DECADE OF VISION
2010-2020
an initiative of the
Alliance For Eye And Vision Research

Sixth Annual Emerging Vision Scientists

Capitol Hill Day

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60 YEARS
Research to Prevent Blindness

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*Age-related Macular Degeneration

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 H. Res. 366 and S. Res. 209 passed in 2009, Congress designated 2010-2020 as the decade of vision and acknowledged AEVR's efforts to provide sustained education about the impact of eye disease and vision impairment through its *Decade of Vision 2010-2020 Initiative.* Visit its Web site at www.eyeresearch.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 $373 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 60 years. Learn more at www.rpbusa.org.

Janet Alexander, MD

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Focus of Vision Research and its Economic/Societal Impact:
My work focuses on cataracts and glaucoma in children, the primary causes of treatable childhood blindness worldwide. Glaucoma occurs in more than 30 percent of children after congenital cataract surgery and presents a diagnostic challenge due to variable timing of onset of glaucoma and children's limited ability to cooperate with testing.

Vision research with sight-saving implications for young children and infants has potential to preserve quality of life and productivity for a lifetime. While congenital cataracts are rare, with a prevalence of 4 in 10,000, the impact in terms of the cost of care and the lost quality of life and productivity spans several decades.

Specific Project Described in the Video:
Advanced image analysis of high frequency ultrasound images may enable clinicians to identify risk factors for glaucoma after congenital cataract surgery earlier and more accurately than ever before. The goal is to identify children at risk for complications such as glaucoma prior to undergoing cataract surgery, thus making prevention possible.

Clinical translational research focused on novel image analysis techniques can improve the diagnosis and treatment of many causes of childhood blindness, allowing for generalization of our novel image analysis techniques to a broad range of eye diseases. Earlier diagnosis of disease, enhanced treatments targeting improved outcomes including vision and quality of life, and optimizing resource allocation toward children at highest risk and reducing invasive testing for children at lowest risk will decrease both cost and unnecessary discomfort.

Raven Diacou, PhD

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Focus of Vision Research and its Economic/Societal Impact:
Patients with vision loss experience significant impact on quality of life, with lost independence and mobility. 3.4 million Americans aged 40 and older are visually impaired or blind. As the aging population is expected to grow, by 2050 the number of visually impaired individuals is expected to reach 7.3 million. Vision loss from degenerative eye diseases such as age-related macular degeneration (AMD) and glaucoma is irreversible. As we enter an era of personalized medicine and consider stem cell-based efforts to cure blindness, it is important to study the genes required for proper eye formation. Genetic research on early eye development informs efforts to generate and advance stem-cell based retinal organoids for accelerated drug discovery and accurate modelling of human eye disease. As a result of early funding support for basic research, we are now able to generate miniature retinas from stem cells which have potential to replace damaged cells of the eye.

Specific Project Described in the Video:
During eye development, retinal progenitor cells in the early eye receive guidance from genes which direct cells to become either retinal neurons or cells destined to become ciliary body and iris. Using a mouse with mutations in genes Six3 and Six6, our data shows that a combination of Six3 and Six6 function is critical for proper development of the retina, ciliary body, and iris, as well as important for proliferation of retinal progenitors. This discovery has direct impact on the field of retinal tissue regeneration and cell replacement therapies for treatment of retinal degenerative eye diseases.

Rebecca G. Edwards, MD, PhD

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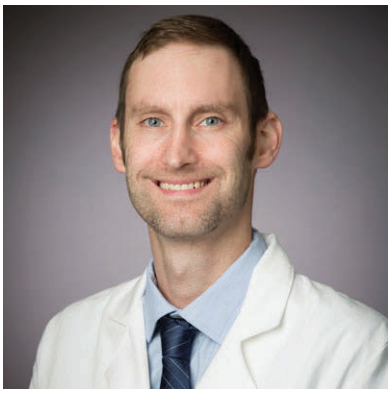
Focus of Vision Research and its Economic/Societal Impact:
Uveitis is a group of conditions involving inflammation of the tissues of the eye that are supplied by blood vessels, including the iris, ciliary body, and choroid, along with neighboring tissues, including the retina, vitreous, and optic nerve. This inflammation may be caused by infection, be associated with systemic diseases, including a variety of autoimmune conditions, or occur in isolation. More than 40,000 new cases of uveitis are diagnosed in the United States each year. Many cases of uveitis are chronic and relapsing, and unchecked inflammation in the eye is associated with vision-threatening comorbidities such as glaucoma, cataract, and retinal problems. Average costs for non-infectious uveitis patients range from 3.1-8.3 times the cost of the average privately insured patients, reflecting the frequent use of the healthcare system by these patients, the prolonged nature of medical therapy, and common need for surgical interventions.

Fortunately for patients, a variety of medications developed for the treatment of other autoimmune conditions have proved useful in the treatment of non-infectious uveitis. These immunosuppressive agents decrease the abnormal immune response in some forms of uveitis. My research focuses on a comparison of the efficacy, tolerability, and cost of steroid-sparing agents in non-infectious intermediate, posterior, and panuveitis (NIIPPU). We aim to identify affordable therapies that preserve efficacy to maximize patient access while balancing cost.

