

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Center for Research Resources

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**National Center for Research Resources
Organizational Chart**

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to

NATIONAL INSTITUTES OF HEALTH

National Center for Research Resources

For carrying out section 301 and title IV of the Public Health Service Act with respect to research resources and general research support grants, [\$1,124,141,000] *\$1,100,203,000*:
Provided, That none of these funds shall be used to pay recipients of the general research support grants program any amount for indirect expenses in connection with such grants [*Provided further*, That \$30,000,000 shall be for extramural facilities construction grants].

[Departments of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Consolidated Appropriations Act for Fiscal Year 2005]

Amounts Available for Obligation 1/

Source of Funding	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Appropriation	\$1,186,183,000	\$1,124,141,000	\$1,100,203,000
Enacted Rescissions	(7,125,000)	(9,051,000)	0
Subtotal, Adjusted Appropriation	1,179,058,000	1,115,090,000	1,100,203,000
Real transfer under NIH Director's one-percent transfer authority to other ICs	12,519,000	0	0
Comparative transfer to Buildings and Facilities	(102,000)	0	0
Comparative transfer to/from other NIH ICs for NIH Roadmap	(12,519,000)	0	0
Subtotal, adjusted budget authority	1,178,956,000	1,115,090,000	1,100,203,000
Unobligated Balance, start of year	27,000	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	1,178,983,000	1,115,090,000	1,100,203,000
Unobligated balance lapsing	(22,000)	0	0
Total obligations	1,178,961,000	1,115,090,000	1,100,203,000

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

FY 2004 - \$1,827,000; FY 2005 - \$7,050,000; FY 2006 - \$7,051,000

Justification

National Center for Research Resources

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

Budget Authority:

FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
88	\$1,178,983,000	92	\$1,115,090,000	92	\$1,100,203,000	0	-\$14,887,000

This document provides justification for the Fiscal Year 2006 activities of the National Center for Research Resources (NCRR), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2006 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

Introduction

To do good work, one must first have good tools—so goes an ancient Asian proverb. As the "research resources" component of the National Institutes of Health, NCRR's mission is to ensure that scientists have the necessary tools and research environments to make the most of their federally funded biomedical studies. With ready access to essential tools, our nation's top investigators are free to think creatively and explore promising new avenues effectively, making scientific advances that enhance human health.

NCCR-supported research tools and infrastructure enable all lines of biomedical inquiry, from studies of molecular structures to large clinical trials that evaluate potential new therapies. Each year more than 35,000 investigators supported by competitive grant support from other NIH components, other federal agencies, and the private sector, use NCCR-supported research resources. The high quality of these investigations is evident in the Science Advances section of this document.

To ensure broad access to essential tools—including high-cost technologies, scarce or novel animal models, state-of-the-art research environments, and specially trained research staff—NCCR encourages the sharing of resources. Resource sharing also leverages federal dollars, thereby maximizing research opportunities in times of budget constraints.

Networks and other shared resources provide a fertile environment for interdisciplinary collaborations among investigators. Such studies are essential for addressing important but

complex research problems—for example, identifying the relationships between genes and clinical characteristics, or genotype and phenotype, which may speed the development of new therapies. N C R R supports several resources that explore genotypic-phenotypic relationships, including a new high-throughput genotyping center that can host integrated investigations for both human and animal studies.

Because patient-oriented research represents the pinnacle of biomedical investigations, N C R R devotes significant resources to support the nationwide network of General Clinical Research Centers (G C R C s). For more than 40 years, the G C R C s have played a significant role in advancing human health, as illustrated in the Story of Discovery below. As clinical research has become more complex, investigators need specialized clinical research resources to identify the cause of disease and also develop effective therapies. To complement the G C R C s, N C R R supports several national research resources, including the National Gene Vector Laboratories, the Regional Human Pancreatic Islet Cell Resource Centers, the National Disease Research Interchange, human embryonic stem cell research resources, and the National Center for High-Throughput SNP Genotyping and Analysis. In addition, clinical investigators need access to secure sophisticated cyberspace-based networks over Internet2 and the National Lambda Rail in order to recruit research subjects across this country and to share research data with colleagues globally.

Story of Discovery: Transplantation—From Organs to Genes

For centuries, health practitioners have recognized the potential of replacing injured or diseased organs and tissues with healthy ones, but only in recent decades has transplantation saved the lives of thousands of people who otherwise had no hope of survival. NIH's nationwide network of General Clinical Research Centers (G C R C s) provided critical research infrastructure for many of these pioneering investigations, from the early days of organ transplantation to current microtransplants of genes into cells. Indeed, ongoing advances in transplantation illustrate how NIH-funded interdisciplinary efforts—among molecular biologists, geneticists, animal researchers, and clinical investigators—lay a solid foundation for improving human health.

One need only look at the data on transplant recipients to appreciate how decades of federal support for transplantation research have enhanced health care. A 34-year-old who received a liver transplant at age 3 now ranks as the longest-surviving liver transplant recipient. The youngest recipient of a heart transplant, as a newborn only 3 hours old, is now a healthy teenager. Indeed, transplantation has become the treatment of choice for failing kidneys, hearts, livers, and lungs.

When the first successful kidney transplantation was performed between identical twins half a century ago, scientists had little understanding of the molecular basis of graft acceptance or rejection. The chief impediment was an immunologic barrier—the body's determination to reject and destroy foreign substances, whether a disease-causing microbe or a life-saving kidney.

A key to understanding the immunologic barrier came from basic science experiments begun in the 1930s. By transferring cells and tissues between genetically identical mice, researchers discovered that transplant success depended on the similarity of cell-surface structures, or antigens, between donor and recipient. By the 1960s, scientists had identified molecules, termed human leukocyte antigens (HLA), that today serve as the basis for human tissue-typing techniques that match compatible transplant recipients and donors. Careful matching enhances the recipients' chances of survival.

While basic scientists pieced together the functions of the H L A complex, clinical investigators were achieving unparalleled success in transplanting organs between unrelated individuals, using drugs to suppress the recipient's immune response. The introduction of the immunosuppressant cyclosporine in the early 1980s revolutionized the field by dramatically improving graft survival. The scientific team that performed the first successful combined heart-lung transplantation in the United States, with support from the G C R C at Stanford University, attributed its success to the use of cyclosporine, as well as previous experience performing heart-lung transplantations in nonhuman primates.

Advances in immunomodulation have progressed rapidly in recent years. By 2001, investigators at Stanford were achieving 100 percent success rates using a therapeutic regimen of three nonsteroidal drugs to suppress immune responses in children undergoing kidney transplantation. In 2004, at the Duke University G C R C, researchers discovered that administering an immunosuppressant drug to babies for three days before they receive thymus tissue transplants helps to prevent immune cells from attacking the new thymus tissue.

Today the focus of transplantation research is not on preventing organ rejection—the primary concern a half-century ago—but rather to meet an urgent and increasing need for appropriate donor organs. Almost 87,000 U. S. citizens now await compatible organs, according to the United Network for Organ Sharing, and each year more than 6,000 Americans die while waiting. To help narrow the gap between organ need and availability, NIH-supported scientists are exploring the potential of generating artificial organs and tissues, developing bridge technologies to keep patients alive while awaiting compatible transplants, and transplanting partially encapsulated organs or cell suspensions.

