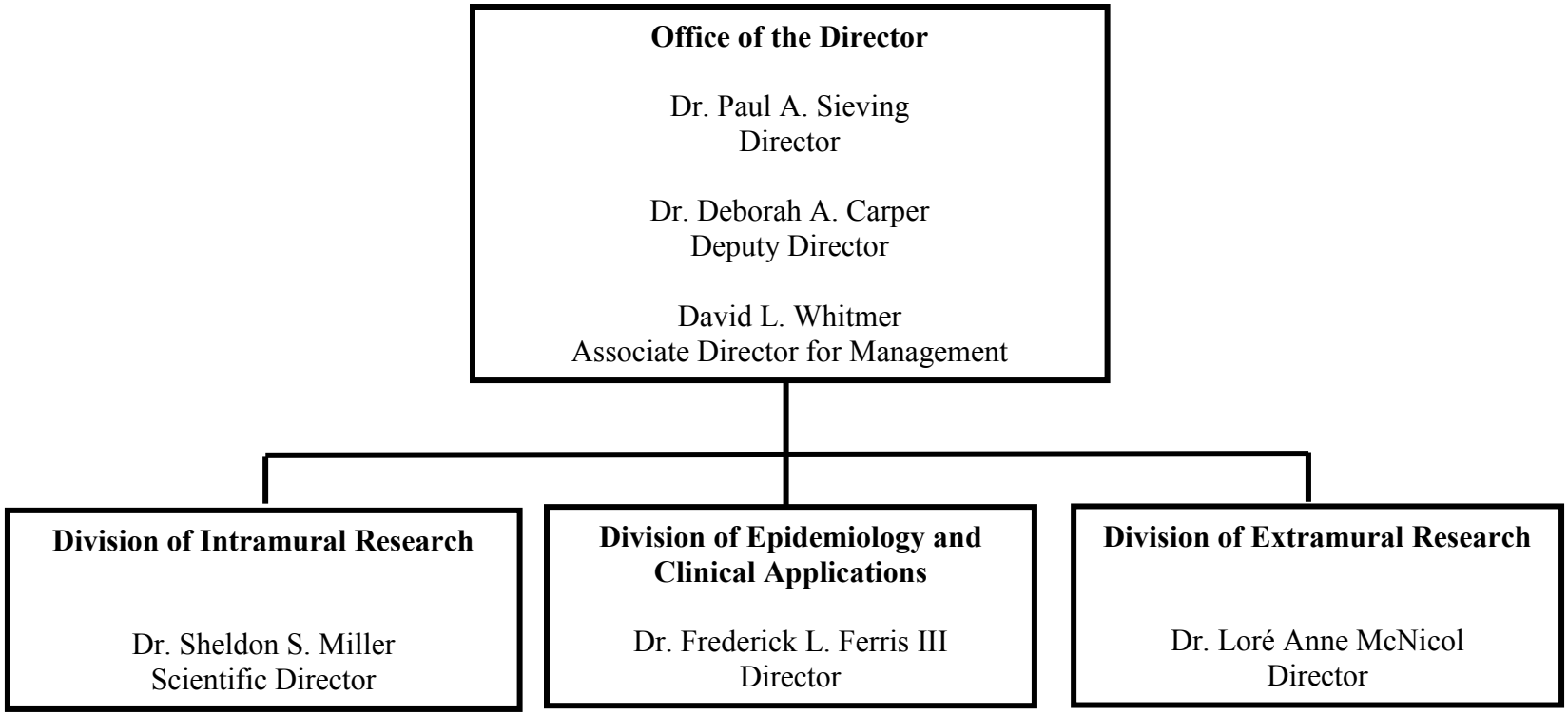
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Eye Institute (NEI)


Office of the Director
Dr. Paul A. Sieving
Director
Dr. Deborah A. Carper
Deputy Director
David L. Whitmer
Associate Director for Management
Division of Intramural Research
Dr. Sheldon S. Miller
Scientific Director
Division of Epidemiology and Clinical Applications
Dr. Frederick L. Ferris III
Director
Division of Extramural Research
Dr. Loré Anne McNicol
Director

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

For carrying out section 301 and title IV of the PHS Act with respect to eye diseases and visual disorders, **[**$682,077,000**]** *$675,168,000*.

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Amounts Available for Obligation[1]
(Dollars in Thousands)

Source of Funding	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
Appropriation	$702,712	$682,077	$675,168
Type 1 Diabetes	0	0	0
Rescission	-1,405	0	0
Sequestration	-35,271	0	0
Subtotal, adjusted appropriation	$666,036	$682,077	$675,168
FY 2013 Secretary's Transfer	-3,885	0	0
OAR HIV/AIDS Transfers	-5,637	-6,890	0
Comparative transfers to NLM for NCBI and Public Access	-787	-938	0
National Children's Study Transfers	565	0	0
Subtotal, adjusted budget authority	$656,291	$674,249	$675,168
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$656,291	$674,249	$675,168
Unobligated balance lapsing	-23	0	0
Total obligations	$656,268	$674,249	$675,168

[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2013 - $15,047 FY 2014 - $17,020 FY 2015 - $17,020