Specific Project Described in the Video:
I will present preliminary results from a meta-analysis of randomized controlled trials of steroid-sparing therapies in NIIPPU. Meta-analyses are studies which aggregate data from many independent, smaller studies in order to understand broader trends. Rather than having to make judgments on every individual study in a body of literature, clinicians may rely on high-quality meta-analyses to provide a global understanding of a specific clinical question. Cochrane Reviews are a collection of systematic meta-analysis-based reviews that are internationally recognized as the highest standard of evidence-based information in health care, and this project is registered as a Cochrane Review through Cochrane Eyes and Vision. Our main objective with this meta-analysis is to compare the efficacy and tolerability of select steroid-sparing, non-biologic agents (methotrexate, mycophenolate mofetil, tacrolimus, cyclosporine, and azathioprine) in the treatment of active, non-infectious intermediate, posterior, and panuveitis in adults. We also plan to do cost analyses of these treatments. Ultimately, we hope to provide a set of recommendations that clinicians around the world may turn to for guidance in the care of their patients with uveitis.



Kevin K. Fuller, PhD

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Focus of Vision Research and its Economic/Societal Impact:
My group studies a potentially blinding infection of the cornea called fungal keratitis (FK). Conventional drug therapy fails in up to 60% of FK patients, resulting in the need for one or more corneal transplants. We therefore seek to identify host and microbial determinants of disease pathogenesis that will guide the development of better non-surgical interventions.

Each year, FK occurs in an estimated 1 million individuals worldwide, with about 30,000 cases in the United States each year. Contact lens wear is an important risk factor for these infections, as illustrated by a recent multi-state outbreak that was traced to a commercial contact lens cleaning solution. However, the major risk factor for FK is agriculture-related ocular trauma, meaning lower socioeconomic populations are disproportionately impacted. Thus, our work aims to mitigate the quality-of-life and economic burden FK imposes on this underserved population.

Specific Project Described in the Video:
A hallmark of FK pathology is severe inflammation that results in pain, photophobia (light sensitivity), and acute vision loss. Even if the infection resolves, inflammatory damage may result in corneal scarring with concomitant long-term visual impairment. Though inflammatory cells that invade the cornea during infection are well described, the corneal resident cells that initiate the response are not. As fibroblasts are one of the few cell-types present in the healthy cornea, we hypothesized they play a central role in early disease pathogenesis.

We developed a novel model of fungal keratitis in which human corneal fibroblasts are cultured and form a 3-dimensional collagen matrix. Following infection of these 3-D constructs with the mold *Fusarium*, we found that fibroblasts internalize the fungal spores, become hyper-inflammatory, and secrete proteins involved in direct corneal damage. Taken together, these data suggest that corneal fibroblasts play an important role in driving the early pathology of infection and that these cells could be the target for fungal keratitis treatment or prophylaxis.

Thomas V Johnson III, MD, PhD

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Focus of Vision Research and Economic/Societal Impact:
Glaucoma is the most common optic nerve disease, affecting approximately 3 million Americans and more than 75 million people worldwide. Disease prevalence will climb as the world's population ages, and by 2040 more than 110 million people will have glaucoma, with 10 million permanently blind in both eyes from it. The disease disproportionally affects racial minorities and represents the leading cause of irreversible blindness for African Americans and Latinos. A combination of glaucoma healthcare costs and productivity loss costs the United States more than $3 billion per year.

Vision lost to optic neuropathies such as glaucoma is permanent because human optic nerve cells (called retinal ganglion cells or RGCs) neither regenerate their communication fibers (axons) nor spontaneously repopulate after injury or when affected by disease. Therefore, currently available treatments are capable only of preserving residual vision by modifying disease risk factors–this is why glaucoma physicians prescribe eye drops, for instance. Unfortunately, glaucoma patients experience irreversible blindness due to late diagnosis and/or suboptimal treatment response. Developing new treatment approaches that could replace RGCs and regenerate the optic nerve could restore vision to millions of people, positively impacting quality of life and healthcare economics. More broadly, proof of principle for human optic nerve regeneration would be a unique advance in neuroscience and could help inform methods for repairing other parts of the central nervous system, such as the spinal cord.

Specific Project Described in the Video:
My laboratory is committed to overcoming the barriers that exist to stem cell transplantation-mediated optic nerve regeneration. We are able to produce human RGCs "in a dish" by differentiating stem cells, including those derived from adult human skin or blood samples. In order for these RGCs to restore vision, they need to be transplanted into living eyes and re-establish connections between the retina within the eye and the visual centers of the brain. By transplanting these RGCs into models of glaucoma and other types of optic nerve degeneration, we have identified critical structural barriers to the integration of transplanted RGCs with the recipient retina. We have developed methods to circumvent these barriers and, in doing so, increased the ability of transplanted RGCs to extend communication fibers into the retina by more than 40-fold. Ongoing work aims to carefully evaluate the neurocircuitry that is established within the retina by these transplanted neurons, with an ultimate goal of translating this technology to human patients.

Arathy Kartha, PhD

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Focus of Vision Research and Economic/Societal Impact:
Visual impairment is associated with reduced functional and economic independence and has a huge impact on patients' quality of life when caused by severe eye disease, where the impact is lifelong. There are currently an estimated 1 million Americans with severe-to-profound visual impairment, and these numbers are expected to double by 2050.

