

# NEI Strategic Plan Vision for the Future 2021-2025



National Eye Institute

## Executive Summary

# Director's Message

I am pleased to share the *National Eye Institute (NEI) Strategic Plan: Vision for the Future*, which outlines our direction over the next five years. Why do we need a strategic plan, and why does our work at NEI matter? Most of all, our work allows us to better understand the eye and visual system, leads to therapies that prevent or eliminate vision loss, and expands opportunities for those who are blind or require vision rehabilitation. Eye and vision disorders can have profound impact on quality of life, and survey data suggest blindness is among the conditions that Americans fear most.<sup>1,2</sup>

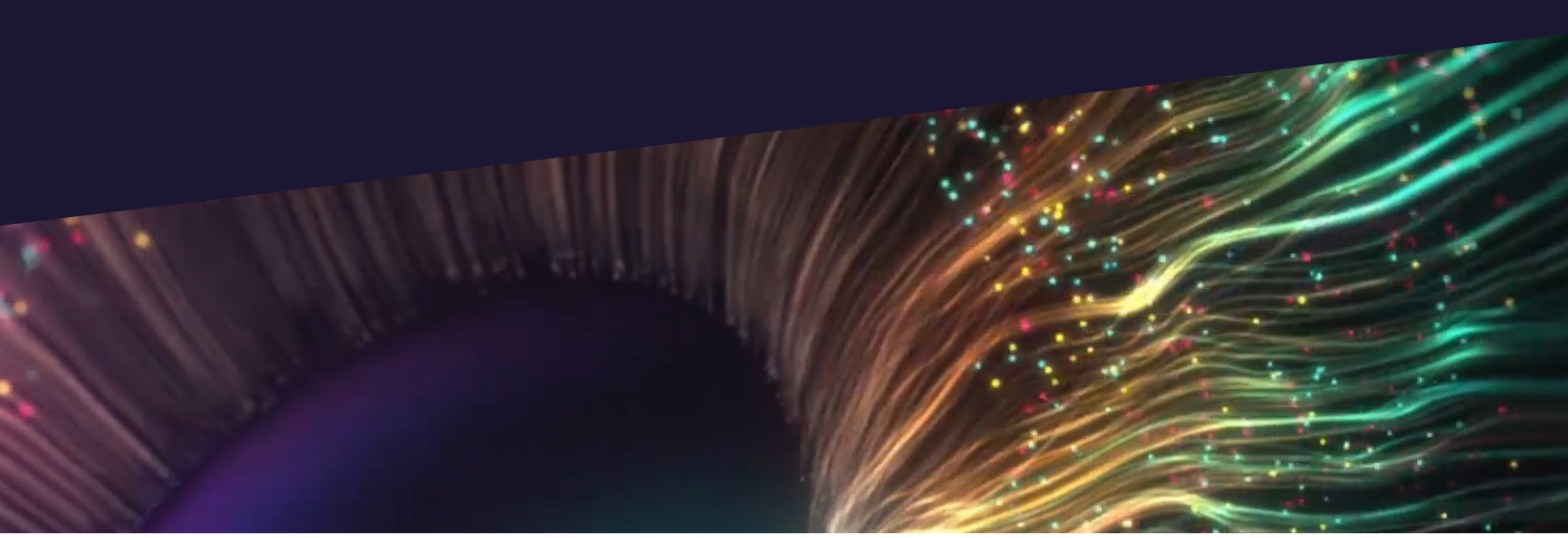


Michael F. Chiang, M.D.

Furthermore, our work matters because it can have enormous, broader impact. NEI is proud to have supported the work of eight Nobel Prize winners, including the foundational brain development studies of Hubel and Wiesel.<sup>3</sup> Many seminal innovations have occurred first in the visual system because it is an accessible setting for conducting research, which can then be generalized to other fields. For example, the first FDA-approved autonomous artificial intelligence system was created for detecting diabetic retinopathy, the first FDA-approved gene therapy for an inherited disease targeted a retinal degeneration, and key discoveries in neural information processing were initially made in the visual system.