NATIONAL INSTITUTES OF HEALTH
National Eye Institute
Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2013 Actual		FY 2014 Enacted[2]		FY 2015 President's Budget		FY 2015 +/- FY 2014	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	764	$295,354	751	$304,906	737	$308,187	-14	$3,281
Administrative Supplements	*(36)*	3,209	*(15)*	1,320	*(19)*	1,704	*(4)*	384
Competing:								
Renewal	99	42,878	100	44,157	96	42,536	-4	-1,621
New	167	62,923	169	64,799	163	62,420	-6	-2,379
Supplements	1	154	0	0	0	0	0	0
Subtotal, Competing	267	$105,956	269	$108,956	259	$104,956	-10	-$4,000
Subtotal, RPGs	1,031	$404,518	1,020	$415,182	996	$414,847	-24	-$335
SBIR/STTR	34	17,420	36	18,517	37	19,125	1	608
Research Project Grants	1,065	$421,938	1,056	$433,699	1,033	$433,972	-23	$273
Research Centers:								
Specialized/Comprehensive	40	$26,118	40	$27,431	40	$27,431	0	$0
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	0	145	0	145	0	145	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	40	$26,263	40	$27,576	40	$27,576	0	$0
Other Research:								
Research Careers	74	$16,432	76	$16,932	71	$15,732	-5	-$1,200
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	37	36,312	36	35,585	36	35,585	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	14	11,211	15	11,711	15	11,711	0	0
Other Research	125	$63,954	127	$64,228	122	$63,028	-5	-$1,200
Total Research Grants	1,230	$512,155	1,223	$525,503	1,195	$524,576	-28	-$927
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	65	$3,226	65	$3,400	65	$3,468	0	$68
Institutional Awards	177	7,662	177	8,000	177	8,160	0	160
Total Research Training	242	$10,889	242	$11,400	242	$11,628	0	$228
Research & Develop. Contracts	41	$39,582	41	$39,978	41	$43,068	0	$3,090
(SBIR/STTR) (non-add)	*(0)*	*(114)*	*(0)*	*(175)*	*(0)*	*(175)*	*(0)*	*(0)*
Intramural Research	180	70,297	180	71,703	180	71,703	0	0
Res. Management & Support	87	23,368	87	23,953	87	24,193	0	240
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NEI	267	$656,291	267	$674,249	267	$675,168	0	$919

[1] All items in italics and brackets are non-add entries. FY 2013 and FY 2014 levels are shown on a comparable basis to FY 2015.

[2] The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

Major Changes in the Fiscal Year 2015 President's Budget Request

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note that there may be overlap between budget mechanisms and activity detail and these highlights will not sum to the total change for the FY 2015 President's Budget for NEI, which is $0.9 million more than the FY 2014 Enacted level, for a total of $675.2 million.

Research Project Grants (+$0.273 million, total $433.972 million):
NEI will support a total of 1,033 Research Project Grants (RPGs) in FY 2015. Noncompeting RPGs will decrease by 14 awards and increase by $3.281 million. Competing RPG awards will decrease by 10 awards and decrease by $4.000 million. SBIR/STTR RPGs will increase by 1 award and increase by $0.608 million.

Research Training (+$0.228 million, total $11.628 million):
Support for NRSA training mechanism will be increased by $0.228 million to cover the cost of increased stipends. The Ruth L. Kirchstein NRSA budget reflects a 2% stipend increase. These increases are consistent with stipend increases recommended by the Advisory Committee to the NIH Director and the National Research Council. In addition, this increase is consistent with 42 USC 288(b)(5), which anticipates periodic adjustments in stipends to reflect increases in the cost of living.

Research and Development Contracts (+$3.090 million, total $43.068 million):
Funds are included in R&D contracts to support trans-NIH initiatives, such as the Basic Behavioral and Social Sciences Opportunity Network (OppNet).

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Summary of Changes[1]

(Dollars in Thousands)

FY 2014 Enacted				$674,249
FY 2015 President's Budget				$675,168
Net change				$919
CHANGES	**FY 2015 President's Budget**		**Change from FY 2014**	
	FTEs	**Budget Authority**	**FTEs**	**Budget Authority**
A. Built-in:				
1. Intramural Research:				
a. Annualization of January 2014 pay increase & benefits		$30,056		$74
b. January FY 2015 pay increase & benefits		30,056		222
c. Zero more days of pay (n/a for 2015)		30,056		0
d. Differences attributable to change in FTE		30,056		0
e. Payment for centrally furnished services		11,629		194
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		30,018		-490
Subtotal				$0
2. Research Management and Support:				
a. Annualization of January 2014 pay increase & benefits		$12,882		$13
b. January FY 2015 pay increase & benefits		12,882		81
c. Zero more days of pay (n/a for 2015)		12,882		0
d. Differences attributable to change in FTE		12,882		0
e. Payment for centrally furnished services		3,050		0
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		8,261		146
Subtotal				$240
Subtotal, Built-in				$240

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Summary of Changes - Continued[1]

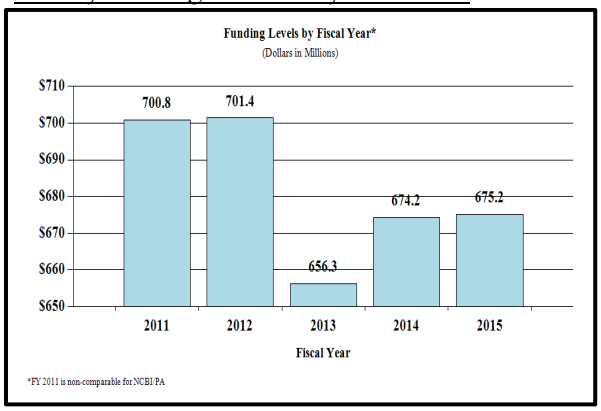
(Dollars in Thousands)

