

DEPARTMENT OF HEALTH AND HUMAN SERVICES

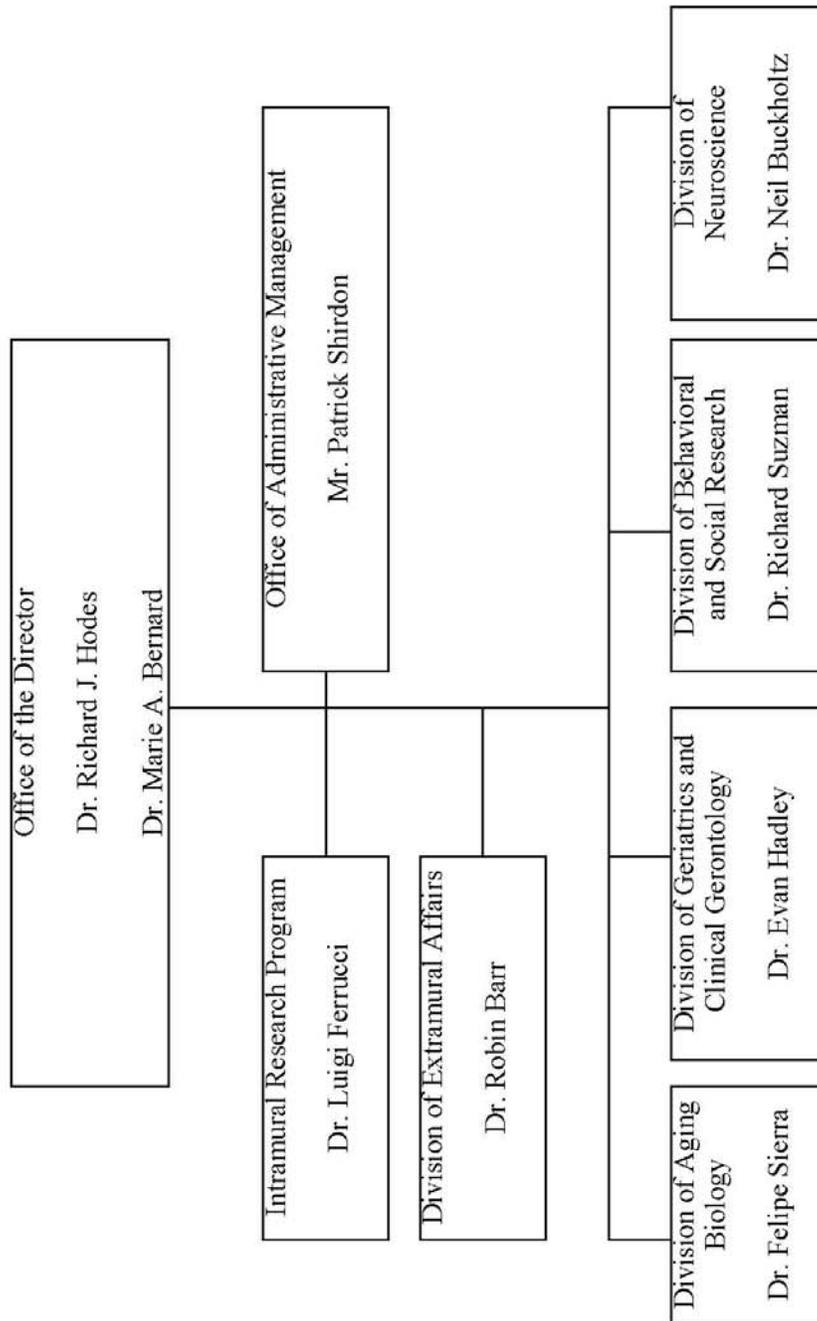
NATIONAL INSTITUTES OF HEALTH

National Institute on Aging (NIA)

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NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Organizational Structure



NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

For carrying out section 301 and title IV of the PHS Act with respect to aging, \$1,193,370,000.

**NATIONAL INSTITUTES OF HEALTH
National Institute on Aging**

Amounts Available for Obligation ¹
(Dollars in Thousands)

Source of Funding	FY 2012 Actual	FY 2013 CR	FY 2014 PB
Appropriation	1,105,530	1,110,194	1,193,370
Rescission	(2,090)	0	0
Subtotal, adjusted appropriation	1,103,440	1,110,194	1,193,370
Secretary's Transfer for Alzheimer's disease (AD)	18,273	0	0
Secretary's Transfer for AIDS authorized by PL 112-74, Section 206	(314)	0	0
Comparative Transfers to NLM for NCBI and Public Access	(1,008)	(1,306)	0
Subtotal, adjusted budget authority	1,120,391	1,108,888	1,193,370
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	1,120,391	1,108,888	1,193,370
Unobligated balance lapsing	(59)	0	0
Total obligations	1,120,332	1,108,888	1,193,370

¹ Excludes the following amounts for reimbursable activities carried out by this account:

FY 2012 - \$6,873 FY 2013 - \$7,000 FY 2014 - \$7,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging
Budget Mechanism - Total ¹
(Dollars in Thousands)