How can we build on this infrastructure to position ourselves best for the future? This is an exciting time because remarkable advances in science, technology, and computing are creating unprecedented opportunities for knowledge discovery, clinical translation, and public health. For these reasons, we have revised our NEI mission statement for the first time in over 50 years, working with both internal and external stakeholders. This strategic plan identifies emerging opportunities for NEI to achieve our mission through





leadership to drive innovative research, inspire and train a talented and diverse next generation, and translate progress into practice. We recognize that the COVID-19 pandemic has exposed many underlying health disparities, and this plan describes steps we propose for making scientific advances more accessible to the entire population.

As NEI Director, I am simply one representative for a large community of scientists, clinicians, patients, advocates, and staff who helped develop this plan. Dr. Paul A. Sieving led NEI from 2001 to 2019, and ushered in a new era of human genetics and regenerative medicine. Our NEI Deputy Director, Dr. Santa Tumminia, served brilliantly as Acting Director during initiation of the planning process. Over 150 panelists and reviewers contributed ideas, which were organized by Dr. Shefa Gordon. The ideas within this plan are bold and ambitious, and I look forward to working with the entire community to implement them and pursue our mission of eliminating vision loss and improving quality of life.

**Michael F. Chiang, M.D.**  
Director, National Eye Institute  
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<sup>1</sup> Scott AW, Bressler NM, Ffolkes S, Wittenborn JS, Jorkasky J. Public attitudes about eye and vision health. *JAMA Ophthalmol* 2016; 134(10):1111-1118.

<sup>2</sup> Brody, J. E. (2017, February). [The worst that can happen? Going blind, people say.](#) *New York Times*.

<sup>3</sup> Wurtz, RH. Recounting the impact of Hubel and Wiesel. *J Physiol* 2009; 587(12):2817-2823.

# Executive Summary



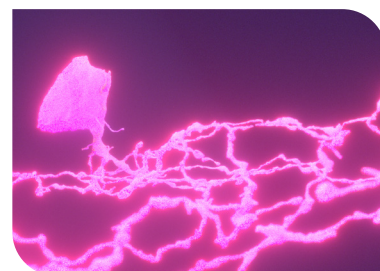
## NEI Redefines its Mission

The National Eye Institute (NEI) has been a world leader in directing and funding eye and vision research since 1968, when Congress and President Lyndon B. Johnson established it as part of the National Institutes of Health (NIH). Since that time, [NEI research](#) has dramatically transformed the treatment of many blinding diseases that were once incurable. Transparent and easily accessible for investigation, the eye and visual system have driven innovation across the entire biomedical domain in areas such as neuroscience, imaging, gene therapy, and artificial intelligence.


Now, remarkable advances in science and computation are rapidly moving us from an era where knowledge discovery was limited by technology to an era where it is increasingly limited only by creativity. *NEI Strategic Plan: Vision for the Future* comes at a particularly exciting time, with unprecedented opportunities for research and translation to clinical care. Meanwhile, the COVID-19 pandemic has not only demonstrated the importance of investments in basic and translational research, but also exposed underlying health disparities and the imperative to better understand and address social determinants of health. It is increasingly clear that scientific and clinical advances must be accessible to the entire population.

In 2020, NEI welcomed its third permanent director, Michael F. Chiang, a practicing pediatric ophthalmologist with a scientific focus on biomedical informatics, artificial intelligence, telehealth, and data science.

To adapt to the changing needs of this new biomedical and public health landscape, we have worked with stakeholders to revise NEI's mission statement for the first time in over 50 years to coincide with the release of this strategic plan as follows:



*The NEI 50 neuron was traced by an EyeWire crowdsourcing exercise in honor of NEI's 50th anniversary*



## **The mission of the National Eye Institute is to eliminate vision loss and improve quality of life through vision research.**

To achieve this mission, NEI provides leadership to:

- Drive innovative research to understand the eye and visual system, prevent and treat vision diseases, and expand opportunities for people who are blind or require vision rehabilitation
- Foster collaboration in vision research and clinical care to develop new ideas and share knowledge across other fields
- Recruit, inspire, and train a talented and diverse new generation of individuals to expand and strengthen the vision workforce
- Educate health care providers, scientists, policymakers, and the public about advances in vision research and their impact on health and quality of life

## **Supporting the Best Science: Extramural and Intramural Research**

The most important mechanism for achieving the NEI mission is supporting the highest quality investigator-initiated research. Funding decisions are based on scientific priorities, potential impact, and opportunities. Of the \$824 million appropriated by Congress to NEI in Fiscal Year (FY) 2020, 85 percent was distributed to universities and research centers across the country (extramural) and 11 percent funded research at NEI facilities (intramural). Extramural programs cover basic research from genetics and cell biology to translational animal models and complex, multi-center clinical studies. NEI also places an emphasis on recruiting, training, and retaining talent, with special consideration for new and early-stage investigators. The NEI extramural portfolio has traditionally been organized into six core programs based on anatomy and disease: retina; cornea; lens and cataract; glaucoma and optic neuropathy; strabismus, amblyopia, and visual processing; and low vision and blindness rehabilitation.

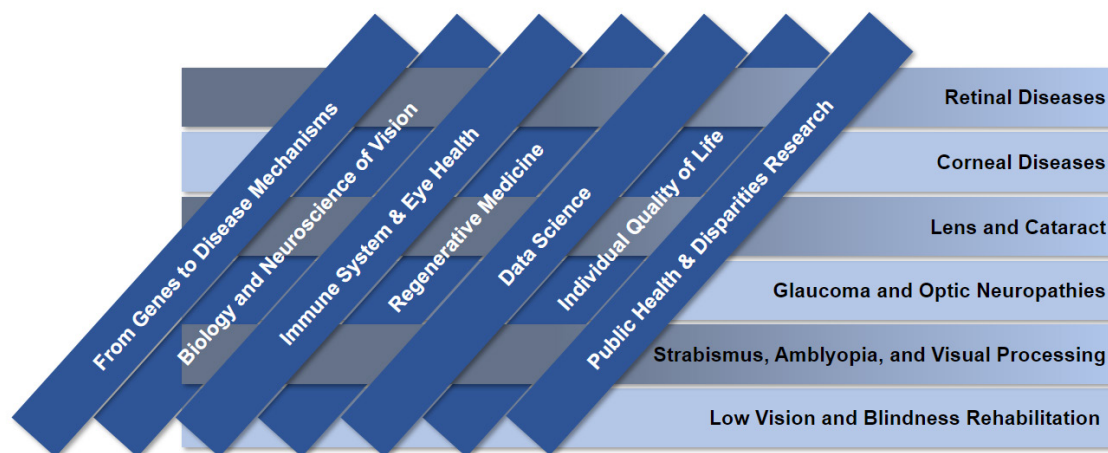
The intramural program is designed to conduct high-risk, high-reward research. Without having to write grants for peer review, intramural investigators can be nimble, quickly reallocating funds to emerging areas. With access to the unparalleled clinical research infrastructure at the NIH Clinical Center and a collaborative environment, the intramural program provides major opportunities for translational research.

## Cross-cutting Strategic Planning: Areas of Emphasis

In developing this strategic plan, NEI hopes to enhance our core research programs by layering on methodological expertise with the goals of addressing challenges across the entire visual system and facilitating translation of promising findings. To accomplish this, the strategic plan is organized across seven cross-cutting Areas of Emphasis (AoE) to highlight important perspectives and expertise that complement the existing core portfolio at NEI. Rather than replacing the existing core programs, they will underscore areas where interdisciplinary approaches can link mechanistic science with clinical applications.

While beginning to develop this plan, NEI considered the National Academies of Sciences, Engineering, and Medicine report, [Making Eye Health a Population Health Imperative](#), which called for stakeholders to establish a common research agenda. Accordingly, NEI issued a Request for Information to researchers, clinicians, patient advocates, professional societies, and the general public soliciting perspectives on research needs. Incorporating this input, NEI created diverse expert panels for each AoE, with the aim of fostering dialogue across traditional fields.