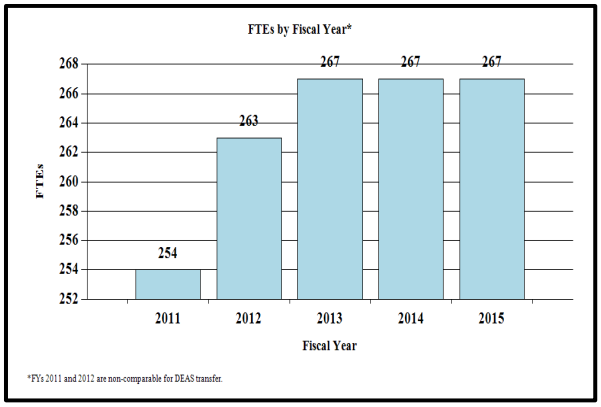
CHANGES	FY 2015 President's Budget		Change from FY 2014	
	No.	Amount	No.	Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	737	$309,891	-14	$3,665
b. Competing	259	104,956	-10	-4,000
c. SBIR/STTR	37	19,125	1	608
Subtotal, RPGs	1,033	$433,972	-23	$273
2. Research Centers	40	$27,576	0	$0
3. Other Research	122	63,028	-5	-1,200
4. Research Training	242	11,628	0	228
5. Research and development contracts	41	43,068	0	3,090
Subtotal, Extramural		$579,272		$2,391
	FTEs		FTEs	
6. Intramural Research	180	$71,703	0	$0
7. Research Management and Support	87	24,193	0	0
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, Program	267	$675,168	0	$2,391
Total changes				$919

[1] The amounts in the Change from FY 2014 column take into account funding reallocations, and therefore may not add to the net change reflected herein.

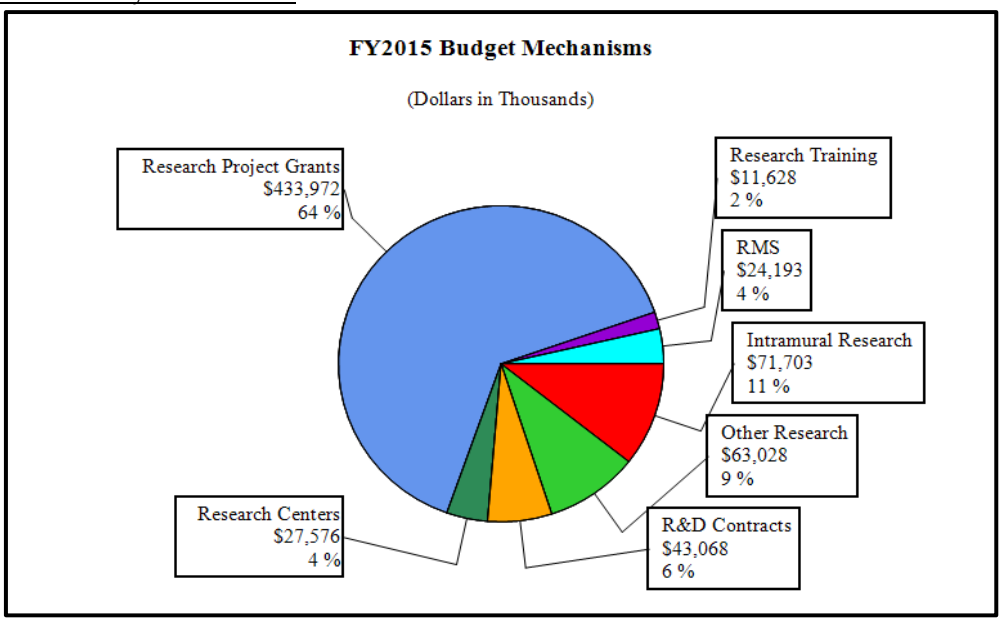
Fiscal Year 2015 Budget Graphs

History of Budget Authority and FTEs:

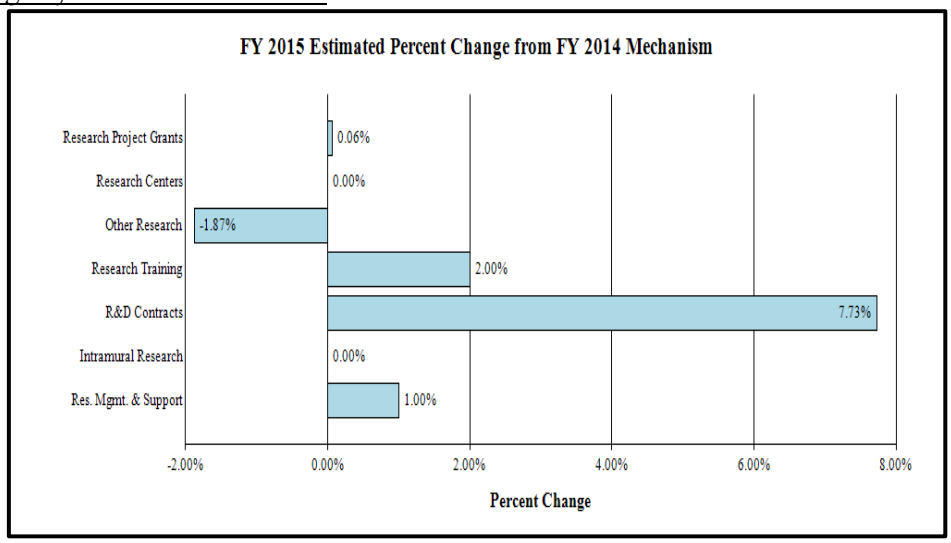




Distribution by Mechanism:



Change by Selected Mechanism:



NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Budget Authority by Activity[1]
(Dollars in Thousands)

