DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute (NCI)

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NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

For carrying out section 301 and title IV of the PHS Act with respect to cancer, \$5,125,951,000, of which up to \$8,000,000 may be used for facilities repairs and improvements at the National Cancer Institute—Frederick Federally Funded Research and Development Center in Frederick, Maryland.

Amounts Available for Obligation 1

(Dollars in Thousands)

	FY 2012	FY 2013	FY 2014
Source of Funding	Actual	CR	PB
Appropriation	5,081,788	5,103,225	5,125,951
Type 1 Diabetes	0	0	0
Rescission	(9,605)	0	0
Supplemental	0	0	0
Subtotal, adjusted appropriation	5,072,183	5,103,225	5,125,951
Secretary's Transfer for Alzheimer Disease (AD)	(3,342)	0	0
Secretary's Transfer for AIDS authorized by PL 112-74, Section 206	(1,445)	0	0
Comparative Transfers to NLM for NCBI and Public Access	(4,634)	(6,000)	0
Subtotal, adjusted budget authority	5,062,762	5,097,225	5,125,951
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	5,062,762	5,097,225	5,125,951
Unobligated balance lapsing	0	0	0
Total obligations	5,062,762	5,097,225	5,125,951

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

FY 2012 - \$52,880 FY 2013 - \$55,000 FY 2014 - \$35,000

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Budget Mechanism - Total¹ (Dollars in Thousands)

	FY	2012	FY	2013	FY	2014		
MECHANISM	Ac	tual	(CR	I	PB	Change vs	. FY 2012
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants								
Research Projects			l		i	I	1	ļ
Noncompeting	3,746	\$1,639,445	3,543	\$1,623,137	3,416	\$1,568,810	-330	-\$70,635
Administrative Supplements	(184)	19,819	(186)	19,819	(186)	19,819	(2)	0
Competing:			1		ł	I		I
Renewal	175	88,083	188	94,740	207	104,244	32	16,161
New	907	325,327	980	351,453	1,078	386,711	171	61,384
Supplements	3	594	3	639	4	703	1	109
Subtotal, Competing	1,085	\$414,004	1,171	\$446,832	1,289	\$491,658	204	\$77,654
Subtotal, RPGs	4,831	\$2,073,268	4,714	\$2,089,788	4,705	\$2,080,287	-126	\$7,019
SBIR/STTR	190	77,355	190	77,989	190	85,103	0	7,748
Research Project Grants	5,021	\$2,150,624	4,904	\$2,167,777	4,895	\$2,165,390	-126	\$14,766
Research Centers			1					
Specialized/Comprehensive	253	612,789	253	614,007	253	620,007	0	7,218
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	0	0	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	253	\$612,789	253	\$614,007	253	\$620,007	0	\$7,218
Other Research			1					
Research Careers	422	73,164	422	73,486	422	73,986	0	822
Cancer Education	93	33,373	93	33,520	93	33,520	0	147
Cooperative Clinical Research	128	229,842	128	230,853	128	231,853	0	2,011
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	3	355	3	357	3	357	0	2
Other	100	70,809	100	71,121	100	71,621	0	812
Other Research	746	\$407,542	746	\$409,337	746	\$411,337	0	\$3,795
Total Research Grants	6,020	\$3,170,954	5,903	\$3,191,121	5,894	\$3,196,734	-126	\$25,780
Res <u>earch Training</u>	FTTPs		FTTPs		FTTPs		FTTPs	
Individual	284	11,740	284	11,792	284	11,977	0	237
Institutional	1,058	54,252	1,058	54,491	1,058	55,356	0	1,104
Total Research Training	1,342	\$65,992	1,342	\$66,283	1,342	\$67,333	0	\$1,341
Research & Development Contracts	497	585,136	497	588,212	497	602,916	0	17,780
SBIR/STTR (non-add)	(67)	(37,650)	(67)	(41,500)	(67)	(42,769)	(0)	+(5,119)
	FTEs		FTEs		FTEs		FTEs	
Intramural Research	1,929	857,841	1.928	864,486	1.928	869,065	-1	11,224
Research Management and Support	1,166	374,919	1.255	379,155	1,255	381,983	89	7,064
Construction	-,	0	-,	0	-,	0		C
Buildings and Facilities		7,920	1	7,968	l	7,920		C
Total, NCI	3.095	\$5,062,762	3,183	\$5,097,225	3,183	\$5,125,951	88	\$63,189

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 NCI, which is \$63.2 million more than the FY 2012 level, for a total of \$5,126.0 million.

<u>Competing Research Project Grants (RPGs) (+\$77.654 million; total \$491.658 million):</u> NCI has the opportunity to support a greater number of new and competing RPGs in FY 2014 due to 330 noncompeting RPGs ending in fiscal year (FY) 2013 and FY 2014. NCI will support 1,289 competing RPGs totaling \$491.7 million in FY 2014, an increase of 204 awards and \$77.7 million above the FY 2012 Actual level. 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.

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

FY 2012 Actual				\$5,062,762
FY 2014 President's Budget				\$5,125,951
Net change				\$63,189
		2014		
	Preside	nt's Budget	Change from	n FY 2012
		Budget		Budget
CHANGES	FTEs	Authority	FTEs	Authority
A. Built-in:				
1. Intramural Research:				
a. Annualization of January				
2012 pay increase & benefits		\$319,888		\$824
b. January FY 2014 pay increase & benefits		319,888		2,357
c. One more day of pay		319,888		1,214
d. Differences attributable to change in FTE		319,888		0
e. Payment for centrally furnished services		134,121		2,408
f. Increased cost of laboratory supplies, materials,				
other expenses, and non-recurring costs		415,056		628
Subtotal				\$7,431
2. Research Management and Support:				
a. Annualization of January				
2012 pay increase & benefits		\$196,869		\$533
b. January FY 2014 pay increase & benefits		196,869		1,456
c. One more day of pay		196,869		744
d. Differences attributable to change in FTE		196,869		0
e. Payment for centrally furnished services		36,566		657
f. Increased cost of laboratory supplies, materials,				
other expenses, and non-recurring costs		148,548		30
Subtotal				\$3,420
Subtotal, Built-in				\$10,851

Summary of Changes--continued

		2014		
	Preside	ent's Budget	Change fi	rom FY 2012
CHANGES	No.	Amount	No.	Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	3,416	\$1,588,629	-330	-\$70,636
b. Competing	1,289	491,658	204	77,654
c. SBIR/STTR	190	85,103	0	7,748
Total	4,895	\$2,165,390	-126	\$14,766
2. Research Centers	253	\$620,007	0	\$7,218
3. Other Research	746	411,337	0	3,795
4. Research Training	1,342	67,333	0	1,341
5. Research and development contracts	497	602,916	0	17,780
Subtotal, Extramural		\$3,866,983		\$44,900
	<u>FTEs</u>		<u>FTEs</u>	
6. Intramural Research	1,928	\$869,065	-1	\$3,792
7. Research Management and Support	1,255	381,983	89	3,644
8. Construction		0		0
9. Buildings and Facilities		7,920		0
Subtotal, program	3,183	\$5,125,951	88	\$52,336
Total changes				\$63,189

