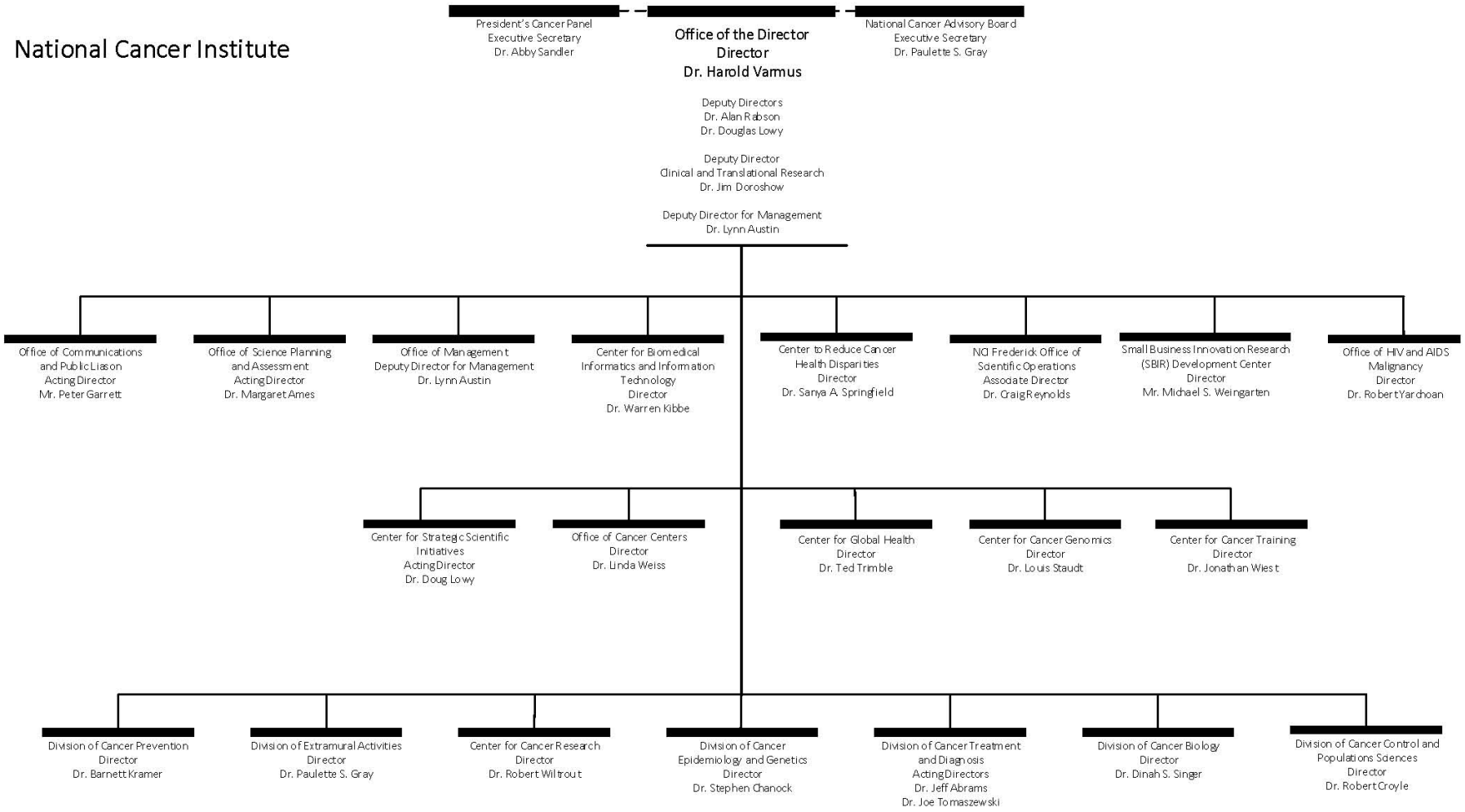
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute (NCI)

National Cancer Institute



NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

For carrying out section 301 and title IV of the PHS Act with respect to cancer, **[**$4,950,396,000]*$5,098,479,000*, of which up to **[**$8,000,000]*$16,000,000* may be used for facilities repairs and improvements at the National Cancer Institute—Frederick Federally Funded Research and Development Center in Frederick, Maryland.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Amounts Available for Obligation[1]

(Dollars in Thousands)

Source of Funding	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget
Appropriation	$4,923,238	$4,950,396	$5,098,479
Type 1 Diabetes	0	0	0
Rescission	0	0	0
Sequestration	0	0	0
FY 2014 First Secretary's Transfer	-12,359	0	0
FY 2014 Second Secretary's Transfer	-965	0	0
Subtotal, adjusted appropriation	$4,909,914	$4,950,396	$5,098,479
OAR HIV/AIDS Transfers	6,307	2,632	0
National Children's Study Transfers	16,181	0	0
Subtotal, adjusted budget authority	$4,932,402	$4,953,028	$5,098,479
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$4,932,402	$4,953,028	$5,098,479
Unobligated balance lapsing	-33	0	0
Total obligations	$4,932,368	$4,953,028	$5,098,479

[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2014 - $20,494 FY 2015 - $60,000 FY 2016 - $60,000

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

(Dollars in Thousands)

MECHANISM	FY 2014 Actual		FY 2015 Enacted		FY 2016 President's Budget		FY 2016 +/- FY 2015	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	3,390	$1,455,389	3,265	$1,434,419	3,141	$1,473,527	-124	$39,108
Administrative Supplements	*(216)*	24,854	*(216)*	25,000	*(216)*	25,000	*(0)*	0
Competing:								
Renewal	147	85,617	155	90,184	173	100,008	18	9,824
New	1,056	363,944	965	370,580	1,076	410,950	111	40,370
Supplements	4	915	4	877	4	972	0	96
Subtotal, Competing	1,207	$450,476	1,124	$461,641	1,253	$511,931	129	$50,290
Subtotal, RPGs	4,597	$1,930,719	4,389	$1,921,060	4,394	$2,010,458	5	$89,398
SBIR/STTR	217	81,841	228	85,188	240	89,500	12	4,312
Research Project Grants	4,814	$2,012,560	4,617	$2,006,248	4,634	$2,099,958	17	$93,710
Research Centers:								
Specialized/Comprehensive	240	$543,839	240	$549,765	240	$552,297	0	$2,532
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	240	$543,839	240	$549,765	240	$552,297	0	$2,532
Other Research:								
Research Careers	399	$67,525	399	$67,525	399	$67,126	0	-$399
Cancer Education	96	32,932	96	32,932	96	32,738	0	-195
Cooperative Clinical Research	102	271,635	102	271,635	102	315,029	0	43,394
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	2	240	2	240	2	239	0	-1
Other	80	57,714	80	57,714	80	57,373	0	-341
Other Research	679	$430,046	679	$430,046	679	$472,504	0	$42,458
Total Research Grants	5,733	$2,986,444	5,536	$2,986,059	5,553	$3,124,759	17	$138,700
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	485	$19,513	485	$19,642	485	$19,771	0	$130
Institutional Awards	947	49,704	947	50,032	947	50,363	0	330
Total Research Training	1,432	$69,217	1,432	$69,674	1,432	$70,134	0	$460
Research & Develop. Contracts	444	$652,316	445	$652,070	439	$642,554	-6	-$9,515
(SBIR/STTR) (non-add)	*(63)*	*(37,418)*	*(63)*	*(37,000)*	*(74)*	*(43,750)*	*(11)*	*(6,750)*
Intramural Research	1,814	845,075	1,824	858,474	1,824	863,401	0	4,927
Res. Management & Support	1,226	371,350	1,233	378,751	1,233	381,630	0	2,879
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(443)*	*(0)*	*(1,254)*	*(0)*	*(0)*	*(0)*	*(-1,254)*
Construction		0		0		0		0
Buildings and Facilities		8,000		8,000		16,000		8,000
Total, NCI	3,040	$4,932,402	3,057	$4,953,028	3,057	$5,098,479	0	$145,451

[1] All items in italics and brackets are non-add entries.

Major Changes in the Fiscal Year 2016 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 2016 President's Budget for NCI, which is $145.451 million more than the FY 2015 Enacted level, for a total of $5,098.479 million. This increase includes $70.000 million for NCI oncology research to advance Precision Medicine and $17.345 million for the NIH-wide Precision Medicine Initiative cohort.

Research Project Grants (RPGs: +$89.398 million; total $2,010.458 million): During FY 2016, NCI will continue to support its established commitment base for non-competing Research Project Grants (RPGs). In addition to the commitment base, NCI will support an increased number of competing RPGs and SBIR/STTR awards, including additional awards that focus on identifying the mechanisms of drug resistance under the NCI component of the Precision Medicine Initiative. The NCI FY 2016 increase in this mechanism also includes amounts to support the NIH-wide Precision Medicine Cohort.

Cancer Centers (+$2.532 million; total $552.297 million): The increase in this mechanism includes amounts in the NCI budget for the NIH-wide Precision Medicine Cohort.

Cooperative Clinical Research (+$43.394 million; total $315.028 million): The FY 2016 increase in this mechanism will allow NCI to expand genetically-based clinical trials and develop and promote best practices under the NCI Precision Medicine Initiative. With the FY 2016 increase for this initiative, NCI will also test new combinations of targeted agents in clinical trials to identify agents that successfully overcome resistance.

R&D Contracts (-$9.515 million; total $642.554 million): During FY 2016, NCI will experience some savings as projects conclude. At the same time, NCI will increase spending under this mechanism to develop an interactive cancer knowledge system to support the NCI Precision Medicine Initiative.

Buildings and Facilities (+$8.000 million; total $16.000 million): During FY 2016, NCI will increase spending to complete priority repair and improvement projects and thereby strengthen the operations of its Federally Funded Research and Development Center (FFRDC), a component that provides high-value support to the NCI mission, the research community, and to patients diagnosed with cancer. NCI faces a backlog of repair and improvement projects on the Fort Detrick campus where the FFRDC is primarily located. The increase will allow NCI to improve laboratories and support facilities that are aged and degrading.