MECHANISM	FY 2012 Actual		FY 2013 CR		FY 2014 PB		Change vs. FY 2012	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants								
<u>Research Projects</u>								
Noncompeting	1,063	\$558,938	963	\$524,597	961	\$516,966	-102	-\$41,972
Administrative Supplements	(91)	17,373	(69)	6,357	(69)	6,357	-(22)	-11,016
Competing:								
Renewal	63	46,119	124	72,435	187	109,607	124	63,488
New	246	93,362	264	100,115	399	151,492	153	58,130
Supplements	5	1,018	5	1,018	5	1,018	0	0
Subtotal, Competing	314	\$140,500	393	\$173,568	591	\$262,117	277	\$121,617
Subtotal, RPGs	1,377	\$716,811	1,356	\$704,522	1,552	\$785,440	175	\$68,629
SBIR/STTR	84	28,483	88	29,627	98	33,191	14	4,708
Research Project Grants	1,461	\$745,295	1,444	\$734,149	1,650	\$818,631	189	\$73,336
<u>Research Centers</u>								
Specialized/Comprehensive	79	87,698	79	87,698	79	87,698	0	0
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	0	1,208	0	1,208	0	1,208	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	79	\$88,906	79	\$88,906	79	\$88,906	0	\$0
<u>Other Research</u>								
Research Careers	218	28,883	218	28,883	218	28,883	0	0
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0	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	41	7,981	41	7,981	41	7,981	0	0
Other Research	259	\$36,864	259	\$36,864	259	\$36,864	0	\$0
Total Research Grants	1,799	\$871,064	1,782	\$859,919	1,988	\$944,401	189	\$73,337
<u>Ruth L. Kirschstein Training Awards</u>	<u>FTIPs</u>		<u>FTIPs</u>		<u>FTIPs</u>		<u>FTIPs</u>	
Individual	190	7,397	190	7,397	188	7,397	-2	0
Institutional	420	17,359	420	17,359	410	17,359	-10	0
Total Research Training	610	\$24,756	610	\$24,756	598	\$24,756	-12	\$0
Research & Development Contracts	123	63,537	123	63,239	123	63,239	0	-298
<i>SBIR/STTR (non-add)</i>	(5)	(61)	(5)	(61)	(5)	(61)	(0)	+(0)
Intramural Research	<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>	
Intramural Research	247	118,602	247	118,601	247	118,601	0	-1
Research Management and Support	150	42,433	172	42,373	172	42,373	22	-60
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NIA	397	\$1,120,391	419	\$1,108,888	419	\$1,193,370	22	\$72,979

¹ All items in italics and brackets are "non-adds."

Major Changes in the Fiscal Year 2014 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 2014 President's Budget for NIA, which is \$73.0 million more than the FY 2012 level, for a total of \$1,193.4 million.

Research Project Grants (+\$73.336 million; total \$818.631 million): NIA will award a total of 1,650 RPGs, an increase of 189 from FY 2012. This includes an \$80.0 million increase for Alzheimer's Disease (AD) research. Projects will facilitate fulfillment of the recommendations of the May 2012 Alzheimer's Disease Research Summit, which was held in response to the passage of the National Alzheimer's Project Act in 2011. Other NIA projects will be decreased by \$6.664 million. NIH budget policy for RPGs in FY 2014, continues FY 2012 policy of eliminating inflationary increases for future year commitments. However adjustments for special needs (such as equipment and added personnel) will continue to be accommodated.

Research and Development Contracts (-\$0.298 million; total \$63.239 million): Funds are included in R&D contracts to support trans-NIH initiatives, such as the Basic Behavioral and Social Sciences Opportunity Network (OppNet).

Intramural Research (-\$0.001 million; total \$118.601 million): NIA will continue work to identify areas of potential savings within the Intramural Research Program that will allow the institute to continue to achieve its program goals and accomplishments.

Research Management and Support (-\$0.060 million; total \$42.373 million, +22 FTE): The NIA oversees 1,988 research grants, 598 full-time training positions, and 123 research and development contracts. Funding will be used to cover the expenses associated with providing for the effective, administrative, planning and evaluation, public information and communications, and scientific leadership of the institute. The apparent increase in estimated FY 2014 FTE compared to the FY 2012 actual FTE usage level is due to the effect of transferring positions previously funded from a centralized support operation (Division of Extramural Activities Support) to individual ICs as of year-end 2012. As a result of the DEAS transfer, estimated salaries and benefits for FY 2014 are proportionately higher than those identified for FY 2012 and previous years.

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging
Summary of Changes
(Dollars in Thousands)

FY 2012 Actual		\$1,120,391		
FY 2014 President's Budget		\$1,193,370		
Net change		\$72,979		
CHANGES	2014 President's Budget		Change from FY 2012	
	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural Research:				
a. Annualization of March				
2013 pay increase & benefits		\$42,482		\$107
b. January FY 2014 pay increase & benefits		42,482		314
c. One more day of pay		42,482		161
d. Differences attributable to change in FTE		42,482		0
e. Payment for centrally furnished services		8,117		146
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		68,002		161
Subtotal				\$890
2. Research Management and Support:				
a. Annualization of March				
2013 pay increase & benefits		\$26,035		\$70
b. January FY 2014 pay increase & benefits		26,035		193
c. One more day of pay		26,035		98
d. Differences attributable to change in FTE		26,035		0
e. Payment for centrally furnished services		5,957		107
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		10,381		0
Subtotal				\$467
Subtotal, Built-in				\$1,357

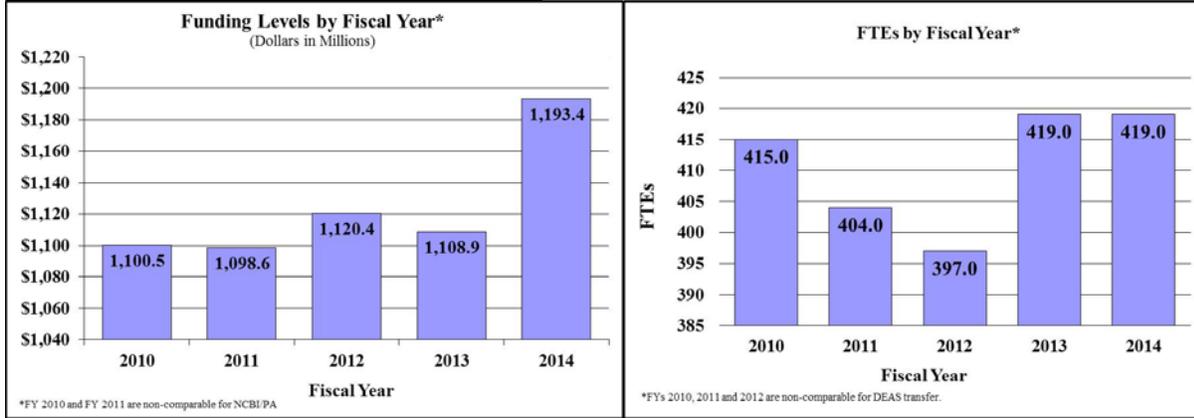
**NATIONAL INSTITUTES OF HEALTH
National Institute on Aging**