	FY 2013 Actual		FY 2014 Enacted [2]		FY 2015 President's Budget		FY 2015 +/- FY 2014	
Extramural Research	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
Retinal Diseases Research		$269,224		$276,046		$277,190		$1,144
Corneal Diseases, Cataract, and Glaucoma Research		163,804		167,953		168,649		696
Sensorimotor Disorders and Rehabilitation Research		129,598		132,882		133,433		551
Subtotal, Extramural		**$562,626**		**$576,881**		**$579,272**		**$2,391**
Intramural Research	**180**	**$70,297**	**180**	**$71,703**	**180**	**$71,703**	**0**	**$0**
Research Management & Support	**87**	**$23,368**	**87**	**$23,953**	**87**	**$24,193**	**0**	**$240**
TOTAL	**267**	**$656,291**	**267**	**$674,249**	**267**	**$675,168**	**0**	**$919**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

[2] The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2014 Amount Authorized	FY 2014 Enacted	2015 Amount Authorized	FY 2015 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$674,249,000	Indefinite	$675,168,000
National Eye Institute	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$674,249,000		$675,168,000

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2005	$671,578,000	$671,578,000	$680,300,000	$674,578,000
Rescission				($5,508,000)
2006	$673,491,000	$673,491,000	$693,559,000	$673,491,000
Rescission				($6,735,000)
2007	$661,358,000	$661,358,000	$666,898,000	$667,166,000
Rescission				$0
2008	$667,820,000	$677,039,000	$681,962,000	$678,978,000
Rescission				($11,862,000)
Supplemental				$3,548,000
2009	$667,764,000	$690,721,000	$687,346,000	$688,276,000
Rescission				$0
2010	$695,789,000	$713,072,000	$700,158,000	$707,036,000
Rescission				$0
2011	$724,360,000		$723,220,000	$707,036,000
Rescission				($6,208,198)
2012	$719,059,000	$719,059,000	$692,938,000	$704,043,000
Rescission				($1,330,641)
2013	$693,015,000		$695,115,000	$702,712,359
Rescission				($1,405,425)
Sequestration				($35,271,328)
2014	$699,216,000		$701,407,000	$682,077,000
Rescission				$0
2015	$675,168,000			

Justification of Budget Request

National Eye Institute

Authorizing Legislation: Section 301 and title IV of the Public Health Service Act, as amended.

Budget Authority (BA):

	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
BA	$656,291,091	$674,249,000	$675,168,000	+$919,000
FTE	267	267	267	0

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

Director's Overview

Blinding eye diseases, such as macular degeneration, diabetic retinopathy, and glaucoma affect millions of Americans of all ages and ethnicities. These and other less common diseases disable productive careers and rob people of their mobility and independence. NEI supports vision research through approximately 1,300 research grants and training awards made to scientists at more than 200 medical centers, hospitals, and universities across the country and around the world. NEI also conducts laboratory and patient-oriented research at its own facilities located on the NIH campus.

Audacious Goal Initiative
NEI launched a new initiative in July 2012, intended to build upon recent advances and opportunities to propel vision research forward based on ideas submitted by the vision research community and the broader public. In the initial idea-gathering phase of the initiative, NEI held a challenge competition, which prompted individuals to submit over 500 ideas, from which 10 winning concepts were evaluated and further developed by scientific experts from within and beyond the vision research community. In May 2013, NEI announced it would focus on the goal of Regenerating Neurons and Neural Connections in the Eye and Visual System. In addition to this goal, NEI also announced two other high priority areas of research: The Intersection of Aging and Biological Mechanisms of Eye Disease and Molecular Therapy for Eye Disease. These three priorities will provide direction for NEI research in the coming decade, and will have huge impacts not only for vision, but for all of biomedicine.

Today's Basic Science for Tomorrow's Breakthroughs
A breakthrough in vision research may have implications for treating Alzheimer's disease (AD) since one hallmark of AD is abnormal deposits of beta-amyloid protein in the brain. These deposits trigger a harmful chain reaction that interrupts the processes that brain cells use to form or maintain connections with each other. NEI neuroscientists, studying visual development and memory formation in the brain, have discovered a missing link in AD progression: LilrB2

protein in humans (or PirB in mice) forms a tight physical bond with beta-amyloid, leading to deleterious consequences. When scientists deleted PirB in a mouse model of AD, they did not observe the beta-amyloid-mediated chain reaction and reduced memory loss. It is thought that LilrB2 plays a similar role in humans, and that a drug that blocks LilrB2 might prevent the effects of beta-amyloid deposits in Alzheimer's disease. These proteins were also found to control brain cell wiring during visual development, providing a possible new target for treating the childhood eye disorder called amblyopia.

Age-related macular degeneration (AMD), the leading cause of visual impairment in older Americans, changes the biology of cells. DNA sequences contain the blueprints for all genes, but individual cells only express a specific subset of genes, determined by complex biological mechanisms. One such mechanism, DNA methylation, is a chemical reaction that switches off genes. NEI investigators found that for patients with AMD, DNA methylation for the interleukin-17 receptor C gene (IL17RC) is reduced, which caused greater IL17RC protein production. This protein enhances immune responses to infections, such as fungal attacks. While the immune system normally protects cells, it is thought that uncontrolled immune activity damages retinal tissues leading to AMD. The investigators plan to determine if these changes are caused by something in the environment and find therapies to reverse the changes.

Recently, genetics and other studies have indicated a connection between cholesterol metabolism and AMD. In the eye, cholesterol accumulation in fatty deposits called drusen is associated with early stages of AMD. Immune cells called macrophages play a role in clearing cholesterol, but this function appears to be compromised with age. Using a mouse model for AMD, investigators discovered that eye drops containing a drug that promotes cholesterol release from macrophages inhibited the accelerated aging effects that lead to disease progression.

