populations. Vision-threatening eye disease impacting these populations the most and which epidemiological and genetic risk factors are associated with the disease outcomes were identified. These populations were either under-represented or not represented at all in the vision research literature. These studies further our understanding of the prevalence of genetic epidemiological risk factors within these populations. Healthcare services developed at a broad level may ignore the needed change to address health disparities between populations, so they must be tailored for each population.

In my current fellowship and with the mentorship of Dr. Maria Woodward and Dr. Paula-Anne Newman-Casey (prior AEVR EVSs), I will apply these concepts to additional populations and communities to further address health inequities in vision care. I will specifically focus on the vision-threatening conditions of glaucoma and corneal ulcers. This research can inform the planning and delivery of accessible, acceptable, quality, and appropriate care to different populations.



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Focus of Vision Research and its Economic/Societal Impact:

Inherited Retinal Disorders (IRDs) are a genetically diverse group of diseases that share a debilitating impact on vision. Affected individuals may be blind at birth or experience progressive vision loss typically beginning in childhood and early adulthood leading to blindness. Although the individual genetic diseases that comprise this group are rare, these conditions are collectively estimated to affect 1-in-1,000 to 1-in-3,000 people worldwide. IRDs have historically been regarded as incurable diseases, and with the exception of one rare early-onset disease, effective treatments remain unavailable. Based upon the age of affected individuals and the severity of vision loss, IRDs have a significant economic impact due to factors including health system costs and altered workforce participation. The non-financial consequences of IRDs, which include the impact of these diseases on well-being and quality of life, are also substantial.

Specific Project Described in the Video:

A growing number of strategies for targeting the specific genetic abnormalities underlying IRDs is creating new therapeutic expectations for these historically untreatable diseases. These investigational treatments can act at a DNA level either by introducing a normal copy of a gene to the retina (gene therapy) or by selectively altering the abnormal gene and DNA that an individual was born with (CRISPR/Cas9 genome editing). Therapies directed at RNA may have the same therapeutic endpoint and are also being evaluated.

My research assesses the effects of these genetic therapies as they are tested in clinical trials for specific IRDs. Assessing their impact first requires an accurate understanding of the natural history of the specific genetic disease being targeted, which can be achieved by prospective observational studies. In interventional trials, careful and repeated evaluations of visual function and retinal structure before and after treatment with one of these investigational drugs provide information about safety and efficacy. Detecting a possible biological signal also requires consideration and design of optimal outcome measures that recognize how these therapies interact with specific diseases and disease stages. Even beyond the successes of individual genetic therapies, the collective lessons learned across these trials will support ongoing improvements and therapies for patients with IRDs.



Archana Jalligampala, PhD

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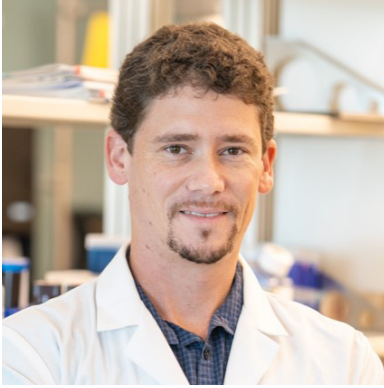
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Focus of Vision Research and its Economic/Societal Impact:

My work focuses on applying gene therapy approaches for Inherited Retinal Dystrophies (IRDs), primarily Retinitis Pigmentosa (RP). In the United States, IRDs result in a socio-economic burden of up to \$33 billion annually. More than 200 genes have been found to be mutated in IRDs, of which more than 60 genes are known to cause RP. Retinitis Pigmentosa is a common inherited retinal disease characterized by the loss of photoreceptor cells—that is, light-sensing cells of the retina. These patients commonly report nyctalopia (night blindness) resulting from loss of rod photoreceptors followed by loss of cones (responsible for daylight vision), eventually leading to blindness. Socially, RP patients struggle to perform day-to-day tasks and economically they experience difficulties in finding employment. Of the various translational approaches for RP treatment, gene therapy represents the most promising therapeutic option for many inherited and acquired retinal diseases. The development of such bench-to-bedside research will improve the quality of life of visually impaired patients and significantly reduce healthcare costs, thereby reducing the long-term socio-economic burden on the country.

Specific Project Described in the Video:

The autosomal dominant form of RP (adRP) accounts for 30-40percent of RP patients. The P23H rhodopsin mutation is a prevalent form of adRP in North Americans. The P23H adRP patients have one copy of the healthy wild-type (WT) allele and one copy of the diseased human P23H (hP23H) mutant allele. This mutation results in misfolding and mis-localization of the rhodopsin—the light-sensing protein of rods—resulting in rod degeneration. Our lab has made a large animal (pig) model of adRP, with six copies of human P23H rhodopsin and two copies of the WT pig rhodopsin. Surprisingly, although there is a fair complement of rod photoreceptors at birth, these transgenic (Tg) pigs do not have any functional rod-driven response, which does not develop with age. Meganucleases are DNA-cutting enzymes that recognize and cleave unique large DNA target sequences. The RHO 1-2 meganuclease, a proprietary of Precision Biosciences, is packaged in a self-complementary AAV5(scAAV5) virus driven by a promoter targeting the photoreceptors. The RHO 1-2 recognizes and cuts the mutant human P23H allele, resulting in a double-stranded DNA break. The cell's DNA repair machinery inactivates the mutant human P23H gene and degradation of the misfolded hP23H rhodopsin, resulting in the expression of the WT pig rhodopsin allele. Pre-clinical results in the pig model of adRP show that RHO 1-2 Meganuclease rejuvenates the rod photoreceptor structure and function up to one year. Such promising results suggest the level of gene editing achieved in this study can effectively treat rod degeneration and facilitate visual improvements in P23H adRP patients.



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Focus of Vision Research and its Economic/Societal Impact:

Uveal Melanoma (UM) is classified as a rare cancer emerging from melanocytes in the uveal tract, which is comprised of the iris, the ciliary body, and the choroid of the eye. Despite being rare, UM is the most common primary eye cancer in adults. While the more common skin melanomas are also derived from melanocytes, UM is a very different tumor—both in regard to the mutations and signaling events changed, as well as treatment approaches. While primary tumor treatment in the eye is very effective, around half of UMs will form metastasis, mainly in the liver, which are notoriously hard to treat and almost uniformly fatal. None of the treatment paradigms currently being used for skin melanoma work well for UM and, unfortunately, treatment options for UM have not progressed significantly in the last decade. New approaches on how to treat UM metastasis are urgently needed. A lot has been learned about the genetics of UM, and we know that, for instance, mutations in the BAP1 gene, as well as expression of the PRAME gene, are highly prognostic of whether UM tumors metastasize or not. However, it is still unclear on how these, and other mutations and expression changes, contribute to tumor development and metastatic spread. More detailed mechanistic insight into the genetics and epigenetics of UM is urgently needed, especially to understand the consequences of genetic and epigenetic aberrations in UM.

My laboratory focusses on understanding how the mutations and gene expression changes we see in metastatic UM cause metastatic spread. A heavy focus lies on epigenetics, as many genes altered in UM modify the genomic structure of cells. We believe that understanding how these tumor-driving events reshape the chromosomal architecture is key in understanding why they are important for tumor development, and in order to develop new treatment options for this highly deadly cancer.

Specific Project Described in the Video:

Two of our main research projects target understanding why BAP1 is mutated in a large majority of metastasizing UMs, and how expression of the PRAME gene is a further key determinant of metastasis. While both are significant biomarkers of whether a UM tumor metastasizes, little is known on the mechanisms by which these genes contribute to UM metastasis. BAP1 loss in UM is classically associated with an increase of repressive histone marks, however, using a developmental model, we show that the main driver of gene expression changes following BAP1 loss are not these repressive marks, but rather activating marks on a distinct subset of genes. Further, we are investigating novel roles for PRAME, and show that PRAME can elicit fundamental cellular changes once expressed, shifting the cell identity and increasing UM adaptability. Both findings are currently being used to explore new treatment options.



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Focus of Vision Research and its Economic/Societal Impact:

Glaucoma is the leading cause of irreversible blindness in the world. It is characterized by loss of retinal ganglion cells—the cells that connect the eye to the brain. All currently approved glaucoma treatments focus on lowering the eye pressure, which is one of the risk factors for the disease. However, many glaucoma patients worsen despite all available medical and surgical therapies, and there are currently no clinically approved treatments that directly promote retinal ganglion cell survival. My research focuses on the role of retinal neuroinflammation in glaucoma, with a particular focus on microglia, the resident immune cells that play a critical role in glaucoma disease progression. By modulating microglial signaling in glaucoma, my research hopes to ultimately develop novel neuroprotective treatments for this common blinding disease.

Specific Project Described in the Video:

By using cutting-edge technologies like RNA sequencing, my research has discovered that, in mouse models of glaucoma, microglia induce a harmful neuroinflammatory molecular signature characterized by production of cytokines and neurotoxic molecules. One of these molecules is APOE, the major lipoprotein in the brain with genetic associations with Alzheimer's disease and glaucoma. Genetic targeting of APOE maintains microglia in the homeostatic state and protects retinal ganglion cells from degeneration despite elevated intraocular pressure. APOE acts through Galectin-3, a toxic downstream mediator whose genetic and pharmacologic targeting is also protective in glaucoma. Furthermore, APOE and Galectin-3 are upregulated in human retinal samples with glaucoma. We propose that microglial APOE-Galectin-3 signaling pathway can be targeted to develop neuroprotective therapies for glaucoma, which would transform the treatment paradigm for this common and devastating eye disease.

Dr. Margeta is a 2019 recipient of a Research to Prevent Blindness Career Development Award.