Fiscal Year 2014 Budget Graphs



History of Budget Authority and FTEs:

Distribution by Mechanism:



Change by Selected Mechanism:



NATIONAL INSTITUTES OF HEALTH National Cancer Institute Budget Authority by Activity ^{1, 2}

(Dollars in Thousands)

	F	Y 2012 Actual	F	Y 2013 CR	F	Y 2014 PB	Chang FY 2	ge vs. 012
Extramural Research Detail:	<u>FTEs</u>	Amount	<u>FTEs</u>	Amount	<u>FTEs</u>	Amount	<u>FTEs</u>	Amount
Understanding the Mechanisms of Cancer		\$756 506		\$761 802		\$765 983		\$9 477
Understanding the Causes of Cancer		1.286.647		1,294,339		1.301.567		\$14,920
Improve Early Detection and Diagnosis		465,053		468,308		470,918		\$5,865
Develop Effective and Efficient Treatments		1,217,012		1,224,265		1,230,899		\$13,887
Cancer Prevention and Control		187,700		189,014		190,048		\$2,348
Cancer Centers		594,476		598,637		601,929		\$7,453
Research Workforce Development		172,529		173,737		174,704		\$2,175
Building and Facilities		7,920		7,968		7,920		\$0
Subtotal, Extramural		\$4,687,843		\$4,718,070		\$4,743,968		\$56,125
Intramural Research (non-add)	1,929	\$857,841	1,928	\$864,486	1,928	\$869,065	(1)	\$11,224
Research Management & Support	1,166	\$374,919	1,255	\$379,155	1,255	\$381,983	89	\$7,064
TOTAL	3,095	\$5,062,762	3,183	\$5,097,225	3,183	\$5,125,951	88	\$63,189

Includes FTEs whose payroll obligations are supported by the NIH Common Fund.
 Includes Transfers and Comparable Adjustments as detailed in the "Amounts Available for Obligation" table.

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	Indelînite		Indefinite	
National Cancer Institute	Section 401(a)	42§281	Indefinite	- \$5,097,225,000	Indefinite	\$5,125,951,000
Total, Budget Authority				\$5,097,225,000		\$5,125,951,000

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2005	\$4,870,025,000	\$4,870,025,000	\$4,894,900,000	\$4,865,525,000
Rescission				(\$40,267,000)
2006	\$4,841,774,000	\$4,841,774,000	\$4,960,828,000	\$4,841,774,000
Rescission				(\$48,418,000)
2007	\$4,753,609,000	\$4,753,609,000	\$4,799,063,000	\$4,797,639,000
Rescission				-
2008	\$4,782,114,000	\$4,870,382,000	\$4,910,160,000	\$4,890,525,000
Rescission Supplemental				(\$85,437,000) \$25,559,000
2009	\$4,809,819,000	\$4,975,039,000	\$4,958,594,000	\$4,968,973,000
Rescission				-
2010	\$5,150,170,000	\$5,150,170,000	\$5,054,099,000	\$5,103,388,000
Rescission				-
2011	\$5,264,643,000	-	\$5,256,409,000	\$5,103,388,000
Rescission				(\$44,810,787)
2012	\$5,196,136,000	\$5,196,136,000	\$5,001,623,000	\$5,081,788,000
Rescission				(\$9,604,579)
2013	\$5,068,864,000	-	\$5,084,227,000	-
Rescission				-
2014	\$5,125,951,000	-	-	-

Justification of Budget Request

National Cancer Institute

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

Budget Authority (BA):

			FY 2014	
	FY 2012	FY 2013	President's	FY 2014 + /-
	Actual	CR	Budget	FY 2012
BA	\$5,062,762,000	\$5,097,225,000	\$5,125,951,000	+\$63,189,000
FTE	3,095	3,183	3,813	+88

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

Director's Overview

The National Cancer Institute (NCI) budget request for FY 2014 is best understood against our current landscape of unmatched promise in the oncological sciences, arriving at a time when the world of cancer research has expanded in talent, facilities, and ideas. Progress in molecular biology, especially in the deciphering of cancer genomes and the probing of the signaling pathways that govern normal and malignant cell growth, has transformed our ability to understand the broken parts of a cancer cell; develop new and more precise therapeutic strategies; reformulate diagnostic categories; and imagine screening for and prevention of some cancers in more powerful ways. In just the past few years, NCI-supported science has delivered a remarkable collection of genetic information about several types of cancers, a number of new targeted therapies for various cancers, compelling examples of successful immunologically based therapies, persuasive evidence that radiographic screening can reduce lung cancer mortality, and many new observations about the genesis of cancer cells, their development, their behavior, and their microenvironment.

These findings all lead toward "precision medicine," an approach in which diagnoses are refined and treatments are custom-tailored based on the molecular make-up of an individual tumor. For some cancers, including leukemias and lung and breast carcinomas, targeted treatments developed based on these findings are already helping patients.

To take better advantage of rapid advances in genomics, NCI established a Center for Cancer Genomics in 2011 with the mission of developing and applying genome science to better diagnose and treat cancer patients, as well as to improve approaches to screening and prevention. NCI is supporting research to identify the genetic drivers of cancer, to advance adoption of precise tumor diagnosis and treatment, to prepare patients and their doctors for the changes in medical care influenced by genomics, and to protect privacy without blocking progress in cancer treatment or research. A flagship effort of the Center is The Cancer Genome Atlas (TCGA), an effort that exemplifies NIH investment in basic science with an eye toward future clinical application. Begun as a pilot project by NCI and the National Human Genome Research Institute (NHGRI) in 2006, TCGA established a research infrastructure and focused initially on the genomic characterization of three cancers: glioblastoma multiforme, ovarian cancer, and lung squamous cell cancer. As one of the NIH's signature programs under the American Recovery and Reinvestment Act, NCI and NHGRI expanded TCGA to characterize 20 cancer types in detail by 2014. TCGA has collected tissue samples (tumor tissue as well as normal tissue) from patients with most of those 20 cancers. A number have reached their 500-sample goal, and others are rapidly heading toward it. About a quarter of TCGA's findings have been published, another quarter are being analyzed, and the remaining half are still in the data-collection stage.

In the past year alone, TCGA findings included confirmation that mutations in a single gene, TP53—a tumor protein involved in cell death and senescence—are present in more than 96 percent of ovarian tumors. TCGA also identified a multitude of less-frequent mutations in other genes in ovarian tumors. TCGA results for colorectal cancer include discovering that the pattern of genomic alterations in colon and rectal tissues is the same regardless of anatomic location or origin within the colon or the rectum, confirming the validity of grouping these two cancer types as one for most chemotherapeutic purposes. The genomic analysis of breast cancer revealed genetic similarities between one of the four primary subtypes of breast cancer and ovarian cancer, leading to speculation that cancer-fighting drugs for some kinds of ovarian cancer might also work for this kind of breast cancer.