In formulating this strategic plan, NEI considered the panel reports and public feedback. The seven AoEs are summarized below, including highlights of progress, followed by key needs, gaps, and opportunities for each area.



**FIGURE 1.** Seven cross-cutting areas of emphasis in this plan intersect with each of the six core extramural programs.



## From Genes to Disease Mechanisms

How can the identification of ocular disease genes be leveraged to develop new strategies, models, and tools for elucidating genetic and environmental interactions at the cellular and systems level, and thereby accelerate mechanistic understanding and therapy development?

With thousands of known genetic mutations that contribute to eye disorders, vision researchers have pioneered innovations in genomics and gene therapy to understand disease mechanisms and to develop treatments to reverse vision loss. However, diseases like macular degeneration, myopia, diabetic retinopathy, and glaucoma often involve complex interactions of many genes and environmental factors. To catalyze progress in understanding these problems, research networks, platforms, and databases are important community resources. Yet ocular tissues and vision health are often underrepresented in publicly available datasets. This AoE builds on previous advances in identifying genetic risk factors and moves toward developing tools to decipher complex disease mechanisms. It prioritizes opportunities such as curating databases to share disparate genetic, transcriptomic, and epigenetic data, as well as establishing standard data representation models for the community. Translating basic research into impactful clinical applications also requires faithful animal- and cell-based model systems that recapitulate disease mechanisms. Additional priorities include understanding the impact of aging on eye disease at the mechanistic level, examining the interacting biochemical pathways underlying common causes of vision loss like angiogenesis and refractive error, targeting genomic studies in minority populations, and addressing gaps in gene-based therapies such as optimizing gene delivery and developing validated outcome measures for clinical trials.

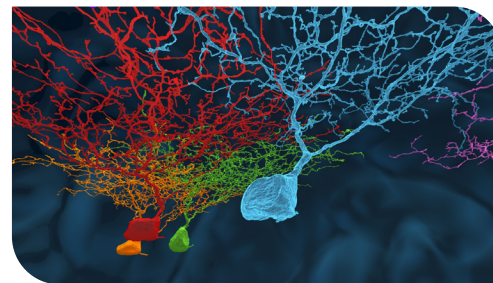


*Zebrafish core resource*

## Biology and Neuroscience of Vision

Visual neuroscience covers disparate specialties including corneal nerves, photoreceptors and phototransduction, retinal circuitry, the optic nerve and oculomotor system, and central visual processing. What are the unifying issues, common problems, and top priorities of visual neuroscience research that NEI should address?

Vision is the dominant sensory modality in humans, occupying roughly one-third of the cortex, and many vision-related problems have a neural component. With NEI playing a major role in the NIH Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative and other large-scale projects, significant progress has been made in characterizing retinal neurons and



*EyeWire crowdsourcing traced retinal ganglion cells and their connections*

their connections. This AoE describes opportunities for addressing gaps in knowledge regarding visual information processing in the retina and higher brain regions. Furthermore, since neuronal connections in the visual system continue to develop after birth, an important opportunity for focus is plasticity, the ability of neurons to reconnect after damage to the brain from injury or disease. In adults, loss of stable neuronal connections is challenging to repair in diseases such as glaucoma, retinal degeneration, and traumatic brain injury. In children, amblyopia arises from maladaptive plasticity. Cerebral (cortical) visual impairment, which can result from perinatal brain damage, will require interdisciplinary collaboration to better understand the condition and explore neuroplasticity-based therapies. Additional visual neuroscience priorities include integrating systems neurobiology and behavior into models of perception, understanding non-image-forming pathways, exploring next-generation visual prostheses, dissecting the biological mechanisms of corneal pain and itch, and promoting synergy between primate research and progress from other animal models.



## Immune System and Eye Health

The eye is a relatively unique, isolated, “immune-privileged” structure, yet many chronic eye diseases including uveitis, dry eye, age-related macular degeneration, and optic neuritis have an immune component. How can NEI develop cross-cutting program priorities and overarching goals for ocular immunology, infection, and inflammation biology?