Another option under development is xenotransplantation, or transplantation from animals to humans. Many researchers consider pig organs to be a reasonable alternative to human organs for transplantation, since they are similar in size. But pig cells display a cell-surface sugar molecule (antigen) that is quickly recognized and attacked by the human immune system, leading to transplant failure. To overcome this hurdle, in 2004, scientists at the University of Missouri-Columbia and their colleagues cloned the world's first knockout pigs that lack both copies of a gene needed to synthesize the notorious sugar, thereby moving a step closer to achieving success in xenotransplantation.

Beyond organ transplantation, NIH also has enabled advances in transplantation on a much smaller scale—of tissues and cells. In the late 1960s, Nobel Prize-winning scientist E. Donnall Thomas depended on the G C R C at the University of Washington for his pioneering clinical studies of bone marrow transplants, a technique that has since saved or enhanced tens of thousands of lives. In April 2004, researchers from Albert Einstein College of Medicine reported advances toward transplanting liver cells instead of the organ itself for the treatment of liver diseases. And for patients with diabetes, NIH recently established a nationwide network of Islet Cell Resource Centers, which retrieve, preserve, and transport insulin-producing islet cells for transplantation.

Genetically modifying cells before inserting them into humans may prove to boost the success rate of cellular microtransplants. Gene therapy researchers have made strides by implanting mice with islet cells that have been genetically engineered to express genes that allow transplanted cells to evade immune system attack. Gene therapy also may hold promise for slowing the aging process. Researchers have shown that degeneration of nerve cells in aged rhesus monkeys could be almost completely reversed by implanting cells in the monkeys' brains with cells that are genetically modified to produce human nerve growth factor. Such grafts may help to slow neurodegenerative conditions, such as Alzheimer's disease.

At an even smaller scale, gene therapy researchers inject encapsulated D N A into the body in hope that the genetic material will transplant itself into target cells. In the first such study, conducted in the early 1990s at the G C R C at the University of Michigan, scientists injected D N A encoding the H L A - B 7 gene directly into melanoma tumors. When taken up by the tumor cells, the D N A caused the cells to produce the cell-surface protein called H L A - B 7, which marked the cells for destruction by the immune system. Continuation of this work has led to the treatment of more patients than all other cancer gene therapy programs in the United States combined and the initiation of the first Phase II gene therapy protocol for cancer.

In another clinical gene therapy trial, conducted in part at the GCRCs at the University of Pittsburgh and the University of North Carolina, scientists successfully transplanted the gene for the human blood-clotting factor VIII into the peripheral blood cells of patients with severe hemophilia A. The protocol was found to be safe and promising in a small clinical trial, with blood cells in some patients continuing to make factor VIII more than a year after the treatment.

By enhancing understanding of the genetic and molecular basis of the normal immune response, transplantation research has improved the health outlook for a large segment of the population, from patients awaiting transplants to anyone at risk for a whole host of immune disorders, ranging from AIDS to influenza.

Science Advances

Genetics

A New Target in the Fight Against Diabetes. Type 2 diabetes arises when the body's tissues fail to respond to what appears to be more than adequate levels of insulin, a condition known as "insulin resistance." Children whose parents have type 2 diabetes are at particularly high risk of developing diabetes if the children are insulin resistant. Scientists at the Yale University's General Clinical Research Center discovered that these high-risk youngsters metabolize glucose in muscle tissues at a remarkably slow rate. The culprit is poor regulation of fatty acid metabolism in muscle cells, probably due to a genetic defect in the cellular mitochondria that generate energy for the cell. This newly identified mitochondrial metabolic defect gives scientists a potential target for preventing and treating type 2 diabetes.

Telltale Mice. Scientists who seek the genetic roots of human disease are often stymied by the fact that common conditions—from obesity to psychiatric disorders—are influenced by multiple genes. Therefore, researchers have turned to inbred mice as an ideal source for detecting genetic regions—known as Quantitative Trait Loci (QTL)—that influence expression of a complex disease. Using unique mouse strains available through the NCRB-supported Jackson Laboratory, investigators examined genetic factors that affect 53 complex traits, including obesity and anxiety. Researchers identified about 150 previously undiscovered QTLs that may serve as a basis for isolating the specific genes affecting the traits of interest. Pinpointing the mouse genes may pave the way for detecting similar genes in humans.

Zebrafish Reveal a New Class of Cancer Genes. A study of mutant zebrafish has identified genes that may hold clues to keeping our bodies cancer-free. When NCRB-supported researchers at the Massachusetts Institute of Technology induced genetic mutations in zebrafish embryos, the cohort of fish had an elevated incidence of cancer. Most of these fish carried one normal and one defective version of particular genes that express proteins found in ribosomes, cellular bodies that help to synthesize proteins. The researchers concluded that normal genes which express ribosomal proteins may act as tumor suppressors in these fish, and perhaps also in humans. Screening for such genes in zebrafish may prove to be a powerful tool for identifying cancer-causing mutations in humans.

Gene Mutations in Skeletal Disorders. Several rare skeletal disorders may be caused by mutant genes that produce abnormal proteins. To identify the factors that underlie these

conditions, a multinational collaboration examined filamin proteins in affected individuals. A family of proteins found within all cells, filamins regulate the structure and activity of the cytoskeleton, a dynamic three-dimensional structure that gives the cell its shape. Researchers identified discrete mutations in the filamin B (*FLNB*) gene that are responsible for some inherited skeletal disorders. Further studies will assist in understanding the specific mechanisms by which *FLNB* mutations produce skeletal defects and abnormalities in other organ systems.

Obesity

Obesity and the Metabolic Syndrome. Patients who have multiple disorders (including diabetes and high blood pressure) that raise the risk of heart disease are said to have a "metabolic syndrome." When scientists at the Yale University's General Clinical Research Center evaluated 439 children and adolescents for the condition, they found that half of the severely obese children had the metabolic syndrome, making it far more common among the severely obese than any other group. Moreover, within a short follow-up period after the study, eight of the participants with metabolic syndrome developed full-blown type 2 diabetes. The increased risk of type 2 diabetes that obese adolescents face has been well documented. However, type 2 diabetes may be only the tip of the iceberg for obese children, who may be heralding an epidemic of cardiovascular disease as well.

Leptin Alters the Brain. The hormone leptin reduces appetite by enhancing the activity of some brain cells and suppressing others. To better understand how nerve cells in the brain respond to leptin, investigators measured neuronal connections in normal and leptin-deficient mice before and after leptin injections. The scientists discovered that leptin can rewire the brain's feeding circuitry, and this rewiring precedes changes in the eating patterns of the mice. Only by monitoring leptin's activities in the brain will researchers understand why obese individuals fail to respond to this hormone's cues.