NCI is dedicated to translating the fruits of its basic science investments into tools that will benefit patients, in part through the support of networks of researchers with complementary knowledge and skills. One example of this is the Cancer Target Discovery and Development network, which brings together scientists with expertise in bioinformatics, genomics, mousebased screening, and small-molecule high-throughput screening to translate the enormous volumes of genomic data generated through TCGA and other efforts into knowledge and tools to support precision medicine.

Deeper understanding of cancer biology driven by genomics, novel tools and techniques, and increasingly powerful supercomputing resources have given scientists an opportunity to ask new "provocative questions" that have stumped us in the past but may be answered by new methods, or that take advantage of new information to pose novel experimental approaches to studying cancer. NCI launched a dedicated Provocative Questions initiative late in 2010, asking investigators to propose intriguing questions, the answers to which could help to overcome obstacles to the control of cancer. From hundreds of questions that were submitted during national workshops and online from researchers, physicians, and advocates, 24 were chosen for solicitation of grant applications. The selected questions build on specific advances in our understanding of cancer and cancer control; address broad issues in the causes, pathogenesis, diagnosis, treatment, and prevention of cancer that have proven difficult to resolve; and take into consideration the likelihood of progress in the foreseeable future. To initiate research focused on these 24 questions, 56 applications totaling just under \$21.5 million were funded in the first year of the program. A new request for applications that includes additional provocative questions

was issued in 2012. The initiative complements NCI's longtime and essential emphasis on funding investigator-initiated research.

Capitalizing on the opportunities in cancer research in the coming years will require a strong and diverse biomedical research workforce. NCI uses several mechanisms to attract and support early-stage investigators, including Ruth L. Kirschstein National Research Service Awards for predoctoral and postdoctoral trainees. The Institute also has programs devoted to supporting individuals from populations currently underrepresented in biomedical research.

NCI's FY 2014 request reflects two important fundamental principles in cancer research: first, different types of cancers are often united by common themes, but also characterized by inherent differences in epidemiological factors, molecular mechanisms, and clinical features; and second, studies of each cancer type are strongly influenced by work on other types of cancer. We must, and we do, balance our knowledge about the public health burden of each cancer type against a consistent historical message: The sources of our greatest advances are difficult to predict and often emerge from unexpected places. Thus, if we are to spend our funds wisely and reward the public's trust, we must take into account scientific opportunity, the richness of experimental ideas, and the talent of investigators, along with the toll taken by individual cancer types.

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

Program Portrait: Provocative Questions "PQ" Program

 FY 2012 Level:
 \$22.5 million

 FY 2014 Level:
 \$77.3 million

 Change:
 +\$54.8 million

In late 2010, NCI launched an initiative to identify a list of intriguing and important questions—the answers to which will surely drive progress against cancer—that have not received sufficient attention or might be answerable using new technologies. Since then, more than 500 Provocative Questions have been proposed through workshops and online. Of these, 24 were chosen for inclusion in a request for applications issued by NCI in 2011. These questions build on specific advances in our understanding of cancer and cancer control, address broad issues in the biology of cancer that have proven difficult to resolve, and take into consideration the likelihood of progress in the foreseeable future. Answers to these could help overcome obstacles to the control of cancer. Fifty-six grants were awarded in response to the first issuance of the Requests for Applications (RFAs). Some of the questions being addressed by researchers supported through the first round of funding include:

- (1) How does obesity contribute to cancer risk?
- (2) How do changes in RNA processing contribute to tumor development?
- (3) Given the recent discovery of the link between a polyomavirus and Merkel cell cancer, what other cancers are caused by novel infectious agents and what are the mechanisms of tumor induction?
- (4) Are there new technologies to inhibit traditionally "undruggable" target molecules, such as transcription factors, that are required for the oncogenic phenotype?

The Provocative Questions initiative is ongoing and input continues to be collected through the Provocative Questions Web site. NCI reissued a set of 8 Provocative Question RFAs in September 2012 with an updated set of 24 questions, which included some of the original Provocative Questions as well as some new questions. More information is available at <u>http://provocativequestions.nci.nih.gov/</u>.

Program Descriptions and Accomplishments

NCI's research spans a variety of activities that can be summarized within five scientific themes: Understanding the Mechanisms of Cancer; Understanding the Causes of Disease; Improving Early Detection and Diagnosis; Developing Effective and Efficient Treatments; and Improving Cancer Prevention and Control. Examples of programs, projects, and progress in each of these areas are described in the following sections.

Understanding the Mechanisms of Cancer: Cancer is driven by alterations of the genome that manifest as aberrant molecular processes favoring survival and uncontrolled growth. A deeper understanding of the genomic and cellular changes that take place in the collection of diseases called cancer is critical for the development of new and improved diagnostic and therapeutic approaches. Large-scale, high-throughput studies provide snapshots of the genes, proteins, and pathways that are altered in cancer, while laboratory studies in model systems, including animal models, probe the activities of these molecules and systems.

<u>Budget Policy</u>: The FY 2014 President's Budget estimate is \$765.983 million, an increase of \$9.477 million, or 1.3 percent above the FY 2012 Actual level. Investigator-initiated research project grants comprise a large proportion of the studies focused on mechanisms of carcinogenesis, but NCI also directs a number of large and small programs in this area. Many of these initiatives bring together groups of researchers to answer scientific questions that cannot easily be addressed by single laboratories. The Center for Cancer Genomics coordinates programs across NCI focused on genome structure and function. A major component of the Center for Cancer Genomics is The Cancer Genome Atlas (TCGA), a joint program with NHGRI. The TCGA is cataloguing the mutations and other alterations that occur in more than 20 types of human cancer with the goal of improving cancer diagnosis, treatment, and prevention. A recent TCGA analysis of primary breast cancers confirmed the existence of four main breast cancer classes and extended the characteristics of these types. One type of breast tumors exhibited striking molecular similarity to a type of ovarian cancer (high-grade serous), suggesting that subsets of cancers at these two sites may arise through similar molecular events and be amenable to similar therapies.

In addition to TCGA, the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) initiative and the Cancer Genome Characterization Initiative are using high-throughput platforms to identify genetic abnormalities in tumors from pediatric and adult patients as well as those from HIV-positive individuals. One TARGET project identified a new subclass of acute lymphoblastic leukemia with high-risk of recurrence that is associated with novel chromosomal translocations. These findings have potential to directly benefit patients in the near future, because the translocations identified involve pathways for which therapies are already available. The Cancer Target Discovery and Development Network is accelerating the transition of the molecular data gained through TCGA and other genomic efforts to new treatments through gene validation studies, as well as high-throughput screening of small molecules and research in mouse models.