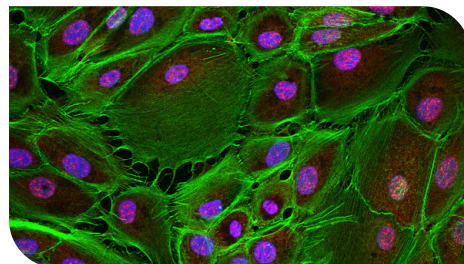
Because so many aspects of eye health are affected by the immune system, understanding immune signaling pathways may lead to new therapies for disease. While the eye may be isolated from the main immune system in the body, it is becoming clear that the eye has its own specialized immune cells that maintain balance between activation and regulation. This AoE recognizes opportunities to elucidate regulatory mechanisms supporting ocular health and function, with goals of designing new therapies to restore tissue homeostasis, and of developing steroid therapy alternatives without side effects such as cataracts or glaucoma. Improved models of chronic immune-mediated disease are required, which permit study of both positive and regulatory responses. Furthermore, aging is a risk factor for many immune-mediated conditions such as dry eye and macular degeneration, so it is also important to create model systems to study how immunosenescence affects disease. Another gap in knowledge involves characterizing the resident microbiome populations in the gastrointestinal tract and ocular surface, and their interactions with the immune system that lead to healthy and diseased states. Data analytics (e.g., applying artificial intelligence to imaging and omics datasets) may help identify new biomarkers for disease detection and surveillance, as well as develop new precision medicine approaches to therapy. Other priorities in this AoE include mitigating ocular infectious diseases and monitoring systemic immune responses to therapy.



## Regenerative Medicine

How can we build upon the leadership that vision research has provided in regenerative medicine through the Audacious Goals Initiative (AGI) to accelerate translation of new therapies that fix or replace damaged or diseased tissues previously thought to be irreparable?

Many blinding diseases, including age-related macular degeneration, glaucoma, and retinal degenerations, cause cell death in the neural retina or retinal pigment epithelium. Regenerative medicine involves replacing, engineering, or regrowing cells, tissues, or organs to establish normal visual function. The NEI Audacious Goals Initiative built academic consortia to catalyze research toward cell-based restoration of vision through neuroregeneration of the retina and optic nerve. This AoE includes a focus on addressing major barriers to translating this cell replacement work into new therapies. It will be important to understand the benefits and limitations of different stem cell sources, as well as the significance of genetic and epigenetic alterations in stem cell lines. Developing safe and effective cell therapies requires increasing the capacity and scale of cell manufacturing. Another focus is assessing transplant survival, tissue integration, and visual function outcomes. Studying material transfer, the phenomenon by which healthy transplanted donor cells transfer RNA or proteins to host cells, may provide new therapeutic options. Additional priorities in this AoE include developing cell reprogramming and gene editing applications for ocular disease, exploring the therapeutic potential of extracellular vesicles, and managing systemic immune responses to cell- and gene-based therapy products.



*Stem-cell derived retinal tissue*

## Data Science

How can NEI identify strategic investments in data science to position vision research to (1) optimize data management and data sharing while preserving safeguards and ethical protections, and (2) maintain leadership in informatics and artificial intelligence?

Exponential advances in technology and computing power have ushered in a new era where researchers have access to large-scale datasets and analytic tools including artificial intelligence and machine learning. This has led, in the past decade, to innovations such as the real-world implementation of autonomous algorithms for diabetic retinopathy screening. NEI has invested in generating clinical data (e.g., imaging, electronic health records, functional testing) and biological data (e.g., single-cell RNA-Seq, whole-genome sequencing, metabolomics). Today, accompanying investments are needed for storing, managing, analyzing, and sharing these data, and for ensuring that datasets are large enough and representative of the entire population. Added to that is the need for inclusion of vision-specific data missing from large-scale research efforts, such as the NIH *All of Us* Research Program and the Genotype-Tissue Expression Project. This AoE addresses additional critical needs such as developing infrastructure and incentives to support data sharing and data harmonization across visual science, improving generalizability and real-world applicability of artificial intelligence systems for ocular care, creating novel methods for integrating cross-modality data for analysis (e.g., clinical, imaging, omics), and expanding the workforce in data science through training programs and collaborations.