NATIONAL INSTITUTES OF HEALTH
National Cancer Institute

Summary of Changes

(Dollars in Thousands)

FY 2015 Enacted	$4,953,028
FY 2016 President's Budget	$5,098,479
Net change	$145,451

CHANGES	FY 2016 President's Budget		Change from FY 2015	
	FTEs	**Budget Authority**	**FTEs**	**Budget Authority**
A. Built-in:				
1. Intramural Research:				
a. Annualization of January 2015 pay increase & benefits		$312,876		$1,041
b. January FY 2016 pay increase & benefits		312,876		3,124
c. One more day of pay (n/a for 2015)		312,876		1,247
d. Differences attributable to change in FTE		312,876		0
e. Payment for centrally furnished services		135,252		3,299
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		415,273		0
Subtotal				$8,711
2. Research Management and Support:				
a. Annualization of January 2015 pay increase & benefits		$195,239		$657
b. January FY 2016 pay increase & benefits		195,239		1,971
c. One more day of pay (n/a for 2015)		195,239		778
d. Differences attributable to change in FTE		195,239		0
e. Payment for centrally furnished services		30,721		749
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		155,670		0
Subtotal				$4,156
Subtotal, Built-in				$12,867

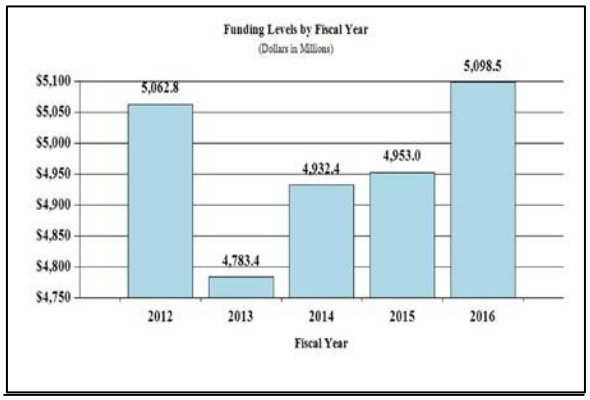
NATIONAL INSTITUTES OF HEALTH
National Cancer Institute

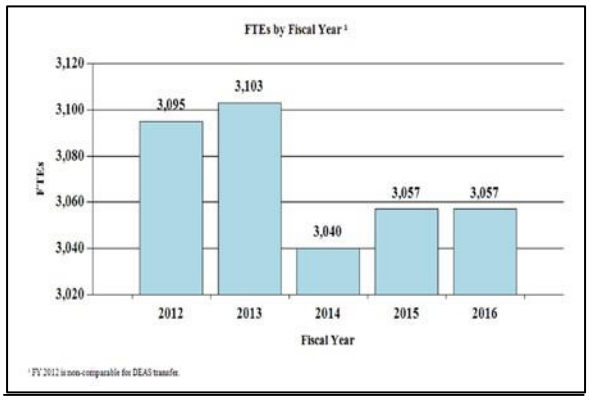
Summary of Changes - Continued

CHANGES	FY 2016 President's Budget		Change from FY 2015	
	No.	Amount	No.	Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	3,141	$1,498,527	-124	$39,108
b. Competing	1,253	511,931	129	50,290
c. SBIR/STTR	240	89,500	12	4,312
Subtotal, RPGs	4,634	$2,099,958	17	$93,710
2. Research Centers	240	$552,297	0	$2,532
3. Other Research	679	472,504	0	42,458
4. Research Training	1,432	70,134	0	460
5. Research and development contracts	439	642,554	-6	-9,515
Subtotal, Extramural		$3,837,448		$129,645
	FTEs		FTEs	
6. Intramural Research	1,824	$863,401	0	-$3,784
7. Research Management and Support	1,233	381,630	0	-1,276
8. Construction		0		0
9. Buildings and Facilities		16,000		8,000
Subtotal, Program	3,057	$5,098,479	0	$132,584
Total changes				$145,451

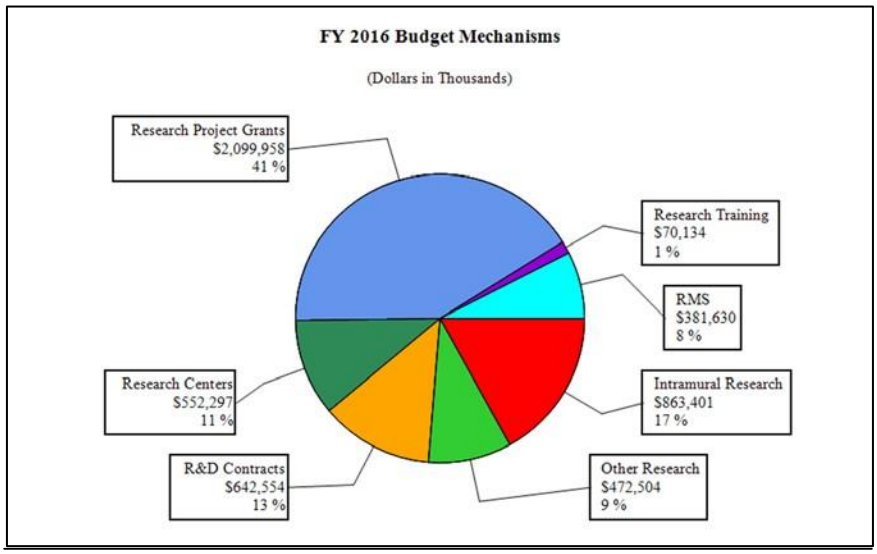
Fiscal Year 2016 Budget Graphs

History of Budget Authority and FTEs:

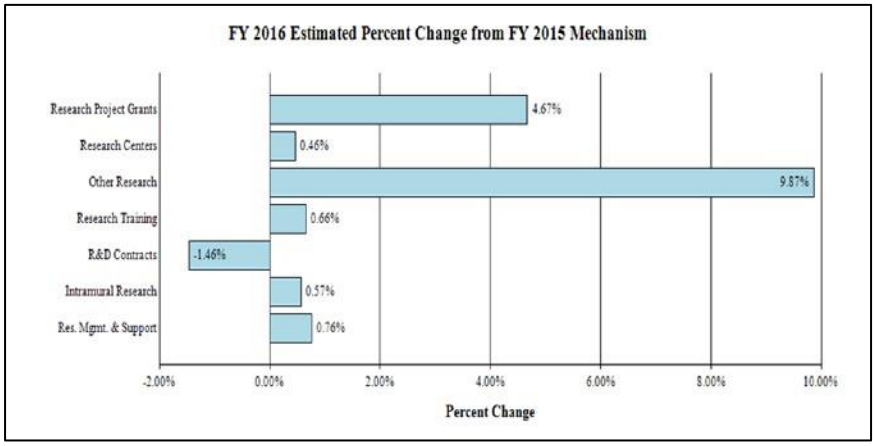




Distribution by Mechanism:



Change by Selected Mechanism:



NATIONAL INSTITUTES OF HEALTH
National Cancer Institute

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

	FY 2014 Actual		FY 2015 Enacted		FY 2016 President's Budget		FY 2016 +/- FY2015	
Extramural Research	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
Understanding the Causes of Cancer		1,253,469		1,257,110		1,294,158		37,048
Understanding the Mechanisms of Cancer		$737,789		$739,932		$761,738		$21,806
Improve Early Detection and Diagnosis		442,701		443,986		457,071		13,085
Develop Effective and Efficient Treatments		1,204,295		1,207,793		1,243,388		35,595
Cancer Prevention and Control		220,869		221,510		228,038		6,528
Cancer Centers		523,681		525,202		540,680		15,478
Research Workforce Development		170,249		170,743		175,775		5,032
Buildings and Facilities		8,000		8,000		16,000		8,000
Subtotal, Extramural		**$4,561,052**		**$4,574,277**		**$4,716,849**		**$142,572**
Intramural Research (non-add)	***1,814***	***$845,075***	***1,824***	***$858,474***	***1,824***	***$863,401***	***0***	***$4,927***
Research Management & Support	**1,226**	**$371,350**	**1,233**	**$378,751**	**1,233**	**$381,630**	**0**	**$2,879**
TOTAL	**3,040**	**$4,932,402**	**3,057**	**$4,953,028**	**3,057**	**$5,098,479**	**0**	**$145,451**

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

NATIONAL INSTITUTES OF HEALTH
National Cancer Institute

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2015 Amount Authorized	FY 2015 Enacted	2016 Amount Authorized	FY 2016 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$4,953,028,000	Indefinite	$5,098,479,000
National Cancer Institute	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$4,953,028,000		$5,098,479,000

NATIONAL INSTITUTES OF HEALTH
National Cancer Institute

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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				$0
2008	$4,782,114,000	$4,870,382,000	$4,910,160,000	$4,890,525,000
Rescission				($85,437,000)
Supplemental				$25,559,000
2009	$4,809,819,000	$4,975,039,000	$4,958,594,000	$4,968,973,000
Rescission				$0
2010	$5,150,170,000	$5,150,170,000	$5,054,099,000	$5,103,388,000
Rescission				$0
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	$5,072,183,421
Rescission				($10,144,367)
Sequestration				($254,588,730)
2014	$5,125,951,000		$5,091,885,000	$4,923,238,000
Rescission				$0
2015	$4,930,715,000			$4,950,396,000
Rescission				$0
2016	$5,098,479,000			

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 Actual	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 + /- FY 2015
BA	$4,932,402,553	$4,953,028,000	$5,098,479,000	+$145,451,000
FTE	3,040	3,057	3,057	0

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

Director's Overview

Cancer research has come to a transformational moment. Thanks to several decades of investment by the NCI to understand the fundamental properties of cancer cells, coupled with the sustained development of genomics, informational sciences, protein chemistry, drug development, immunology, and other disciplines by several components of the NIH, including the NCI, a new view of cancer has emerged. We have already begun to use that vision to assess the risks, refine the diagnoses, and improve the treatments for several kinds of cancer. And we are poised to enter an era of medical practice in which detailed genetic and other molecular information about a patient's cancer is routinely used to properly categorize the disease and deploy more effective patient-specific remedies to treat it. Moreover, we now understand enough about the current limitations of these molecularly-based approaches to propose research programs intended to overcome them.

This new era of medicine is commonly called "Precision Medicine," in accord with a perceptive report issued by the Institute of Medicine (IOM) in 2011, and it has the potential to influence many branches of medicine – not just oncology, where its influence has been felt most quickly. These early effects have occurred in oncology because cancers are fundamentally "diseases of the genome," and they are therefore best understood by identifying the abnormal genes and proteins that: confer risk, determine diagnostic categories, influence preventive strategies, hold promise for more efficient screening, and (most obviously thus far) dictate the development and use of targeted therapies.

Several examples of "precision oncology" have gradually accumulated over the past decade or two: identification of mutant *BRCA1* and *BRCA2* genes to define high risk of breast and ovarian cancers; use of a monoclonal antibody (trastuzamab) to treat certain breast cancers or reduce the risk of metastases when the *HER2* gene is amplified or over-expressed; restoration of health and normal life expectancy to patients with chronic myeloid leukemia by deploying imatinib (and related drugs) to inhibit the abnormal protein made by a deranged *ABL* oncogene; and more

effective treatment of metastatic melanoma with drugs that block a mutant *BRAF* oncogene and with antibodies that enhance immune responses to the cancer.