J. Patrick Mayo, PhD

Current Position: Assistant Professor, Departments of Ophthalmology and Bioengineering, Center for the Neural Basis of Cognition (CNBC), Visual-Motor Neuroscience Lab

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Focus of Vision Research and its Economic/Societal Impact:

The vast majority of visual disorders—including glaucoma ("tunnel vision"), strabismus ("crossed eyes"), and macular degeneration ("central vision loss")—not only affect the eyes but also impact processing in the brain. Visual abnormalities affect millions of Americans yearly and produce tens of billions of dollars in annual health care costs. These societal impacts are only expected to increase in the coming years as population demographics skew towards older age groups.

While an abundance of research is focused on unraveling the biological underpinnings of disease states in the eyes, substantially less work focuses on the more basic role of the brain in translating incoming visual signals into what we see. Our laboratory investigates how visual information and eye movements are coordinated between brain hemispheres. Eye movements are the dominant way in which we explore the world, and how eye movement patterns change due to disorders of the eye is an ongoing field of active research. Each half of the brain largely represents the opposite half of the visual world (the left hemisphere represents the right visual field, and vice versa). Because individual visual neurons are sensitive to particular regions in space, and those regions are linked to where we are looking, instructed eye movements allow us to experimentally control what visual information is processed by each hemisphere. Understanding how these anatomically separate sources of visual information are unified will provide a critical first step towards the development of novel treatments and interventions that act at the level of the brain for mitigating vision loss.

Specific Project Described in the Video:

Our laboratory records simultaneously from populations of neurons in key oculomotor regions of the brain in both hemispheres. We use precisely measured, visually guided eye movements to probe different parts of the visual world at predetermined time intervals. This approach allows us to confidently measure where a subject is looking and when the eyes move. Eye movements provide a vital reference point for interpreting corresponding changes in inter-hemispheric neuronal activity—by cueing subjects to look to the left or right, we can reliably activate neurons in each hemisphere and determine when the "hand-off" between hemispheres occurs. More detailed investigations of vision and eye movements near the vertical meridian, alongside modern techniques for labeling anatomically connected neurons, will pave the way for a comprehensive map of inter-hemispheric brain function needed for advanced clinical treatments and the restoration of vision.



Mallory McLaughlin, OD

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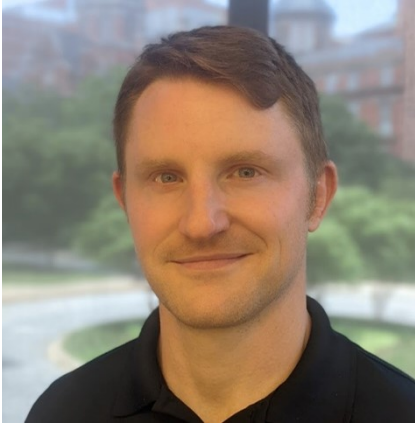
Focus of Vision Research and its Economic/Societal Impact:

Currently, approximately 3 million Americans have glaucoma. It is estimated that 7.32 million Americans will have glaucoma by 2050. Glaucoma is one of the leading causes of visual impairment and blindness in the United States. It is estimated that half of people who have glaucoma are unaware of their disease. Development and validation of technology to increase accessibility and availability of glaucoma diagnosis and treatment is imperative.

Specific Project Described in the Video:

Glaucoma is diagnosed and monitored with peripheral visual field testing. The gold-standard Humphrey Visual Field test requires the patient to hold their head still for several minutes on chin and forehead rests inside of the bowl-shaped instrument. The test is stationary and is not accessible to all patients, especially those with limited mobility. Virtual reality-based visual field testing could be a cost-efficient, portable alternative to the gold standard visual field test. The head-mounted design allows the test to be performed in any comfortable position, thereby increasing accessibility. It can also be performed in any room of the clinic, improving clinical efficiency.

Virtual reality-based visual field technology could be expanded to allow for remote monitoring or home monitoring of glaucoma, increasing access to glaucoma care for patients who do not live within reasonable proximity to a glaucoma specialist. This study compared a commercially available virtual reality-based visual field test to the gold standard Humphrey Visual Field test to determine if it can comparably detect vision loss from glaucoma. The study also examined the effect of fogging due to facemask wear on both types of visual field tests.



Joseph Mertz, PhD

Current Position: Post-Doctoral Research Fellow

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Institution: Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland

Focus of Vision Research and its Economic/Societal Impact:

The goal of my work is to inform the development of neuroprotective-based treatment strategies for glaucoma and other optic neuropathies. Glaucoma alone is the world's leading cause of irreversible blindness, with more than 3 million experiencing it in the United States and more than 70 million worldwide. Glaucoma patients suffer detriments to their quality of life, safety, mobility, numerous everyday necessities, and psychological and emotional health.

The costs of glaucoma to the American healthcare system are approaching \$3 billion annually, including direct medical costs, loss of productivity, and costs to family and caregivers. Sadly, the number of Americans with glaucoma and the costs to society are projected to rise as our population ages.