## Individual Quality of Life

Since vision research is often focused on preventing or reversing vision loss, how can NEI address the needs and perspectives of individuals, including those living with blindness or low vision, to advance their independence and improve quality of life?

Eye and vision health covers a range of experiences, from correctable problems such as using eyeglasses for work and school, to experiencing pain from dry eyes, to developing a blind spot from macular degeneration impacting an individual's ability to drive, to complete blindness in a young child with retinopathy of prematurity. This AoE describes opportunities to empower individuals as partners with their vision care providers and to develop resources for education, employment, and navigation. There is growing recognition about the value of incorporating patient perspectives in vision-related quality-of-life assessments for clinical research studies and patient-reported outcomes for measuring quality of care. There are currently over 7 million Americans and 250 million people globally with blindness or uncorrectable low vision.<sup>4</sup> Individuals with irreversible vision loss must learn to adapt to their conditions by relying on their other senses and making use of accessibility devices, adaptive equipment, and social support. This AoE highlights opportunities to maximize visual function and mental well-being for these individuals by developing and evaluating personalized approaches to rehabilitation based on medical and social factors, and by incorporating integrated care management, information technology, and neuroscience with vision rehabilitation research.



*Perceptions11 was created by artist John Bramblitt. After losing his vision in 2001, he taught himself how to paint using raised lines to help him find his way around the canvas, and through something called haptic visualization, which enables him to "see" his subjects through touch.*

<sup>4</sup> Flaxman AD, et al. Prevalence of visual acuity loss or blindness in the US: a Bayesian meta-analysis. *JAMA Ophthalmol* 2021; 139: 717-723.

## Public Health and Disparities Research

Visual impairment and blindness are significant public health problems in the United States despite major biomedical research advances to detect and treat eye disease. What research can facilitate application of basic and clinical advances to improve vision and preserve sight for all? This population health perspective explores the intersecting fields of epidemiology, health services, and health disparities, including women's and minority health.

Vision loss and blindness are a leading cause of disability in the United States. The public health and economic impacts are enormous, particularly when considering associated problems such as lost productivity, social isolation, and acceleration of dementia. There are often significant barriers to accessibility of vision care for high-risk groups such as elderly people, children, communities of color, and those in rural or urban underserved communities. Existing population health initiatives have been working to address these challenges, and NEI can provide a focal point for coordinated research strategies aimed at delivering clinical advances and vision health services to all. This AoE recognizes opportunities to develop large-scale representative epidemiological data on eye diseases and conditions through data sharing and harmonization of research methods. Also, new models for improving quality and accessibility of vision care delivery, such as telehealth, must be developed and evaluated. Other key priorities include understanding the social determinants of vision care and eye health, especially those impacting preventable vision loss, as well as the promotion of health equity by expanding diversity in research, workforce, and environment.



# Bold Predictions

The following “Bold Predictions” are aspirational vision research goals, potentially within reach. They are not an exhaustive list but were chosen to illustrate the range of NEI research. Despite the risks associated with making short-term predictions, it is important that NEI continues to place high hopes on the ability to push the boundaries of innovation.

1. Efficacy of the first induced pluripotent stem cell (iPSC)-derived products will be demonstrated in patients with age-related macular degeneration (AMD).
2. Artificial intelligence tools will improve detection and management of conditions such as glaucoma and diabetic retinopathy, and educational programs will be developed to help clinicians apply these tools in real-world settings to result in improved patient outcomes.
3. A complete catalog of retinal cells types will be created in multiple mammals and will reveal gene-expression profiles, circuit connectivity, and contributions to visual function and disease.
4. Control over the expression of genes in specific cell types will enable the restoration of vision to those suffering from retinal degeneration.
5. Strategies for treating chronic intractable inflammatory eye disease will be developed based on manipulating the gut microbiome through a combination of antibiotics, dietary interventions, fecal transplants, and probiotics.
6. Telehealth will be used for remote screening and management of common eye and visual diseases, and will improve eye care accessibility for people with limited mobility or residing in medically underserved areas.