But this is only the beginning. During the past few years, the NCI (in partnership with the National Human Genome Research Institute) has dramatically increased the amount of genetic information available about a wide range of cancers through The Cancer Genome Atlas (TCGA) project; computational scientists have generated some of the new tools required to build the kind of "knowledge network" emphasized in the IOM report; NCI-supported scientists and many pharmaceutical and biotechnology firms have produced candidate drugs that need to be validated in model systems and tested in patients; and, after many years of uncertainty, proponents of immunotherapies have seen long-term responses with a wide range of cancer types and are beginning to define the characteristics of tumors that predict success.

At the same time, the obstacles to faster progress have been recognized in both laboratory and clinical settings: the complexities of the mutational profile of each tumor (the large numbers, varied combinations, and kinds of mutations); the frequent appearance of resistance to targeted drugs; the difficulties of organizing efficient clinical trials to test the large number of new drugs – both singly and in the combinations that are likely to avoid drug resistance; the lack of suitable pre-clinical models for screening the effects of such drugs and drug combinations; and the computational and legal issues that must be faced to build an information network that brings new knowledge to health care workers in an understandable and convenient manner.

The Budget we are requesting for FY 2016 is built in large part on the coming of Precision Medicine to oncology – both on its promises and on the need to confront the problems that remain to be solved. Among the many plans described in the body of our budget justification are programs that: will expand the genomic data sets and increase our understanding of cancer genomes and their relationship to a patient's inherited gene variants; will extend the novel kinds of clinical trials we have already begun – testing new therapies against childhood cancers and several common adult cancers; will study mechanisms of drug resistance, develop better animal and cell-based models of cancer, and learn to use new therapies in combination; and will build cancer information systems that integrate molecular and clinical knowledge in ways that are useful to both scientists and clinicians.

As will be evident in the text that follows, the precepts of Precision Medicine are also being felt in all facets of oncology, not only in diagnostics and therapeutics, but also in the development of prevention and cancer screening strategies; in the assessment of the causes of cancer identified through epidemiology; and in the monitoring of tumors through molecular and imaging methods.

In addition NCI will participate in the NIH-wide effort to launch a national research cohort of one million or more Americans – to propel our understanding of health and disease and set the foundation for a new way of doing research through engaged participants and open, responsible data sharing. Participants who voluntarily choose to join this effort will be able to share their genomic data, biological specimens, and behavioral data, and, if they choose, link it to their electronic health records (EHRs), taking advantage of the latest in social media and mobile applications, and with appropriate privacy protections in place. Bona fide researchers from across the country will have access to data voluntarily provided, thereby crowdsourcing rich data to the brightest minds in biomedical research. The cohort will be built largely by linking existing

cohorts together taking advantage of infrastructure, data security and expertise already in place. NIH will help to connect these existing cohorts, but the current sponsors of the cohorts will maintain their ownership and management. Research on this scale promises to lead to new prevention strategies, novel therapeutics and medical devices, and improvements in how we prescribe drugs – on an individual and personalized basis.

As in the past, the NCI's budget request is broad in its range, encompassing three major areas – basic research (in genetics, cell biology, immunology, nanotechnology, and other fields); translational and clinical sciences (to develop and test drugs, molecular markers, imaging technologies, diagnostics, and radiotherapies); and population sciences (including epidemiological, environmental, and behavioral approaches). While many of these disciplines are affected by new visions of cancer that drive Precision Medicine, others depend on more traditional methods that have proved their value during the past decade, helping to decrease cancer mortality rates, to improve the management of the symptoms of cancer, and to monitor the prevalence of cancers and the factors that confer the risks of cancers in the United States and throughout the world.

Now, as in the past, virtually all major advances that contribute to preventing, diagnosing, and treating cancer depend on many kinds of science. This diversity of approach is evident in the pages that follow, reflecting NCI's conviction that immediate investments in multiple disciplines are required to provide tangible clinical benefits in the future for those suffering from cancer, those at risk of cancer, and the growing population of cancer survivors.

Overall Budget Policy:
The FY 2016 President's Budget request is $5,098.479 million, an increase of $145.451 million, or 2.9 percent compared with the FY 2015 Enacted level. The Budget includes $70 million for Precision Medicine.

Program Descriptions and Accomplishments

NCI basic and applied research activities advance five broad scientific goals:

- Understanding the Causes of Cancer
- Understanding the Mechanisms of Cancer
- Improving Early Detection and Diagnosis
- Developing Effective and Efficient Treatments
- Improving Cancer Prevention and Control

To pursue these goals, NCI issues grants to support investigator-initiated research, conducts clinical trials, and finances many other programs; selects and provides support to cancer centers; conducts basic and clinical research through its intramural programs; issues and manages contracts, including a Federal Funded Research and Development Contract (FFRDC); operates research facilities to support intramural and certain FFRDC activities; funds training to maintain a strong workforce of cancer researchers; and provides essential management and support for NCI cancer research programs.

NCI uses these various mechanisms to support cancer research in pursuit of the five major scientific goals. For example, investigator-initiated research project grants represent a large portion of the research investment in all five of NCI's major scientific areas. During FY 2014, NCI issued 5,733 new and non-competing grant awards across all grant mechanisms, including 3,403 traditional (R01) grants and 648 exploratory (R21) grants to support research that advances these goals.

The narratives that follow highlight some of the programs – including recent NCI progress and future plans – within each scientific area. A few general points should be made at the outset. First, virtually all NCI research activities influence the approaches taken to advance other goals, in addition to the goal area that an activity is assigned to. For example, identifying human papillomavirus (HPV) many years ago as the causative infectious agent of cervical cancer led to major advances in understanding the mechanism by which cervical cancer develops, which led to the development of HPV vaccines to prevent infection and to improved screening for early stages of cervical cancer.

Second, one of the driving forces behind the FY 2016 budget request is the opportunity to make rapid progress towards an era of precision medicine, as described in the NCI Director's Overview. Although the concept of precision medicine is most simply illustrated by the use of therapies that are designed based on an accurate account of the molecular and genetic alterations in a specific cancer, the concept applies to virtually all aspects of cancer research and cancer control, including epidemiology, prevention, screening, diagnosis, and risk assessment. These relationships are briefly noted in the sections that follow.

Third, the size and complexity of the research program that NCI supports precludes a complete account of all its programs in this budget text. The examples chosen provide a meaningful overview of the current state of NCI operations, but inevitably under estimate the vast amount of valuable work underway in all areas of cancer research at this promising time.

I. Understanding the Causes of Cancer: Cancer develops through the complex interplay of genetic background, lifestyle, and environmental factors. All of these factors probably influence the likelihood of contracting every cancer. In some cases, however, cancer risk is most strongly influenced by inheriting a mutation (or a variant) of a single gene or a combination of genes. More commonly, cancer risk is determined principally by external factors, such as exposure to tobacco or infectious agents, but responses to these factors are likely to differ depending on a person's genetic background. One of the tasks of precision medicine is to understand the relationships of these factors and to use that information to improve the assessment of risk, the understanding of individual behaviors, and the prevention and early detection of cancers.

NCI-funded studies of cancer causation range from small-scale laboratory research to large-scale projects that use population cohorts or case-controlled comparisons of subpopulations. They may also involve modeling to predict cancer risks within an individual or population. In addition, NCI also supports research to identify new causes of cancer.

Budget Policy:
The FY 2016 President's Budget request is $1,294.158 million, an increase of $37.048 million, or 2.9 percent compared with the FY 2015 Enacted level.

Population Cohorts – NCI investments in population cohorts provide a framework for identifying factors associated with cancer risk. For example, NCI's Cohort Consortium – a large, international collaboration of cohorts that includes data on more than four million people – is evaluating the role of genetic susceptibility, lifestyle, environmental exposures, and gene-environment interactions for a range of cancers. Recent findings uncovered by the Cohort Consortium include:

- The continued increase in the risk of death from cigarette smoking among women
- Many new genetic susceptibility regions for common cancers (breast, prostate, lung, colon, and bladder) and uncommon cancers (osteosarcoma and chronic lymphocytic leukemia)
- A biomarker that may predict head and neck cancers caused by HPV

The Cohort Consortium offers the promise of answering important questions related to cancer risks in African-Americans, Hispanics, and other understudied populations in the United States, questions about the interaction between environmental exposures and genetic endowment, and questions about how medical practices may affect cancer risks. NCI researchers are also conducting a genome-wide association study in collaboration with the Childhood Cancer Survivor Study to assess the genetic component of risk in treatment-related subsequent cancers.

Obesity and Cancer Risk – In addition to its association with other health risks, obesity is associated with increased risks of cancers of the esophagus, breast (postmenopausal), endometrium (the lining of the uterus), colon and rectum, kidney, pancreas, thyroid, gallbladder, and possibly other cancer types. Through the National Collaborative on Childhood Obesity Research (NCCOR), NCI is partnering with four NIH institutes, the Centers for Disease Control and Prevention (CDC), the Robert Wood Johnson Foundation, and the U.S. Department of Agriculture to improve the efficiency, effectiveness, and application of childhood obesity research. NCCOR seeks to:

- Increase surveillance of childhood obesity
- Identify, design, and evaluate practical and sustainable interventions
- Support coordination and collaboration to halt and reverse childhood obesity

Since 2013, NCI has been operating two web-based NCCOR tools: the Catalogue of Surveillance Systems and the Measures Registry. Combined, these web tools have experienced more than 1.5 million visits by individuals accessing these tools. Through the Catalogue of Surveillance Systems, for the first time researchers and practitioners can assess a range of childhood obesity resources, identify possible gaps, and plan innovative multilevel obesity prevention research. The Measures Registry contains more than 1,000 measures and is an invaluable resource for researchers interested in using standard measures to describe, monitor, and evaluate interventions related to obesity and cancer risk.

Exposure to Therapeutic Radiation – Investigating the cancer risks associated with medical exposures to ionizing radiation has become increasingly important, given that radiation exposure from medical sources in the United States has increased six-fold since 1980. To address this concern, NCI scientists are investigating cancer risks associated with historic and emerging

medical radiation sources, including diagnostic and screening radiation exposures (which are lower dose) and radiotherapy treatments for cancer (which are high dose). For example, NCI research suggests that there is a significantly increased risk of brain tumors and leukemia among patients exposed to radiation from CT scans during childhood, and NCI is supporting additional studies to assess whether these findings are confirmed in other populations.