Summary of Changes--continued

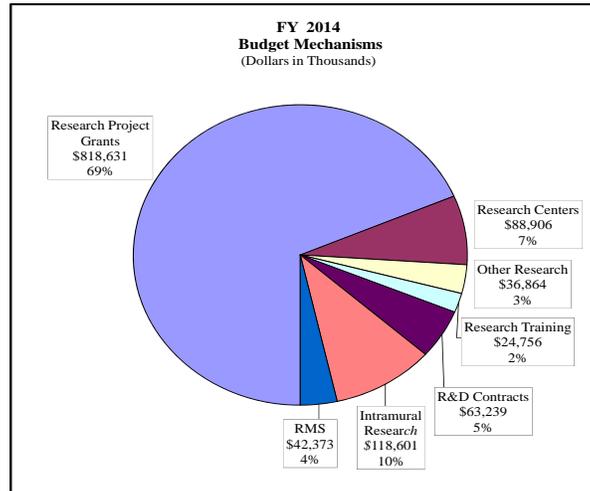
CHANGES	2014 President's Budget		Change from FY 2012	
	No.	Amount	No.	Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	961	\$523,323	-102	-\$52,989
b. Competing	591	262,117	277	121,617
c. SBIR/STTR	98	33,191	14	4,708
Total	1,650	\$818,631	189	\$73,336
2. Research Centers	79	\$88,906	0	\$0
3. Other Research	259	36,864	0	0
4. Research Training	598	24,756	-12	0
5. Research and development contracts	123	63,239	0	-298
Subtotal, Extramural		\$1,032,396		\$73,038
6. Intramural Research	<u>FTEs</u> 247	\$118,601	<u>FTEs</u> 0	-\$890
7. Research Management and Support	172	42,373	22	-527
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, program	419	\$1,193,370	22	\$71,621
Total changes				\$72,979

Fiscal Year 2014 Budget Graphs

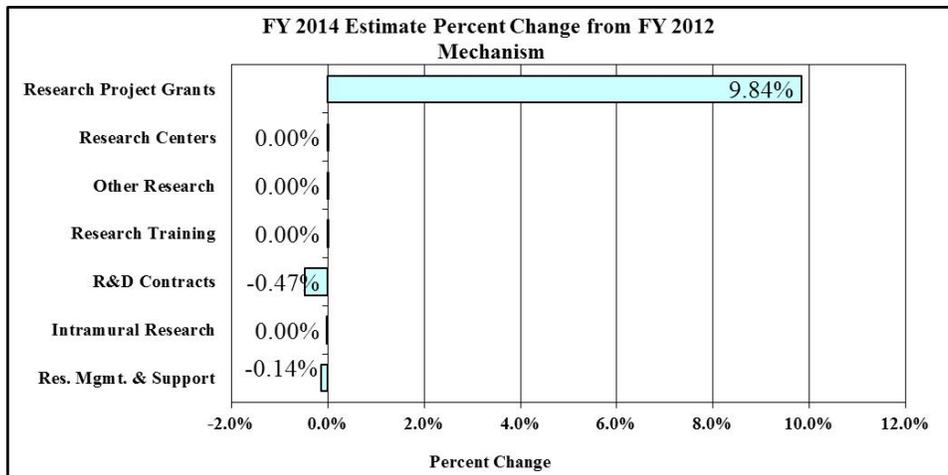
History of Budget Authority and FTEs:



Distribution by Mechanism:



Change by Selected Mechanism:



NATIONAL INSTITUTES OF HEALTH
National Institute on Aging
Budget Authority by Activity ¹
(Dollars in Thousands)

	FY 2012 Actual		FY 2013 CR		FY 2014 PB		Change vs. FY 2012	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural Research								
<u>Detail:</u>								
Aging Biology		\$181,895		\$179,725		\$180,575		-\$1,320
Behavioral & Social Research		187,547		185,310		186,186		-\$1,361
Neuroscience ²		437,444		432,226		514,270		\$76,826
Geriatrics & Clinical Gerontology		152,471		150,653		151,365		-\$1,106
Subtotal, Extramural		\$959,357		\$947,914		\$1,032,396		\$73,039
Intramural Research	247	\$118,602	247	\$118,601	247	\$118,601	0	(\$1)
Research Management & Support	150	\$42,433	172	\$42,373	172	\$42,373	22	(\$60)
TOTAL	397	\$1,120,391	419	\$1,108,888	419	\$1,193,370	22	\$72,979

¹ Includes Transfers and Comparable Adjustments as detailed in the "Amounts Available for Obligation" table.

² Neuroscience includes an \$80 million increase for Alzheimer's disease (AD) related work and a \$3.1 million decrease for non-AD related work.

**NATIONAL INSTITUTES OF HEALTH
National Institute on Aging**

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2013 Amount Authorized	FY 2013 CR	2014 Amount Authorized	FY 2014 PB
Research and Investigation	Section 301	42§241	Indefinite	\$1,108,888,000	Indefinite	\$1,193,370,000
National Institute on Aging	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				\$1,108,888,000		\$1,193,370,000

**NATIONAL INSTITUTES OF HEALTH
National Institute on Aging**

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2005	\$1,055,666,000	\$1,055,666,000	\$1,094,500,000	\$1,060,666,000
Rescission				(\$8,676,000)
2006	\$1,057,203,000	\$1,057,203,000	\$1,090,600,000	\$1,057,203,000
Rescission				(\$10,572,000)
2007	\$1,039,828,000	\$1,039,828,000	\$1,039,828,000	\$1,039,828,000
Rescission				-
2008	\$1,047,148,000	\$1,062,833,000	\$1,073,048,000	\$1,047,260,000
Rescission				(\$18,621,000)
2009	\$1,048,278,000	\$1,084,321,000	\$1,077,448,000	\$1,080,796,000
Rescission				-
2010	\$1,093,413,000	\$1,119,404,000	\$1,099,409,000	\$1,110,229,000
Rescission				-
2011	\$1,142,337,000	-	\$1,140,547,000	\$1,110,229,000
Rescission				(\$9,748,472)
2012	\$1,129,987,000	\$1,129,987,000	\$1,088,091,000	\$1,105,530,000
Rescission				(\$2,089,452)
2013	\$1,102,650,000	-	\$1,124,265,000	-
Rescission				-
2014	\$1,193,370,000	-	-	-

Justification of Budget Request

National Institute on Aging

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

Budget Authority (BA):

	FY 2012 Actual	FY 2013 CR	FY 2014 President's Budget	FY 2014 +/- FY 2012
BA	\$1,120,391,000	\$1,108,888,000	\$1,193,370,000	+72,979,000
FTE	397	419	419	+22

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

Director's Overview

By 2030, there will be some 72 million Americans ages 65 or older – more than double the number in that age group in 2000. The number of “oldest old” – people age 85 or older – is expected to more than triple between 2010 and 2050.¹ Age is a primary risk factor for many disabling diseases and conditions, and recent demographic studies have shown a modest increase in activity limitations among members of the enormous baby boom cohort. For these reasons it is imperative that we discover new and effective ways to make added years as healthy and productive as possible.