The Clinical Proteomic Tumor Analysis Consortium (CPTAC) is a comprehensive and coordinated effort to systematically identify proteins that result from alterations in cancer genomes and related biological processes. CPTAC investigators are characterizing the protein contents of three types of human cancer and integrating these findings with genomic data (including that collected through TCGA), with the goal of improving cancer diagnosis, treatment, and prevention. All data, as well as all assays and protocols developed through CPTAC, will be made available to the research community. The Office of Physical Sciences-Oncology coordinates NCI activities that apply principles and approaches from the physical sciences to oncology. The Physical Sciences-Oncology Centers Program promotes a deeper understanding of the mechanisms of cancer initiation and progression by incorporating physical measurements and spatial and temporal information with genomic and epigenomic alterations. This may facilitate prediction of viable pathways to develop novel interventions.

NCI is interested in investigating how metabolic processes contribute to cancer risk. Intramural investigators have identified several renal tumors with mutations within the Krebs cycle pathway (a series of chemical reactions that organisms use to generate energy from carbohydrates, fats, and proteins) and are poised to study potential interventions targeting these lesions. In addition they will use imaging techniques to evaluate oxidative metabolism directly within tumors with the hope to move these techniques forward in the clinic. The Transdisciplinary Research on Energetics and Cancer Program was developed to foster collaboration among scientists and accelerate progress toward reducing cancer incidence, morbidity, and mortality associated with obesity, low levels of physical activity, and poor diet.

The trans-NCI Innovative Molecular Analysis Technologies program exemplifies high-risk, high-reward investments to catalyze highly innovative technology development with the potential for truly transformative impact across the broad continuum of basic, translational, and clinical cancer research. This program has a proven record for catalyzing the development of a variety of well-known and emerging technologies that have delivered significantly on this goal.

Understanding the Causes of Cancer: Cancer develops through the complex interplay of genetic background, lifestyle, and environmental factors. In some cases, cancer risk is strongly influenced by inheritance of a mutation of a single gene or a combination of genes. More commonly, however, known cancer risk is determined mainly by external factors (e.g., exposure to tobacco or an infectious agent), the effects of which may differ depending on a person's genetic background.

<u>Budget Policy</u>: The FY 2014 President's Budget estimate is \$1,301.567 million, an increase of \$14.920 million, or 1.2 percent above the FY 2012 Actual level. NCI's past investment in population cohorts has laid the groundwork for additional studies to identify factors associated with cancer risk and to determine how these factors interact. Studies through NCI's Cohort Consortium—a large-scale, international collaboration of cohorts that include over four million people—are evaluating the role of genetic susceptibility, environmental exposures (including nutrition), and gene-environment interactions for a range of cancer types.

NCI also has several ongoing genome-wide association studies (GWAS) examining the genetic determinants of a variety of cancers (breast, prostate, lymphoma, lung, bladder, renal, endometrial, ovarian, upper GI, testicular, pancreatic, and glioma), as well as genetic factors that may contribute to obesity and tobacco use. One GWAS is investigating possible genetic contributions to the increased risk of tobacco-induced lung cancer among African-Americans. This intramural-extramural collaborative study includes more than 4,000 African-American lung cancer patients and twice as many population controls. GWAS results are being further examined through the Post-Genome Wide Association Initiative, the goal of which is to translate GWAS findings into clinical and prevention applications by replicating findings, more accurately pinpointing genomic regions that cause cancer, unraveling the functions of genetic variants, and determining how environmental factors alter genetic risk. NCI is also following up on detectable genetic mosaicism in GWAS data as a marker of genomic instability associated with aging and a possible biomarker for increased risk of cancer and other late-onset diseases. NCI is also supporting more than 50 grants focused on epigenetic factors that contribute to cancer through the Epigenetic Approaches in Cancer Epidemiology initiative.

Some initiatives are focused on the causes of cancer at specific sites. The Breast Cancer and the Environment Research Program, which is a transdisciplinary approach involving basic scientists, epidemiologists, clinicians, and community partners, is investigating the effects of environmental exposures that may predispose a woman to breast cancer throughout her lifetime. Intramural investigators also are working to characterize and define molecular mechanisms that drive progression of the precursor disease of monoclonal gammopathy of undetermined significance and smoldering myeloma to full-blown multiple myeloma. It is hoped that knowledge gained through these efforts will identify new rational approaches for treating multiple myeloma and its high-risk precursors.

NCI research also focuses on the important roles of infectious agents and the tumor microenvironment in cancer. Current evidence indicates that as many as one in five cancers may have an infectious cause. When infectious causes are discovered, the agent can represent a molecular target for intervention—prevention or treatment—or can serve as a biomarker for screening (e.g., human papillomavirus infection of the cervix, infection of the liver with the hepatitis B and C viruses). Five grants funded through the first Provocative Questions RFAs are focused on identifying novel infectious agents involved in cancer—including viruses, bacteria, and parasites—using a variety of approaches. The complex interactions between tumors and surrounding cells that influence cancer progression are being characterized by projects funded through the Integrative Cancer Biology Program and the Tumor Microenvironment Network. Projects funded through the recent Advanced In Vivo Imaging to Understand Cancer Systems initiative are focused on integrating advanced in vivo imaging technologies with systems biology approaches to understand complex cancer phenomena at the highest available resolution.

Improving Early Detection and Diagnosis: Many of the deadliest cancers are often diagnosed at late stages due to the lack of screening tests capable of identifying cancers at early stages, when they may be more likely to respond to treatment. Researchers are working to identify molecules—nucleic acids, proteins, metabolites, and other substances—as well as imaging modalities that can be used to identify the presence of cancer cells earlier and help guide

decisions about treatment. The risks associated with screening and early detection modalities must be assessed and measures must be taken to ensure that harms do not outweigh benefits.

<u>Budget Policy</u>: The FY 2014 President's Budget estimate is \$470.918 million, an increase of \$5.865 million, or 1.3 percent above the FY 2012 Actual level. NCI is working to identify and evaluate tools for early detection and diagnosis of a variety of cancers. Many projects related to the identification of potential biomarkers are driven by researchers supported through investigator-initiated research project grants. Specialized Programs of Research Excellence (SPORE) investigators also are using annotated biospecimens to identify cellular and molecular markers of cancer. For example, one group of SPORE investigators developed a new urine test for detection of the TMPRSS2:ERG gene fusion in exfoliated prostate cancer cells. In combination with the existing prostate cancer marker PCA3, this test may help avoid an invasive needle biopsy, while identifying men at highest risk for clinically significant disease. NCI also established the Early Detection Research Network to support the identification and validation of candidate biomarkers of early disease, with the goal of developing clinically useful diagnostic tests. The efforts of investigators working on early detection and improved diagnosis can be augmented by findings from genomic and proteomic studies (e.g., TCGA, TARGET, CPTAC) and the results from the Cancer Target Discovery and Development Network.