New and Improved Treatments

The Age-Related Eye Disease Study 2 (AREDS2) improved upon a landmark NEI study from 2001, which pioneered an antioxidant vitamin and mineral formulation that delays the onset of severe vision loss in late stage AMD. Since the original formulation, several studies have linked high doses of beta-carotene to an increased risk of lung cancer in smokers, but AREDS2 showed that replacing beta-carotene with two other anti-oxidants, lutein and zeaxanthin, was as effective without the increased cancer risk. Other changes such as adding omega-3 fatty acids or lowering zinc levels did not change therapeutic outcomes. The new formulation provides a safe and more effective treatment for people at risk of advanced AMD.

Results of another NEI study help identify patients who would most benefit from early AMD therapy. Researchers found that high levels of the C-reactive protein (CRP) indicated increased risk of developing AMD. CRP plays a role in inflammation and is also a risk factor for cardiovascular disease.

In February 2013, the Food and Drug Administration approved the Argus II Retinal Prosthesis System, the first implanted device that allows patients with advanced retinitis pigmentosa (RP) to regain ambulatory vision. RP is a rare, untreatable degenerative eye disease that damages the retina. Approval of the device was made possible in part by continued NEI-support of clinical trials.

Big Opportunities in Big Data
The AMD Gene Consortium, a NEI-led network of international investigators representing 18 research groups, identified seven new regions of the human genome associated with increased risk of AMD. To find these hard-to-detect genes that confer small yet significant risk of disease, the consortium employed a statistical tool called meta-analysis, which analyzed 77,000 patient and control samples. The results implicate a variety of biological functions, including regulation of the immune system, fat metabolism, and the buildup of fats in the arteries, which is called atherosclerosis.

Next-generation sequencing is a powerful new tool used to quickly process large amounts of DNA. NEI researchers used this technology to study patients with a severe form of near-sightedness, called high myopia, which can lead to glaucoma, cataract, and detached retina. They recently identified a mutation of the SCO2 gene in patients with high myopia. SCO2, involved in copper metabolism, helps maintain proper oxygen levels, which is important in tissues with high energy demands, such as the retina. SCO2 mutations are now being examined for effects on other diseases.

Overall Budget Policy:
The FY 2015 President's Budget request is $675.168 million, an increase of $0.919 million or 0.1 percent above the FY 2014 Enacted level. The most important priority is to support the highest quality research that will help achieve the mission of the NEI. NEI recognizes that the main engine for scientific discovery is investigator-initiated research project grants (RPGs). As such, these RPGs comprise the vast majority of the NEI portfolio. With the new Audacious Goal initiative, NEI will solicit new applications from multidisciplinary teams in three areas of emphasis (*see Program Portraits*). These solicitations are expected to attract new investigators from disciplines that do not typically work in vision research.

Program Descriptions and Accomplishments

Corneal Diseases, Cataract, and Glaucoma Research: Corneal diseases, cataract, and glaucoma cause more visits to ophthalmologists than any other vision disorders. NEI supports research to address all three conditions.

- *Corneal disease research*. Corneal injuries, infections, and diseases can be extremely painful and require immediate medical attention. NEI grantees are exploring how infectious, inflammatory, and immunological processes affect the cornea, ocular pain, and how the cornea heals after a wound. Important proteins that promote or deter wound healing have been identified, providing an opportunity to develop therapies that prevent or ameliorate corneal disease.
- *Cataract research*. Worldwide, cataracts are the leading cause of blindness. NEI cataract research seeks to understand the physiological basis of lens transparency at the cellular and molecular levels and investigates strategies to prevent cataract formation and progression.
- *Glaucoma research*. Glaucoma is a blinding disease that results from damage to the optic nerve, the bundle of fibers that transmit signals from the eyes to the brain. Current therapies focus on reducing excessive fluid pressure in the eye, which causes nerve damage in the most common form of glaucoma. NEI investigators aim to understand the complex genetic and

biological factors that cause the disease and to develop early detection strategies and treatments that protect optic nerves and prevent vision loss.

Budget Policy:
The FY 2015 budget request for these activities is $168.649 million, an increase of $0.696 million or 0.4 percent above the FY 2014 Enacted level. The Audacious Goal to *Regenerate Neurons and Neural Connections in the Eye and Visual System* would prioritize glaucoma research focused on regenerating the optic nerve and understanding how the regenerated nerve can form appropriate connections with its targets in the brain. The cornea also has nerves involved in pain or in tear secretion that may be damaged by trauma or surgery. The new area of emphasis exploring the intersection of aging and biological mechanisms of eye disease will promote research on environmental factors of aging affecting cataract formation and progression.

Program Portrait: NEI Audacious Goal to Regenerate Neurons and Neural Connections in the Eye and Visual System

FY 2014 Level: $0.0 million
FY 2015 Level: $3.0 million
Change: +$3.0 million

In 2013, NEI embarked on a novel strategic planning initiative to identify highly ambitious goals in vision research. After soliciting ideas from the scientific community and general public for The NEI Audacious Goals in Vision Research program, NEI leadership identified the "regeneration of neurons and neural connections in the eye and visual system" as the biggest challenge to restoring vision for the millions of Americans who are blind or visually impaired. NEI will pursue this audacious goal over the next 10-15 years with a coordinated effort to understand plasticity and neuroregeneration in the visual system and to develop therapies that replace or restore neurons damaged by eye disease. It is hoped this initiative will not only make important contributions to vision research, but also to regenerative medicine for spinal cord injuries and central nervous system diseases.