The National Institute on Aging (NIA) leads a national scientific effort to understand the nature of aging in order to promote the health and well-being of older adults. NIA's mission is to support and conduct genetic, biological, clinical, behavioral, social, and economic research related to the aging process, diseases and conditions associated with aging, and other special problems and needs of older Americans; foster the development of research and clinician-scientists for research on aging; and communicate information about aging and advances in research on aging with the scientific community, health care providers, and the public. We carry out our mission by supporting extramural research at universities, research centers, and medical centers across the United States and around the world as well as a vibrant intramural research program at NIA laboratories in Baltimore and Bethesda, Maryland.

A major priority for NIA is investment in research on the aging process at its most fundamental levels. Exciting basic research findings, such as the discovery that removing small populations of senescent cells, which have lost their capacity to divide but continue to send and receive signals within the body, delayed onset of disease-related changes in skeletal muscle, fat, and eye tissues in mice and that removing senescent cells later in life slowed progression of established

¹ *Federal Interagency Forum on Aging-Related Statistics. Older Americans 2012: Key Indicators of Well-Being. Federal Interagency Forum on Aging-Related Statistics. Washington, DC: U.S. Government Printing Office. 2012. <http://www.agingstats.gov>.*

age-related disorders, are suggesting new avenues for the development of interventions for age-related diseases and conditions. The establishment of the trans-NIH Geroscience Interest Group, which was formed to accelerate and coordinate efforts to promote further discoveries on the common risks and mechanisms behind age-related diseases and conditions, is expected to stimulate an increased research interest in the basic biology of aging.

NIA also maintains an ongoing commitment to supporting basic behavioral and social research in aging. Ongoing initiatives in social neuroscience, behavioral and social consequences of natural and man-made disasters on the elderly, and effects of the economic downturn on older individuals will be active into FY 2014, and NIA remains an active participant in the trans-NIH Basic Behavioral and Social Science Opportunity Network (OppNet). In addition, NIA recently began to solicit research applications to use newly-available genetic data in the Health and Retirement Study, the nation's premier study of health, retirement, pensions, and Social Security, to advance our understanding of how genetic, behavioral, and psychosocial factors affect the health and well-being of older Americans.

The translation of new interventions to clinical practice is another area of focus at NIA. NIA supports 13 Edward R. Roybal Centers for Translation Research in the Behavioral and Social Sciences of Aging; the Centers currently support research on health and mobility, disease and pain management, decision making and behavior change. Center investigators are also developing better data collection and measurement techniques and working to forecast the consequences of medical breakthroughs on health and health care spending. NIA also continues to support 13 Claude D. Pepper Older Americans Independence Centers, which investigate ways to maintain or restore independence in older adults. Ongoing studies such as Lifestyle Interventions and Independence for Elders (LIFE), in which researchers are testing an intervention to preserve mobility in older people, and the ASPirin in Reducing Events in the Elderly (ASPREE) trial, designed to determine whether the benefits of aspirin outweigh the risks in people over 70, further exemplify NIA's commitment to reducing disease and disability in the elderly. NIA also initiated 17 clinical trials on a variety of conditions in FY 2012.

NIA's comprehensive Alzheimer's disease (AD) research program spans the spectrum of discovery, from basic neuroscience through translational research and clinical application. In 2012, the National Alzheimer's Plan and Research Summit, as well as additional funding provided for FY 2012, generated new momentum in this field. Under four new funding opportunity announcements, projects covering development and validation of new therapeutics and prevention and treatment trials will be active in FY 2014. In addition, over 40 compounds are currently under development as part of the NIH AD Translational Initiative, and NIH supports over 35 AD-related clinical trials.

Recent AD-related advances include the discovery that misfolded tau protein, a pathological hallmark of the disease, spreads among neurons in a predictable pattern throughout vulnerable brain regions and the development of technology to convert skin cells from patients with familial AD into functional neurons. Separately, in a highly promising pilot trial, a nasal-spray form of insulin delayed memory loss and preserved cognition in people with cognitive deficits ranging from mild cognitive impairment to moderate AD. A larger-scale study to confirm and extend these results began in 2012 and will continue through 2014. In addition, a five-year study

of whether crenezumab, which is designed to bind to and possibly clear abnormal amounts of amyloid protein in the brains of people with Alzheimer's, can prevent cognitive decline in familial (early-onset) AD will continue through 2014.

Finally, NIA supports several innovative programs dedicated to the critical task of training the next generation of aging researchers. For example, the prestigious Paul B. Beeson Career Development Awards in Aging Research, co-funded by NIA and several philanthropic concerns, support outstanding junior and mid-career faculty committed to academic careers in aging-related research, training, and practice. Beeson scholars are emerging as leaders in the field of aging research. NIA's new Grants for Early Medical/Surgical Specialists Transition to Aging Research (GEMSSTAR) program provides support for early stage clinician-scientists who have recently completed their clinical training and are embarking on a career in aging research in their specialty area. Recognizing the urgent need to promote diversity in the research workforce, in 2012 NIA established the Advancing Diversity in Aging Research through Undergraduate Education Program, which supports academic institutions that propose creative and innovative research education programs to diversify the workforce in aging at the undergraduate level.

For a comprehensive overview of NIA's plans and priorities, see *Living Long and Well in the 21st Century: Strategic Directions for Research on Aging*, at <http://www.nia.nih.gov/about/living-long-well-21st-century-strategic-directions-research-aging>

Overall Budget Policy: The FY 2014 President's Budget request is \$1,193.370 million, an increase of \$72.979 million, or 6.5 percent above the FY 2012 Actual level. This includes an \$80.0 million increase in Research Project Grants (RPGs) for Alzheimer's Disease (AD) and a decrease of \$7.021 million to other program areas, including a \$6.664 million decrease to RPGs.

Funds are included in R&D contracts to support trans-NIH initiatives, such as the Basic Behavioral and Social Sciences Opportunity Network (OppNet).