The Hormones Behind Obesity. Key targets of researchers studying obesity are the hormones that modulate appetite and metabolism. Investigators at the N C R R-supported General Clinical Research Center at the University of California, Los Angeles, measured blood levels of obesity-related hormones in lean and obese volunteers. Concentrations of the hormone ghrelin, which is believed to boost appetite, did not increase at night in obese men, as it did in healthy volunteers. The same research group also reversed a genetically induced leptin deficiency in three obese adult volunteers and monitored the dramatic results. When taking leptin injections, the volunteers lost up to 54 percent of their body weight, began pubertal development that had been delayed by leptin deficiency, and transformed from emotionally and behaviorally immature individuals to mature adults. The researchers note that more work is needed to determine what role leptin may play in other types of obesity.

Biomedical Computing/Informatics

Defining a New Branch of Biomedical Informatics. An online N C R R resource called PhysioNet is helping to define a new branch of informatics. Dubbed complex signal informatics, this previously neglected area focuses on the physiological signals recorded from patients every day. It tracks important information such as heartbeats, brain waves, pulmonary recordings, and

measurements of blood counts and hormone levels. Scientists at the Harvard Medical School in Boston have detailed how PhysioNet provides online access to signal archives and to software for analyzing physiological data. Information gleaned from PhysioNet signal data has already uncovered ways to enhance the diagnosis and monitoring of irregular heartbeats.

New Method Details Dynamics of Macromolecules. By integrating sophisticated mathematical modeling with high-tech images of molecular structures, scientists can more precisely chart the dynamic changes that occur as large macromolecules move, interact, and change shape. Scientists at The Scripps Research Institute applied the new technique to three cellular proteins and to the ribosome, which translates genetic information within the cell. The researchers began with electron-microscope images showing the shapes of macromolecules at specific points during their molecular motions. Using structural details derived from X-ray crystallography, the scientists then determined how the molecular structures would change in the intervals between those time points. The reconstructed motions agreed with predictions based on the imaging data. The new method may help to shed light on many other macromolecular complexes, including viruses.

Neuroscience

Effects of Pregnant Women's Cocaine Use on Their Children. The effects of cocaine on fetuses have long been an issue of concern because cocaine is a commonly abused drug that easily crosses the placenta into the fetal brain. However, researchers have reported conflicting results in many short-term studies focusing on cocaine use in pregnant women and how it affects their children. Scientists at Case Western University recently studied 376 children, including some who had been exposed to cocaine and some who had not. By age 4, those prenatally exposed to cocaine showed deficits in visual-spatial skills, general knowledge, and arithmetic skills. However, the study showed that cocaine-exposed children placed in foster or adoptive homes had better vocabulary skills and attained similar IQ scores to unexposed children in familial homes. They also had higher scores than cocaine-exposed children in familial homes. These findings suggest that the environment of cocaine-exposed children after birth has a big impact on their intelligence and learning performance later in life.

A Mouse Brain Atlas. Researchers at the NCRF-supported Laboratory of Neuro Imaging at the University of California, Los Angeles, have developed a digital atlas of the brain of the adult mouse, an animal model key to biomedical science. The atlas allows researchers to relate experimental data on genes and protein expression to the anatomical structures where the gene expression takes place. With the digital atlas, scientists from around the world also can readily share and compare information from their respective laboratories. These collaborations may ultimately point to new therapeutic options for brain disorders.

Brain-Scanning Method May Improve Management of NeuroAIDS. A new type of brain scan may for the first time allow diagnosis of encephalitis in AIDS patients before permanent brain damage occurs. This encephalitis can lead to a condition known as AIDS dementia complex, or neuroAIDS. NCRF-supported scientists at the University of Pittsburgh found that a new type of positron emission tomography (PET) detected early-stage encephalitis in monkeys infected with simian immunodeficiency virus (SIV), a pathogen similar to the human

immunodeficiency virus (HIV) that leads to neuroAIDS. The new PET technique detected the condition by identifying elevated levels of a molecule present on brain cells affected by HIV or SIV encephalitis. The researchers hope the technique also will enable early detection in AIDS patients.

How Human and Chimp Brains Differ. Although humans are more advanced behaviorally and cognitively than other primates, human DNA sequences differ only about 1 percent from those of chimpanzees. But human and nonhuman primates may diverge to a greater extent in their control of how specific genes are expressed in various tissues. Researchers at the Salk Institute for Biological Studies in La Jolla, California, and their colleagues compared gene expression in the cerebral cortex of humans and chimpanzees. They identified 169 genes expressed differently in the two species, most of which related to cell metabolism or neuronal activity. These genes may be more active in humans because of our high levels of cerebral activity, but further study is needed to determine the roles of the specific genes identified.

Mouse Vaccine Offers Hope for Parkinson's Disease. A variety of medications can relieve the symptoms of Parkinson's disease, but no available treatment can stop or reverse the progressive loss of nerve cell function that characterizes the disease. Now a new vaccine, tested in mice with a Parkinson's-like condition, shows promise for halting some destruction to the central nervous system. Based on a drug called Copaxone, the vaccine targets the inflammation that damages nerve cells. Compared to unvaccinated mice, vaccinated animals had less inflammation, which preserved more brain neurons, and a greater density of nerve fibers. Vaccinated mice also had higher levels of an important nerve cell growth factor and of dopamine, a substance essential to proper brain function. Given the established safety of Copaxone, which is currently used to treat multiple sclerosis, this vaccine offers a promising clinical approach that might be readily evaluated in patients.

Biodefense

Drugs Thwart Deadly Anthrax Toxin. The anthrax bacterium is unusual because it produces large amounts of a toxin that can kill a patient even after antibiotics have destroyed the bacteria. The toxin is unresponsive to antibiotics. A research team used the NCCR-supported resource at the Stanford Synchrotron Radiation Laboratory to learn the structures of inhibitor molecules bound to the deadly toxin associated with inhalational anthrax. Attacking inhalational anthrax via these toxin-disabling inhibitors offers several advantages. While an antiserum would require the vaccination of whole populations, the availability of antibiotics and inhibitor drugs might be used only in cases of actual illness. This would reduce the side effects from vaccinations and also could prove economical.

New Method Improves DNA Fingerprinting of Pathogens. A new technology is boosting scientists' capacity to identify microbes from the infectious agent's DNA — a critical advance in this age of bioterrorism and emerging infectious diseases. Using laser technology, scientists at the NCCR-supported National Flow Cytometry Resource at Los Alamos National Laboratory analyzed and measured tiny samples of DNA from a Staphylococcus bacterium. The analysis can be completed in just 30 minutes, compared to the 24 hours normally required to analyze

D N A . Advanced computational methods linked to the new technology should boost efforts to detect and track microbial threats.

AIDS/HIV

Optimizing Drug Therapy for Patients with HIV/HCV. Patients infected with both HIV and the hepatitis C virus (HCV) who receive aggressive antiretroviral therapy are more likely to die of HCV-related complications than patients infected with HCV alone. The AIDS Clinical Trials Group tested a new combination of antiviral drugs. The study revealed that patients who took the new combination had lower levels of HCV than those treated with an older combination. Antiviral therapy for HCV did not lead to progression of HIV disease, nor did it reduce patient response to HIV therapies.