Increasing knowledge about the molecular traits of tumors coupled with advancements in imaging technology is creating opportunities for molecular imaging of cancer. NCI's intramural Molecular Imaging Program is focused on the development of *in vivo* imaging agents targeted to cancer for early detection and monitoring. The program is conducting clinical and preclinical tests of potential imaging agents and is also striving to create new technologies that will improve image quality. A collaborative pilot program supported by TCGA and the NCI Cancer Imaging Program is collecting clinical imaging scans from patients whose tumor tissue has been analyzed through TCGA in order to assess whether noninvasive imaging techniques can provide information about the genomic fingerprint of tumors. The pilot initially focused on collecting magnetic resonance images of patients with glioblastoma multiforme; collections of images from breast and renal cell carcinoma patients are also underway. An image archive with user support has been established with both public and limited access collections.

Nanotechnology has potential to benefit early detection and diagnosis efforts. The NCI Alliance for Nanotechnology in Cancer is supporting development of materials and instrumentation for imaging specific cancer biomarkers in patients. Nanotechnology enabled in vitro diagnostic devices offer higher sensitivity and new capabilities, such as single cell proteomic analysis, for molecular stratification of patient prognosis.

NCI is also working to improve existing approaches for cancer screening. The National Lung Screening Trial (NLST) of high risk current and former smokers found that screening with lowdose helical computed tomography (CT) decreased lung cancer mortality by 20 percent. However, many of the lesions detected by CT were subsequently found to be noncancerous. To help address these false-positive cases, the NCI Cancer Biomarkers Research Group is developing an initiative aimed at integrated imaging and biomarker(s) approaches to improve lung cancer screening, early cancer detection, and diagnosis. NCI also is working to find ways to distinguish indolent lesions that do not require extensive treatment from lesions that are progressive and/or potentially life threatening through the Improving the Diagnosis of Early Lesions Detected by Cancer Screening initiative. The goal of this effort, which is focused on breast, prostate, and lung cancers as well as melanoma, is to maintain the benefits of early detection while minimizing the harms.

Screening tests for breast, colon, and cervical cancers have been shown to reduce mortality from these diseases, but there is evidence that these tests are not optimally implemented in community settings. The Population-based Research Optimizing Screening through Personalized Regimens initiative funds research to improve the screening processes for these cancers with respect to recruitment, screening, diagnosis, and referral for treatment.

NCI has dedicated efforts to develop new strategies for early detection. One example, the Barrett's Esophagus Translational Research Network (BETRNet), consists of multiple centers collaborating to develop an understanding of the basis of Barrett's esophagus and its conversion to esophageal adenocarcinoma. BETRNet investigators are following up on potential biomarkers, utilizing animal models and studying information from human populations in hopes of finding ways to identify individuals at risk for Barrett's esophagus and esophageal adenocarcinoma and to determine which patients with Barrett's esophagus are likely to develop esophageal cancer.

Developing Effective and Efficient Treatments: Increasing knowledge about the molecular fingerprints of tumors and the ways in which cancer cells interact with their environments is creating opportunities for interventions targeted to specific molecules and signaling pathways. The ultimate goal is to match patients with the treatments most likely to help them based on specific characteristics of their tumors.

<u>Budget Policy</u>: The FY 2014 President's Budget estimate is \$1,230.899 million, an increase of \$13.877 million, or 1.1 percent above the FY 2012 Actual level. NCI investments in basic and translational research lead to identification of therapeutic targets, many of which are validated and developed by commercial interests. NCI-supported clinical research activities also are developing and testing interventions in many cancer sites, both through the intramural work in the NIH Clinical Center and through support of extramural clinical research networks. NCI does not seek to compete with the private sector, but rather works to complement the work being undertaken by other players in the cancer field.

NCI has a number of programs designed to promote development of drugs and assays for clinical trials. The NCI Experimental Therapeutics Program (NExT) aims to shorten the typical 10- to 12-year drug development timeline by getting promising drugs into human trials and rapidly eliminating those likely to be ineffective. The NExT platform will facilitate the many handoffs that occur between academic research laboratories and the private sector in order to achieve the ultimate goal of utility in patients. The Chemical Biology Consortium, a component of NExT, develops chemical tools for probing signaling pathways involved in cancer, with a focus on molecules that have traditionally been difficult to target. The Clinical Assay Development Program facilitates movement of promising clinical laboratory assays from the research setting into robust platforms ready for federal certification and clinical testing. The Clinical Assay Development Network is developing laboratory capacity at selected sites nationwide to perform

molecular profiling on human tumors for patients entering clinical trials. In support of the NExT initiative, the Center for Advanced Preclinical Research will accelerate development of therapeutics and diagnostics for human diseases by providing state-of-the-art animal models that are genetically programmed to develop diseases that mimic human diseases.

NCI is working to develop treatments and tools that will make cancer treatments more effective while reducing the often debilitating side effects that often accompany them. Whole genome sequencing through TCGA of squamous cell lung cancer, which has proven resistant to existing treatments for lung cancer, has resulted in identification of several mutations and should stimulate clinical trials of targeted therapies.

NCI also is investigating ways to harness the immune system to treat cancer. The Center for Excellence in Immunology is an intramural program focused on discovery, development, and delivery of novel immunologic approaches—including cell-based therapies, therapeutic vaccines, and novel cytokines—for prevention and treatment of cancer. Basic discoveries in immunology are being moved into early clinical trials via the Cancer Immunotherapy Trials Network (CITN). CITN performs early trials with new immunomodulators with a heavy emphasis on real-time immunomonitoring to predict response and/or resistance.

Efforts are underway to enhance traditional radiation therapy and chemotherapy. The Radiation Research Program (RRP) tests NCI-developed drugs for their efficacy as radiosensitizers under a variety of in vitro environmental conditions and carries out in vivo radiation response studies. The Physical Sciences-Oncology Centers program is using physical science approaches to investigate the evolution of cancer resistance to radiation and/or chemotherapy.

Clinical trials are a critical step in moving potential therapies into clinical practice. NCI supports clinical trials through a number of mechanisms, especially the Cooperative Group Program. The Cooperative Groups are now being reorganized to streamline the development and execution of trials, to select and prioritize trials through stringent peer review, and to fund the most promising studies. As part of the Towards Precision Oncology initiative, Cooperative Groups are incorporating genomic science into a wide array of trials, including tests of targeted drugs as adjuvant therapies for mutationally defined types of lung adenocarcinoma (the ALKEMIST trial) and trials that will dramatically expand the number of patients who are given targeted therapies based on determined genotypes. Similarly, the new Exceptional Cases Initiative involves retrospective and prospective studies to understand how the molecular properties of tumors affect responses to standard and targeted therapies, with a focus on those tumors that have unusual characteristics and/or demonstrate unusual responses to treatment. NCI also has implemented the Biomarker, Imaging, and Quality of Life Studies Funding Program, which supports promising correlative studies related to biomarkers, imaging, patient quality of life studies, and cost effectiveness analysis in association with phase III and large phase II trials. In order to facilitate management and coordination of the clinical trials portfolio, NCI is creating the Clinical Trials Reporting Program, a comprehensive database that will contain regularly updated information on all interventional trials.