Program Descriptions and Accomplishments

Biology of Aging Program:

Understanding Aging Processes, Health, and Longevity

Investigators supported by NIA's Biology of Aging Program seek to improve our understanding of the basic biological mechanisms underlying the process of aging and age-related diseases. Basic biochemical, genetic, and physiological studies are carried out primarily in animal models, including both mammals and non-mammalian organisms (e.g., flies, worms, yeast). The program's goal is to provide the biological basis for interventions in the process of aging, which is the major risk factor for many chronic diseases affecting the American population. Ongoing initiatives that will remain active during FY 2014 include the Interventions Testing Program to identify compounds that extend median and/or maximal life span in a mouse model, along with a similar program to identify such compounds in the worm model *Caenorhabditis elegans*; an initiative to explore the basic biology of aging from a systems perspective – i.e., by investigating the complex interactions at the single-cell level among individual gene products, biochemical pathways, and cell biological mechanisms that impact aging, as well as interactions between tissues; and studies to enhance our understanding of the molecular

mechanisms that control circadian clocks in aging tissues. The program also coordinates the Nathan Shock Centers of Excellence in the Basic Biology of Aging, as well as the NIH Geroscience Interest Group (GSIG), which was established in 2012 to accelerate and coordinate efforts to promote discoveries on the common risks and mechanisms behind age-related diseases and conditions by developing a collaborative framework that includes multiple NIH Institutes and Centers.

Budget Policy: The FY 2014 President's Budget estimate is \$180.575 million, a decrease of \$1.320 million, or 0.7 percent below the FY 2012 Actual level.

Program Portrait: Inflammation and Aging

FY 2012 Level: \$18.0 million

FY 2014 Level: \$18.2 million

Change: + \$0.2 million

Acute inflammation, such as that which occurs with an injury, is transient and usually resolves as the injury heals. Chronic inflammation, on the other hand, can be present over many years, and is associated with blood and tissue levels of pro-inflammatory molecules that are lower than those seen with acute inflammation but still higher than in healthy adults. Scientists increasingly view chronic inflammation as a likely common thread linking a number of diseases and conditions for which aging is the primary risk factor, including cardiovascular disease, Alzheimer's disease, osteoarthritis, and cancer. This hypothesis is bolstered by current research, using mice, demonstrating two linked findings: a) the process of cellular senescence (conversion to a nondividing state) is associated with secretion of pro-inflammatory molecules, and b) removing senescent cells delayed the onset of disease-related changes and slowed progression of known age-related disorders in several tissues.

NIA supports a robust program of research to understand the causes and consequences of inflammation in aging tissues. For example, one study is evaluating the relationships among age-related changes in angiotensin receptors, which are found on the surface and on the inside of virtually all human cells, and determining how these changes might influence chronic inflammation, frailty, and late life vulnerability. In a large program project, investigators are looking in greater detail at the effects on health resulting from the removal of senescent cells. Other studies explore inflammation's role in immune response and specific diseases, including heart disease, infectious diseases, and cancer.

In September 2012, the trans-NIH Geroscience Interest Group held a workshop on Inflammation and Age-Related Diseases, which brought together experts in aging biology and in age-related pathology to explore the mechanistic relationships between inflammation and age-associated disease. A report is being prepared that should direct our efforts to identify outstanding questions concerning the impact of inflammation on the diseases of aging and what tools, technologies, resources, or community efforts are required to address these questions. The report is expected to inform NIA's efforts, including the development of funding opportunity announcements, through FY 2014.

Behavioral and Social Research Program:

Understanding and Addressing the Behavioral, Emotional, and Social Dynamics of Aging

NIA's Behavioral and Social Research Program supports social and behavioral research to increase our understanding of the processes of aging at the individual, institutional, and societal levels. Research areas include the behavioral, psychological, and social changes individuals experience over the adult lifespan; participation of older people in the economy, families, and communities; the development of interventions to improve the health and cognition of older adults; and the societal impact of population aging and of trends in labor force participation,

including fiscal effects on the Medicare and Social Security programs. The program also supports research training; development of research resources such as publicly available, cross-nationally comparable studies that support research to understand the sources of international variations in health outcomes; interdisciplinary studies that integrate biological and genetic measures with traditional social, behavioral and economic measures; longitudinal studies; and interventions to maximize active life and health expectancy. The program coordinates the long-running Health and Retirement Study, the nation's leading source of combined data on health and financial circumstances of Americans over age 50; the Centers on the Demography and Economics of Aging; the Roybal Centers for Translational Research on Aging; and the Resource Centers for Minority Aging Research (RCMARs). Major program activities for FY 2014 will include studies of social neuroscience and the neuroeconomics of aging and identification of practical interventions to improve medication adherence in the primary care setting.

Budget Policy: The FY 2014 President's Budget estimate is \$186.186 million, a decrease of \$1.361 million, or 0.7 percent below the FY 2012 Actual level.

Neuroscience Program:

Understanding, Preventing, and Treating Cognitive Decline and Disability

NIA's Neuroscience Program supports a broad spectrum of research and training aimed at better understanding age-related normal and pathological changes in the structure and function of the aging nervous system and how such changes affect behavior. The program's basic mission is to expand knowledge on the aging nervous system to allow improvement in the quality of life of older people. Ongoing activities include basic and clinical studies of the nervous system, clinical trials of treatments and preventive interventions for neurological disease, and epidemiological research to identify risk factors and to establish prevalence and incidence estimates of pathologic conditions. Additionally, this program supports research relevant to problems arising from psychiatric and neurological disorders associated with aging. NIA is also the lead federal agency for research on Alzheimer's disease (AD). The Institute supports a national network of Alzheimer's Disease Centers to translate research advances into improved diagnosis and care of AD patients while pursuing development and testing of effective preventive and treatment interventions for AD, as well as a broad array of initiatives aimed at improving our understanding of this disease.

Budget Policy: The FY 2014 President's Budget estimate is \$514.270 million, an increase of \$76.827 million, or 17.6 percent above the FY 2012 Actual level. This includes an \$80.0 million increase for Alzheimer's Disease (AD) research and a decrease of \$3.174 million to other program areas.