Toward the Design of HIV Vaccines. HIV vaccine development is increasingly focused on eliciting certain white blood cells that will recognize and kill HIV-infected cells. However, the AIDS virus mutates as it replicates and spreads, leading to the development of "escape variants" that the immune system has trouble recognizing. Collaborating researchers at the Wisconsin and New England National Primate Research Centers and elsewhere studied escape variants using the simian immunodeficiency virus (SIV) macaque model of AIDS. The researchers infected macaques with a cloned SIV bearing escape mutations and followed the evolution of viral changes during infection. The mutations reduced the fitness of the virus, leading to viruses that the host immune system could recognize. The findings suggest that HIV may revert to forms that the immune systems can recognize once it has originally escaped immune detection. This promising result will inform development of HIV vaccines.

Autoimmune Disease

Identifying Lupus Risk. Lupus, formally known as systemic lupus erythematosus, is one of many autoimmune diseases in which antibodies attack the body's normal tissues and organs. Early detection and treatment can slow the progression and lessen the severity of lupus. Researchers at the Oklahoma Medical Research Foundation's Center of Biomedical Research Excellence (COBRE) evaluated serum samples from 130 people who later were diagnosed with lupus. Although the blood samples were collected years before the diagnosis, they revealed autoantibodies indicative of the disease. In a related study, researchers at the NCCR-supported General Clinical Research Center at the University of Alabama at Birmingham found a particular genetic pattern that may increase a person's chance of developing lupus. This genetic pattern enhances expression of a receptor gene and therefore boosts receptor levels on the surfaces of immune cells. Since the receptor performs different tasks on different types of immune cells, the rise in receptor levels may contribute to autoimmune disease in several ways. These discoveries may help identify people at risk for lupus and also may lead to better drugs to combat lupus and other autoimmune disorders.

Scientists Explore Mechanism Behind Autoimmune Disease. A detailed study of the immune system's B cells sheds light on why the immune system sometimes attacks the body's own tissues. The new findings may provide insights for developing improved therapies for conditions caused by this so-called autoimmunity. B cells normally produce antibodies that target invading

pathogens, but errant B cells, termed autoreactive, create antibodies that launch a misdirected autoimmune attack. Scientists found that autoreactive B cells undergo an abnormal process of genetic mutation when they are readying their antibodies for an assault, resulting in antibodies that target the body's own cells. Further research may reveal which molecules in the body are most likely to be targets of autoreactive antibodies, and why.

A Novel Approach To Treating Juvenile Arthritis. Juvenile arthritis is an often-devastating disease in which white blood cells target the body's own tissues. Chemicals released by this misdirected attack damage tissues, causing inflammation and pain. Effective treatments are available, but it is difficult to predict which patients will respond to specific drugs, or to know when to try a new drug. Scientists at the Oklahoma Medical Research Foundation evaluated nine children with juvenile rheumatoid arthritis prior to beginning therapy. By identifying the genes expressed in inflammatory arthritis, the scientists learned which genes influenced a child's response to therapy. This approach also may help identify and predict treatment responses to other autoimmune diseases.

Cardiovascular Disease

New Drug Boosts "Good" Cholesterol. A new drug that raises blood levels of high-density lipoprotein (HDL), the "good" cholesterol, may provide a much-needed addition to the statin drugs now commonly used to prevent cardiovascular disease. The new drug, torcetrapib, is designed to improve health by raising HDL, rather than lowering low-density lipoprotein (LDL), the "bad" cholesterol. Researchers at NCCR-supported General Clinical Research Centers at the New England Medical Center in Boston and the University of Pennsylvania in Philadelphia found that HDL levels increased 46 to 106 percent in people with low HDL levels given torcetrapib. Combination therapy that included a statin drug further boosted the rise in HDL levels. Torcetrapib has the added benefit of also lowering LDL levels, which fell as much as 17 percent in study subjects.

New Approach Limits Damage After Heart Attack. A heart attack launches a destructive sequence of events that includes a failure of oxygen to reach the heart, fluid buildup in the heart, and rapid cell death. A team from The Scripps Research Institute is experimenting with a potential treatment to disrupt this often-deadly progression. The scientists are blocking an enzyme (Src kinase) that promotes fluid leakage from the heart's blood vessels, thereby preventing fluid buildup in the heart and, possibly, long-term damage to the heart. The researchers assessed fluid accumulation in animal hearts using a high-strength magnetic resonance scanner funded through the NCCR Shared Instrumentation Grant Program. The study suggests that Src kinase might be a useful target for new therapies that aim to prevent tissue injury following heart attack.

NIH Roadmap

As a significant partner of the NIH Roadmap for medical research, NCCR's programs complement a variety of the NIH Roadmap initiatives. Many of the NIH Roadmap initiatives will be implemented using NCCR research resources, repositories, and research resource centers.

The interdisciplinary nature of N C R R ' s existing clinical research resources provides a national network that can be leveraged to facilitate several of the Roadmap goals, including those under the theme of Re-engineering the Clinical Research Enterprise. N C R R serves as the lead institute/center partnering with other N I H components to support Exploratory Centers for Interdisciplinary Research, an initiative that seeks to lower the artificial barriers that divide researchers and impede scientific progress. N C R R is the lead N I H institute/center in support of the National Technology Centers for Networks and Pathways to develop new technologies to study the dynamics of molecular interactions within cells. N C R R program staff have assumed the leadership for another Roadmap initiative, the National Centers for Biomedical Computing. This effort will establish the computational infrastructure for biomedical computing, ranging from basic research in computational science to providing the tools and resources that biomedical and behavioral investigators need to do their research.

Initiatives

Accelerate Informatics Support of Clinical Research. N C R R has initiated a needs assessment to ascertain the capabilities that exist for state-of-the-art electronic communication and information management and to determine future capabilities that will be required for biomedical research across its research centers—including biomedical technology research centers, Research Centers in Minority Institutions, Centers of Biomedical Research Excellence and General Clinical Research Centers. The intent of this assessment is to identify the informatics and communication tools and networks investigators need to facilitate biomedical research and also support collaborations among investigators located in less densely populated states. The needs assessment will be completed by the beginning of FY 2006 and will require periodic updating thereafter to be responsive to investigator needs. Based on discussions with the research community, N C R R recognized the need for cyberspace infrastructure to significantly enable information sharing, access and management of vast datasets and transmitting large data objects—for example, brain images. A Biomedical Informatics Research Network (BIRN) has been developed and is the Nation's first test bed for online sharing of research resources and expertise, and for effective data mining for both basic and clinical research. The initial effort focuses on neuroscience since that discipline holds the largest data sets and requires the capacity to transmit large images. Ultimately, the network will enhance the translation of basic research to the clinical research arena. In addition, the network will link researchers with databases in the health-care sector, including NIST, industry, N I H , e-gov, and others. N C R R proposes to introduce and implement the architecture and interface standards that are identified by the needs assessment process.