As part of the Audacious Goal program, NEI will support research to develop stem cell-based technologies that can replace diseased neurons, explore tissue transplantation approaches that promote integration with the host visual system without evoking damaging immune responses, elucidate the biological processes that stimulate nerve fibers to form connections in the brain, uncover how nerve synapses form in developing and adult neural tissue, and understand the mechanisms that activate self-repair of neural tissue.

Because this initiative is so ambitious, NEI is working with leading neuroscientists to identify specific ocular targets, develop an implementation plan, and define outcome measures to track success. NEI plans to issue funding opportunities announcements in 2014, and is expected to ramp up support in this area to make this audacious goal a reality in the coming decade.

Sensorimotor Disorders, Visual Processing, and Rehabilitation Research: NEI supports important research in sensorimotor control, visual processing, and rehabilitation for individuals with low vision.

- *Sensorimotor disorder research*. Strabismus (misalignment of the eyes) and amblyopia (known as "lazy eye") are common disorders that develop during childhood. Program goals center on gaining a better understanding of the neuromuscular control of gaze and the development of the visual system in children at high risk for these disorders.

- *Visual processing research*. Refractive errors, such as nearsightedness, farsightedness, and astigmatism, are commonly correctable with eye glasses or contact lenses in the United States but remain a tremendous economic and personal burden globally. Major goals of this program are to discover the biochemical pathways that govern eye growth and to uncover the risk factors associated with refractive errors. NEI-supported vision scientists seek to understand how the brain processes the visual information that floods our eyes, how neural activity is related to visual perception, and how the visual system interacts with cognitive and motor systems.
- *Rehabilitation research*. Low vision is the term used to describe chronic visual conditions that are not correctable by eye glasses or contact lenses. NEI supports rehabilitation research on improving the quality of life of persons with visual impairments by helping them maximize the use of remaining vision and by devising improved aids and strategies to assist those without useful vision.

Budget Policy:
The FY 2015 budget request for these activities is $133.433 million, an increase of $0.551 million or 0.4 percent from the FY 2014 Enacted level. FY 2015 program plans include pursuing research to identify genetic risk factors for strabismus, myopia, and other ocular diseases. In 2013, NEI-supported investigators participated in an international genome wide association study (GWAS) of refractive error which found nine different risk genes. This was the largest GWAS for refractive error with over 20,500 DNA samples sequenced. Future work will focus on the function of these genes in health and disease.

Within this program area, the Neuro-Ophthalmology Research Disease Investigator Consortium, a clinical trials network dedicated to diseases of the optic nerve, will collaborate with Quark Pharmaceuticals, Inc. to conduct a multi-center study to determine the safety of the company's proprietary drug, QPI-1007, a neuroprotectant developed to treat non-arteritic anterior ischemic optic neuropathy (NAION) and other optic neuropathies in which loss of retinal ganglion cells (RGCs) leads to irreversible vision loss. A study in mice reveals an essential circuit within the developing visual system that fosters the neural connections between the eyes and the brain, a finding with implications for understanding and treating amblyopia.

Retinal Diseases Research: The light-sensitive retina is susceptible to many sight-threatening conditions, including age-related macular degeneration (AMD), diabetic retinopathy, retinopathy of prematurity, retinitis pigmentosa, Usher syndrome, ocular albinism, retinal detachment, and uveitis (inflammation). The goals of this program are to increase the understanding of disease mechanisms that cause vision loss and to develop improved methods of prevention, diagnosis, and treatment. To meet these goals, NEI supports research on the cell biology, physiology, and immunology of the retina and on the role of gene expression, gene regulation, and the environment in retinal health and disease. NEI investigators have identified gene variants for many of these diseases and have made significant progress in discovering the underlying biological mechanisms of vision loss.

Based on recent advances in a gene therapy-based strategy in retina, NEI investigators prevented central vision loss in a mouse model of retinitis pigmentosa (RP), a group of rare, untreatable diseases resulting from mutations in rod photoreceptor cells. These cells form our peripheral

vision and allow us to see in dim and dark environments. As RP progresses, patients experience night blindness and severely restricted visual fields. The loss of rods eventually leads to the degeneration and death of cones, the photoreceptor cells in the central portion of the retina that allow us to perceive fine visual detail and color. Without central vision, it is impossible to perform essential tasks such as reading, walking without assistance, or recognizing faces and objects. NIH-supported investigators genetically reprogrammed rods cells to become cones, thereby eliminating the deleterious effect of rod cell mutations that lead to cone loss. Saving cones would prevent central vision loss and would improve the quality of life for an estimated 200,000 Americans who live with RP.

Budget Policy:
The FY 2015 budget request for these activities is $277.190 million, an increase of $1.144 million or 0.4 percent from the FY 2014 Enacted level. New areas of emphasis, research on the intersection of aging and eye disease, and developing therapies at the molecular level have many applications in the retina program, including building on recent advances in gene transfer, photosensitive replacement molecules, and visual prostheses.

Program Portrait: New Initiatives to Support the Development of Molecular Therapies for Eye Disease and to Explore the Intersection of Aging & Biological Mechanisms of Eye Disease

FY 2014 Level: $ 2.5 million
FY 2015 Level: $12.5 million
Change: +$10.0 million

As part of NEI's Audacious Goal strategic planning initiative in 2013, the vision community identified two areas of research which leverage recent scientific and technological breakthroughs in both areas.

One area of emphasis, molecular therapies, was selected in part because NEI-supported gene therapy research has shown promise in early stage clinical trials. Technologies for precise gene correction are becoming a reality. NEI investigators have engineered light-sensitive molecules that restore the function of retinal cells lost to disease. Other therapeutic molecules that rescue diseased cells and restore lost function in preclinical studies have been identified. To exploit these and other specific, mechanistically targeted treatments, NEI issued a Funding Opportunity Announcement (FOA) in 2013 to encourage grant applications for molecular therapy development.