Inflammation Studies – Chronic inflammation due to persistent infection, harmful exposures, or obesity may increase cancer risk by directly damaging DNA and by the process of tissue remodeling and scarring. NCI investigators are conducting studies within well-characterized patient cohorts to identify associations between inflammation markers and various cancers, particularly cancers already linked to inflammation and for other rarer cancers that are poorly understood. Ongoing research focuses on identifying associations between more than 70 inflammation markers and various cancers, including lung, non-Hodgkin lymphoma, multiple myeloma, ovary, endometrium, colon, gallbladder, cervix, and stomach. NCI researchers have discovered that several markers are associated with increased lung cancer risk, independent of smoking, and this research suggests that other inflammatory response markers play a role in survival for early-stage lung cancer patients.

Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer – The recent increase in the prevalence of Type 2 diabetes may be contributing to a parallel increase in the incidence of pancreatic ductal adenocarcinoma. In 2014, the NCI joined with NIDDK and NIAAA to establish the Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer (CSCPPC), a multidisciplinary network of research centers focusing on the relationship between diabetes and pancreatic ductal adenocarcinoma. To support the Consortium, NCI is funding research that focuses on factors that increase the risk of pancreatic cancer in patients with chronic pancreatitis or diabetes.

II. Understanding Mechanisms of Cancer: Cancer is driven by alterations of a cell's genome (DNA) and its associated proteins. As a consequence, abnormal kinds and amounts of proteins are made that cause a variety of molecular abnormalities and result in inappropriate tumor cell survival, inadequately controlled tumor growth, and other hallmarks of cancer. Precision medicine, in all of its forms, depends on a deeper understanding of the genetic and physiological changes that take place in cancer cells.

To better understand these mechanisms, NCI supports large-scale, high-throughput studies of the genes, proteins, and pathways altered in cancer. In addition, NCI supports studies related to basic cell biology, cell interactions, angiogenesis, immune responses, and other areas of research that are essential to better understand the mechanisms of cancer. NCI also supports laboratory studies in model systems, including animal models, to investigate the functions of molecules within these systems.

Budget Policy:
The FY 2016 President's Budget request is $761.738 million, an increase of $21.806 million, or 2.9 percent compared with the FY 2015 Enacted level.

Genomic Research to Support Precision Medicine – Cancer genomics research at NCI is using high-throughput techniques to identify and study small mutations, rearrangements, and

chemical modifications of DNA and to detect changes in the production of RNA and proteins. These NCI programs in genomics provide essential support for the research and related translational and clinical science activities that serve to advance precision medicine.

• **TCGA –** The Cancer Genome Atlas (TCGA) is a major collaborative initiative of NCI and the National Human Genome Research Institute (NHGRI). Although the major five-year phase of the program has concluded successfully, TCGA continues to support the comprehensive analysis of the alterations in DNA and RNA found in more than 20 human cancers. TCGA achieved a milestone at the close of FY 2013 when it accrued 10,000 tumor samples and control samples from patients for characterization. The Center for Cancer Genomics is now focusing on the final analytic phases of TCGA and extending the use of TCGA methods to larger collections of certain tumor types, to experimental models of cancers, and to potential therapeutic targets.

• **TARGET –** The Therapeutically Applicable Research to Generate Effective Treatments (TARGET) initiative uses high-throughput methods to identify abnormalities in tumors from pediatric patients. During the past year, a TARGET team helped to develop a clinical trial, scheduled to start in 2015, that will identify patients with a subclass of acute lymphoblastic leukemia who have a high-risk of recurrence due to chromosome-based abnormalities (translocations). Another TARGET project identified novel causes of pediatric kidney cancers.

• **Cloud Pilots on Cancer Genomics** – The NCI Center for Biomedical Informatics and Information Technology, in collaboration with the Center for Cancer Genomics, is coordinating a program to support the design, implementation, and documentation of a new model for computational analysis and sharing very large biological data sets. The goal is to develop a set of Cancer Genomics Cloud Pilots that will provide more open and secure access to genomic data that NCI generates. Cloud computing will be a valuable tool to support studies related to the mechanisms of cancer. This capability will also be equally valuable to other NCI scientific areas, including clinical trials and other types of patient-focused research.

• **Cancer Target Discovery and Development (CTD^2) Network** – The Cancer Target Discovery and Development (CTD^2) Network is accelerating the use of molecular data gained through TCGA, TARGET and other genome-focused initiatives. Through validation studies that rely on high-throughput screening of molecules and research that involve mouse models, the CTD^2 Network supports research that capitalizes on a growing volume of molecular data in ways that can identify new cancer treatments. Highlights of CTD^2 progress during the past year include:

- determining that mutations in known cancer genes function through new cellular mechanisms
- discovering that an oncogene can be a therapeutic target for high grade neuroendocrine lung cancers
- identifying a subtype of triple negative breast cancer that will likely respond to the FDA-approved drug dasatinib

Integrative Cancer Biology – The Integrative Cancer Biology Program (ICBP) applies systems biology to cancer research to develop predictive computational models of cancer initiation, progression, and metastasis. Systems biology is a multi-disciplinary science that depends on the

contributions of cancer biologists, computer scientists, engineers, mathematicians, physicists, and contributions from other areas of cancer research.

ICBP investigators have made seminal contributions in some of the most challenging areas of cancer research, ranging from basic understanding of molecular and cellular processes to improved clinical outcomes for patients. For example, using a novel strategy to conduct cross-species computational analysis of gene regulatory networks, ICBP investigators identified novel cancer mutations that drive prostate tumor growth. During 2014, ICBP investigators also completed a critical mathematical analysis of the effect of estrogen in breast cancer. The ICBP analysis revealed novel signaling relationships within the cancer cell that affect cell fate decisions and the response to endocrine-based therapies. The ICBP also developed new computational models to predict drug response in cancer cell lines. These approaches are providing deeper insights into the underlying biology of cancer and could lead to better diagnosis and therapies.

Tumor Microenvironment Network (TMEN) – There is growing evidence of the extent to which cancer cells depend on and influence the non-tumor cells in the microenvironment where they live. This tumor microenvironment affects tumor development, progression, and metastasis, even at the earliest stage of disease. The tumor microenvironment may also contribute to inefficient drug delivery and drug resistance. NCI's Tumor Microenvironment Network (TMEN) studies how interactions between cancer cells and their microenvironment affect tumor growth and therapeutic response. For example, TMEN researchers discovered that in pancreatic cancer the non-cancer cells in the tumor microenvironment serve to restrain tumor growth, and that removing the non-cancer cells results in aggressive cancer. TMEN researchers have also discovered that prostate cancer cells migrate to the bone where they can lie dormant for many years. Recent studies show that dormancy is actively maintained by the balance of opposing signals from the tumor microenvironment to the cancer cell.

III. Improving Early Detection and Diagnosis: Many cancer deaths occur because cancers are diagnosed at late stages, when treatment often proves futile. This is generally a consequence of a lack of screening tests to identify cancers earlier, when they may respond more effectively to treatment. Investigator-initiated research project grants are the primary mechanism that NCI relies on to support and improve early detection and diagnosis of cancer, but other larger research programs also play important roles. NCI researchers are working to identify molecules – nucleic acids, proteins, glycans, metabolites, and other substances – and develop imaging methods to identify the presence of cancer cells earlier.

These efforts are part of – or closely linked to – components of the Precision Medicine Initiative, since they depend on the characterization and interpretation of cancer genomes and the computationally based methods to interpret and disseminate the findings. Clinicians will increasingly be using this detailed, tumor-specific information to find tumors early and to guide categorization of tumors (diagnosis) as well as to select the best treatment for each patient (therapy). NCI also supports research to assess the risks associated with screening and early detection, and to ensure that the potential harms of screening do not outweigh the benefits.

Budget Policy:
The FY 2016 President's Budget request is $457.071 million, an increase of $13.085 million, or 2.9 percent compared with the FY 2015 Enacted level.

Cancer Intervention and Surveillance Modeling Network (CISNET) – In 2000, NCI established CISNET, a consortium of statisticians that use biostatistical modeling to improve the understanding of cancer control interventions in prevention, screening, and treatment. CISNET researchers develop models using data from randomized controlled trials, meta-analyses, observational studies, national surveys, and studies of practice patterns to evaluate the past and potential future impact of clinical and public health interventions. CISNET created models to interpret the results from the National Lung Screening Trial (NLST). The U.S. Preventive Services Task Force used those models to make national recommendations on CT screening that have been adopted by the Centers for Medicare and Medicaid Services. Also relying on NCI-supported models supplied by CISNET, the Task Force recommended screening for colorectal cancer using fecal occult blood testing, sigmoidoscopy, or colonoscopy in adults between the ages of 50 to 75 years. Continued funding of CISNET will enhance the ability of the cancer community to develop and deploy new interventions and determine how to best use these tools to optimize their benefits to patients.

Program Portrait: Frederick National Laboratory for Cancer Research

FY 2015 Level: $161.2 million
FY 2016 Level: $161.2 million
Change: $0.0 million

Established in 1971 under the National Cancer Act, NCI's Frederick National Laboratory for Cancer Research (FNLCR) is a major part of the only Federally-Funded Research and Development Center dedicated to biomedical research. NCI's FNLCR is a national asset and a unique resource. FNLCR brings public and private partners together to address the most difficult cancer research challenges. Examples of FNLCR programs include:

The Biopharmaceutical Development Program (BDP) produces novel antibodies and proteins as therapeutics when industry is not prepared to develop them. For example, when the Children's Oncology Group could not find a manufacturer to produce ch14.18, a monoclonal antibody being evaluated as a treatment for neuroblastoma tumors in children, BDP manufactured the antibody for the clinical trial. The trial demonstrated that ch14.18 reduced the risk of recurrence when given to children whose cancer responded to chemotherapy. The monoclonal antibody has become the standard of care for children with certain types of neuroblastoma, and the pharmaceutical company United Therapeutics is now manufacturing the antibody.

The Nanotechnology Characterization Laboratory (NCL) accelerates the development of nanotechnology for basic and applied cancer research. Working in collaboration with FDA and the National Institute of Standards and Technology, NCL standardizes the preclinical characterization of nanomaterials that academic, government, and industry researchers are developing as cancer therapeutics and diagnostics. NCL has evaluated more than 200 nanoparticle formulations, many of which have gone forward into clinical testing.

NCI's Experimental Therapeutics (NExT) program shortens the timeline for new drug development and advances breakthroughs into new cancer therapies. For example, through the NExT program, promising molecules such as the angiogenesis inhibitor cediranib and olaparib, which inhibits the repair of DNA damage, are being tested as a combination treatment for ovarian cancer and mesothelioma. The NExT Program is also supporting another promising therapeutic (selumetinib) to treat childhood brain tumors.