My postdoctoral research mainly focuses on people with profound visual impairment or ultra-low vision (ULV). ULV refers to vision <20/1600, that is the inability to read the top line of letters on an eye chart at 0.5m. People with ULV are those with end-stage diseases of the eye and congenital defects.

Methods to quantify ULV have received limited attention, yet can have critical impact to guide visual rehabilitation and improved quality of life, and to understand and improve visual potential of various sight restoration clinical trials for visual prosthetics, gene therapy, or stem cell therapy that enroll patients with vision at the ULV level and rely on these methods to assess treatment benefit.

Specific Project Described in the Video:
Along with my mentor Dr. Gislin Dagnelie, I am currently developing and validating tests to assess functional vision in people with ULV. Using virtual reality, we have developed a series of tests to assess visual information gathering, eye/hand coordination, and visual wayfinding in people with ULV. Virtual reality offers a robust and unique platform for developing functional assessment because it not only allows the ability to measure performance under controlled settings but also is portable for community and in-home assessments.

T. Y. Alvin Liu, MD

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Focus of Vision Research and Economic/Societal Impact:
My research centers on the application of deep learning (DL) in ophthalmology, currently the cutting-edge artificial intelligence (AI) approach for medical image analysis, with three areas of focus:

- We aim to use DL to develop a novel survival prediction tool based on digitized pathology images of uveal melanoma, the most common primary intraocular malignancy in adults.

- We aim to use DL for large-scale, automatic Optical Coherence Tomography (OCT) analysis in age-related macular degeneration (AMD). OCT imaging has revolutionized the field of ophthalmology, and AMD is the most common reason for central vision loss in persons over 50 years in age in the United States. The burden of AMD is expected to increase exponentially as our society ages. Currently, measurement of OCT metrics in AMD clinical trials is done manually at certified reading centers and is labor-intensive and time-consuming. Our approach will allow for automatic quantification of OCT lesions and detailed phenotyping of disease, which could further maximize the impact of OCT technology and largely replace the costly process of manual OCT grading.

- I am working with a multi-disciplinary team within Johns Hopkins Medicine to integrate IDX, a completely automatic AI system for diabetic retinopathy screening at primary points of care, into our health care system. We plan to measure the cost savings and value of implementing IDX at a systems level to demonstrate that a particular AI technology, when deployed appropriately, can improve outcomes and value for various stakeholders. This, to our knowledge, has never been substantiated and will help define the evolving relationship between AI tools, clinical practice, and healthcare delivery.

Specific Project Described in the Video:
Survival Prediction in Uveal Melanoma Using Deep Learning
Our approach harnesses the incredible pattern-recognition power of DL to extract useful prognostication information from digital pathology slides that would otherwise be indiscernible to human pathologists. This represents a paradigm-shifting method for cancer survival prediction. This tool could be utilized remotely around the world with a quick turn-around time and become an alternative to the current gold standard, which is a costly gene expression profile test that is only available in the US. In addition, the technical pipeline that we develop can be adapted and generalized to DL analysis for a wide range of malignancies beyond uveal melanoma.

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Focus of Vision Research and Economic/Societal Impact:
My research is centered on investigating the feasibility of tele-rehabilitation in low vision rehabilitation. Low vision is defined as a visual impairment which cannot be corrected with glasses, contact lenses, surgery, or medication. Low vision causes difficulty performing daily activities and often results in the loss of independence as well as difficulty performing simple tasks such as reading, which negatively impacts an individual's quality of life. Low vision has also been shown to increase the risk of depression, anxiety, and mortality. The number of visually impaired individuals has increased drastically over the years. In 2004, 3.5 million Americans older than 40 years of age had low vision. Prevalence is now estimated at 5.7 million individuals in the United States, with cases predicted to double by 2050. Vision research can reveal methods of improving quality of life for the increasing numbers of visually impaired individuals, reducing the negative impacts of low vision on individuals.

Specific Project Described in the Video:
I have implemented a novel concept which involves the use of remote access of a Smartphone to provide tele-rehabilitation to individuals with low vision. Participants are seen for their initial low vision rehabilitation in an office, with the follow-up rehabilitation session scheduled via teleconference. The follow-up session is conducted by a low vision provider who remotely accesses a participant's Smartphone and provides training on how to use the low vision aid prescribed during the initial office visit. The overall goal is to determine whether this method of rehabilitation is feasible in allowing visually impaired patients to have access to training without leaving the comfort of their homes, enabling them to preserve their quality of life.

Freya Mowat, BVSc, PhD

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Focus of Vision Research and Economic/Societal Impact:
Aging predisposes people to vision impairment and increases the risk for blinding diseases such as age-related macular degeneration (AMD, the most common cause of vision loss in persons over the age of 65). There is both an economic and personal burden of vision impairment. By year 2050, age-related eye disorders in the United States will cost more than $700 billion. Visually impaired adults experience difficulties with self-care, transportation, and medication administration, which compounds many of the physical difficulties associated with aging. Vision impairment is also associated with a decline in mental ability (cognitive function). This combined visual and cognitive decline increases the risk of loneliness and depression, resulting in an urgent need to study vision and cognitive impairment in our aging population to develop early interventions that limit the economic and psychological burdens.