Program Portrait: Alzheimer's Disease Research

FY 2012 Level: \$335.2 million

FY 2014 Level: \$415.2 million

Change: +\$80.0 million

In FY 2014, the NIH anticipates allocating an additional \$80 million to research project grants aimed at speeding drug development and testing new therapies for Alzheimer's disease (AD). Projects will facilitate fulfillment of the recommendations of the May 2012 Alzheimer's Disease Research Summit, which was held in response to the passage of the National Alzheimer's Project Act in 2011. The goal of the Summit was to formulate a strategy for a new integrated, multidisciplinary research agenda that will enable the development of effective therapies across the disease continuum and to identify the resources, infrastructure, and public-private partnerships necessary to implement this translational agenda.

This investment will be targeted at preclinical, translational, and clinical development of preventive and treatment interventions for AD. Specific research areas will include:

Identification of novel therapeutic targets. New discoveries have opened a variety of approaches to identifying candidate molecular targets for prevention and treatment of AD. For example, ongoing and extensive whole genome sequencing has the potential for identifying new genetic variants that either increase risk (risk factors) or reduce risk (protective factors) of AD. Our FY 2014 investment will facilitate the analysis of the sequencing data being generated, supporting efforts of experts in genomics, informatics, and Alzheimer's disease biology to identify the most promising leads for further target identification. A key aspect of these efforts will be the emphasis on the creation of new translational teams consisting of researchers across a broad array of disciplines within a framework that will enable cross-talk and collaboration among basic and translational scientists with the goal of identification and preclinical validation of novel therapeutic targets within molecular networks involved in different stages of Alzheimer's disease pathogenesis.

Preclinical development of new therapies. Translation of basic discoveries will be accelerated by application of new technologies and research paradigms. For example, researchers who have promising small molecule compounds, but lack outside drug development expertise and infrastructure support to advance these compounds to the clinic, will have access to a "virtual pharma" network of contract research organizations, technical and regulatory experts, and project managers, all with extensive biopharma/industry experience. The long-term goal is to advance projects from medicinal chemistry optimization through Phase I clinical trials and facilitate industry partnership for their further development.

AD clinical trials. Recent discovery of genetic causes and risk factors for Alzheimer's disease has allowed identification of individuals who are at high risk for developing disease. Recent studies have also led to the discovery of brain imaging changes and other biomarkers that identify early stages of Alzheimer's well before the appearance of any clinical manifestations. These advances will permit the design of novel clinical trials that: Initiate prevention intervention before symptoms occur or at very early stages of disease; determine the effectiveness of these interventions by monitoring sensitive changes in brain imaging or other biomarkers, allowing more rapid determination of effectiveness than has previously been possible by monitoring Alzheimer's symptoms; test new agents – e.g., monoclonal antibodies and small molecules - as well as the re-purposing of agents currently approved for use against other diseases; and test non-pharmacologic interventions that have shown effects on cognition in initial studies. Clinical trials may range from Phase I studies to evaluate the metabolic and pharmacological actions of a variety of agents in humans to larger-scale interventions of drugs, exercise, or other lifestyle changes to prevent or ameliorate AD symptoms.

Alzheimer's Disease Program Portrait continued

Example: Repurposing Drugs for Alzheimer's Disease

One strategy NIA is pursuing is "repurposing" drugs originally approved for other conditions as therapeutics for AD and mild cognitive impairment (MCI), which is often a precursor to the disease. In addition to the ongoing NIA efforts, the newly launched repurposing program at the National Center for Advancing Translational Sciences (NCATS), while more broad in nature, will open additional avenues for possible repurposing in AD therapy development. An advantage to the repurposing approach is that detailed information is already available on these drugs' pharmacology, formulation, dosing, and potential toxicity, meaning that they can be moved into clinical testing much more rapidly than a new compound. Findings from repurposing studies can also inform our knowledge of disease mechanisms, suggesting additional paths for therapeutic development. For example, the NIA-supported investigators who recently found that the skin cancer drug bexarotene reversed cognitive defects and improved function in a mouse model of AD also elucidated the mechanism behind a major genetic risk factor for the disease, ApoE4. ApoE4 is hindered in its ability to clear toxic beta-amyloid from the brain. Bexarotene boosts the levels of functional ApoE in the brain, promoting beta-amyloid clearance. These findings suggest that increasing ApoE levels in the brain may be an effective therapeutic strategy.

NIA is currently supporting studies on several established compounds in patients with cognitive decline, MCI, or AD. For example, an 18-month phase II clinical trial in the NIA Intramural Research Program is exploring the use of exenatide, which is widely prescribed as a treatment for type 2 diabetes, in patients with MCI or early AD. Enrollment will continue in 2013, with analysis and follow-up continuing in the following years. NIA is also supporting a major five-year study of insulin delivered via nasal spray in patients with MCI and mild AD. This study will be ongoing in 2014. Other studies in AD patients include a pilot trial of the beta-blocker carvedilol and a pilot trial of a selective serotonin reuptake inhibitor antidepressant citalopram. Additional compounds will be considered for clinical study as scientifically justified.

Geriatrics and Clinical Gerontology Program: Reducing Disease and Disability among Older People

As people age, the risk for many types of disease and/or disability increases dramatically. NIA's Geriatrics and Clinical Gerontology Program supports research on health, disease, and disability in the aged (other than neurodegeneration, which is the focus of the NIA's Neuroscience Program). Areas of focus include age-related physical changes and their relationship to health outcomes, the maintenance of health and the development of disease, and specific age-related risk factors for disease. Program staff work closely with other NIH Institutes to coordinate research on diseases and conditions that are common among older people or represent a growing threat (for example, an ongoing collaboration with NIAID addresses the increasing incidence of HIV/AIDS among older Americans). The program also plans and administers clinical trials for a number of age-related conditions. In addition, the program coordinates the Claude D. Pepper Older Americans Independence Centers Program, the goal of which is to increase scientific knowledge leading to better ways to maintain or restore independence in older persons.

Budget Policy: The FY 2014 President's Budget estimate is \$151.365 million, a decrease of \$1.106 million, or 0.7 percent below the FY 2012 Actual level.