NCI is launching a new initiative in 2014 called Understanding and Managing Baseline Chronic Conditions and Cachexia in Clinical Trials, that aims to improve understanding of the clinical

manifestations and biological impact of comorbidities and coexisting diseases on clinical management of cancer patients. About half of cancer patients suffer from cachexia (a disorder characterized by loss of weight, muscle atrophy, severe loss of appetite, etc.), which can interfere with the effectiveness and tolerability of cancer treatments and lead directly to the death of some patients.

NCI has made significant efforts to expand access to clinical trials for patients being treated in community settings and for minority and underserved populations. The Community Clinical Oncology Programs (CCOPs) enroll patients onto approved cancer prevention, control, and treatment trials, enrolling one-third of all participants on NCI trials nationwide. The 49 current CCOPs represent 340 hospitals and 2,900 physicians. The Minority-Based Community Clinical Oncology Programs (MBCCOPs) enroll patients onto approved trials in areas with at least 30 percent underserved or minority populations. The 17 current MBCCOPs comprise 55 hospitals and 475 physicians, including 100 minority investigators. MBCCOPs have an average of 64 percent minority participants on trials at their sites. The NCI Community Cancer Centers Program (NCCCP) is a network of 21 community hospitals in 16 states dedicated to improving the quality of cancer care for cancer patients from rural, inner-city, and underserved communities each year and providing them the opportunity to participate in cancer research. NCI is in the process of planning for the consolidation of its three community-based oncology research programs (CCOPs, MBCCOPs, and NCCCP).

NCI also invests in research to elucidate the factors that contribute to cancer health disparities. The Basic Research in Cancer Health Disparities initiative supports research to understand the biological mechanisms for cancer disparities among various racial and ethnic populations. The Centers for Population Health and Health Disparities program supports transdisciplinary research involving social, behavioral, biological, and genetic studies to improve knowledge of the causes of health disparities and devise effective methods of preventing, diagnosing, and treating disease and promoting health. Using a regional approach, the Geographical Management of Cancer Health Disparities Program (G/BMaP) is working to support biospecimen collection, development of bioinformatics platforms, clinical trials recruitment and retention, emerging technologies applications, and the development of health disparities research projects in racial/ethnic minority and underserved communities. As part of a broader Center to Reduce Cancer Health Disparities Biospecimen Awareness/Education and Collection Campaign, G/BMaP is also working to raise awareness about the importance of biospecimens and to educate minority populations about biospecimen research.

NCI supports the development and use of technologies with potential to enhance treatment and related research. The Advanced Technology Program accelerates the delivery of new treatments to patients by developing and applying advanced technologies, such as biomedical imaging. The NIH Center for Interventional Oncology offers new and expanded opportunities to investigate cancer therapies using imaging technology to diagnose and treat localized cancers in a targeted and minimally or noninvasive manner. Researchers funded through the Quantitative Imaging Network are developing and validating quantitative imaging methods and software tools for the measurement of response to drug or radiation therapy for use in clinical trials. NCI's Cancer Imaging Program has worked with the American College of Radiology Imaging Network to develop guidelines for advanced imaging for sites participating in NCI-sponsored clinical trials

in order to decrease variability in procedures; this effort has qualified NCI-designated comprehensive cancer centers to be Centers of Quantitative Imaging Excellence.

Nanotechnology-based constructs are being developed to facilitate better delivery of chemotherapeutic drugs, reducing their toxic systemic effects and increasing therapeutic efficacy. These constructs are being tested in clinical trials, as are nanotechnology-based approaches to deliver RNA molecules capable of silencing specific genes to targeted cells. In addition, the NCI Nanotechnology Characterization Laboratory supports standardized preclinical characterization of nanomaterials to ease regulatory approval of these new constructs. Recently, the NCI developed a suite of Web-based tools called CellMiner that allows the research community to compare data derived from large collections of genomic information against thousands of drugs. By comparing drugs and genetic targets, researchers can more easily identify pharmaceuticals that could be effective against different forms of cancer.

Program Portrait: Lymphoma/Leukemia Molecular Profiling Project

FY 2012 Level:\$2.7 millionFY 2014 Level:\$2.7 millionChange:\$0.0 million

The Leukemia/Lymphoma Molecular Profiling Project (LLMPP) is a consortium of NCI intramural and extramural investigators who have pooled resources and talent to develop molecular classifications for human lymphoid malignancies that can play roles in disease diagnosis, determination of prognosis, and selection of appropriate therapy. Dr. Louis Staudt in the NCI Center for Cancer Research leads the consortium. The large number of samples made available through this collaborative effort—substantially more than any single institution could have acquired—has facilitated significant increases in knowledge and identified potential ways to improve treatment for patients with leukemia and lymphoma. LLMPP coordinates with other NCI efforts, including the Center for Cancer Genomics and the Center for Global Health.

LLMPP researchers recently conducted a study of Burkitt lymphoma (BL), a fast growing form of non-Hodgkin lymphoma. There are three subtypes of BL: sporadic BL, which is the form most commonly seen in the United States and other developed countries; endemic BL, which is associated with infection with the Epstein Barr virus and is the most common form of BL in developing countries; and an HIV-associated subtype. Extensive RNA sequencing of tumor cells from BL patients and BL cell lines identified a number of mutations that occur commonly in BL and confirmed that BL is distinct from other types of non-Hodgkin lymphoma. Researchers found that the gene that encodes for the protein TCF3, which controls the production of many genes within normal B cells, is mutated in many of the sporadic BL cases. Endemic BL exhibited different patterns of mutations, including a high rate of mutation in cyclin D3, a protein that regulates cell division. Although neither TCF3 nor cyclin D3 are likely to be a therapeutic target, there are already drugs that target proteins or pathways that interact with or are activated by these mutated proteins, opening up the possibility of testing targeted therapies in BL in the near future. In the United States and other developed countries, many patients with BL can be cured with high-dose chemotherapy regimens. However, cure rates are substantially lower in developing countries; high-dose therapies cannot be used in these settings because the immunosuppressive and other toxic effects of intensive chemotherapy cannot be managed. There is tremendous potential for targeted therapies to supplement the minimal chemotherapy that can be administered in developing areas and improve outcomes for patients. These therapies may also help BL patients in the developing world who do not respond to or cannot withstand standard chemotherapy.

Improving Cancer Prevention and Control: Cancer prevention research draws on knowledge of the mechanisms and causes of cancer. Interventions can reduce cancer risk by reducing exposure to environmental factors through approaches such as education, behavior modification, vaccination, or policy changes. Chemopreventive agents that interfere with processes known to be involved in cancer initiation also have potential to counteract the elevated risk of cancer in some individuals due to genetic or biologic factors. Research in the area of cancer control seeks to better understand the factors that influence cancer outcomes, quality of care, quality of life, and cancer-related health disparities, in part through surveillance.