The RAS Initiative supports development of therapies against tumors that contain mutations in members of the RAS family of oncogenes. In contrast to progress in other areas of cancer therapeutics, researchers have not successfully developed effective treatments against proteins produced by RAS oncogenes. RAS genes are mutated in about 1/3 of all cancers, including the vast majority of pancreatic adenocarcinomas, about 45% of colorectal cancers, and about 35% of lung adenocarcinomas. To address this challenge, FNLCR launched the RAS Initiative, a large-scale collaboration to identify therapeutic strategies for patients with RAS-driven cancers. NCI's Advanced Technology Research Facility at FNLCR serves as the program hub that engages academia, the pharmaceutical industry, and NCI intramural labs as collaborating spokes in the RAS Initiative.

Assessing Treatment of Early Anal Lesions in HIV-Infected Patients – NCI has built the AIDS Malignancy Clinical Trials Consortium to study cancers associated with long-standing infection by HIV. Compared to the general population, HIV-infected individuals are at increased risk – by more than 100-fold – of developing anal cancer, even when the individuals are successfully treated with combination antiretroviral therapy. To address this situation, NCI is supplementing the AIDS Malignancy Clinical Trials Consortium to support a multicenter study that will determine the effectiveness of treating anal high-grade squamous intraepithelial lesions (HSIL) and thereby reduce the incidence of anal cancer in HIV-infected men and women. In addition, the study will collect specimens to examine the molecular pathogenesis of progression from HSIL to cancer, to discover biomarkers to identify those at highest risk, and to identify new avenues for treating anal HSIL and cancer.

Characterizing Screen-Detected Early Lesions – Increased sensitivity in the screening for a variety of cancers (such as breast, lung, prostate, and melanoma) permits detection of very early lesions. Unfortunately, screening detects lesions, but usually does not distinguish between

lesions that are likely to progress and those that are indolent and require no immediate treatment. To address this problem, NCI launched a new program to identify cellular and molecular characteristics that distinguish progressive from non-progressive lesions. The goal of the program is to achieve a comprehensive characterization of screen-detected lesions that will include the tumor cells and the surrounding non-cancerous tissue as well as growth factors and other mediators of tumor behavior. New enabling technologies (including genomics, epigenomics, proteomics and imaging, including single cell analyses) and the availability of appropriately annotated sets of tissue specimens provide the means to determine the cellular and molecular patterns in early lesions and to assess the degree to which the behavior of these lesions is predictable.

Multiparametric MRI for Prostate Biopsies – Until recently, PSA screening served as the primary basis for determining whether to perform prostate biopsies in the general population. However, relying on PSA screening has resulted in over-diagnosis and over-treatment, without a definite survival benefit. To address the limitations of current blind prostate biopsies, a team of NIH scientists developed the technology to perform MRI-guided prostate biopsies using real time ultrasound. With this technology, urologists can guide their ultrasound biopsies directly into suspicious lesions using the superior resolution of multiparametric magnetic resonance imaging. This technology has been commercialized, and in 2013 was unveiled as UroNav. The technology and others based on the same idea are likely to be widely adopted to diagnose and treat prostate cancer.

Technologies to Detect Breast Cancer – The NCI SBIR Development Center provided Phase I/II funding to two SBIR applicants to support FDA clearance of technologies that improve early detection and diagnosis of cancer in soft tissue. Mammography, the current standard for breast imaging, has poor sensitivity in women with dense breasts.

The first product is SoftVue, a technology that is not compromised by breast density and allows faster through-transmission imaging of the whole breast. The second product, Clear Guide ONE, received FDA approval in 2014 as a device that attaches directly to an ultrasound probe and uses computer vision algorithms to calibrate the system, find the needle, and guide the practitioner to the target lesion. This technology reduces the number of biopsy events, patient discomfort, and ultimately the cost of patient care.

IV. Developing Effective and Efficient Treatments: Research on cancer therapeutics has many facets that go beyond developing and testing drugs, radiotherapy, immunotherapy, and surgery. These other aspects include control of symptoms and palliation of fatal and non-fatal cancers. Still, developing new drugs, immune-based therapies, and means to monitor cancers before and during treatment are the central efforts to advance this goal. Increasingly, progress is linked to new knowledge about the molecular fingerprints of tumors, about how cancer cells interact with the host environment and the immune system, and about the altered behaviors of cancer cells.

These are the elements most well recognized as components of Precision Medicine in the control of cancer, because they are critical to the design of interventions that target specific molecules and signaling pathways. Although several successful applications of precision medicine to therapeutics have been documented, it is also apparent that fully realizing of its potential will

require the wide use of combined therapies, an understanding of drug resistance, better models for pre-clinical testing, and a better integration of drug-based and immunologically-based approaches.

To support the development of effective and efficient cancer treatments, NCI invests in basic and translational research. These investments have identified therapeutic targets and strategies, and commercial interests have frequently validated and developed many of these targets. NCI-supported clinical research develops and tests interventions at many sites throughout the country and at the NIH Clinical Center, often through clinical research networks.

Budget Policy:
The FY 2016 President's Budget request is $1,243.388 million, an increase of $35.595 million, or 2.9 percent compared with the FY 2015 Enacted level.

Therapeutic Studies to Advance Precision Medicine – The most conspicuous application of the precepts of precision medicine are occurring in the realm of targeted therapeutics, where new drugs are tested against tumors identified through molecular methods to have genetic or epigenetic abnormalities that the new agents are designed to counteract. A few examples appear below.

• **Molecular Analysis for Clinical Choice (NCI-MATCH) –** NCI clinical initiatives are taking advantage of cancer genomics and data generated through TCGA. For example, NCI is developing NCI-MATCH, a new national clinical trial conducted through the NCI-supported Cooperative Group network. NCI-MATCH is a prospective clinical trial for patients with advanced cancers of any type and will involve the sequencing of a patient's tumor biopsy. The sequencing will serve as the basis for defining a precision medicine approach that assigns patients to treatments that target specific molecular abnormalities. The trial will evaluate FDA approved drugs outside of their approved indication as well as unapproved compounds that have demonstrated evidence of activity against a known target in a specific human tumor. About 20 to 25 compounds will be available to treat 1,000 patients through this study, based on the molecular findings on their biopsy. [ECOG-ACRIN will conduct the study with NCI through the Cancer Trials Support Unit. ECOG-ACRIN is a clinical research alliance of the American College of Radiology Imaging Network (ACRIN) and the Eastern Cooperative Oncology Group (ECOG).]

• **Pediatric and Tumor-Specific Trials –** Under the Precision Medicine initiative, NCI will extend this type of trial to pediatric patients with tumors refractory to currently approved therapies and to specific types of adult cancer that are also being subjected to extended genomic characterization.

• **Exceptional Responders –** The NCI recognizes that in the past many individuals received and responded favorably to investigation agents or conventional chemotherapy that had a small chance of success. Since such patients did not have the benefit of prior genetic characterization of their tumors, the NCI has launched an effort to perform TCGA-type assessments of tumors from these exceptional responders, in hopes of learning the basis of such successes. A few examples of important lessons learned from this approach have already been published from

investigators at NCI-designated cancer centers, and the NCI is now receiving substantial numbers of samples from such patients for further study.

Immune-Therapy of Cancer – During the past few years, some remarkable successes with immune-therapy of several cancer types has revolutionized thinking about the prospects for immunotherapy, vindicating several NCI investigators who remained committed to such approaches and creating optimism that immunotherapies may become a standard form of cancer treatment under suitable circumstances. Although products of the immune system, especially monoclonal antibodies directed against cancer cell surface proteins have been standard instruments in the treatment of breast, cancer and certain lymphomas for many years, the new therapies employ the cells of the immune system in novel ways – by inhibiting inherent "brakes" on immune responses to tumors ("breakpoint inhibition") or by instructing immune cells of the T cell type to attack cancer cells that contain peptides (antigens) that provoke the immune system. Moreover, as the rules that govern responsiveness to immunotherapies are now beginning to emerge, immunotherapy is becoming an integral part of precision medicine, based on characterization of the altered coding potential of individual tumors and the likelihood of generating potent antigens. NCI continues to support many extramural grantees and intramural investigators working on these problems. Some examples follow:

• **Center for Excellence in Immunology –** To study ways to harness a patient's own immune system to treat cancer, the NCI's intramural Center for Excellence in Immunology is comprised of investigators from labs and branches across the Center for Cancer Research. These researchers are developing novel immunologic approaches, including cell-based therapies, therapeutic vaccines, and cytokines, and combination therapies to treat cancers.

• **Cancer Immunotherapy Trials Network (CITN) –** Basic discoveries in tumor immunology are moving into early clinical trials through the Cancer Immunotherapy Trials Network (CITN), which performs trials with new drugs that modulate the immune system. These trials emphasize immune system monitoring to predict tumor response and resistance. CITN trials using new immunomodulatory agents have been opened during the past two years. The research objective is to identify important immune subsets that can attack tumor cells or to block a significant immune suppression mechanism in the tumor microenvironment, and thereby enhance immune defenses against tumors.

• **Promising Approaches for Cancer Immunotherapy –** Scientists at NCI's Center for Cancer Research have developed a new method using immunotherapy to specifically attack tumor cells that have mutations unique to a patient's cancer. The researchers recently demonstrated that the human immune system can mount a response against mutant proteins expressed by cancers that arise in epithelial cells that line certain internal and external surfaces of the body. These cells give rise to many types of common cancers, such as those of the digestive tract, lung, pancreas, bladder and other sites. NCI research suggests that this immune response can be harnessed for therapeutic benefit in patients.

Program Portrait: NCI's National Clinical Trials Network

FY 2015 Level: $151.3 million
FY 2016 Level: $151.3 million
Change: $0.0 million

Since 1955, NCI has been the sole support for a clinical trials enterprise that conducts large-scale cancer treatment trials. Originally organized as the Clinical Trials Cooperative Group Program and reorganized in FY 2014 as the National Clinical Trials Network (NCTN), the program's network of researchers, cancer centers, and community physicians enroll approximately 20,000 patients annually in clinical trials. With the involvement of more than 3,100 institutions and 14,000 clinical investigators, this clinical trials enterprise has changed the face of clinical oncology by establishing the safety and efficacy of many therapies now commonly used to treat cancer patients.

Cancer patients enjoy longer lives in large part due to strategies that have come from the NCI clinical trials program. For example, during FY 2014 a clinical study found that adults with low-grade gliomas, a form of brain tumor, who received a chemotherapy regimen after they completed radiation therapy, lived significantly longer than patients who received radiation therapy alone. In addition, early results from another clinical trial demonstrated that men with hormone-sensitive metastatic prostate cancer who received the chemotherapy drug docetaxel at the start of hormone therapy lived longer than patients who received hormone therapy alone. These trials and clinical findings were possible only because of sustained NCI investment in NCTN.