Specific Project Described in the Video:
I study vision in dogs—important companion animals that live with us in our home environment and experience similar lifestyles to us. Our hypothesis is that by monitoring the health of pet dogs, we may provide an early warning for risk factors that will affect their human owners. We have studied the anatomy and function of the retina in normal dogs and have begun to explore what happens to pet dogs' vision and mental abilities as they age.

Human age-related visual and cognitive decline has been studied for many decades by University of Wisconsin researchers. They have received NIH funding to consistently follow the health of a group of people living in Beaver Dam, Wisconsin. Many of these human participants have pet dogs, and our long-term goal is to study the age-related visual and cognitive decline in pet dogs compared with their human companions. If dogs are indeed early warning systems, we can understand more quickly what environment and lifestyle factors negatively impact aging and what treatments may have promise for translation to humans. Dogs could truly prove themselves to be "man's best friend"!

Lucy Mudie, MD MPH

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Institution: University of Colorado, Denver, Colorado

Focus of Vision Research and its Economic/Societal Impact:
The focus of my work is prevention of avoidable vision impairment—81 percent of all vision impairment could be avoided if diagnosed and treated on time, and $102 billion could be saved if avoidable vision impairment was eliminated in the United States. Minorities are often disproportionately affected, for example, African Americans are more likely to experience vision loss from glaucoma while Hispanic populations are more like to have vision-threatening complications from diabetes.

Although population-based screening programs have shown promise in preventing some causes of avoidable vision loss, studies to improve inequity in eyecare delivery have yet to provide guidance for eyecare professionals in daily clinical practice. At a safety-net hospital, which sees a disproportionate share of minorities and non-English speakers, eyecare providers need to be able to take care of these patients in a way that is efficient, cost-effective, and successful in preventing avoidable vision loss.

Specific Project Described in the Video:
Focusing on non-English speakers compared to English speakers, my study evaluates how eyecare delivery varies by patient demographic factors at our large, safety-net hospital. The data show that non-English speaking patients have the same time or less spent with a provider when compared to English speakers. Since you would expect the language barrier to require more time for translation, this suggests that less care is being delivered to non-English speaking patients. This data is a jumping off point for those involved in eyecare, alerting us to the problem and then forming a baseline from which we can improve, ensuring that the patients at our safety-net hospital are receiving quality care and resources are being utilized efficiently.

Tareq Issam Nabhan, OD

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Focus of Vision Research and its Economic/Societal Impact:
The basis of this project is to determine viral transmission risk associated with modern non-contact tonometry (NCT) tools through novel computer vision techniques performing the evaluation. NCT differs from contact tonometric methods in that no physical contact between patient cornea and device occurs. The NCT measures intraocular pressure (IOP) via a burst of air which applanates the cornea of the eye (known generally as the "air-puff" test). Many ophthalmologic and optometric offices use NCT to measure IOP of patients.

In the age of pandemic, two fundamental questions must be answered:

- Do COVID-19 particles exist on the ocular surface tear-film?
- Do modern NCTs cause invisible tear-film splatter and/or aerosolization?

According to a retrospective case series published March 31, 2020 in *JAMA Ophthalmology*, nearly 30 percent of COVID-19+ patients hospitalized in Hubei Province, China had ocular findings. Several other studies published in the *Journal of Medical Virology* and the *New England Journal of Medicine* have shown that SARS-CoV-2 RNA has been detected in ocular secretions of COVID-19+ conjunctivitis patients. More still, Britt et al. published a paper in 1991 that determined splatter and micro-aerosol potential of the tear-film by currently antiquated NCT instruments—however, artificially added tear-film volume was needed for improved detection due to photographic limitations at that time. Based on the study claims mentioned, it is possible that COVID-19 associated conjunctivitis could have viral particles in ocular secretions. Moreover, it is apparent that improved aerosol image detection methods using novel computer vision techniques to test modern NCT equipment is warranted. Said results could help determine viral transmission risk and potentially guide clinical best-practices.

Specific Project Described in the Video:
We propose the use of modern hardware/software solutions using the processing and communications power of mobile devices coupled with image processing and computer vision techniques to evaluate and analyze splatter and aerosolization potential of the ocular tear-film layer from modern noncontact tonometry machines. The study is meant to collect data for use in development and validation of software to perform the analysis. The results of splatter and aerosolization risk by modern NCT tools may help guide both proper disinfection techniques and best-practice intraocular measuring methodologies globally.

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Focus of Vision Research and its Economic/Societal Impact:
The focus of my work is the mitigation of vision loss after ocular trauma. More than 2.4 million eye injuries occur yearly in the United States, rendering patients unable to return to their work. Such injuries require intense treatment and the burden of visual impairment falls not only on the families, but also to the economy and society as a whole. According to the World Health Organization (WHO), corneal blindness is the fourth leading cause of vision loss, responsible for 5.1 percent of the total world blindness after cataract, glaucoma, and age-related macular degeneration. Considering that ocular traumas also lead to retinal pathologies and glaucoma, such injuries represent a major reason for permanent vision loss in our societies. Development of new treatment modalities to protect and restore the eye after trauma is, therefore, a fundamental need in clinical ophthalmology.