Specific Project Described in the Video:

All current treatments for glaucoma act by reducing high intraocular pressure (IOP), the major risk factor for the disease, but reducing IOP does not always stop vision loss. It is ultimately the death of a particular set of neurons in the retina, the retinal ganglion cells (RGCs), that causes loss of vision in glaucoma. These neurons comprise the information carrying fibers in the optic nerve and are the sole conduit of visual information from the eye to the brain. As they are lost during glaucoma progression, and because they cannot be replaced, the visual information they once carried is permanently lost. If we can directly protect these neurons, we might be able to supplement or replace pressure-related therapies and save vision for millions of people. If we could replace lost RGCs, we could potentially even restore sight to patients who have already lost vision.

Using a combination of state-of-the-art technologies, we have identified candidates for important mediators of RGC death during stress conditions. First, we generate RGCs from human stem cells, which allows us to closely replicate the cell and molecular biology of the cells present in the human body—a key factor for informing treatment of human patients. This also affords the opportunity for careful and well-controlled manipulations in the culture dish, such as CRISPR-Cas9 gene editing and precise administration of treatment conditions. Lastly, through powerful and comprehensive proteomics and interactomics methods, we can examine this cellular system as a whole, thereby revealing unforeseen molecular behavior and interactions that bring about cell death. By these approaches, we have identified a handful of genes and molecular pathways and are examining their utility as targets for future treatment strategies to preserve and restore vision.



Ann Morrison, OD, PhD

Current Position: Clinical Instructor

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Institution: The Ohio State University College of Optometry, Columbus, Ohio

Focus of Vision Research and its Economic/Societal Impact:

Most infants are born with a moderate amount of hyperopia, also known as farsightedness. This is not generally a problem because there is a process called emmetropization that reduces the amount of farsightedness, placing most infants' eyes right where they need to be in order for them to see clearly by their first birthday. However, up to 10 percent of infants do not emmetropize properly and end up with eyes that are shorter than normal in length and a very high farsighted prescription (refractive error). Farsighted children are at increased risk of vision problems such as strabismus ("eye turn") or amblyopia ("lazy eye") later in childhood, as well as difficulties with early literacy and academic performance.

If emmetropization can be enhanced in highly hyperopic infants, the risk of developing strabismus and amblyopia could be reduced, preventing the need for more aggressive and costly treatment such as surgery, patching, and other therapies. Enhancing emmetropization may also promote clear and comfortable vision that is essential for learning, by reducing a child's accommodative (eye focusing) burden. The lifelong need for spectacles, contact lenses, or refractive surgery for high amounts of farsightedness would also be reduced. Positive results might provide evidence-based guidelines for detecting and prescribing for hyperopia in pediatric populations, which is not currently standardized among eye care practitioners.

Specific Project Described in the Video:

The goal of my work is to determine if early refractive error correction (wearing glasses) and eye exercises to promote more robust eye focusing can enhance the emmetropization process in highly farsighted infants. My research includes a current clinical trial that randomizes two-month-old infants to observation (current standard of care) or to this new treatment regimen. The hypothesis of my study is that more active and accurate accommodation (eye focusing), promoted by spectacle under-correction and accommodative exercises, will increase the rate of eye growth to reduce high amounts of hyperopia. The prediction is that more accurate accommodation will modulate eye growth by creating a less oblate, or more prolate eye shape through the action of the ciliary muscle to accentuate elongation. To determine if the hypothesis is correct, my research is paying close attention to accommodation and eye shape during a 15-month period, which will help determine what mechanisms are responsible for effective emmetropization.



Alex Muntz, PhD, MScOptom

Current Position: Research Fellow, Department of Ophthalmology, Faculty of Medical and Health Sciences

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Focus of Vision Research and its Economic/Societal Impact:

Dry Eye Disease (DED) is one of the most common eye conditions, affecting up to one-in-three individuals, including often older people worldwide. Patients experience chronic eye discomfort and poor vision, impacting their quality of life and work productivity. Stress, depression, anxiety, and insomnia are common in severe dry eye. Its burden on the United States healthcare and economy is estimated at more than \$55 billion per year, which is rising steadily given our aging population, but also due to a new patient category—children.

Evidence increasingly suggests that extended digital screen usage from an early age may be causing the incidence of more dry eye in younger people, including children. This is a result of decreased blinking during screen use, which dries out the eye surface, causing discomfort, poor vision, and structural changes. Over time, these effects can become chronic or permanent.

With no cure for DED, today's early and ubiquitous use of screens for learning and leisure may predispose children to an earlier onset of dry eye, with more severe consequences for their overall health and wellbeing. As seen with COVID-19, the solution may be an evidence-based approach to develop guidelines and promote education for the safe use of screens in and outside of the classroom.

Specific Project Described in the Video:

Our team at the Ocular Surface Laboratory in Auckland, New Zealand, sought to better understand the relationship between extended screen use, blinking and dry eye in young people. For this, we targeted a young population who were expected to spend considerable time on screens—gamers at a gaming convention. Using iPads that were customized to track blinking, participants completed a survey on screen-use habits, eye comfort, quality of life, and demographics. They then played a “staring contest”—a validated measure for ocular surface health. The results indicated that more than 90 percent of the study population reported clinically significant levels of dry eye symptoms. The young people who reported longer daily screen use also had poorer blinking, eye comfort, tear quality, and self-reported quality of life.