Expand the Research Subject Advocate (RSA) Program. As clinical research becomes more complex, the risk of adverse reactions in study subjects increases. To help address the public's concern about patient safety, N C R R established support for Research Subject Advocates or Ombudsmen (R S A or R S O) to assure appropriate safety monitoring of research subjects for G C R C -based studies. N C R R initiated the R S A program in 2001, but only for studies conducted on G C R C s across the country. The R S A s serve as advocates for research subjects and also work closely with clinical investigators to be certain they are aware of their responsibilities to research subjects as articulated within federal and state regulations, laws and guidelines that protect

human subjects participating in clinical research studies. In view of the positive impact of the R S A program, N C R R plans to gradually extend the R S A program as a complement to existing institutional activities for human subject protection within the entire G C R C host institution.

Expand Availability of Embryonic Stem Cells from Several Nonhuman Primates. Stem cells hold the potential for providing replacement tissues, damaged by trauma or abnormal development. However, extensive studies in suitable animal models need to be undertaken to determine the factors that modulate stem cell differentiation and may be adapted for therapeutic interventions. N C R R proposes to support research to identify the factors or cytokines, which modulate stem cell differentiation and will support the isolation of several different embryonic stem cell (ESC) lines from the rhesus macaque, baboon, and a few other nonhuman primate species. Isolated cell lines will be distributed via a national resource upon request from qualified investigators and a companion database will track relevant data for each cell line. Information gleaned from these studies also may be applicable to the study of human ESCs.

Career Development for Veterinarians. There is a growing need for well-trained veterinary scientists to manage the specialized animal resource facilities that provide the animal models needed for research on human disease. N C R R will initiate a new program for training veterinarians in animal resource facility management, in combination with research training. This combined approach will be invaluable in view of the rapidly expanding volume of genetic mutants that are frequently immunocompromised and in need of special facilities and husbandry to be certain they are free of infectious disease.

Expand the Capacities for Health Disparities Research. N C R R will extend three initiatives in collaboration with several other N I H Institutes and Centers, with special emphasis on enhancing the clinical research capacity of the eight medical schools affiliated with the Research Centers in Minority Institutions (R C M I) Program to conduct health disparity research. The initiatives to be expanded include the Comprehensive Centers on Health Disparities (C C H D), designed to augment and strengthen institutional clinical research capabilities in an effort to identify the factors contributing to health disparities in racial and ethnic minority populations. The Stroke Prevention and Intervention Research Program (S P I R P) is the first program specifically focused on clinical intervention for stroke, a major health disparity. Finally, the Clinical Research Education and Career Development (C R E C D) award supports the development and implementation of curriculum-based programs in minority institutions. The C R E C D awards support the clinical research training of promising doctoral and postdoctoral candidates, leading to a Master of Science in Clinical Research or a Master of Public Health in a clinically relevant area.

The NIH Neuroscience Blueprint

Overview -- The Blueprint is a framework to enhance cooperation among fifteen N I H Institutes and Centers that support research on the nervous system. Over the past decade, driven by the science, the N I H neuroscience Institutes and Centers have increasingly joined forces through initiatives and working groups focused on specific disorders. The Blueprint builds on this foundation, making collaboration a day-to-day part of how the N I H does business in neuroscience. By pooling resources and expertise, the Blueprint can take advantage of

economies of scale, confront challenges too large for any single Institute, and develop research tools and infrastructure that will serve the entire neuroscience community.

FY2005 -- For fiscal year 2005, the Blueprint participants are developing an initial set of initiatives focused on tools, resources, and training that can have a quick and substantial impact because each builds on existing programs. These initiatives, with the participation of all Blueprint Institutes, include an inventory of neuroscience tools funded by the N I H and other government agencies, enhancement of training in the neurobiology of disease for basic neuroscientists, and expansion of ongoing gene expression database efforts. N C R R ' s current efforts in developing a Biomedical Informatics Research Network (B I R N) serves as the Nation's test bed for online access and management of vast datasets and transmitting large data objects, such as brain images.

FY2006 -- Advances in the neurosciences and the emergence of powerful new technologies offer many opportunities for Blueprint activities that will enhance the effectiveness and efficiency of neuroscience research. Blueprint initiatives for fiscal year 2006 will include systematic development of genetically engineered mouse strains of critical importance to research on nervous system and its diseases and training in critical cross cutting areas such as neuroimaging and computational biology. N C R R ' s support will continue to provide shared biomedical research resources needed by the neuroscience community.

Other Area of Interest

Based on the input of biomedical investigators, high-level administrators in research organizations, scholarly organizations, and N I H senior program staff, N C R R developed its 2004–2008 Strategic Plan: *Challenges and Critical Choices*. At least half of the participants of a two-day forum had no prior history as former N C R R grantees or resource users, which allowed N C R R to receive fresh ideas to address new areas of research. The Strategic Plan is guiding N C R R ' s priorities for programmatic investments, including local and cyberspace-based national networks, research resources, technology development, instrumentation, biological models, and biomedical informatics tools to facilitate research intended to prevent, alleviate, or treat human disease. The initiatives described above are the first steps that N C R R is taking towards addressing the many recommendations included within the Strategic Plan—*Challenges and Critical Choices*.

The following table shows a programmatic display of N C R R funding.

National Center for Research Resources
Funding by Division and Selected Program Areas
(Dollars in thousands)

	FY 2004	FY 2005	FY 2006
	Actual	Approp.	Estimate
Clinical Research:	347,025	359,409	359,410
General Clinical Research Centers (M01's)	275,318	286,118	286,118
Career Development Program	34,407	35,867	35,867
Science Education Partnership Award	16,141	16,141	16,141
Clinical Research Resources	21,159	21,283	21,284
Biotechnology Research	173,664	168,984	170,369
Biotechnology Research Resources	102,927	102,908	104,189
Shared Instrumentation Grants	70,737	66,076	66,180
Comparative Medicine	177,374	177,355	186,921
PRCs (P51's)	71,949	71,949	75,086
Career Development Program	3,720	3,720	3,720
Comparative Medicine - Other	101,705	101,686	108,115
Research Infrastructure	398,150	318,531	289,221
Research Ctrs in Minority Institutions (Ctrs)	52,754	52,754	53,204
Construction & Animal Facilities Improvement	131,398	42,650	12,890
Institutional Development	213,044	222,208	222,208
Other Research Infrastructure	954	919	919
SBIR/STTR	27,132	27,943	28,339
RMS	26,285	27,618	28,402
Roadmap (non RMS)	3,591	6,496	8,855
Non Program R & D Contracts	25,735	28,754	28,686
TOTAL	1,178,956	1,115,090	1,100,203

The FY 2004 amounts of \$213.0 million for the Institutional Development Award Program (IDeA) and \$275.3 million for General Clinical Research Centers (GCRC) reflect reallocations that were not identified in the September 16, 2004 letter to the Appropriations Committees on anticipated FY 2004 NIH budget reallocations. The additional reallocations were as follows:

IDeA: The conference bill provided \$213.7 million for IDeA (post-rescission). The September 16, 2004 letter indicated that \$9 million was being reallocated from IDeA center grants to fund RPGs in IDeA states. NCRR did not use the entire \$9 million and reallocated \$1.5 from RPG's and an additional \$4.0 from Research Centers to Other Research to support additional research infrastructure grants in the IDeA states.