Intramural Research at NIA

Investigators with NIA's Intramural Research Program (IRP) conduct research in the areas of basic, behavioral, clinical, epidemiologic, and translational research. High priority research endeavors and areas of specific focus include: *Molecular and Cellular Biology*, including caloric restriction, cell cycle control, signal transduction, DNA damage and repair, physiology, and medicinal chemistry; *Neuroscience*, including neurodegenerative diseases, drug design and development, and neuronal cell apoptosis; *Genetics*, particularly genetic determinants of aging as an integrated part of human development; *Behavioral Research*, including personality, cognition, and psychophysiology; *Clinical and Translational Research* in cardiology, oncology, immunology, neurology, and endocrinology; and *Epidemiology*, including studies of frailty, cognition, body composition, disability, and molecular biomarkers of aging. The clinical research effort focuses on the translation of basic research findings, prevention and therapeutic clinical trials focused on age-associated diseases, modulation of treatment efficacy and toxicity in older patients, and establishment of and maintenance of diverse longitudinal cohorts for aging research. Many studies focus on common age-related diseases such as Alzheimer's disease, Parkinson's disease, stroke, atherosclerosis, and diabetes. Others, such as the groundbreaking Baltimore Longitudinal Study of Aging, explore the determinants of healthy aging. Work is also continuing on the Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS) study, which is examining the influences of race and socioeconomic status on the development of age-related health disparities among socioeconomically diverse African Americans and whites living in Baltimore. In 2012, the IRP underwent a major review and reorganization which included the formation of a Translational Gerontology Branch; the number of laboratory units was reduced from 15 to 10, and plans were made to consolidate a number of operations at the NIA Biomedical Research Center in Baltimore. IRP investigators also identified a protein, PGC-1alpha, in mice that may play an important role in forming and maintaining healthy dendrites and synapses in the hippocampus (a brain region important to learning and memory); PGC-1alpha may be a promising therapeutic target for Alzheimer's disease and other neurodegenerative disorders. Other IRP investigators began to elucidate the pathways through which the *CRI* gene influences Alzheimer's disease risk, determining that the amount of brain amyloid (one of AD's hallmark pathologies) is influenced by the interaction of *CRI* the *APOE* gene, but that individuals carrying the AD risk allele of *CRI* have significantly *lower* brain amyloid burden than those without the risk allele. These findings suggest that the risk of AD associated with *CRI* may not be mediated by increasing brain amyloid but through some other means.

Budget Policy: The FY 2014 President's Budget estimate is \$118.601 million, a decrease of \$0.001 million from the FY 2012 Actual level.

Program Portrait: Identifying the Genetic Bases for Neurological Diseases: NIA's Laboratory of Neurogenetics

FY 2012 Level: \$10.0 million ¹

FY 2014 Level: \$10.3 million

Change: +\$0.3 million

¹ Estimate, includes personnel and proportion of overhead costs.

Understanding a disease at its most basic levels is an important first step toward developing interventions to prevent, slow, halt, or reverse disease progression. Since 2001, the NIA Laboratory of Neurogenetics (LNG) has had one overarching goal: to find genetic variation and gene mutations that cause or contribute to neurological disease.

The LNG has been a key laboratory in furthering the basic understanding of neurodegenerative diseases, including Alzheimer's disease and related dementias. In addition, LNG investigators explore the genetic bases of a number of other neurological disorders, including amyotrophic lateral sclerosis, dystonia, ataxia, and Parkinson's disease. LNG investigators were the first to describe a triplication mutation of the alpha-synuclein gene that causes a severe, early-onset form of Parkinson's disease. The laboratory was at the forefront of the international research team that was the first to identify mutations in the LRRK2 gene as a cause of familial Parkinson's disease, as well as the more common sporadic Parkinson's disease. More recently, the LNG identified the most common genetic cause of both amyotrophic lateral sclerosis and frontotemporal dementia, and was a leading contributor on the international team that identified variations in the TREM2 gene as risk factors for Alzheimer's. The LNG has also focused on the complex genetics of Parkinson's disease, describing more than 15 common genetic risk factors for this disease. Integrated with this basic genetic approach are groups within LNG that focus on understanding the biology of these varied diseases using genetic modeling in cell and animal systems. This work has shed significant light on the processes underlying Parkinson's disease and Alzheimer's disease. In addition, the LNG has active research programs investigating genetic diversity and the consequences of genetic alterations, particularly in the context of the brain and aging, using systems biology-based approaches. One of the laboratory's strengths is its broad network of collaborators, including laboratories within NIA and NIH, across the nation, and internationally.

In FY 2014, the LNG anticipates continuing its groundbreaking work in the genetics of neurological disease, taking the well-established approach of studying rare familial forms of disease and then extrapolating the function of genes involved to related conditions.

Research Management and Support (RMS)

NIA RMS activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, training awards and research and development contracts. RMS functions also encompass strategic planning, coordination, and evaluation of the Institute's programs, regulatory compliance, international coordination, and liaison with other Federal agencies, Congress, and the public. The Institute currently oversees more than 1,600 research project grants and centers, as well as 598 full-time training positions and 123 research and support contracts.

Budget Policy: The FY 2014 President's Budget estimate is \$42.373 million, a decrease of \$0.060 million, or 0.1 percent below the FY 2012 Actual level.

Common Fund

The NIA participates in the support of the following initiatives funded through the NIH Common Fund:

- Interdisciplinary Research Consortium
- Using Metabolomics to Investigate Biological Pathways and Networks
- Supplements for Methodological Innovations – Behavioral and Social Science

NATIONAL INSTITUTES OF HEALTH
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Budget Authority by Object Class
(Dollars in Thousands)