Leah Owen, MD, PhD

Current Position: Assistant Professor of Ophthalmology and Visual Sciences

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Institution: John Moran Eye Center, University of Utah School of Medicine, Salt Lake City, Utah

Focus of Vision Research and its Economic/Societal Impact:

Retinopathy of Prematurity (ROP) is a blinding disease that affects preterm infants. ROP impairs the maturation of blood vessels in the back of the eye within a tissue called the retina—the light-sensitive back of the eye essential for visual function. Retinal blood vessels do not naturally mature until an infant is full term, so when born early it is expected that these blood vessels will need to continue their growth. However, for reasons we don't understand, when they do this in an environment that is different than the in-utero environment, problems can arise which we call ROP. ROP can range from mild to severe disease, and while severe disease is associated with complete blindness, even mild disease can cause life-long vision loss. As a result, ROP represents a significant clinical problem, with up to 20,000 children suffering blindness every year, cumulatively accounting for up to 40 percent of childhood vision loss worldwide. The clinical impact of ROP to preterm infant life-long vision is predicted to increase as advancing technology allows for improved preterm infant survival, particularly in developing nations.

Specific Project Described in the Video:

ROP is not present at birth, instead it develops approximately 4-6 weeks following preterm birth. Despite this “preclinical” window of opportunity, we cannot prevent or cure ROP. Gold-standard treatment requires laser scarring of all retinal tissue lacking blood vessels and is indicated to prevent complete blindness—although it causes permanent scarring, loss of peripheral vision, and other visual co-morbidities. Importantly, our current interventions cannot facilitate normal, healthy blood vessel maturation, promoting healthy eye and vision development. My research targets this knowledge gap by seeking to better understand the molecular changes occurring in the “pre-clinical” window which predisposes infants to development of ROP rather than healthy vessel development. My group uses a systems biology approach to identify molecular factors within the preclinical window that correlate either with subsequent normal retinal vascularization or with ROP development. To accomplish this, we are analyzing comprehensive genomic changes, including those at the DNA, RNA, and protein levels, within natural models of ROP protection. This will allow for identification of protective molecular signatures, which can then be used to inform preventive interventions which mimic the protective preclinical environment. Ultimately, we hope our work will shift the paradigm from one of destructive treatment toward ROP prevention and facilitation of healthy retinal blood vessel maturation.



Jennifer Patnaik, PhD

Current Position: Assistant Professor, Division of Ophthalmic Epidemiology, Department of Ophthalmology

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Focus of Vision Research and its Economic/Societal Impact:

My work involves conducting epidemiologic research and analyzing data on a variety of topics in clinical medicine and public health. My recent focus in ophthalmology has included research in the areas of Age-Related Macular Degeneration (AMD), Retinopathy of Prematurity (ROP), cataract and glaucoma surgeries, and other pediatric and adult ophthalmic diseases. My work includes assisting ophthalmology faculty, fellows, residents, and medical students with their ophthalmic research; instructing an epidemiology and database class to incoming residents in the Department of Ophthalmology; researching disparities in eye diseases, specifically for disadvantaged populations, and assessing differences by gender, race/ethnicity and socio-economic status; and analyzing the use of “Big Data sources in ophthalmology.

Specific Project Described in the Video:

My project discussion focuses on two research projects supported by Orbis, a global nonprofit organization whose mission is to fight blindness worldwide—vision screening and productivity among two different groups of disadvantaged workers in Bangladesh, including female garment workers and male bus drivers. Orbis conducted a cohort study of more than 1,000 female garment workers to assess prevalence of vision impairment and explore associations with income. More than one-quarter of women screened had near and distance vision impairment (25 percent and 27 percent, respectively). Women garment workers with near vision impairment earned significantly less (\$6-9 per month). Near vision correction could be a strategy for alleviating poverty in this setting and to alleviate the gender disparities that exist in lower income countries. The second project was performed because road traffic injuries are the leading cause of death globally for children and young adults, and rates are disproportionately increasing in low- and middle-income countries. We surveyed 700 males who drive buses in Bangladesh to assess vision and predictors of self-reported motor vehicle crashes. A majority of drivers (70 percent) had near or distance refractive error and most (88 percent) could be improved with glasses or cataract surgery. Traffic crashes were self-reported among 9 percent of participants. Drivers with visual impairment were 2.5-times more likely to have had a motor vehicle accident. This study demonstrates that, to ensure traffic safety, specific vision standards are needed for licensure and once enacted, need to be enforced by rigorous and regular vision testing. Referral for affordable and accessible eye care should be made for all drivers failing vision screening.

Dr. Patnaik is a 2021 recipient of a Research to Prevent Blindness/American Academy of Ophthalmology IRIS Registry® Research Award.