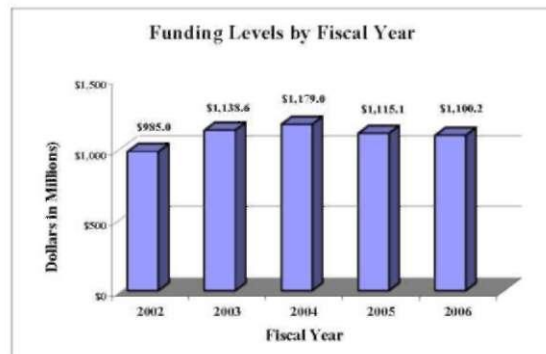
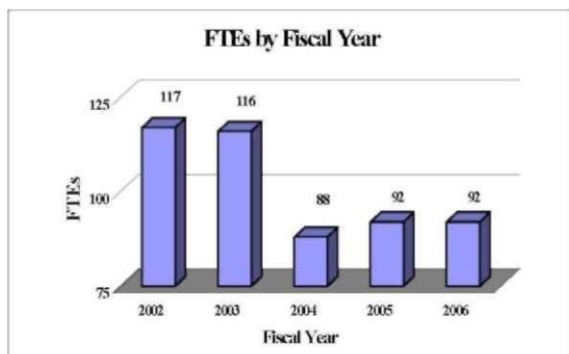
G C R C : The Conference Report identified \$320.0 million for G C R C . In subsequent interactions with the Subcommittees, it was determined that \$285.2 million was the intended amount, as the higher figure included other activities such as research career awards at G C R C 's . However, without informing the Appropriations Committees, N C R R reallocated \$9.9 million from G C R C grants to other mechanisms to support additional research career scholars, expansion of the biomedical research informatics networks, and other high priority clinical research resources.

N C R R has taken steps to implement a new funds management system in FY 2005. This, along with more rigorous management oversight, will ensure that the funds received in FY 2005 are used in accordance with Congressional intent and the plans that have been provided.

Budget Policy

The Fiscal Year 2006 budget request for the N C R R is \$1,100,203,000 a decrease of \$14,887,000 and 1.35 percent from the FY 2005 Appropriation. Also included in the FY 2006 request, is N C R R 's support for the trans-NIH Roadmap initiatives, estimated at 0.89% of the FY 2006 budget request. This Roadmap funding is distributed through the mechanisms of support, consistent with the anticipated funding for the Roadmap initiatives. A full description of this trans-NIH program may be found in the N I H Overview.

A five year history of FTEs and Funding Levels for N C R R are shown in the graphs below.



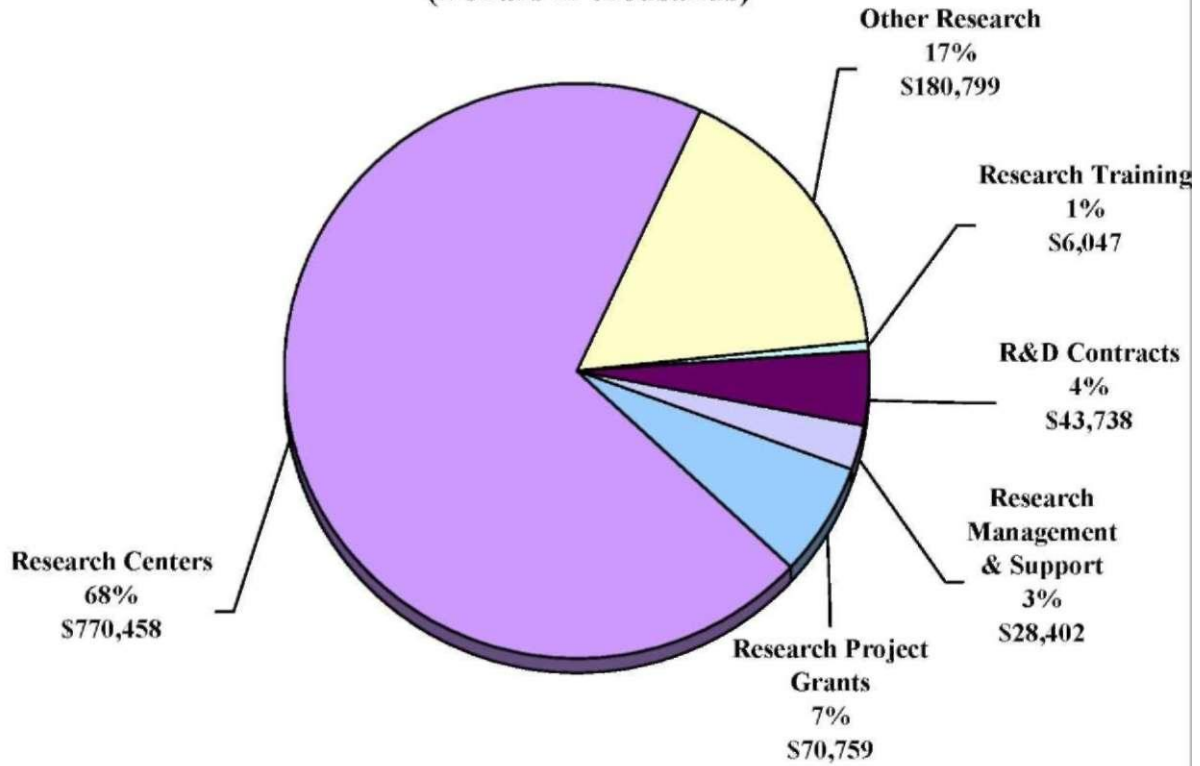
NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while pursuing new research opportunities. We estimate that the average cost of competing RPG's will be \$277,000 in FY 2006. While no inflationary increases are provided for direct, recurring costs in non-competing RPG's, where the N C R R has committed to a programmatic increase in an award, such increases will be provided.

Advancement in medical research is dependent on attracting, training, and retaining the best and the brightest individuals to pursue careers in biomedical and behavioral research. In the FY 2006 request, most stipend levels for individuals supported by the Ruth L. Kirschstein National Research Service Awards are maintained at the FY 2005 levels. To help prevent the potential attrition of our next generation of highly trained post-doctoral trainees, stipend levels for post-docs with 1-2 years of experience are increased by 4.0 percent. This will bring these stipends closer to the goal NIH established for post-doc stipends in March 2000. In addition, individual post-doctoral fellows will receive an increase of \$500 in their institutional allowance for rising health benefit costs. The need for increased health benefits is particularly acute for these post-doctoral trainees, who, because of their age and stage of life are more likely to have family responsibilities. The increases in stipends and health insurance are financed within the FY 2006 request by reducing the number of Full-Time Training Positions. The NIH believes that it is important to properly support and adequately compensate those who are participating in these training programs so that the programs can continue to attract and retain the trainees most likely to pursue careers in biomedical, behavioral and clinical research.