Specific Project Described in the Video:
My work focuses on vision restoration after ocular trauma. To this end, I am implementing engineering and molecular biology techniques to restore corneal clarity after injury and to protect the most vulnerable retinal tissue from subsequent degeneration. Most notably, our lab is developing novel designs for artificial corneas, such as the Boston Keratoprosthesis and Lucia, both FDA-approved for replacing the injured cornea with a bioengineered clear window. Moreover, our groundbreaking work using high-throughput single cell RNA sequencing led to the discovery of immune mechanisms implicated in glaucoma pathogenesis after injury, as well as to the development of new therapies for retinal protection.

Most importantly, our mechanistic work extends beyond the eye providing important insights into the regulation of the immune cells in other compartments of the central nervous system (CNS). As such, these findings may also be relevant for the treatment of other degenerative conditions of the CNS.

Jolene Rudell, MD, PhD

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Focus of Vision Research and its Economic/Societal Impact:
I am a pediatric ophthalmologist, and the focus of my research is strabismus, or eye misalignment, which is a common and serious eye disorder that affects 2-6 percent of the population worldwide. Strabismus is associated with amblyopia, or “lazy eye”, which is the leading cause of irreversible vision loss in children and results in significant visual morbidity that continues into adulthood. Despite its prevalence and its effects on visual morbidity and quality of life, the underlying mechanisms of strabismus remain largely unknown. The treatment for strabismus is primarily surgery—the third most common eye surgery in the United States with more than 1.2 million performed each year. However, long-term studies show that approximately half of these surgeries fail over time, with outcomes highly unpredictable and variable.

My research focuses on studying tissue samples from patients with strabismus to examine its cause. I am also examining new drugs that show promise as an effective therapy for strabismus to determine why they work. With this research, I am looking to find better therapies to improve my patients’ quality of life.

Specific Project Described in the Video:
The challenge is that, although strabismus patients present with the same type of strabismus and eye misalignment, we suspect that the underlying causes are not the same. My project analyzes the extraocular muscles in patients with the same type of strabismus (specifically overelevation in adduction), and in this cohort we examine the patients who have a genetic syndrome (Apert syndrome) and patients without this syndrome (patients with primary inferior oblique overaction). We found that the extraocular muscles in these patients were very different, with Apert syndrome patients having extraocular muscles that were significantly smaller with increased muscle regeneration compared to patients with primary inferior oblique overaction and patients without strabismus.

In conclusion, the muscles from both sets of subjects were significantly different compared from control muscles. This supports the idea that, despite having the same type of strabismus, the potential mechanism behind its occurrence in patients is significantly different. Knowing more about the underlying causes of strabismus will improve treatment outcomes.

Benjamin Sivyer, PhD

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Focus of Vision Research and its Economic/Societal Impact:
Glaucoma, the leading cause of irreversible blindness in the world, is a group of diseases that injures the optic nerve, a bundle of fibers that connects the eye with the brain. Often called a 'silent' disease, glaucoma progresses slowly and can remain unnoticed until vision loss is advanced. It affects more than 3 million Americans and disproportionately afflicts African Americans and Hispanics. In the next 10 years, the annual economic impact of glaucoma in the United States is projected to rise from $2.8 billion to $4 billion.

The cause of glaucoma remains unclear. Although early diagnosis can significantly reduce this financial burden by allowing early treatment, it is currently limited to lowering intraocular pressure (IOP). This highlights the importance of basic science research to improve early detection and provide new cures that will protect optic nerves that continue to deteriorate despite current pressure-lowering therapy.

Specific Project Described in the Video:
My laboratory, with the help of a team of Casey Eye Institute glaucoma researchers, is approaching this problem from two ends:

- We study early changes in retinal neurons following axon injury in glaucoma models with the goal of developing new tools to aid in early detection.

- We study neurons that uniquely survive injury and aim to apply this knowledge to develop new glaucoma treatments that would be used alongside IOP lowering. We have identified, in specific retinal neurons, early markers of injury that may become visible in patients using technologies being developed by clinical researchers.

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Focus of Vision Research and its Economic/Societal Impact:
Glaucoma is one of the most common causes of irreversible blindness in the world, disproportionately affecting the African-American and Latinx communities. More than 3 million Americans suffer from glaucoma. Age, family history, and elevated intraocular pressure (IOP) are key risk factors for developing this disease. As the United States population continues to grow older, more Americans will seek ophthalmic care for glaucoma. Retinal ganglion cells are lost in glaucoma, leading to thinning of the retinal nerve fiber layer (RNFL), a specific part of the retina. This structural damage subsequently leads to the manifestation of defects in a patient's peripheral vision. If untreated, the disease can progress to central vision loss and irreversible blindness. The economic burden of caring for these low-vision individuals is immense, with reports indicating expenditures of $27,000 per-year, per-individual.

Optical Coherence Tomography (OCT) provides information regarding structural damage caused by glaucoma, while standard automated perimetry provides details regarding functional damage using visual field testing. Structure-function correlation is essential when treating glaucoma in order to provide an accurate assessment of the nature of a patient's degree of disease and to predict how rapidly they may worsen without further treatment. My research focus is in developing large structure-function databases at the Bascom Palmer Eye Institute in order to improve our ability to risk-stratify glaucoma patients. This work is essential to minimizing visits for patients who are stable or low risk, while ensuring appropriate attention is given to those at high risk for vision loss. My research involves utilizing higher-order statistical methodologies, such as Artificial Intelligence (AI), to refine our predictive abilities.