7. Infrastructure for large-scale sharing and analysis of vision-related data, including definitions and standardization of data elements and biomarkers across multiple data types, will enable knowledge discovery and predictive disease modeling.
8. Neuroplasticity research will enable therapeutic strategies that reprogram an adult brain to behave like a developing brain with the ability to form and reorganize synaptic connections in response to injury or vision loss.
9. Newly discovered genes will be leveraged to develop candidate therapies for glaucoma.
10. New therapies to control the balance between immune tolerance and immune reaction will transform treatment of ocular inflammatory disease, greatly reducing the need for risky steroid medications.
11. Mobile applications utilizing cameras and other sensors will be developed for individuals with low vision by rendering graphical information into non-visual forms (e.g., auditory or tactile) and by applying computer vision methods to identify objects in the environment.
12. Improved understanding of the circuitry and mechanisms of corneal pain from conditions such as dry eye, neurological diseases, and refractive surgery will lead to new therapies.
13. Multi-omic analysis will help identify new pathogenic mutations in ocular disease genes and improve understanding of their mechanisms.
14. Vision-related quality of life and patient-reported outcome instruments will be developed for common diseases and will be incorporated into outcome measures for clinical trials and quality improvement programs.
15. Development of advanced, noninvasive functional imaging technologies at the cellular level will enable real-time assessment of regenerative interventions in the visual system.
16. Research incorporating social determinants of health will lead to new strategies for improving eye and vision disease prevention behaviors such as compliance with eye exams and medications, particularly in populations that experience health disparities.
17. Immunosuppression strategies needed for successful gene- and cell-based therapies will be developed and applied to provide optimal treatments that are tailored to the disease, the individual, and the regenerative medicine approach.



## Summary and Future Directions

Moving forward, NEI is beginning to implement ideas from this strategic plan, using the framework of the new mission statement as described below.

**Drive innovative research:** Identification of key initiatives described in this plan for implementation as solicited projects will be led by NEI staff, with input from external stakeholders. A preliminary step, announced in February 2021, was creation of new NEI coordinating offices for data science and population health.