The second area of emphasis, the intersection of aging and the biological mechanisms of eye disease, is motivated by the fact that many blinding eye diseases such as cataracts, diabetic retinopathy, glaucoma, presbyopia, and macular degeneration are associated with aging. The common theme of aging in such a diverse set of eye diseases represents a challenge and opportunity. In 2013, NEI issued an FOA: to address how the failure of basic physiological processes might lead to disease, to better define the staging and pathophysiology of disease by identifying early biomarkers, to distinguish normal ocular changes associated with aging from pathologic conditions, and to explore new therapeutic interventions.

Intramural Research: NEI clinical and translational studies are focused on the cause, prevention, and treatment of major eye diseases and vision disorders; cellular and molecular mechanisms of eye development, including the expression and function of genes within the eye; immunology and infectious diseases of the eye; mechanisms of visual perception by the brain; and developing a better understanding of our ability to guide movements under sensory control. The National Ophthalmic Disease Genotyping Network (eyeGENE), an NEI intramural collaboration with patients, clinicians, and investigators throughout the United States, has

expanded its operations by collecting more than 4,700 patient DNA samples. eyeGENE enables patients to receive a genetic diagnosis for many rare eye diseases in exchange for donating DNA samples for research and participating in a clinical trial registry. Through this unique collaboration, eyeGENE is enhancing patient care, education, and research.

Budget Policy:
The FY 2015 budget request for these activities is $71.703 million, the same as the FY 2014 Enacted level. As the NEI develops priorities based on the Audacious Goal initiative, NEI intramural investigators are pioneering stem cell therapeutics (*see program portrait)*. Recognizing the many hurdles that confront the field, the NEI scientific director hosted a stem cell meeting to discuss common principles, concerns, and issues across the entire clinical development pipeline. The goal of the meeting was to identify and share information in the so-called pre-competitive space to remove road-blocks in the clinical development pipeline, and more efficiently and economically move stem cell based therapies for retinal degenerative diseases towards the clinic. The meeting proceedings will be published in 2014.

Ocular albinism, results from defects in the tyrosinase gene, is characterized by a lack of pigmentation in the skin and retinal pigment epithelial cells, which support the function of photoreceptor cells. Children with ocular albinism have varying degrees of visual impairment, including blindness. In 2012, NEI investigators in the NIH Clinical Center increased pigmentation in a mouse model of ocular albinism using nitisinone, an FDA approved drug that was found to boost tyrosinase production. In 2013, NEI intramural clinicians launched a clinical trial to evaluate this treatment.

Program Portrait: NEI Intramural Program in Stem Cell Therapeutics

FY 2014 Level: $2.5 million
FY 2015 Level: $2.5 million
Change: $0.0 million

NEI's Intramural Regenerative Medicine Program is centered on the use of induced pluripotent stem (iPS) cells. These iPS cells can be generated from any adult cell, and then converted into a variety of other types of cells such as retinal pigment epithelial (RPE) cells and photoreceptor cells. The RPE cells lie underneath the neural retina and support the function of photoreceptor cells, the light-sensitive cells that capture light and convert it to an electrical signal that is transmitted to areas of the brain where images are processed. These cell types are implicated in several diseases, including AMD, retinitis pigmentosa, and Leber congenital amaurosis.

Generating tissue-specific iPS cells is a powerful technique with several applications. A major thrust of this program is to derive iPS cells from patients with retinal degenerative diseases. Then, the iPS cells are differentiated to form RPE cells or photoreceptors and studied to identify disease-causing pathways. Diseases of interest currently include AMD, Best disease, late-onset retinal degeneration, Stargardt's disease, and retinitis pigmentosa. This program is exploiting these techniques to develop high-throughput drug screens to identify potential therapeutic compounds for treating retinal degenerative diseases.

Another potentially powerful application of iPS cell technology is to generate iPS cells from normal tissue and then differentiate those cells into monolayer sheets of RPE for tissue transplants. NEI intramural investigators are engineering a bio-degradable scaffold in order to grow the RPE tissue and transfer it to patients with RPE-associated retinal degenerative diseases.

In FY 2015, the stem cell program will expand to explore therapies for ocular albinism and coloboma, two blinding eye disorders. It will also use stem cell technologies to evaluate synaptic connections in 3-D retinas derived from iPS cells.

Research Management and Support: Research Management and Support (RMS) sustains, guides, and monitors the extramural and intramural research programs. Included in these funds is the support necessary for personnel to carry out leadership and management functions, human resource support, training, travel, purchasing, facilities, budget, planning, information technology, and extramural grant award and management. NEI currently oversees more than 1,300 grants and contracts, including research project grants, core center grants, research career development awards, cooperative clinical research agreements, and research and development contracts.

Budget Policy:
The FY 2015 budget request for these activities is $24.193 million, an increase of $0.24 million or 1.0 percent from the FY 2014 Enacted level. The research management plans for FY 2015 include the continued prudent use of RMS funds while implementing strategic changes through continuous improvement and business process reengineering to promote efficient spending.