Specific Project Described in the Video:
While thinning of the RNFL is known to increase the overall risk of subsequent visual field loss, the association between the rate of RNFL loss and rate of subsequent visual field loss has not been clearly demonstrated. By evaluating our large retrospective data repository of more than 800 glaucoma patients, we demonstrated that the rate of initial RNFL loss due to glaucoma is correlated with the rate of concurrent or subsequent visual field damage; rapid structural loss over the initial 3 years led to faster visual field loss over 6 years. In addition, baseline glaucoma severity was noted to affect the rate of visual field loss. Our work shows that rapid changes noted on structural glaucoma testing should warrant the augmentation of treatment, even before visual field changes are noted. Identifying those patients with fast rates of structural change is essential to preventing functional vision loss.

Christopher Patrick Taylor, PhD

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Institution: New England College of Optometry, Boston, Massachusetts

Focus of Vision Research and its Economic/Societal Impact:
The focus of my work is myopia control. Myopia arises from the dysregulated growth of the eye, which results in refractive error. If myopic refractive error is not corrected or controlled, educational outcomes, particularly among vulnerable populations, are poorer. The global productivity loss due to vision impairment caused by uncorrected refractive error is estimated to be $202 billion annually. Myopia can lead to blindness and is a substantial risk factor for developing age-related eye diseases such as age-related macular degeneration (AMD) and tunnel vision (glaucoma). The risk of eye disease associated with myopia is equivalent to the risk that hypertension signals for cardiovascular disease.

Myopia control is an advancing field. It has recently been discovered that the role of the visual environment plays a crucial role in altering the eye's anatomy. However, more basic and applied vision research is needed to discover and translate cost-effective and scalable solutions to the public.

Specific Project Described in the Video:
I am investigating the response of the choroid to the visual environment. The choroid's response to the visual environment influences refractive error via signals that guide eye-growth. For example, viewing positive or negative contrast stimuli affects the choroid. The choroid thickens when the eye is exposed to positive contrast (e.g., white on black text) and thins in response to negative contrast (e.g., black on white text) stimuli. The choroid plays a vital role because a thinning choroid is a precursor to myopia development in animal models. We used a large sample of observers that had a range of refractive error and axial lengths. We looked at how identifying positive/negative contrast letters affected choroid thickening and thinning and how an observer's axial length mediates the thickening or thinning response. Night modes, where white on black text predominates, have become a popular mode to use on phones, tablets, and computers. This project is the first step in a series investigating whether changing the contrast mode of devices could be used, along with traditional treatments, to slow the development of myopia.

Matthew B. Veldman, PhD

Current Position: Assistant Professor, Department of Cell Biology, Neurobiology, and Anatomy

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Institution: Medical College of Wisconsin, Milwaukee, Wisconsin

Focus of Vision Research and its Economic/Societal Impact:
My laboratory studies the molecular mechanisms of retinal degenerative diseases with an emphasis on glaucoma. Glaucoma, a leading cause of irreversible blindness, affects about 2 percent of Americans over 40 years old with increasing incidence as we age. This translates to more than 3 million patients at risk of blindness. Once diagnosed, there are some treatments to prevent progression of the disease, but there is no cure and lost vision cannot be recovered. We are working to identify the basic mechanisms of this disease using animal models to test new ways to prevent neurodegeneration, as well as reverse vision loss through regenerative medicine. Glaucoma costs the United States $1.9 billion in direct medical costs.

Specific Project Described in the Video:
Loss of vision in glaucoma is caused by damage to the optic nerve and death of the cells in the eye that project visual information to the brain. In order to reverse the effects of this disease, cell death must be prevented and new connections between the eye and brain need to be generated. Although patients and commonly used laboratory animals such as mice and rats cannot regenerate optic nerve connections lost to injury, zebrafish can. Zebrafish have 70 percent evolutionary conservation of total genes and 84 percent conservation of disease genes with humans, including all known glaucoma-linked disease genes. Using technologies for analyzing gene expression and epigenetic state in zebrafish, we have identified thousands of gene expression changes and genomic loci that correlate with cell survival and nerve regeneration. Some of these changes are evolutionarily conserved with mammals while others are fish-specific. We are currently testing the identified genes and pathways for their role in zebrafish optic nerve regeneration with the goal of translating these findings first to pre-clinical mammalian models of glaucoma and eventually to enhance the treatment and visual recovery in patients.

Lauren K. Wareham, PhD

Current Position: Research Assistant Professor, Department of Ophthalmology and Visual Sciences

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Institution: Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, Tennessee

Focus of Vision Research and its Economic/Societal Impact:
The focus of my research is glaucoma, the second leading cause of irreversible blindness worldwide. There are more than 3 million people in the United States suffering from the disease, and many of these patients will go blind despite receiving current treatment options. The number of people worldwide estimated to be blind as a result of glaucoma is 4.5 million, which accounts for approximately 12 percent of all global blindness. As such, the World Health Organization (WHO) recognizes glaucoma as a "priority eye disease".