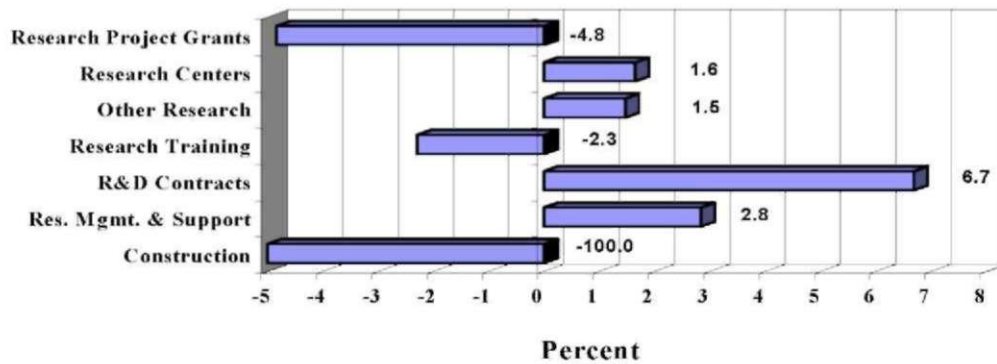
The Fiscal Year 2006 request includes funding for 337 research centers, 493 other research grants, including 174 clinical career awards, and 75 R & D contracts. Research Management and Support receives an increase of 2.8%. In FY 2006, funds are also provided for support of the national repository and characterization center for human embryonic stem cell lines currently eligible for Federal funding. N C R R is also participating in the NIH Neuroscience Blueprint. The FY 2006 request includes \$400,000 for a variety of Neuroscience Blueprint initiatives, including neuroscience cores, training initiatives, and the Neuromouse project. Consistent with the FY 2005 President's Budget Request, no funds for extramural construction are included in the FY 2006 request

The mechanism distribution by dollars and percent change are displayed below:

**FY 2006 Budget Mechanism
(Dollars in thousands)**



**FY 2006 Estimate
Percent Change from FY 2005 Mechanism**



Budget Mechanism - Total

MECHANISM	FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research Grants:						
Research Projects:						
Noncompeting	83	\$29,058,000	87	\$35,501,000	82	\$26,712,000
Administrative supplements	(6)	875,000	(1)	155,000	(0)	0
Competing:						
Renewal	10	5,459,000	12	6,550,000	12	6,616,000
New	30	11,768,000	27	4,275,000	45	9,161,000
Supplements	1	179,000	0	0	0	0
Subtotal, competing	41	17,406,000	39	10,825,000	57	15,777,000
Subtotal, RPGs	124	47,339,000	126	46,481,000	139	42,489,000
SBIR/STTR	98	27,078,000	100	27,874,000	100	28,270,000
Subtotal, RPGs	222	74,417,000	226	74,355,000	239	70,759,000
Research Centers:						
Specialized/comprehensive	95	201,214,000	106	217,419,000	106	225,360,000
Clinical research	108	287,475,000	106	298,424,000	106	298,424,000
Biotechnology	52	79,959,000	52	80,218,000	52	81,216,000
Comparative medicine	55	108,973,000	55	109,168,000	55	112,254,000
Research Centers in Minority Institutions	18	52,754,000	18	52,754,000	18	53,204,000
Subtotal, Centers	328	730,375,000	337	757,983,000	337	770,458,000
Other Research:						
Research careers	185	38,347,000	171	40,146,000	174	40,580,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	0	0	0	0	0	0
Biomedical research support	163	71,843,000	145	66,101,000	145	66,210,000
Minority biomedical research support	0	0	0	0	0	0
Other	171	74,045,000	174	71,940,000	174	74,009,000
Subtotal, Other Research	519	184,235,000	490	178,187,000	493	180,799,000
Total Research Grants	1,069	989,027,000	1,053	1,010,525,000	1,069	1,022,016,000
Research Training:	FTEs		FTEs		FTEs	
Individual awards	2	73,000	2	89,000	2	89,000
Institutional awards	139	5,753,000	148	6,100,000	146	5,958,000
Total, Training	141	5,826,000	150	6,189,000	148	6,047,000
Research & development contracts (SBIR/STTR)	78 (1)	39,310,000 (54,000)	74 (0)	40,998,000 (69,000)	75 (0)	43,738,000 (69,000)
	FTEs		FTEs		FTEs	
Intramural research	0	0	0	0	0	0
Research management and support	88	26,312,000	92	27,618,000	92	28,402,000
Cancer prevention & control	0	0	0	0	0	0
Construction		118,508,000		29,760,000		0
Buildings and Facilities		0		0		0
Total, N C R R	88	1,178,983,000	92	1,115,090,000	92	1,100,203,000
(RoadMap Support)		(4,049,000)		(7,050,000)		(9,828,000)
(Clinical Trials)		(94,792,000)		(98,361,000)		(97,885,000)

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2004		FY 2005		FY 2006		Change	
	Actual		Appropriation		Estimate			
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural Research:								
Extramural Research Resources		\$1,152,671		\$1,087,472		\$1,071,801		(\$15,671)
Subtotal, Extramural Research		1,152,671		1,087,472		1,071,801		(15,671)
Research Management & Support	88	26,312	92	27,618	92	28,402	0	784
Total	88	1,178,983	92	1,115,090	92	1,100,203	0	(14,887)

Summary of Changes

FY 2005 Estimate	\$1,115,090,000																																																																																																			
FY 2006 Estimated Budget Authority	1,100,203,000																																																																																																			
Net change	(14,887,000)																																																																																																			
	<table border="1"> <thead> <tr> <th rowspan="2">CHANGES</th> <th colspan="2">FY 2005</th> <th colspan="2">Change from Base</th> </tr> <tr> <th>FTEs</th> <th>Budget Authority</th> <th>FTEs</th> <th>Budget Authority</th> </tr> </thead> <tbody> <tr> <td>A. Built-in:</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td> 1. Intramural research:</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td> a. Within grade increase</td> <td></td> <td align="right">\$0</td> <td></td> <td align="right">\$0</td> </tr> <tr> <td> b. Annualization of January 2005 pay increase</td> <td></td> <td align="right">0</td> <td></td> <td align="right">0</td> </tr> <tr> <td> c. January 2006 pay increase</td> <td></td> <td align="right">0</td> <td></td> <td align="right">0</td> </tr> <tr> <td> d. One less day of pay</td> <td></td> <td align="right">0</td> <td></td> <td align="right">0</td> </tr> <tr> <td> e. Payment for centrally furnished services</td> <td></td> <td align="right">0</td> <td></td> <td align="right">0</td> </tr> <tr> <td> f. Increased cost of laboratory supplies, materials, and other expenses</td> <td></td> <td align="right">0</td> <td></td> <td align="right">0</td> </tr> <tr> <td> Subtotal</td> <td></td> <td></td> <td></td> <td align="right">0</td> </tr> <tr> <td> 2. Research Management and Support:</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td> a. Within grade increase</td> <td></td> <td align="right">11,398,000</td> <td></td> <td align="right">200,000</td> </tr> <tr> <td> b. Annualization of January 2005 pay increase</td> <td></td> <td align="right">11,398,000</td> <td></td> <td align="right">106,000</td> </tr> <tr> <td> c. January 2006 pay increase</td> <td></td> <td align="right">11,398,000</td> <td></td> <td align="right">202,000</td> </tr> <tr> <td> d. One less day of pay</td> <td></td> <td align="right">11,398,000</td> <td></td> <td align="right">(45,000)</td> </tr> <tr> <td> e. Payment for centrally furnished services</td> <td></td> <td align="right">3,030,000</td> <td></td> <td align="right">15,000</td> </tr> <tr> <td> f. Increased cost of laboratory supplies, materials, and other expenses</td> <td></td> <td align="right">11,590,000</td> <td></td> <td align="right">140,000</td> </tr> <tr> <td> Subtotal</td> <td></td> <td></td> <td></td> <td align="right">618,000</td> </tr> <tr> <td> Subtotal, Built-in</td> <td></td> <td></td> <td></td> <td align="right">618,000</td> </tr> </tbody> </table>	CHANGES	FY 2005		Change from Base		FTEs	Budget Authority	FTEs	Budget Authority	A. Built-in:					1. Intramural research:					a. Within grade increase		\$0		\$0	b. Annualization of January 2005 pay increase		0		0	c. January 2006 pay increase		0		0	d. One less day of pay		0		0	e. Payment for centrally furnished services		0		0	f. Increased cost of laboratory supplies, materials, and other expenses		0		0	Subtotal				0	2. Research Management and Support:					a. Within grade increase		11,398,000		200,000	b. Annualization of January 2005 pay increase		11,398,000		106,000	c. January 2006 pay increase		11,398,000		202,000	d. One less day of pay		11,398,000		(45,000)	e. Payment for centrally furnished services		3,030,000		15,000	f. Increased cost of laboratory supplies, materials, and other expenses		11,590,000		140,000	Subtotal				618,000	Subtotal, Built-in				618,000
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Summary of Changes—continued