	FY 2012 Actual	FY 2014 PB	Increase or Decrease
Total compensable workyears:			
Full-time employment	397	419	22
Full-time equivalent of overtime and holiday hours	0	0	0
Average ES salary (in whole dollars)	\$154,190	\$155,732	\$1,542
Average GM/GS grade	12.0	11.0	(1.0)
Average GM/GS salary (in whole dollars)	\$95,463	\$96,418	\$955
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207) (in whole dollars)	\$107,696	\$108,773	\$1,077
Average salary of ungraded positions (in whole dollars)	\$138,616	\$140,002	\$1,386
OBJECT CLASSES	FY 2012 Actual	FY 2014 PB	Increase or Decrease
Personnel Compensation:			
11.1 Full-time permanent	\$27,214	\$29,947	\$2,733
11.3 Other than full-time permanent	14,800	15,305	505
11.5 Other personnel compensation	739	806	67
11.7 Military personnel	597	661	64
11.8 Special personnel services payments	7,343	7,465	122
Total, Personnel Compensation	\$50,694	\$54,184	\$3,490
12.0 Personnel benefits	\$12,919	\$13,839	\$920
12.2 Military personnel benefits	442	494	52
13.0 Benefits for former personnel	0	0	0
Subtotal, Pay Costs	\$64,055	\$68,517	\$4,462
21.0 Travel and transportation of persons	\$1,157	\$1,157	\$0
22.0 Transportation of things	85	84	(1)
23.1 Rental payments to GSA	0	0	0
23.2 Rental payments to others	4	4	(0)
23.3 Communications, utilities and miscellaneous charges	1,055	1,055	(0)
24.0 Printing and reproduction	17	17	(0)
25.1 Consulting services	3,649	3,634	(15)
25.2 Other services	16,205	13,526	(2,679)
25.3 Purchase of goods and services from government accounts	87,163	89,328	2,165
25.4 Operation and maintenance of facilities	10,096	10,095	(1)
25.5 Research and development contracts	52,153	30,671	(21,482)
25.6 Medical care	287	287	(0)
25.7 Operation and maintenance of equipment	2,156	2,156	(0)
25.8 Subsistence and support of persons	0	0	0
25.0 Subtotal, Other Contractual Services	\$171,709	\$149,697	(\$22,012)
26.0 Supplies and materials	\$8,475	\$8,475	(\$0)
31.0 Equipment	2,707	2,707	0
32.0 Land and structures	0	0	0
33.0 Investments and loans	0	0	0
41.0 Grants, subsidies and contributions	871,127	961,657	90,530
42.0 Insurance claims and indemnities	0	0	0
43.0 Interest and dividends	0	0	(0)
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	\$1,056,336	\$1,124,853	\$68,517
Total Budget Authority by Object Class	\$1,120,391	\$1,193,370	\$72,979

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

NATIONAL INSTITUTES OF HEALTH
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Salaries and Expenses
(Dollars in Thousands)

OBJECT CLASSES	FY 2012 Actual	FY 2014 PB	Increase or Decrease
Personnel Compensation:			
Full-time permanent (11.1)	\$27,214	\$29,947	\$2,733
Other than full-time permanent (11.3)	14,800	15,305	505
Other personnel compensation (11.5)	739	806	67
Military personnel (11.7)	597	661	64
Special personnel services payments (11.8)	7,343	7,465	122
Total Personnel Compensation (11.9)	\$50,693	\$54,184	\$3,491
Civilian personnel benefits (12.1)	\$12,919	\$13,839	\$920
Military personnel benefits (12.2)	442	494	52
Benefits to former personnel (13.0)	0	0	0
Subtotal, Pay Costs	\$64,054	\$68,517	\$4,463
Travel (21.0)	\$1,157	\$1,157	\$0
Transportation of things (22.0)	85	84	(1)
Rental payments to others (23.2)	4	4	0
Communications, utilities and miscellaneous charges (23.3)	1,055	1,055	0
Printing and reproduction (24.0)	17	17	0
Other Contractual Services:			
Advisory and assistance services (25.1)	3,649	3,634	(15)
Other services (25.2)	16,205	13,526	(2,679)
Purchases from government accounts (25.3)	56,480	54,325	(2,155)
Operation and maintenance of facilities (25.4)	10,096	10,095	(1)
Operation and maintenance of equipment (25.7)	2,156	2,156	0
Subsistence and support of persons (25.8)	0	0	0
Subtotal Other Contractual Services	\$88,586	\$83,736	(\$4,850)
Supplies and materials (26.0)	\$8,473	\$8,473	\$0
Subtotal, Non-Pay Costs	\$99,377	\$94,526	(\$4,851)
Total, Administrative Costs	\$163,431	\$163,043	(\$388)

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Details of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2012 Actual			FY 2013 CR			FY 2014 PB		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Office of the Director									
Direct:	25	-	25	31	-	31	31	-	31
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	25	-	25	31	-	31	31	-	31
Intramural Research Program									
Direct:	245	2	247	245	2	247	245	2	247
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	245	2	247	245	2	247	245	2	247
Office of Administrative Management									
Direct:	41	-	41	42	-	42	42	-	42
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	41	-	41	42	-	42	42	-	42
Division of Extramural Affairs									
Direct:	27	-	27	37	-	37	37	-	37
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	27	-	27	37	-	37	37	-	37
Division of Aging Biology									
Direct:	14	-	14	15	-	15	15	-	15
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	14	-	14	15	-	15	15	-	15
Division of Geriatrics & Clinical Gerontology									
Direct:	11	1	12	12	1	13	12	1	13
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	11	1	12	12	1	13	12	1	13
Division of Behavioral & Social Research									
Direct:	13	-	13	14	-	14	14	-	14
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	13	-	13	14	-	14	14	-	14
Division of Neuroscience									
Direct:	16	2	18	19	1	20	19	1	20
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	16	2	18	19	1	20	19	1	20
	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-
Total	392	5	397	415	4	419	415	4	419
Includes FTEs whose payroll obligations are supported by the NIH Common Fund. FTEs supported by funds from Cooperative Research and Development Agreements.									
FISCAL YEAR	Average GS Grade								
2010	11.5								
2011	12.0								
2012	12.0								
2013	12.0								
2014	11.0								

NATIONAL INSTITUTES OF HEALTH

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Detail of Positions

GRADE	FY 2012 Actual	FY 2013 CR	FY 2014 PB
Total, ES Positions	1	1	1
Total, ES Salary	\$ 154,190	\$ 154,190	\$ 155,732
GM/GS-15	29	29	29
GM/GS-14	44	44	44
GM/GS-13	55	55	55
GS-12	61	62	62
GS-11	28	29	29
GS-10	1	1	1
GS-9	31	36	36
GS-8	12	18	18
GS-7	16	21	21
GS-6	0	2	2
GS-5	0	2	2
GS-4	2	2	2
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	279	301	301
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	4	4	4
Senior Grade	0	0	0
Full Grade	0	0	0
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	4	4	4
Ungraded	103	103	103
Total permanent positions	287	309	309
Total positions, end of year	389	411	411
Total full-time equiv (FTE) at YE	397	419	419
Average ES salary	\$ 154,190	\$ 154,190	\$ 155,732
Average GM/GS grade	12.0	12.0	11.0
Average GM/GS salary	\$ 95,463	\$ 95,463	\$ 96,418

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