In response to a 2010 Institute of Medicine report that NCI requested, NCI retooled its clinical trials enterprise as the NCTN to facilitate a system that responds more rapidly to scientific opportunities, particularly genomically based clinical trials. Many of the new trials planned through the NCTN depend on new drugs, genetically-based diagnostics, and immunotherapies that offer great promise for cancer patients and are a direct outgrowth of the NCI commitment to basic and early translational science.

Conducting a new generation of clinical trials requires sophisticated and expensive technology and clinical processes to collect tissue, conduct advanced DNA and RNA sequencing, and run complex algorithms to distinguish normal genetic variants from tumor-specific changes. These, in turn, entail new expenses for surgery, interventional radiology, molecular pathology, and bioinformatics that are not typically part of clinical trials.

In addition, the NCI Community Oncology Research Program (NCORP), which also launched during FY 2014, will play a critical, complementary role to NCTN. NCORP is a community-based initiative that builds upon NCI's networks to bring clinical trials and cancer care delivery research to patients – including minority and underserved populations – in the communities where they live.

NCORP – Bringing State-of-the-Art Clinical Trials to Communities – During FY 2014, NCI replaced several existing programs when it launched the NCI Community Oncology Research Program (NCORP). This new program expands on the success of the Community Clinical Oncology Program (CCOP) Network and the Minority-Based CCOPs, and includes elements of the NCI Community Cancer Centers Program (NCCCP). NCORP is a national network of investigators, cancer care providers, academic institutions, and other healthcare organizations that provide cancer care to diverse populations in community-based healthcare practices across the United States.

In August 2014, NCI awarded 53 new five-year NCORP grants to researchers across the country to conduct multi-site studies. Through NCORP, NCI will support an expanded portfolio of clinical trials and other studies. The portfolio will emphasize cancer care delivery research that focuses on diverse, multi-level factors that affect access to and quality of care in a community setting. In addition, the program will enhance patient and provider access to treatment and imaging trials under the National Clinical Trials Network. Overall, NCORP will bring state-of-the art clinical trials for cancer prevention, control, treatment and imaging, as well as cancer disparities, cancer care delivery, and clinical effectiveness research to individuals in their communities.

Advances in Treating Leukemia – There are an estimated 6,000 cases of chemotherapy-resistant B-cell acute lymphoblastic leukemia diagnosed in the United States. More than half of these cases occurred in children and young adults (from age 1 to age 30). The children and young adults with chemotherapy-resistant leukemia who do not achieve remission have very poor outcomes. Results from an ongoing clinical trial led by the Center for Cancer Research (CCR) demonstrated that a new immunotherapy treatment had anti-leukemia effects in patients and that the treatment was feasible and safe. Fourteen of the 21 patients in this trial experienced complete remission. In 12 of the patients, highly sensitive techniques could not detect evidence of leukemia following the therapy. CCR is continuing to study this treatment.

The Experimental Therapeutics Clinical Trials Network (ETCTN) – The Cancer Therapy Evaluation Program (CTEP) supports an early phase experimental therapeutics clinical trials program to develop new clinical agents. CTEP also assesses various cancer-relevant molecular changes for developing targeted drug agents designed to exploit specific abnormalities. CTEP recently redesigned this program, creating an NCI Experimental Therapeutics Clinical Trials Network (ETCTN) that develops novel anticancer agents for patients most likely to respond to these agents, based on recognized biomarkers. ETCTN clinical trials are designed to identify the dose, schedule, and evidence of activity to help guide future disease-specific, large randomized phase 2 and phase 3 clinical trials conducted by the National Clinical Trials Network.

Imaging in Precision Medicine – Precise measures to diagnose and monitor tumor progression and regression are essential in modern therapy, so the NCI makes major investments in these methods. Two examples of such investments include:

- **Quantitative Imaging Network for Measuring Therapy Response –** The Quantitative Imaging Network (QIN) includes 24 research teams, and each team is dedicated to improving the role of quantitative imaging for clinical decision-making. The teams develop and validate data acquisition, analysis methods, and tools to tailor treatment to individual cancer patients and to predict or monitor response to drug or radiation therapy. The multidisciplinary teams include oncologists, radiologists, imaging specialists, medical physicists, computer informatics scientists, and others. QIN teams are studying cancers such as non-small-cell lung cancer, cancers of the central nervous system, breast cancer, and hepatic cell carcinoma (liver), to name a few. In single- and multisite phase 1 through phase 3 clinical trials, these teams are applying a variety of imaging modes to quantitatively measure tumor response to drug or radiation treatments. The network is developing algorithms that could eventually become clinical tools to help oncologists make decisions about cancer treatment pathways for individual patients.

- **The Cancer Imaging Archive (TCIA) –** A primary goal of TCIA is to collect and make publicly available clinical images of patients matched with TCGA tissue specimens to allow researchers to explore the connectivity between cancer image phenotypes and emerging publically accessible genomic data. Using the data hosted in TCIA, researchers across the world have published important new scientific findings. Thus far, data submitted by multiple institutions generated 13 TCGA-matched imaging collections that are now publically available. One informatics team coordinated tumor-specific, TCGA-related phenotype-to-genotype science explorations. A team investigating glioma tissue types generated fourteen peer-reviewed publications detailing advanced imaging analyses used to identify specific molecular subclassifications.

Improving Survival for Pancreatic Cancer Patients – The NCI SBIR program is supporting phase 1 / phase 2 trials for a potential treatment for pancreatic cancer. There currently are no approved therapies beyond first-line treatment for pancreatic cancer after it has metastasized. Overall, patients diagnosed with pancreatic cancer have a 6.7 percent chance of surviving 5 years or more, and more than half (53 percent) of all pancreatic cancer is diagnosed after it has already metastasized.

Recently, the FDA granted Breakthrough Therapy Designation following the results of a phase 2A clinical study of a two-vaccine combination that showed significant improvements for patients who had failed prior therapies. The therapy is a combination of the GVAX Pancreas vaccine and CRS-207 vaccine. Together, the combined vaccine improves patient survival from 3.9 months (GVAX only) to 6.1 months (GVAX + CRS-207). A phase 2B clinical trial for the combination therapy is ongoing, with enrollment expected to be completed by the end of 2015. NCI has also funded NCI SBIR grant to the same sponsor to develop the novel adjuvant to increase the potency of the combination vaccine therapy to treat pancreatic cancer.

V. Improving Cancer Prevention and Control: Cancer prevention research draws on knowledge of the mechanisms and causes of cancer, and is therefore closely associated with aspects of the precision medicine initiative. But prevention also depends on population-based surveys to obtain epidemiological information, such as the incidence of specific types of cancers and their association with possible causative factors. Through education, behavior modification, vaccination, and policies that limit exposures to known carcinogens, the risk of cancer can be reduced by one-third to one-half. Measures (such as vaccines or behavioral changes) that interfere with processes that initiate cancer (such as virus infections and smoking tobacco) have the potential to counteract the elevated risk of cancer. To improve cancer prevention and control, NCI also supports research to understand the factors that influence cancer outcomes, quality of care, and quality of life. NCI also promotes studies in disadvantaged communities in the United States and globally to advance the goal of controlling cancer more effectively for all populations.

Budget Policy:
The FY 2016 President's Budget request is $228.038 million, an increase of $6.528 million, or 2.9 percent compared with the FY 2015 Enacted level.

Surveillance, Epidemiology and End Results Program – Since 1973, the Surveillance, Epidemiology and End Results (SEER) program has been collecting data on cancer incidence, mortality, and prevalence. The registries that comprise SEER cover approximately 28 percent of the U.S. population within their catchment areas. The SEER database contains information on 5.7 million cancer cases, with 380,000 new cancer cases added each year. This database is a critical resource for identifying cancer trends. It also serves as a powerful resource for researchers, and the database includes population data associated by age, sex, race, year of diagnosis, and geographic areas. SEER data is used to create the Annual Report to the Nation on the Status of Cancer, a collaboration of the NCI, the CDC, the American Cancer Society, and the North American Association of Central Cancer Registries.

The December 2013 report revealed that overall cancer mortality rates for men and women continued to decline at an average rate of about 1.5 percent per year, after adjusting for age. It

also described the prevalence and impact of comorbidities (other coexisting noncancerous diseases) in patients over 66 years of age with breast, prostate, lung, or colorectal cancer. Because comorbidities affect cancer care and survival, NCI has funded several grants that specifically consider issues related to comorbidities in cancer patients.

Monitoring and Interpreting Cancer Trends Across Diverse Populations – NCI captures high-quality data and makes it widely available for analysis to guide cancer research. For example, a SEER study out of Yale University, published in June 2014 in Cancer, found that widespread screening for colorectal cancer has helped prevent an estimated half-million cases of the disease since the mid-1970s. The December 2013 edition of Cancer published the *Annual Report to the Nation on the Status of Cancer, 1975-2010, Featuring Prevalence of Comorbidity and Impact on Survival Among Persons with Lung, Colorectal, Breast, or Prostate Cancer*. The next report, due in January 2015, will feature breast cancer as a special topic. This will be the first opportunity to provide data in more clinically relevant strata, specifically acknowledging that molecular subtypes represent differing risks. SEER will continue to be an important resource for the public health community, using population-based science to document our nation's progress in cancer control.

Translational Epidemiology and Genomics – Epidemiologic and genomic findings generated by NCI research are leading to cost-effective screening and clinical applications that directly benefit public health and medical practice. Importantly, NCI research has helped the U.S. Preventive Services Task Force (USPSTF) and professional society guideline committees to issue sound evidence-based cancer screening recommendations over many years. For example, NCI biostatisticians used recent findings from NCI's National Lung Cancer Screening trial to develop a risk-based lung cancer screening protocol using low dose CT. The USPSTF cited the NCI analysis in their recent lung cancer screening guidelines.

NCI researchers are also translating findings from genome-wide association studies into potential clinical applications. Recently, NCI scientists discovered a novel interferon (IFN-λ4) that is created by a genetic variant associated with spontaneous and treatment-induced clearance of the hepatitis C virus (HCV). NCI has developed a genotyping test for this gene variant that is now certified and in use by the U.S. Department of Veterans Affairs to tailor patient treatment options for HCV therapy. NCI's discovery also has potential to contribute to future drug development.

Tobacco – Tobacco use is the leading cause of preventable death and disease worldwide. The World Health Organization has estimated that globally, smoking is responsible for almost six million deaths annually. Based on current patterns, by the year 2030, smoking-related deaths are projected to rise to more than eight million annually. While tobacco use has been slowly declining in most high-income nations, including the United States, it is increasing in many low- and middle-income countries.