Margaret Reynolds, MD

Current Position: Assistant Professor of Ophthalmology and Visual Sciences

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Institution: Washington University, St. Louis, Missouri

Focus of Vision Research and its Economic/Societal Impact:

My work focuses on how decreased visual acuity impacts development. Children who have low vision can suffer from developmental delay and decreased school performance. We are studying how different interventions, such as refractive surgery among children with Autism Spectrum Disorder (ASD) or an occupational therapy intervention among children with low vision, can impact development and school performance. Children who have low vision in early childhood can suffer from developmental delay and impaired communication, cognition, and school performance leading to lifelong decreased productivity and impaired quality of life. Early intervention can lead to improved lifelong productivity and quality of life.

Specific Project Described in the Video:

My research studies how improved visual acuity secondary to refractive surgery impacts the phenotype of children with ASD. Uncorrected refractive error in young children can cause substantial visual impairment. Typically, spectacles are sufficient to correct refractive error, but a subset of children exists who refuse to wear glasses even though their vision is degraded to the point of legal blindness. To treat the visual impairments, we have been performing refractive surgery on these children for the past 18 years. The impact of decreased visual acuity on ASD has not been well described. We hypothesize that improving visual acuity in this patient population will improve the ASD phenotype. We additionally hypothesize that improved visual acuity will lead to improvement in eye tracking behavior. Refractive surgery, therefore, has the potential to be behavior-modifying intervention in ASD.



Rokhsana Sadeghi, MSc

Current Position: PhD student in Biomedical Engineering

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Focus of Vision Research and its Economic/Societal Impact:

In 2020, an estimated 43.3 million individuals had blindness worldwide. Currently, there is no treatment or cure for the many causes of blindness. Blindness is among the health problems about which most individuals have the greatest fear because it affects a person's health and economic livelihood, significantly reducing a person's quality of life.

In our laboratory, we are trying to improve the visual performance of individuals with blindness by creating visual perception using electrical stimulation via electrodes implanted either in the eye or the primary visual cortex located along the back surface of the brain. Electrical stimulation of the neurons in the visual pathway can create visual perception. Even though this prosthetic visual perception is limited to moving shadows and lights—and thus very different from normal vision—it can help individuals avoid obstacles while walking and orienting themselves in a room by locating ceiling lights, doorways, and windows. We are also combining other technologies, such as Artificial Intelligence (AI), with these visual implants that can help perform daily life activities independently and, hence, enhance their quality of life.

Specific Project Described in the Video:

The visual cortex in the brain stays normal in many diseases that result in blindness. Therefore, by implanting the electrodes in the visual cortex, many people can benefit from it. There is no commercially available cortical visual implant that uses real-time stimulation based on a head-mounted camera. Our team is developing and testing novel methods to optimize visual perception with an intracortical visual prosthesis in humans.



Daisy Shu, BOptom, PhD

Current Position: Postdoctoral Research Fellow

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Focus of Vision Research and its Economic/Societal Impact:

My research is focused on understanding the disease mechanisms underlying Age-Related Macular Degeneration (AMD) and in doing so, developing novel therapeutic strategies to combat the disease and restore vision. AMD is the leading cause of irreversible blindness in the elderly. With our aging population, AMD cases are expected to increase to 288 million by 2040. The global cost of visual impairment due to AMD is approximately \$343 billion, including \$255 billion in direct health care costs. Not only does AMD carry a significant economic burden, but also a severe societal burden due to visual impairment. The central vision loss suffered by AMD patients can result in a reduced quality of life with difficulties in everyday functions such as reading, driving and self-care. The emotional distress and higher rates of depression associated with visual impairment further emphasize the urgent need to study AMD and develop more effective therapies to limit the devastating long-term effects of this disease.

Specific Project Described in the Video:

My research project explores how metabolism plays a role in AMD. With age, our metabolic function declines and our mitochondria (energy-generating powerhouses in our cells) become dysfunctional. During AMD, the retinal pigment epithelial (RPE) cells in our eyes degenerate, leading to blindness. RPE cells are highly metabolically active and are packed with mitochondria. My research shows that during AMD, the mitochondria in RPE lose their normal function and take on an aberrant appearance, shifting the metabolic activity of RPE towards a disease state. By testing drugs that target metabolism and promote mitochondrial health, my research has found some promising therapeutic avenues to restore RPE and thus, combat AMD.