<u>Budget Policy</u>: The FY 2014 President's Budget estimate is \$190.048 million, an increase of \$2.348 million, or 1.3 percent above the FY 2012 Actual level. In addition to identifying therapeutic targets, molecular characterization of tumors may also provide targets for chemoprevention. The Consortia for Early Phase Prevention Trials include five major research centers that lead collaborative networks to assess the cancer prevention potential of new agents, with a focus on phase 0, I, and II clinical trials. Continued emphasis will be placed on identifying molecular targets, developing successful prevention strategies, and translating findings into clinical practice.

Concurrently, NCI is working to enhance understanding of cancer prevention and control interventions that are known to be effective, from the molecular level to the policy level. NCI is supporting a biospecimen repository for the NIA-sponsored ASPirin in Reducing Events in the Elderly (ASPREE) study, a landmark placebo-controlled trial testing the effects of aspirin in healthy participants from the United States and Australia. The specimens, which will include those collected from participants who develop cancer over the course of the study, will be used to study the molecular mechanisms that support the cancer preventive effects of aspirin, including changes in specific DNA biomarkers. NCI is also interested in elucidating the protective effects of the diabetes drug metformin against some kinds of cancer using both preclinical and clinical approaches. On the policy level, the State and Community Tobacco Control Policy and Media Research initiative will investigate the effectiveness of the state and community tobacco control efforts. Focus areas include secondhand smoke policies, tax and pricing policies, tobacco industry marketing and promotion, mass media countermeasures, and community and social norms.

The Surveillance, Epidemiology and End Results (SEER) program, which has collected data since 1973, regularly samples approximately 26 percent of the U.S. population and has obtained information on 5.7 million cancer cases—380,000 cases are added each year. This database provides critical data on cancer trends. The Health Maintenance Organization, Cancer Research Network conducts cancer prevention, early detection, treatment, long-term care, and surveillance research, using data systems of 14 Health Maintenance Organizations nationwide. Studies of lifestyle change include research into energy balance (integrated effects of diet, physical activity, and genetics on growth and body weight) as a way to control cancer incidence.

Cancer Centers: The NCI-designated cancer centers program recognizes centers around the country that meet rigorous criteria for state-of-the-art programs in multidisciplinary cancer research. These centers put significant resources into developing research programs, faculty, and facilities that will lead to better approaches to prevention, diagnosis, and treatment of cancer.

<u>Budget Policy</u>: The FY 2014 President's Budget estimate is \$601.929 million, an increase of \$7.453 million, or 1.3 percent above the FY 2012 Actual level. The 67 NCI-designated Cancer Centers perform a high proportion of the research supported by NCI. This includes high quality laboratory, clinical, and population science research to improve cancer prevention, diagnosis, and treatment in addition to efforts to stimulate innovative pilot projects in new investigational areas. Investigators at NCI-designated cancer centers have played central roles in many groundbreaking findings in cancer research over the past decades.

Research Workforce Development: NCI is committed to supporting the development of a strong workforce of cancer researchers that span the career continuum. Investment in early-stage investigators is needed to attract strong talent and ensure the future of cancer research, but continued support is also needed for established investigators who have proven their ability to conduct robust science and who provide mentoring for the next generation of researchers.

<u>Budget Policy</u>: The FY 2014 President's Budget estimate is \$174.704 million, an increase of \$2.175 million, or 1.3 percent above the FY 2012 Actual level. NCI has a number of intramural opportunities for training in basic, clinical, and behavioral research. In addition, NCI supports fellowships, research career development awards, and training/education programs at universities and institutions across the country. Awardees span the career continuum, including predoctoral candidates, postdoctoral fellows, new faculty in independent research positions, and midcareer and established investigators.

NCI is committed to enhancing diversity within the cancer research workforce. Many efforts in this regard are coordinated through the NCI Center to Reduce Cancer Health Disparities. The Partnerships to Advance Cancer Health Equity (formerly known as the Minority Institution Cancer Center Partnership) is a program that links institutions serving racial/ethnic and/or underserved communities with cancer health disparities and NCI-Designated Cancer Centers to train scientists from diverse backgrounds in cancer research and to effectively deliver cancer advances to racially and ethnically diverse communities. There are currently 13 established partnerships, and an additional six pairs of institutions have received funding to explore the feasibility of creating partnerships. The Continuing Umbrella of Research Excellence program aims to increase the cadre of underrepresented investigators engaging in cancer research by identifying and providing opportunities for promising candidates from high school through junior investigator levels.

Buildings and Facilities: Buildings and Facilities: The renovation and improvement funds for the facilities at the NCI-Frederick campus, located in Frederick, Maryland, were budgeted as facilities funds beginning in FY 2005. The funds are necessary to maintain the operation of these facilities for the scientific missions of NCI, NIH, other government agencies, and the extramural community.

<u>Budget Policy</u>: The FY 2014 President's Budget request is \$7.920 million, the same amount as the FY 2012 Actual level.

Research Management and Support: NCI's research management and support personnel fulfill a key and indispensable role within the Institute by supporting and enabling the activities and success of all NCI-funded researchers. This staff conducts activities that include but are not limited to central administration, overall program direction, grant and contract administration, human resources, program coordination, and financial management.

<u>Budget Policy</u>: The FY 2014 President's Budget estimate is \$381.983 million, an increase of \$7.064 million, or 1.9 percent above the FY 2012 Actual level. 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.

Budget Authority by Object Class

(Dollars in Thousands)

		FY 2012 Actual	FY 2014 PB	Increase or Decrease
Total co	ompensable workyears:			
	Full-time employment	3,095	3,183	88
	Full-time equivalent of overtime and holiday hours	3	3	0
		¢170.017	¢175 777	¢4.960
	Average ES salary (in dollars)	\$170,917	\$1/5,///	\$4,860
	Average GM/GS grade	12.3	12.3	0.0
	Average GM/GS salary (in dollars)	\$99 884	\$102 724	\$2.840
	Average salary grade established by act of	\$77,004	\$102,724	φ2,040
	July 1, 1944 (42 U.S.C. 207) (in dollars)	\$95.572	\$96.528	\$956
	Average salary of ungraded positions (in dollars)	129,835	131,133	1,298
				-,-, -, -, -, -, -, -, -, -, -, -, -, -,
		FY 2012	FY 2014	Increase or
	OBJECT CLASSES	Actual	PB	Decrease
	Personnel Compensation:			
11.1	Full-time permanent	\$206,953	\$220,153	\$13,200
11.3	Other than full-time permanent	123,148	126,246	3,098
11.5	Other personnel compensation	8,413	8,961	548
11.7	Military personnel	4,378	4,549	171
11.8	Special personnel services payments	47,931	49,126	1,195
	Total, Personnel Compensation	\$390,822	\$409,035	\$18,213
12.0	Personnel benefits	\$99,743	\$104,520	\$4,777
12.2	Military personnel benefits	3,092	3,202	110
13.0	Benefits for former personnel	0	0	0
	Subtotal, Pay Costs	\$493,657	\$516,757	\$23,100
21.0	Travel and transportation of persons	\$14,609	\$14,609	(\$0)
22.0	Partal accurate to CSA	948	947	(1)
23.1	Rental payments to GSA	1,562	1,628	00
23.2	Communications utilities and	98	99	1
23.3	miscellaneous charges	7 649	7 649	(0)
24.0	Printing and reproduction	850	851	(0)
25.1	Consulting services	16 957	17 167	210
25.1	Other services	220.098	215 117	(4 981)
25.2	Purchase of goods and services from	220,070	213,117	(1,001)
2010	government accounts	601.621	630.923	29,302
25.4	Operation and maintenance of facilities	10.648	10.382	(266)
25.5	Research and development contracts	461,505	374,814	(86,691)
25.6	Medical care	4,013	4,013	(0)
25.7	Operation and maintenance of equipment	17,531	17,531	0
25.8	Subsistence and support of persons	17	17	(0)
25.0	Subtotal, Other Contractual Services	\$1,332,391	\$1,269,964	(\$62,427)
26.0	Supplies and materials	\$33,723	\$33,724	\$1
31.0	Equipment	15,645	15,646	1
32.0	Land and structures	9	9	(0)
33.0	Investments and loans	0	0	0
41.0	Grants, subsidies and contributions	3,161,617	3,264,067	102,450
42.0	Insurance claims and indemnities	0	0	0
43.0	Interest and dividends	2	1	(1)
44.0	Retunds	0	0	0
	Subtotal, Non-Pay Costs	\$4,569,105	\$4,609,194	\$40,089
	Total Budget Authority by Object Class	\$5,062,762	\$5,125,951	\$63,189