Ten years ago, NCI, the Fogarty International Center and other partners launched the International Tobacco and Health Research and Capacity Building Program. This program supports transdisciplinary research and capacity building that addresses the burden of tobacco consumption in low- and middle-income nations. The program is designed to promote international cooperation between investigators in the United States (and other high-income nations) and scientists and institutions in low- and middle-income countries where tobacco consumption is an urgent public health concern.

NCI also disseminates evidence-based findings to prevent, treat, and control tobacco use and provides the scientific evidence base to inform policy makers and public health practitioners. For example, the NCI Cancer Intervention and Surveillance Modeling Network study estimated that tobacco control was associated with avoiding 8 million premature deaths and extending mean life span by 19 to 20 years.

To address emerging developments related to smoking, in November 2013, NCI co-sponsored the NIH Electronic Cigarette Workshop: Developing a Research Agenda. Proceedings from the workshop were published in the October 2014 volume of *Nicotine and Tobacco Research*. Research needs identified by the workshop participants included:

- standards to measure the contents and emissions of e-cigarettes
- biomarkers of exposure
- physiological effects of e-cigarettes on tissues and organ systems
- information on e-cigarette users and how the devices are used
- factors that drive use and influence patterns of use
- methods to evaluate a potential role for e-cigarettes in smoking or nicotine cessation

The NCI research portfolio includes grants that are investigating electronic cigarettes. These include five-year grants funded by the FDA Center for Tobacco Products in September 2013 through the Tobacco Regulatory Science Program (TRSP), an NIH-FDA collaboration. NCI will continue supporting research to increase our understanding of tobacco product design and composition, nicotine addiction, tobacco product marketing, and use by youth and adults. In addition, NCI will support research and efforts to harness social media interactions, with the goal of improving tobacco prevention, cessation, and control, focusing especially on youth and underserved populations.

HPV Infection and Cancer – As a result of long-term investments by the NCI, effective vaccines and screening strategies exist to prevent cervical cancer. However, additional research is needed to understand HPV infection and carcinogenesis at cervical and non-cervical sites and to define the most effective vaccination, screening and clinical management approaches for HPV-related diseases. Researchers are currently working to develop and evaluate biomarkers for risk of HPV-related pre-cancers and cancers that will help identify women at highest risk of HPV-associated cancers. NCI also continues its critically important work on developing risk models to inform clinical management of women with various cervical cancer screening and colposcopy outcomes.

The NCI HPV Vaccine Trial has demonstrated the ability of the vaccine to protect against HPV-16/18 infection and associated disease. Extended follow-up on vaccinated and screened groups will provide a detailed assessment of the vaccine's long-term impact. Results from this effort have already demonstrated high efficacy in preventing new infections with HPV vaccine types, a lack of efficacy in treating established HPV infections, and excellent protection against anal, vulvar, and oral HPV infections.

During FY 2015, NCI will begin planning a randomized controlled clinical trial to investigate the efficacy of a one-dose regimen vs. two-dose regimen of HPV vaccine. Completing the three-

dose vaccine series continues to be a challenge, even in wealthy nations. Evidence of protection from a single-dose of HPV vaccine may enable countries that cannot afford multi-dose regimens to achieve extensive population coverage by vaccinating a much larger number of girls, which in combination with community immunity will result in decreased cervical cancer incidence and mortality over time. Evidence from this NCI-supported research should provide the scientific information that public health policy makers need to make evidence-based decisions and implement large-scale, sustainable, and cost-effective HPV vaccination programs.

Program Portrait: Cancer Prevention and Early Detection

FY 2015 Level: $356.6 million
FY 2016 Level: $356.6 million
Change: $0.0 million

NCI research into the causes and mechanisms of cancer supports progress across all areas of cancer control, prevention, and detection. However, the greatest progress in reducing cancer mortality has come through prevention. Prominent examples of prevention success include reduced tobacco use and tests that identify pre-malignant lesions and early cancers, such as screening for lesions in the large intestine and uterine cervix.

The NCI investments in epidemiology, genomics, cancer biology, behavioral sciences, health services research, and other areas of our research portfolio are all integral to making advances in prevention and screening. For example, careful epidemiologic observations supported by NCI have contributed to reduced tobacco use and other advances in cancer prevention. Experimental validation – such as the fall in lung cancer rates after smoking rates decline and the recent findings of tobacco mutagen signatures within the genomic profiles of tumors – have strengthened confidence in our ability to identify epidemiological associations and to discover genomic signatures linked to cancer.

NCI supports a range of other initiatives intended entirely or in part to improve cancer prevention and screening. Examples of these NCI initiatives include:

- NCI's Provocative Questions Initiative highlights important questions in all domains of research, including questions focused on prevention that may lead to a better understanding the association between obesity and cancer risk and questions that may uncover ways to identify additional infectious agents that cause cancer.
- NCI's Early Detection Research Network works to identify and validate candidate biomarkers that can detect early or recurrent cancers.
- A Forthcoming NCI Request for Applications seeks to address one of the confounding problems in early cancer detection, the challenge of distinguishing lesions destined to become life-threatening cancers from those likely to remain non-cancerous.
- NCI Collaborations, such as collaborations with CDC that focus on developing and implementing more effective approaches to reduce tobacco consumption and a collaboration with FDA and other NIH institutes to study new tobacco products, including electronic cigarettes.
- NCI Population-Based Cancer Screening, such as the National Lung Screening Trial, which demonstrated a 16 percent relative reduction in cancer mortality through screening 50,000 high-risk participants with low-dose computed tomography (CT).

The progress that NCI is achieving in cancer prevention and screening demonstrates the importance of continuing to fund a research portfolio that spans across a broad spectrum of science.

New Cancer Prevention Indications for Non-Cancer Drugs – Repurposing existing drugs is a growing area of research for cancer prevention. Numerous studies during the past two decades have suggested that aspirin may lower a person's risk of developing or dying from cancer. However, the research findings are not clear, and aspirin's safety and potential side effects are of concern. NCI and the National Institute on Aging (NIA) are collaborating on a primary prevention trial on low-dose aspirin use, Aspirin in Reducing Events in the Elderly (ASPREE),

that is on track to reach the recruitment goal of 19,000 participants by the end of 2014, and participant retention remains high.

The study results have the potential to alter clinical practice and resolve uncertainty about whether there is an upper age where the harms outweigh the benefits of aspirin use. Based on suggestions that metformin, a diabetes prevention drug, also may reduce the risk of cancer, NCI is studying metformin in collaboration with NIDDK to assess cancer endpoints in the Diabetes Prevention Program and follow-up cohort. NCI is also supporting several early stage clinical trials to investigate metformin's potential to prevent an array of cancers, including colorectal, prostate, endometrial, and breast cancer.

Center for Global Health – The global success in controlling infectious diseases suggests that using a similar approach – coordinated basic research, translational research, clinical trials, implementation science, and capacity building – will also be effective against non-communicable diseases such as cancer. With this approach in mind, NCI established the Center for Global Health (CGH) in 2011 to advance global cancer research, build expertise, and leverage resources across borders in an effort to reduce cancer deaths worldwide, especially in low- and middle-income countries. CGH engages other NCI divisions, offices, and centers, as well as the NIH, to create sustainable international partnerships to address global gaps in research and scientific training. CGH also disseminates information and best practices to improve cancer research and cancer control.

Basic Research in Cancer Health Disparities – NCI also invests in research to identify factors that contribute to cancer health disparities. The Basic Research in Cancer Health Disparities Initiative supports research to understand biological factors that may contribute to the unexplained differences observed in cancer incidence, prevalence, and mortality rates among racial and ethnic populations. The Centers for Population Health and Health Disparities supports transdisciplinary research involving social, behavioral, biological, and genetic studies to improve knowledge of the causes of health disparities and to devise methods to prevent, diagnose, and treat disease and promote health.

Immunotherapy and Vaccine Development – Building on recent successes in harnessing the immune system to treat advanced cancer, NCI is also examining the potential of vaccines and immune-preventive approaches to prevent cancer. These approaches include vaccines directed against cancer-causing viruses and vaccines directed against antigens abnormally expressed during cancer development. Vaccines developed to target early cancers have shown promise in preclinical studies, and the approach offers an excellent strategy to combat early cancers with minimal toxicity. In related work, NCI is studying the use of biological agents and relevant biomarkers in vaccines to prevent cancer. One example is a clinical trial, currently funded through the Consortia for Early Phase Prevention Trials, of a Mucin 1 (MUC1) vaccine in colorectal polyps. MUC1 is abnormally expressed in a variety of cancers, so this vaccine approach may also have potential application for other human cancers.

Trans-NCI Innovative Molecular Analysis Technologies (IMAT) – The IMAT program is a high-risk, high-reward investment to foster development of innovative technologies. Grants awarded through the IMAT program support 25-30 research projects each year. Projects are selected for their strong potential to transform cancer research or clinical care of cancer patients.

Since the program's inception, NCI has awarded more than 500 IMAT grants, leading to more than 100 platforms that are now either commercially available or accessible through collaboration with NCI-supported scientists.

VI. Cancer Centers: The NCI Cancer Centers program is one of the anchors of the nation's cancer research effort. There are currently 68 cancer centers, located in 35 states and the District of Columbia, that form the backbone of NCI's programs for studying and controlling cancer.

Budget Policy:
The FY 2016 President's Budget request is $540.680 million, an increase of $15.478 million, or 2.9 percent above the FY 2015 Enacted level.

Cancer Centers are the nation's single most important source of new insights into the causes of cancer and strategies for prevent, diagnosis, and treat cancer. Research proposals from Cancer Center investigators account for about three-quarters of the successful investigator-initiated grants that NCI awards.

At any given time, hundreds of research studies are under way at NCI Cancer Centers, ranging from basic laboratory research to clinical assessments of new treatments. Many of these studies are collaborative and may involve several research centers and other partners in industry and the community. In addition to conducting meritorious basic and applied research, the cancer centers deliver quality cancer care to patients and their families, including in communities with underserved and understudied populations. In addition to 68 NCI-designated cancer centers, NCI supports more than 100 other more specialized centers.

VII. Research Workforce Development: NCI is committed to training and developing a strong workforce of cancer researchers that spans the career continuum. NCI's investment in early-stage investigators helps attract strong talent and ensure the strength of future cancer research. In addition to NCI's direct support for training, our support for established investigators – scientists that have proven their ability to conduct robust science – also fosters mentoring for the next generation of cancer researchers.

Budget Policy:
The FY 2016 President's Budget request is $175.775 million, an increase of $5.032 million, or 2.9 percent above the FY 2015 Enacted level.