The cost to the US economy is, on average, around $2.86 billion every year in direct costs and productivity losses. Glaucoma accounts for more than 10 million visits to physicians each year with the average direct cost of glaucoma treatment for patients with late-stage glaucoma in excess of $2,511. Loss of vision in patients also positively correlates with increased depression, due to loss of independence and lifestyle changes. The highest risk demographic for the disease are the elderly, and this population is the fastest growing. Current therapies in the clinic, if the disease is caught early, only serve to delay progression of the disease; there is no cure currently available. We need novel therapeutics that not only delay progression of the disease but also help to prevent degeneration of the cells at the back of the eye that results in vision loss.

Specific Project Described in the Video:
Current therapy for glaucoma only delays progression of the disease by lowering intraocular pressure (IOP) with eye drops, or in extreme cases, surgical intervention. Despite these interventions, the disease still progresses, and patients develop irreversible blindness. Therefore, investigation into other pertinent risk factors for the disease is crucial in the development of novel therapies.

In some cases of glaucoma, such as normal tension glaucoma, there are no overt elevations in IOP, which suggests that there are other risk factors for the disease that are not yet fully understood. Glaucoma involves significant comorbidity with multiple vascular conditions, including migraine, arterial hypertension and hypotension, and diabetes, which suggests that vascular dysfunction may be a risk factor and a primary driver of disease progression. My research, which uses animal models, aims to understand how the retinal vasculature (blood vessels) changes with glaucoma disease progression—for example, do glaucoma patients have defective blood vessels and does this affect the loss of cells at the back of the eye which ultimately results in blindness? Findings from these studies may then be translated into novel areas of interest for the design of new therapeutic interventions in the clinic.

Benjamin Xu, MD, PhD

Current Position: Assistant Professor of Clinical Ophthalmology

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Institution: University of Southern California Roski Eye Institute, Los Angeles, California

Focus of Vision Research and its Economic/Societal Impact:
Glaucoma affects approximately 4 percent of Americans over the age of 40, and care costs the United States healthcare system an estimated $2.5 billion annually. Due to aging of the US population, the prevalence of glaucoma in America is expected to rise by more than 50 percent over the next two decades. This will place a heavy burden on the healthcare system and its limited number of eyecare providers.

As the prevalence of glaucoma continues to rise, eyecare providers need new clinical methods to detect and evaluate patients with strong risk factors for the disease. One such risk factor is angle closure, in which the drain that normally carries away the fluid produced inside the eye is obstructed. Angle closure leads to a buildup of fluid pressure inside the eye, a strong risk factor for glaucoma. Ideally, these clinical methods would be automated, to reduce reliance on eyecare providers, and could be conducted remotely to eliminate the risk of in-person doctor visits in the post-COVID era.

Specific Project Described in the Video:
My laboratory combines computer science and ocular imaging to develop Artificial Intelligence (AI) algorithms that detect patients with angle closure. We have developed a non-invasive ocular imaging system that can detect angle closure with a high degree of accuracy in only a few seconds. My overall research goal is to develop automated methods that can be used not only to screen patients remotely for angle closure, but to detect patients with high risk for glaucoma who would benefit from an evaluation or even treatment by an eyecare provider. These methods could be combined with other AI advances in ophthalmology to enhance the care of patients with or at risk for glaucoma-related vision loss.

Philip Yuhas, OD, PhD

Current Position: Assistant Professor

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

Focus of Vision Research and its Economic/Societal Impact:
Traumatic Brain Injury (TBI) as a disruption in brain function caused by an external force such as a bump, blow, jolt, or penetrating wound to the head. TBI is not a rare condition in the United States. In 2013, physicians diagnosed TBI in 2.5 million emergency department visits, resulting in 282,000 hospitalizations, and its incidence in the general population is rising. Among soldiers serving in the Middle East, the incidence of TBI is even higher, with nearly 350,000 diagnoses since the year 2000. Most TBIs experienced by civilians and by soldiers are classified as “mild,” but this label can be misleading. Individuals suffering from mild TBI can experience emotional, behavioral, and physical impairments that can persist for months or for years after the initial injury. The visual system is not immune from the negative effects of TBI, as blurred vision, reading difficulties, visual field loss, and photophobia (light sensitivity) are common eye-related sequelae of TBI. Currently, there is no definitive, objective marker for the diagnosis of TBI. As a result, many individuals with TBI never receive the appropriate care and support after their injury, impeding their ability to work. In fact, the economic impact on TBI in the United States is immense, with a productivity loss of $1.1 billion annually. The eye is an attractive platform for the detection of TBI pathology. The retina in the back of the eye is a direct extension of the brain. Its structure and function are easily assessed. The overall goal of my laboratory is to develop objective, accessible, and cost-effective diagnostic tests for TBI by detecting damage to retinal neurons after TBI using existing clinical equipment.

Specific Project Described in the Video:
Repeated traumatic brain injuries cause a distinct pathophysiology in the brain. Specifically, they cause the breakdown of microtubules in neurons. Microtubules are rigid, hollow rods that give neurons structure and facilitate the movement of proteins and other molecules within the cell. My project seeks to detect these same changes in the neurons of the retinas of subjects who have suffered from repeated TBIs. Using established retinal imaging technologies, I am measuring the structure of microtubules in two different types of retinal neurons, retinal ganglion cells and photoreceptors. I am also measuring the function of these cells by using electroretinography to measure their electrophysiological response to flashing lights. I expect to detect alterations to both the structure and to the function of retinal neurons in subjects who have suffered from repeated TBIs but not in healthy control subjects. If successful, this project will provide proof of principle that microtubule-associated pathology can be detected in human subjects with a history of repeated TBI. Future studies will be able to use its results to establish best practices for detecting TBI in the retina using readily available, inexpensive technologies and easy-to-administer techniques.