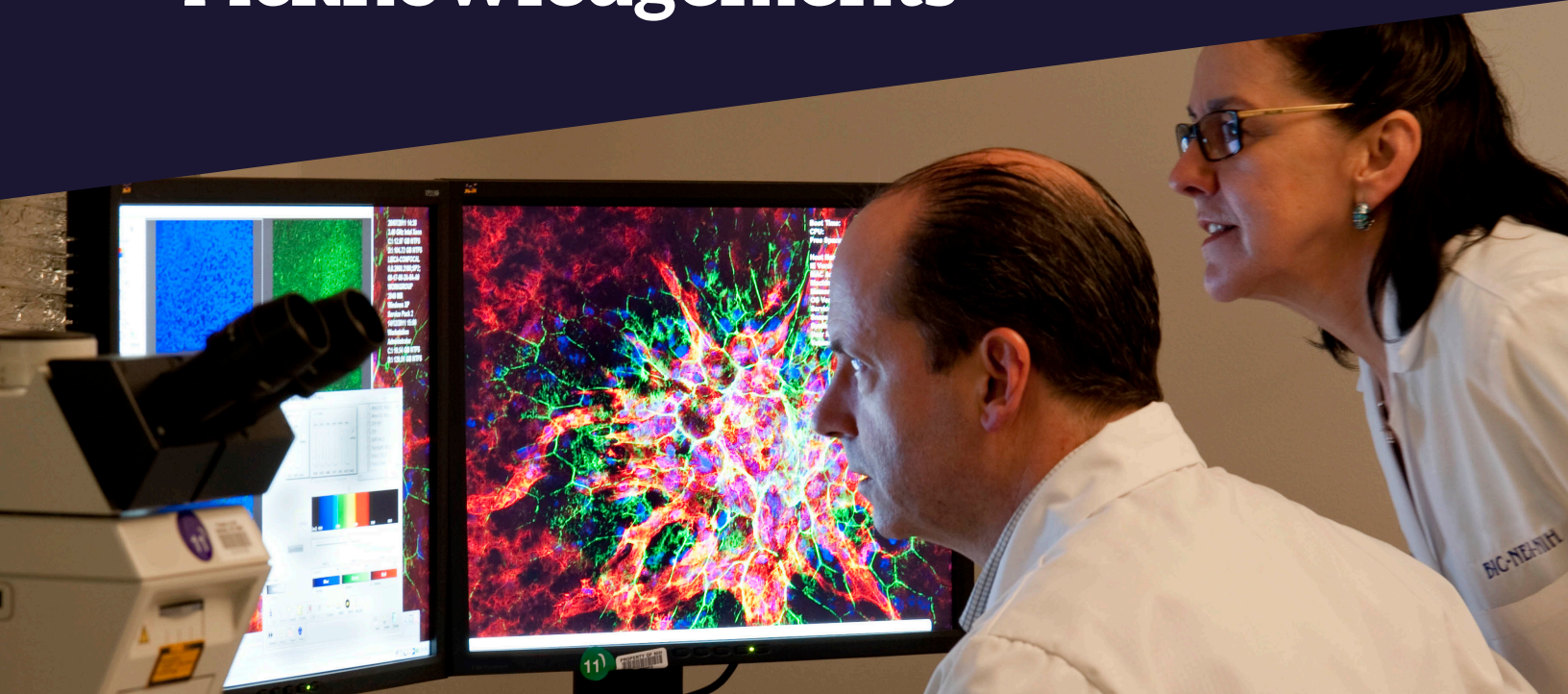
**Foster collaboration:** NEI is exploring collaborative initiatives within NIH and with other organizations. This will require a workforce of people trained in different disciplines, and NEI will examine approaches to identify the most talented scientists and engineers with methodological expertise. NEI seeks to train clinicians (e.g., M.D., O.D., D.V.M.) for the scientific workforce to create more opportunities for translational and population-based research.

**Recruit a talented and diverse workforce:** NEI is expanding workforce diversity initiatives in both extramural and intramural programs and recognizes that meaningful change will require long-term effort that engages the entire community. To focus on priorities at the Institute level, NEI established a Diversity, Equity, Inclusion, and Accessibility (DEIA) Council in March 2021.

**Educate providers, scientists, policymakers, and the public:** NEI is developing approaches to improve communication through conferences, publications, social media, collaboration with other organizations, and mechanisms such as the National Eye Health Education Program.

NEI is excited by opportunities to eliminate vision loss and improve quality of life through vision research and looks forward to working with the entire community toward this goal.

# Acknowledgements



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Digital representation of an eye; Image courtesy of Selman Keles.

### Page 4 (top)

James H. Shannon Building (Building One); NIH campus, Bethesda MD; Image courtesy of NIH.

### Page 4 (bottom)

The NEI50 neuron was traced by an EyeWire crowdsourcing exercise in honor of NEI's 50th anniversary. Image courtesy of EyeWire.

### Page 7

At the largest zebrafish facility in the country, Kevin Bishop, NHGRI Zebrafish Core staff member, holds up a tank of zebrafish to observe their behavior and physiology; Image courtesy of Ernesto del Aguila III, NHGRI, NIH.

### Page 8

Ganglion cells and their connections; Image courtesy of EyeWire.

### Page 10

Immunostaining of human iPSC-derived retinal pigment epithelium (RPE) seeded at low density; Cell nuclei (blue), actin protein filaments (green), and Transcription Factor EB (red); Confocal microscopy; Image courtesy of NEI Media Library.

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Image courtesy of John Bramblitt.

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NEI Imaging Core.



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