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Budget Authority by Object Class[1]
(Dollars in Thousands)

		FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
Total compensable workyears:				
	Full-time employment	267	267	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$167	$167	$0
	Average GM/GS grade	12.2	12.2	0.0
	Average GM/GS salary	$102	$103	$1
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$99	$100	$1
	Average salary of ungraded positions	$128	$130	$1
	OBJECT CLASSES	**Enacted**	**President's**	**+/-**
	Personnel Compensation			
11.1	Full-Time Permanent	$16,685	$16,852	$167
11.3	Other Than Full-Time Permanent	12,017	12,137	120
11.5	Other Personnel Compensation	454	459	5
11.7	Military Personnel	388	392	4
11.8	Special Personnel Services Payments	3,538	3,573	35
11.9	**Subtotal Personnel Compensation**	**$33,082**	**$33,412**	**$331**
12.1	Civilian Personnel Benefits	$8,959	$9,272	$314
12.2	Military Personnel Benefits	251	253	3
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**$42,291**	**$42,938**	**$647**
21.0	Travel & Transportation of Persons	$774	$787	$13
22.0	Transportation of Things	59	60	1
23.1	Rental Payments to GSA	0	0	0
23.2	Rental Payments to Others	14	15	0
23.3	Communications, Utilities & Misc. Charges	560	569	10
24.0	Printing & Reproduction	4	4	0
25.1	Consulting Services	$61	$62	$1
25.2	Other Services	6,333	5,941	-392
25.3	Purchase of goods and services from government accounts	56,968	58,720	1,752
25.4	Operation & Maintenance of Facilities	$191	$194	$3
25.5	R&D Contracts	19,038	19,102	63
25.6	Medical Care	84	87	3
25.7	Operation & Maintenance of Equipment	4,004	4,072	68
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal Other Contractual Services**	**$86,680**	**$88,178**	**$1,498**
26.0	Supplies & Materials	$4,505	$4,173	-$332
31.0	Equipment	2,458	2,239	-219
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	536,903	536,204	-699
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	0	0	0
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$631,958**	**$632,230**	**$272**
	Total Budget Authority by Object Class	**$674,249**	**$675,168**	**$919**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

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Salaries and Expenses
(Dollars in Thousands)

OBJECT CLASSES	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
Personnel Compensation			
Full-Time Permanent (11.1)	$16,685	$16,852	$167
Other Than Full-Time Permanent (11.3)	12,017	12,137	120
Other Personnel Compensation (11.5)	454	459	5
Military Personnel (11.7)	388	392	4
Special Personnel Services Payments (11.8)	3,538	3,573	35
Subtotal Personnel Compensation (11.9)	**$33,082**	**$33,412**	**$331**
Civilian Personnel Benefits (12.1)	$8,959	$9,272	$314
Military Personnel Benefits (12.2)	251	253	3
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	**$42,291**	**$42,938**	**$647**
Travel & Transportation of Persons (21.0)	$774	$787	$13
Transportation of Things (22.0)	59	60	1
Rental Payments to Others (23.2)	14	15	0
Communications, Utilities & Misc. Charges (23.3)	560	569	10
Printing & Reproduction (24.0)	4	4	0
Other Contractual Services:			
Consultant Services (25.1)	61	62	1
Other Services (25.2)	6,333	5,941	-392
Purchases from government accounts (25.3)	38,216	36,988	-1,228
Operation & Maintenance of Facilities (25.4)	191	194	3
Operation & Maintenance of Equipment (25.7)	4,004	4,072	68
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$48,805**	**$47,257**	**-$1,548**
Supplies & Materials (26.0)	$4,505	$4,173	-$332
Subtotal Non-Pay Costs	**$54,723**	**$52,866**	**-$1,857**
Total Administrative Costs	**$97,014**	**$95,804**	**-$1,210**

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2013 Actual			FY 2014 Est.			FY 2015 Est.		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Epidemiology and Clinical Applications									
Direct:	13		13	13		13	13		13
Reimbursable:			-			-			-
Total:	13		13	13		13	13		13
Division of Extramural Research									
Direct:	33	1	34	33	1	34	33	1	34
Reimbursable:			-			-			-
Total:	33	1	34	33	1	34	33	1	34
Division of Intramural Research									
Direct:	133		133	133		133	133		133
Reimbursable:	2		2	2		2	2		2
Total:	135		135	135		135	135		135
Office of the Director									
Direct:	81	3	84	81	3	84	81	3	84
Reimbursable:	1		1	1		1	1		1
Total:	82	3	85	82	3	85	82	3	85
Total	263	4	267	263	4	267	263	4	267
Includes FTEs whose payroll obligations are supported by the NIH Common Fund.									
FTEs supported by funds from Cooperative Research and Development Agreements.	0	0	0	0	0	0	0	0	0

FISCAL YEAR	Average GS Grade
2011	12.1
2012	12.3
2013	12.2
2014	12.2
2015	12.2

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Detail of Positions

GRADE	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
Total, ES Positions	1	1	1
Total, ES Salary	167,441	167,441	167,441
GM/GS-15	32	32	32
GM/GS-14	22	22	22
GM/GS-13	34	34	34
GS-12	31	31	31
GS-11	32	32	32
GS-10	1	1	1
GS-9	5	5	5
GS-8	6	6	6
GS-7	3	3	3
GS-6	4	4	4
GS-5	0	0	0
GS-4	0	0	0
GS-3	0	0	0
GS-2	2	2	2
GS-1	0	0	0
Subtotal	172	172	172
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	0	0	0
Director Grade	1	1	1
Senior Grade	2	2	2
Full Grade	1	1	1
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	4	4	4
Ungraded	89	89	89
Total permanent positions	173	173	173
Total positions, end of year	266	266	266
Total full-time equivalent (FTE) employment, end of year	267	267	267
Average ES salary	167,441	167,441	167,441
Average GM/GS grade	12.2	12.2	12.2
Average GM/GS salary	101,334	102,094	103,115

Includes FTEs whose payroll obligations are supported by the NIH Common Fund.