NCI supports opportunities for training in basic, clinical, and behavioral research through formal training programs, individual fellowships, and career development awards. NCI training occurs at universities and institutions across the country. In addition, NCI supports research experiences for high school, college, graduate and medical school students, and many domestic and foreign post-doctoral fellows working in NCI's intramural research programs. Beneficiaries of training and career development grants span the career continuum, including pre-doctoral candidates, postdoctoral fellows, new faculty in independent research positions, and established midcareer investigators.

NCI is committed to enhancing diversity within the cancer research workforce. These efforts are coordinated through the NCI Center to Reduce Cancer Health Disparities. Initiated in 2001, the Partnerships to Advance Cancer Health Equity (PACHE) supports cancer research, training,

education, and outreach programs that build infrastructure and capacity at institutions serving underserved health disparity populations and underrepresented students. PACHE also supports cancer health disparities research at NCI Cancer Centers. PACHE seeks to achieve a greater understanding of the underlying causes of cancer health disparities in underserved populations and to train the next generation of investigators in cancer and health disparities research.

Recently, the NCI intramural programs formed a task force to identify opportunities to enhance the diversity of the long-term staff, especially tenure-track investigators.

The Continuing Umbrella of Research Experiences (CURE) program provides students and trainees educational and career development opportunities that extend from high school through professional appointment. This holistic training program constitutes a pipeline through which students and trainees from groups that are underrepresented in health research gain the skills and knowledge needed to become successful independent scientists.

The Cancer Prevention Fellowship Program provides a unique training mentorship for research at NCI, as well as leadership and professional development opportunities in a range of areas, including basic, quantitative, and social and behavioral sciences as well as in clinical cancer prevention. The program provides scientists and clinicians with a strong foundation of training in the field of cancer prevention and control. Trainees are mentored by NCI investigators and provided opportunities to conduct important research in basic, quantitative, social and behavioral sciences, and in clinical cancer prevention. Fellows have the opportunity to develop original scientific projects and to report their findings at scientific meetings and in leading journals. Recently, the program conducted outreach to recruit more physicians and to expand the cadre of trained clinical research scientists. Many alumni of this program have gone on to serve in prominent research and leadership positions at leading scientific institutions around the country.

VIII. Research Management and Support: NCI research management and support personnel fulfill a key and indispensable role by supporting and enabling the activities and success of all NCI-funded activities.

Budget Policy:
The FY 2016 President's Budget request is $381.630 million, an increase of $2.879 million, or 0.8 percent above the FY 2015 Enacted level.

IX. Repairs and Improvements: Established in 1971 under the National Cancer Act, the NCI's Frederick National Laboratory for Cancer Research is the only Federally-Funded Research and Development Center dedicated to biomedical research. This NCI enterprise headquartered on the campus on Fort Detrick, Maryland, is a national asset and a unique resource. .

Budget Policy:
The FY 2016 President's Budget request is $16 million, an increase of $8 million, or 100 percent above the FY 2015 Enacted level. During the past decade, the value of the $8 million R&I allocation for the FFRDC has declined by approximately 25 percent due to inflation. At the same time, the laboratory and support facilities – much of which was aged and needed to be modernized when NCI received its Fort Detrick facilities – has continued to age, wear, and

degrade. The additional $8 million would have a substantial impact on improving the facilities that host essential cancer research. R&I projects would include repairs related to laboratory operations, repairs to correct deficiencies, and repairs to infrastructure.

The FY 2016 increase in the R&I allocation from $8 to $16 million will allow NCI to complete priority repair and improvement projects and thereby strengthen FFRDC operations that provide high-value support to the NCI mission, the research community, and to patients diagnosed with cancer.

NATIONAL INSTITUTES OF HEALTH
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Budget Authority by Object Class[1]
(Dollars in Thousands)

		FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Total compensable workyears:				
	Full-time employment	3,057	3,057	0
	Full-time equivalent of overtime and holiday hours	3	3	0
	Average ES salary	$181	$183	$2
	Average GM/GS grade	12.1	12.1	0.0
	Average GM/GS salary	$102	$103	$1
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$101	$102	$1
	Average salary of ungraded positions	$134	$135	$1
	OBJECT CLASSES	**FY 2015 Enacted**	**FY 2016 President's Budget**	**FY 2016 +/- FY 2015**
	Personnel Compensation			
11.1	Full-Time Permanent	$212,365	$215,347	$2,982
11.3	Other Than Full-Time Permanent	117,840	119,494	1,654
11.5	Other Personnel Compensation	9,179	9,308	129
11.7	Military Personnel	4,123	4,181	58
11.8	Special Personnel Services Payments	44,269	44,891	622
11.9	**Subtotal Personnel Compensation**	**$387,776**	**$393,221**	**$5,444**
12.1	Civilian Personnel Benefits	$108,700	$111,974	$3,273
12.2	Military Personnel Benefits	2,820	2,921	101
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**$499,296**	**$508,115**	**$8,819**
21.0	Travel & Transportation of Persons	$13,536	$13,752	$217
22.0	Transportation of Things	1,115	1,133	18
23.1	Rental Payments to GSA	14,453	14,684	231
23.2	Rental Payments to Others	11	11	0
23.3	Communications, Utilities & Misc. Charges	6,396	6,498	102
24.0	Printing & Reproduction	132	134	2
25.1	Consulting Services	$19,562	$19,875	$313
25.2	Other Services	377,679	344,748	-32,931
25.3	Purchase of goods and services from government	599,512	639,373	39,861
25.4	Operation & Maintenance of Facilities	$18,039	$18,167	$128
25.5	R&D Contracts	334,788	340,145	5,357
25.6	Medical Care	3,039	3,115	76
25.7	Operation & Maintenance of Equipment	19,083	19,388	305
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal Other Contractual Services**	**$1,371,702**	**$1,384,811**	**$13,109**
26.0	Supplies & Materials	$33,691	$34,229	$539
31.0	Equipment	30,204	30,687	483
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	2,982,492	3,104,422	121,931
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	1	1	0
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$4,453,732**	**$4,590,364**	**$136,632**
	Total Budget Authority by Object Class	**$4,953,028**	**$5,098,479**	**$145,451**

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

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National Cancer Institute

Salaries and Expenses

(Dollars in Thousands)

OBJECT CLASSES	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Personnel Compensation			
Full-Time Permanent (11.1)	$212,365	$215,347	$2,982
Other Than Full-Time Permanent (11.3)	117,840	119,494	1,654
Other Personnel Compensation (11.5)	9,179	9,308	129
Military Personnel (11.7)	4,123	4,181	58
Special Personnel Services Payments (11.8)	44,269	44,891	622
Subtotal Personnel Compensation (11.9)	**$387,776**	**$393,221**	**$5,444**
Civilian Personnel Benefits (12.1)	$108,700	$111,974	$3,273
Military Personnel Benefits (12.2)	2,820	2,921	101
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	**$499,296**	**$508,115**	**$8,819**
Travel & Transportation of Persons (21.0)	$13,536	$13,752	$217
Transportation of Things (22.0)	1,115	1,133	18
Rental Payments to Others (23.2)	11	11	0
Communications, Utilities & Misc. Charges (23.3)	6,396	6,498	102
Printing & Reproduction (24.0)	132	134	2
Other Contractual Services:			
Consultant Services (25.1)	10,949	11,124	175
Other Services (25.2)	377,679	344,748	-32,931
Purchases from government accounts (25.3)	460,709	471,989	11,280
Operation & Maintenance of Facilities (25.4)	10,030	10,030	0
Operation & Maintenance of Equipment (25.7)	19,083	19,388	305
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$878,451**	**$857,280**	**-$21,171**
Supplies & Materials (26.0)	$33,691	$34,229	$539
Subtotal Non-Pay Costs	**$933,331**	**$913,038**	**-$20,293**
Total Administrative Costs	**$1,432,628**	**$1,421,153**	**-$11,474**

NATIONAL INSTITUTES OF HEALTH
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Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2014 Actual			FY 2015 Est.			FY 2016 Est.		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Center for Cancer Research									
Direct:	1,399	21	1,420	1,407	21	1,428	1,407	21	1,428
Reimbursable:	2	-	2	2	-	2	2	-	2
Total:	1,401	21	1,422	1,409	21	1,430	1,409	21	1,430
Division of Cancer Biology									
Direct:	51	-	51	51	-	51	51	-	51
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	51	-	51	51	-	51	51	-	51
Division of Cancer Control and Population Sciences									
Direct:	167	3	170	168	3	171	168	3	171
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	167	3	170	168	3	171	168	3	171
Division of Cancer Epidemiology and Genetics									
Direct:	150	5	155	151	5	156	151	5	156
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	150	5	155	151	5	156	151	5	156
Division of Cancer Prevention									
Direct:	95	1	96	95	1	96	95	1	96
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	95	1	96	95	1	96	95	1	96
Division of Cancer Treatment and Diagnosis									
Direct:	229	4	233	231	4	235	231	4	235
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	229	4	233	231	4	235	231	4	235
Division of Extramural Activities									
Direct:	103	-	103	104	-	104	104	-	104
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	103	-	103	104	-	104	104	-	104
Office of the Director									
Direct:	806	4	810	810	4	814	810	4	814
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	806	4	810	810	4	814	810	4	814
Total	3,002	38	3,040	3,019	38	3,057	3,019	38	3,057
Includes FTEs whose payroll obligations are supported by the NIH Common Fund.									
FTEs supported by funds from Cooperative Research and	0	0	0	0	0	0	0	0	0

FISCAL YEAR	Average GS Grade
2012	12.3
2013	12.1
2014	12.1
2015	12.1
2016	12.1

NATIONAL INSTITUTES OF HEALTH
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Detail of Positions[1]

GRADE	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget
Total, ES Positions	1	1	1
Total, ES Salary	179,700	181,497	183,312
GM/GS-15	261	262	262
GM/GS-14	462	465	465
GM/GS-13	419	421	421
GS-12	480	483	483
GS-11	187	188	188
GS-10	14	14	14
GS-9	133	134	134
GS-8	94	95	95
GS-7	68	68	68
GS-6	18	18	18
GS-5	7	7	7
GS-4	5	5	5
GS-3	5	5	5
GS-2	5	5	5
GS-1	3	3	3
Subtotal	2,161	2,173	2,173
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	0	0	0
Director Grade	18	18	18
Senior Grade	9	9	9
Full Grade	4	4	4
Senior Assistant Grade	4	4	4
Assistant Grade	0	0	0
Subtotal	35	35	35
Ungraded	865	870	870
Total permanent positions	2,170	2,182	2,182
Total positions, end of year	3,062	3,079	3,079
Total full-time equivalent (FTE) employment, end of year	3,040	3,057	3,057
Average ES salary	179,700	181,497	183,312
Average GM/GS grade	12.1	12.1	12.1
Average GM/GS salary	101,137	102,148	103,169

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