Nazlee Zebardast, MD, MSc

Current Position: Instructor, Department of Ophthalmology

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Institution: Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, Massachusetts

Focus of Vision Research and its Economic/Societal Impact:
Glaucoma, the leading cause of irreversible vision loss, and affects 75 million people worldwide and is projected to increase to 112 million by 2040 due to an aging population. Glaucoma is a progressive optic neuropathy resulting from retinal ganglion cell degeneration and leads to gradual loss of vision and accounts for 14 percent of global blindness. Glaucoma vision loss is associated with poor quality of life, increased falls, decreased mobility, and increased economic burden. The annual burden of glaucoma treatment is estimated at $5.8 billion, with additional loss of productivity due to glaucoma-related vision loss estimated to cost the United States economy $2.9 billion annually.

While there is no cure for glaucoma, early detection and treatment can delay progression. Glaucoma is clinically heterogeneous and disease course can be highly variable. While some patients progress to blindness, many individuals left untreated never progress to vision loss. We currently lack the ability to pre-symptomatically distinguish patients at risk of severe and progressive disease from those individuals unlikely to develop glaucoma-related vision loss. The goal of my research is to use a precision medicine approach to improve our assessment of disease risk for any individual. Detecting glaucoma earlier and accurately assessing individual disease risk will significantly reduce costs and burden of blindness.

Specific Project Described in the Video:
The goal of my work is to use data from two large biobanks and machine learning methods to discover novel image-based endophenotypes or markers for primary open angle glaucoma that can be used to understand the genetic underpinning of disease etiology and clinical course. We will use machine learning methodologies to define image based structural endophenotypes for glaucoma aligned with disease subtype and disease progression. We will then use these endophenotypes for genetic association studies to discover novel genetic variants associated with disease subtypes, as well as novel variants predisposing to progressive disease. Using a comprehensive set of genetic risk factors, we will create a series of polygenic risk scores and test their ability to detect glaucoma cases. We will build prediction models based on imaging endophenotypes and genetic risk scores for glaucoma case detection. This work will lay the foundation for individualized screening and diagnostic tests built on fundus image and genetic risk profiling.

Xiaoying Zhu, OD, PhD, MD, MS, FAAO

Current Position: Assistant Clinical Professor

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Institution: State University of New York College of Optometry, New York, New York

Focus of Vision Research and its Economic/Societal Impact:
My principal research interests encompass emmetropization (normal refraction condition of the eye in which light accurately focuses on the retina), visual development, and myopia (nearsightedness). Myopia is currently a major public health concern because of its rapidly increasing prevalence worldwide and the threat to vision. Myopia can cause a wide spectrum of complications, such as cataracts, glaucoma, retinal detachment, and myopia maculopathy. It is the leading cause of blindness in Asia, and the World Health Organization (WHO) recognizes myopia as a significant cause of visual impairment if not fully corrected. The global productivity losses associated with visual impairment from uncorrected myopia and myopia-related complications in 2015 were estimated to be $244 billion and $6 billion, respectively.

I have been studying the signaling molecules regulating emmetropization and temporal integration of defocus, using animal models, in search of potential methods for preventing and/or treating myopia in school-aged children. I also studied some intrinsic, non-visual factors involved in emmetropization and eye growth. I am currently conducting multiple clinical trials to investigate the effects of multifocal soft contact lenses and glasses with a novel design on myopia progression in school-aged children.

Specific Project Described in the Video:
Change in accommodation and in children treated with multifocal soft contact lens for myopia control.

Myopia (nearsightedness) progression is caused by elongation of the eye. Multifocal soft contact lenses (MFCLs) are one of the most promising treatment modalities used for myopia control. However, the efficacies of MFCLs present with considerable variability, potentially explained by reduced accommodation during MFCL wear. We measured the accommodative response over time in children treated with MFCLs for myopia control and correlated it with the change in eye growth in a clinical setting.

We discovered that children's accommodative response may predict future elongation of the eye and myopia progression. Specially, myopia in children who accommodate less accurately during reading may progress faster, compared with children who accommodate more accurately. These promising findings have important clinical significance. They help explain why some children respond better to MFCL treatment for myopia control than others. They also support future studies aiming to improve MFCL's efficacy by training children to maintain accommodation during reading using biofeedback technique.

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Educating about the Value of Vision Research

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 2020 has increased NEI's enacted budget to $824.1 million—21 percent more than its pre-sequester FY2012 funding level of $702 million—meaning that over those eight fiscal years it has averaged a 2.6 percent increase as compared to the average biomedical inflation rate of 2.8 percent, resulting in a loss of purchasing power.

The annual cost of vision disorders in the U.S. is $172 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 FY2020 enacted budget of $824.1 million is less than 0.5 percent of the $172 billion annual cost of vision disorders. The U.S. spends only $2.50 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 and incidence of eye disease, especially glaucoma and diabetic retinopathy.

- 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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