Katelyn Swindle-Reilly, PhD

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Institution: The Ohio State University, Columbus, Ohio

Focus of Vision Research and its Economic/Societal Impact:

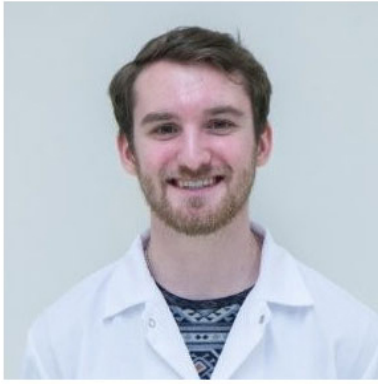
My research focuses on the development of new ocular biomaterials and drug delivery systems to improve outcomes after ophthalmic surgery and prevent permanent blindness. My aim is to develop treatments for age-related ocular diseases which impact millions of American patients. As the aging population continues to grow, the number of patients and annual health care costs associated with both treatment and loss of productivity continues to rise. My research is exploring ways to prevent complications associated with common ophthalmic surgeries such as cataract extraction and vitrectomy to reduce visual impairment and eliminate the need for costly secondary surgeries. It also investigates therapies for traumatic optic neuropathy, which currently has no treatment available and disproportionately affects military personnel. Other ongoing projects seek to improve the wound healing response using biomaterials-based approaches in the lens and cornea.

In particular, my lab focuses on engineering approaches to preventing irreversible vision loss from eye diseases such as Age-Related Macular Degeneration (AMD). This research has the potential to prevent blindness, improve patient comfort, and reduce costs associated with treatment. For example, AMD treatments incur huge costs that are a burden to the patients, caregivers, and the health care system, with half a million injections performed every month in the United States alone, exceeding \$500 million per year in direct medical costs.

Specific Project Described in the Video:

My research is interdisciplinary and engages engineers, scientists, and ophthalmologists to develop sustained release technologies to reduce frequency of injection for AMD patients. There is no treatment for dry AMD, and vision is only preserved in wet AMD with frequent injections into the eye as often as every month. My lab has used polymers to develop biodegradable, injectable drug delivery systems to preserve visual function. In particular, we are developing tunable, injectable microcapsules capable of sustained release of AMD therapeutics for six months to more than one year. This small capsule offers tunable, predictable drug release and biodegradation while protecting bioactivity of costly therapeutics used for treatment of AMD.

My research, which bridges the gap between basic and translational vision research, informs technology development, with the ultimate goal of bringing new treatments to improve quality of life for patients with blinding diseases, including AMD.



Brian Thompson, PhD

Current Position: PhD Candidate, Department of Environmental Sciences

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Focus of Vision Research and its Economic/Societal Impact:

My research is focused on understanding the role of oxidative stress in eye development and microphthalmia. Microphthalmia is a disease where one or both of the eyes fail to develop properly and can cause blindness in the most severe cases. Microphthalmia is a major cause of childhood blindness cases worldwide. Childhood blindness causes lifelong loss of independence and reduces quality of life. Additionally, it is estimated that global childhood blindness costs upwards of \$270 billion annually. Current treatments for microphthalmia can address the associated cosmetic abnormalities but are unable to restore vision. Given this, it is essential that we more fully elucidate the etiology of microphthalmia. In doing so, it will enable us to design therapeutic strategies to prevent the development of microphthalmia and/or effectively treat it, thereby reducing the burden of childhood blindness.

Specific Project Described in the Video:

Epidemiological studies have associated oxidative stress-inducing environmental factors with microphthalmia. However, little research has mechanistically explored the link between oxidative stress and the development of microphthalmia. My research aims to address this knowledge gap with next-generation “omics” experiments in a genetically modified mouse model of oxidative stress. It has demonstrated that oxidative stress can impair eye development by disrupting the morphogenesis of many ocular structures including the cornea, lens, iris, and retina. My research then directed “omics” experiments on the dysmorphogenic lens and found that oxidative stress impairs the proper differentiation of lens epithelial cells into lens fiber cells, likely through the impairment of a critical transcription factor, PAX6. These results are the among the first to suggest that maintenance of oxidative stress is critical for normal eye and lens development and provides further evidence that members of the PAX protein family can be redox regulated, which could have important implications for myriad diseases.



Edmund Tsui, MD

Current Position: Assistant Professor of Ophthalmology

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Focus of Vision Research and its Economic/Societal Impact:

Uveitis refers to a group of eye diseases that are characterized by intraocular inflammation from autoimmune, infectious, or idiopathic causes. Uveitis is the fifth leading cause of blindness in the United States and accounts for 10 percent of patients with legal blindness. Although uveitis in children is less common than in adults, children tend to have more chronic and severe courses than adults and thus require more frequent examinations for screening and monitoring of inflammation. The prevalence of uveitis in children is 30 cases per 100,000, and anterior uveitis is the most common form of uveitis in children. Oftentimes, children with anterior uveitis can be asymptomatic at disease onset and during exacerbations and may not report any visual changes or symptoms until vision-limiting complications occur, such as cataracts and glaucoma. Thus, routine screening and monitoring play a central role in long-term preservation of vision. My research focuses on improving the diagnosis, monitoring, and detection of intraocular inflammation using instrument-based measures of intraocular inflammation. With these new methods of evaluating inflammation, we may be able to identify children at greatest risk of vision loss and promptly implement treatment, which may help prevent blindness and improve their quality of life.