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

Salaries and Expenses

(Dollars in Thousands)

	FY 2012	FY 2014	Increase or
OBJECT CLASSES	Actual	PB	Decrease
Personnel Compensation:			
Full-time permanent (11.1)	\$206,953	\$220,153	\$13,200
Other than full-time permanent (11.3)	123,148	126,246	3,098
Other personnel compensation (11.5)	8,413	8,961	548
Military personnel (11.7)	4,378	4,549	171
Special personnel services payments (11.8)	47,931	49,126	1,195
Total Personnel Compensation (11.9)	\$390,823	\$409,035	\$18,212
Civilian personnel benefits (12.1)	\$99,743	\$104,520	\$4,777
Military personnel benefits (12.2)	3,092	3,202	110
Benefits to former personnel (13.0)	0	0	0
Subtotal, Pay Costs	\$493,658	\$516,757	\$23,099
Travel (21.0)	\$14,609	\$14,609	\$0
Transportation of things (22.0)	948	947	(1)
Rental payments to others (23.2)	98	99	1
Communications, utilities and			
miscellaneous charges (23.3)	7,649	7,649	0
Printing and reproduction (24.0)	850	851	1
Other Contractual Services:			
Advisory and assistance services (25.1)	16,957	17,167	210
Other services (25.2)	220,098	215,117	(4,981)
Purchases from government accounts (25.3)	450,721	459,242	8,521
Operation and maintenance of facilities (25.4)	8,227	8,227	0
Operation and maintenance of equipment (25.7)	17,531	17,531	0
Subsistence and support of persons (25.8)	17	17	(0)
Subtotal Other Contractual Services	\$713,551	\$717,301	\$3,750
Supplies and materials (26.0)	\$32,930	\$32,930	\$0
Subtotal, Non-Pay Costs	\$770,635	\$774,386	\$3,751
Total, Administrative Costs	\$1,264,293	\$1,291,143	\$26,850

Details of Full-Time Equivalent Employment (FTEs)

		FY 2012			FY 2013			FY 2014	
OFFICE/DB/JSION	Civilian	Actual	T-4-1	C'-ilian	CR	T-4-1	C'!!!	PB	Total
OFFICE/DIVISION	Civilian	Mintary	Total	Civilian	Mintary	Total	Civilian	Mintary	Total
Office of the Director									
Direct:	830	4	834	838	4	842	838	4	842
Reimbursable:	0	0	-	-	-	-	-	-	-
Total:	830	4	834	838	4	842	838	4	842
Center for Cancer Research									
Direct:	1,511	23	1,534	1,512	23	1,535	1,512	23	1,535
Reimbursable:	3	0	3	-	-	-	-	-	-
Total:	1,514	23	1,537	1,512	23	1,535	1,512	23	1,535
Division of Cancer Biology									
Direct:	42	-	42	46	-	46	46	-	46
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	42	-	42	46	-	46	46	-	46
Division of Extramural Activities									
Direct:	95	-	95	115	-	115	115	-	115
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	95	-	95	115	-	115	115	-	115
Division of Cancer Treatment and Diagnosis									
Direct:	193	4	197	221	4	225	221	4	225
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	193	4	197	221	4	225	221	4	225
Division of Cancer Prevention									
Direct:	80	1	81	92	1	93	92	1	93
Reimbursable:	-	-	-		-	-	-	-	-
Total:	80	1	81	92	1	93	92	1	93
Division of Cancer Control and Population Sciences									
Direct:	143	3	146	161	3	164	161	3	164
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	143	3	146	161	3	164	161	3	164
Division of Cancer Epidemiology and Genetics									
Direct:	156	7	163	156	7	163	156	7	163
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	156	7	163	156	7	163	156	7	163
Total	3,053	42	3,095	3,141	42	3,183	3,141	42	3,183
Includes FTEs whose payroll obligations are supported by the	NIH Common Fu	ind.							
FTES supported by funds from Cooperative Research and Devi	elopment Agreen	ients.							
FISCAL YEAR	_			Av	verage GS Gra	de			
2010					12.0				
2011					12.0				
2012	1				12.3				
2013	1				12.3				
2014					12.3				

Detail of Positions

	FY 2012	FY 2013	FY 2014
GRADE	Actual	CR	PB
Total, ES Positions	3	3	3
Total, ES Salary	512,751	527,330	527,330
GM/GS-15	252	259	259
GM/GS-14	464	477	477
GM/GS-13	393	404	404
GS-12	508	522	522
GS-11	208	214	214
GS-10	11	11	11
GS-9	131	135	135
GS-8	97	100	100
GS-7	47	48	48
GS-6	8	8	8
GS-5	7	7	7
GS-4	10	10	10
GS-3	1	1	1
GS-2	2	2	2
GS-1	0	0	0
Subtotal	2,139	2,198	2,198
Grades established by Act of			
July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	23	24	24
Senior Grade	8	8	8
Full Grade	5	5	5
Senior Assistant Grade	6	6	6
Assistant Grade	0	0	0
Subtotal	42	43	43
Ungraded	949	976	976
Total permanent positions	2,187	2,249	2,249
Total positions, end of year	3,136	3,225	3,225
Total full-time equiv (FTE) at YE	3,095	3,183	3,183
Average ES salary	170,917	175,777	175,777
Average GM/GS grade	12.3	12.3	12.3
Average GM/GS salary	99,884	102,724	102,724

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