Specific Project Described in the Video:

My research utilizes non-invasive imaging platforms called Anterior Segment Optical Coherence Tomography (AS-OCT) and Laser Flare Photometry (LFP) to identify imaging-derived biomarkers of inflammation in children with uveitis. Current clinical evaluation of uveitis is by slit lamp examination, which results in a semi-quantitative grading system and is subject to bias due to the subjective estimation of the observer. Both AS-OCT and LFP are rapid imaging techniques that can provide reproducible, objectively quantifiable measurements of inflammation. Children with uveitis are a unique, at-risk population and quantitative techniques are of paramount importance as these patients are often unable to cooperate with prolonged examination at the slit lamp while assessing for inflammation. By using instruments to identify imaging-based biomarkers, my goal is to develop an innovative platform to objectively quantify intraocular inflammation in children. My long-term goal is to validate these instrument-based imaging biomarkers and incorporate them into clinical trials and to create a risk stratification model for children with uveitis.



Kevin Willeford, OD, MS, PhD

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Focus of Vision Research and its Economic/Societal Impact:

Humans have six extraocular muscles in each eye. The brain continually adjusts the amount of innervation directed to each muscle to maintain binocular alignment. This process is called “motor fusion” and helps people use their eyes together in many situations. For example, most people can look upward, downward, leftward, rightward, far-away, and up-close while using their eyes together as a team. However, there are two types of people who have trouble doing so. Patients with non-strabismic disorders have difficulty maintaining motor fusion and may experience blur, double vision, and headaches. On the other hand, patients with strabismus do not have motor fusion at all. This results in a loss of stereopsis (“3D vision.”) The reductions in visual function associated with both non-strabismic and strabismic disorders may limit one’s academic achievements, reduce their range of possible jobs and hobbies, and impose psychosocial challenges.

Specific Project Described in the Video:

My research is interested in learning how much motor fusion people typically exert to keep their eyes aligned. My project asks two questions related to this general fascination. First, does the required amount of motor fusion change as we look in different directions? This may be the case for those with muscle weaknesses in one of their eyes. Second, is motor fusion a limited resource? If so, this may explain why some non-strabismic and strabismic patients only have difficulties in specific situations (e.g., while looking up-close). My research will address both questions by repeatedly measuring eye alignment in several gaze positions following both removal and addition of motor fusion. The results will paint a broader picture of the continuum between normal and abnormal motor fusion and in turn help eye care professionals create diagnostic and therapeutic paradigms which optimize visual function.



Thomas Wubben, MD, PhD

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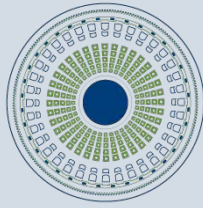
Focus of Vision Research and its Economic/Societal Impact:

The retina is a highly organized neural tissue at the back of the eye that contains photoreceptors, which are specialized neurons capable of changing the light we see into a series of biological processes the brain can process into an image. Photoreceptor death contributes to vision loss in many retinal disorders, including Age-Related Macular Degeneration (AMD), Inherited Retinal Diseases (IRDs), and retinal detachment. AMD is estimated to affect 200 million people worldwide, while IRDs affect approximately 2 million and retinal detachment about 850,000 people worldwide. The visual decline that people experience due to these retinal disorders results in decreased quality of life, life-long medical care, and loss of productivity for both the patient and their caregiver. Although hundreds of mutations cause IRDs, there is currently only one Food and Drug Administration (FDA)-approved treatment for a single IRD-causing mutation. Despite intensive study and recent clinical trials, new AMD therapies have failed to demonstrate efficacy. Therefore, there is an urgent unmet need for therapies that improve photoreceptor survival and prevent vision loss. The retina is one of the most metabolically demanding tissues, and this is driven by the metabolic needs of photoreceptors. Interestingly, mutations affecting key components of cell metabolism—common to almost all cells throughout the body—have been linked to isolated retinal degenerations, thereby suggesting that precise control of metabolism is necessary for the continued survival of photoreceptors. Understanding the metabolic pathways that support photoreceptor function/survival may provide a framework for developing novel therapies that slow/prevent vision loss in these blinding retinal disorders.

Specific Project Described in the Video:

My laboratory is committed to addressing the critical gap in our knowledge regarding retinal cell metabolism and how it is altered in disease. Glucose, or sugar, is the primary fuel for the retina, and its breakdown into energy and building blocks for the cell has been central to the study of photoreceptor metabolism. Yet, photoreceptors obtain only a fraction of their energy from the breakdown of glucose and recent evidence suggests photoreceptors have the flexibility to use other fuels to meet their metabolic demands. Glutamine is an amino acid, or protein building block, that can act as a fuel source for energy, cellular building blocks, and combating cellular stress. My laboratory has recently been the first to demonstrate that, in a mouse model where a key component of glutamine metabolism is deleted in photoreceptors, the photoreceptors undergo rapid degeneration. Our ongoing work is defining the pathways by which photoreceptors use glutamine to survive and function in hopes of developing therapies that improve photoreceptor survival and prevent vision loss in many retinal degenerations.

Dr. Wubben is a 2020 recipient of a Research to Prevent Blindness Career Development Award.



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