CHANGES	2005 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	87	\$35,656,000	(5)	(\$8,944,000)
b. Competing	39	10,825,000	18	4,952,000
c. SBIR/STTR	100	27,874,000	0	396,000
Total	226	74,355,000	13	(3,596,000)
2. Research centers	337	757,983,000	0	12,475,000
3. Other research	490	178,187,000	3	2,612,000
4. Research training	150	6,189,000	(2)	(142,000)
5. Research and development contracts	74	40,998,000	1	2,740,000
Subtotal, Extramural				14,089,000
6. Intramural research	0	0	0	0
7. Research management and support	92	27,618,000	0	166,000
8. Construction		29,760,000		(29,760,000)
Subtotal, program		1,115,090,000	0	(15,505,000)
Total changes	92		0	(14,887,000)

**NATIONAL INSTITUTES OF HEALTH
National Center for Research Resources**

Budget Authority by Object

	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	92	92	0
Full-time equivalent of overtime & holiday hours	0	0	0
Average ES salary	\$149,897	\$153,345	\$3,448
Average G M / G S grade	12.8	12.8	0.0
Average G M / G S salary	\$77,556	\$79,340	\$1,784
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	\$0	\$0	\$0
Average salary of ungraded positions	\$132,507	\$135,555	\$3,048
OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	\$8,259,000	\$8,594,000	\$335,000
11.3 Other than Full-Time Permanent	769,000	801,000	32,000
11.5 Other Personnel Compensation	215,000	224,000	9,000
11.7 Military Personnel	0	0	0
11.8 Special Personnel Services Payments	24,000	24,000	0
Total, Personnel Compensation	9,267,000	9,643,000	376,000
12.0 Personnel Benefits	2,131,000	2,218,000	87,000
12.1 Military Personnel Benefits	0	0	0
13.0 Benefits for Former Personnel	0	0	0
Subtotal, Pay Costs	11,398,000	11,861,000	463,000
21.0 Travel & Transportation of Persons	434,000	448,000	14,000
22.0 Transportation of Things	47,000	48,000	1,000
23.1 Rental Payments to G S A	0	0	0
23.2 Rental Payments to Others	1,000	1,000	0
23.3 Communications, Utilities & Miscellaneous Charges	118,000	120,000	2,000
24.0 Printing & Reproduction	337,000	349,000	12,000
25.1 Consulting Services	8,508,000	9,060,000	552,000
25.2 Other Services	490,000	648,000	158,000
25.3 Purchase of Goods & Services from Government Accounts	38,900,000	42,824,000	3,924,000
25.4 Operation & Maintenance of Facilities	5,000	5,000	0
25.5 Research & Development Contracts	5,285,000	5,604,000	319,000
25.6 Medical Care	0	0	0
25.7 Operation & Maintenance of Equipment	895,000	913,000	18,000
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	54,083,000	59,054,000	4,971,000
26.0 Supplies & Materials	166,000	174,000	8,000
31.0 Equipment	430,000	458,000	28,000
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	1,048,074,000	1,027,690,000	(20,384,000)
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	2,000	0	(2,000)
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	1,103,692,000	1,088,342,000	(15,350,000)
Total Budget Authority by Object	1,115,090,000	1,100,203,000	(14,887,000)

Salaries and Expenses

OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	\$8,259,000	\$8,594,000	\$335,000
Other Than Full-Time Permanent (11.3)	769,000	801,000	32,000
Other Personnel Compensation (11.5)	215,000	224,000	9,000
Military Personnel (11.7)	0	0	0
Special Personnel Services Payments (11.8)	24,000	24,000	0
Total Personnel Compensation (11.9)	9,267,000	9,643,000	376,000
Civilian Personnel Benefits (12.1)	2,131,000	2,218,000	87,000
Military Personnel Benefits (12.2)	0	0	0
Benefits to Former Personnel (13.0)	0	0	0
Subtotal, Pay Costs	11,398,000	11,861,000	463,000
Travel (21.0)	434,000	448,000	14,000
Transportation of Things (22.0)	47,000	48,000	1,000
Rental Payments to Others (23.2)	1,000	1,000	0
Communications, Utilities and Miscellaneous Charges (23.3)	118,000	120,000	2,000
Printing and Reproduction (24.0)	337,000	349,000	12,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	1,536,000	1,867,000	331,000
Other Services (25.2)	490,000	648,000	158,000
Purchases from Govt. Accounts (25.3)	10,228,000	11,579,000	1,351,000
Operation & Maintenance of Facilities (25.4)	5,000	5,000	0
Operation & Maintenance of Equipment (25.7)	895,000	913,000	18,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	13,154,000	15,012,000	1,858,000
Supplies and Materials (26.0)	166,000	174,000	8,000
Subtotal, Non-Pay Costs	14,257,000	16,152,000	1,895,000
Total, Administrative Costs	25,655,000	28,013,000	2,358,000

NATIONAL INSTITUTES OF HEALTH

National Center for Research Resources

SIGNIFICANT ITEMS IN HOUSE AND SENATE APPROPRIATIONS COMMITTEE REPORTS

FY 2005 House Appropriations Committee Report Language (H. Rpt. 108-636)

Item

Institutional Development Award (IDeA) - The Committee has identified \$222,000,000 for this program, which is the same as the Administration request and \$8,000,000 above the fiscal year 2004 level. (page 100)

Action taken or to be taken

As instructed by the Senate, N C R R provided \$224,000,000 to the Institutional Development Award program in FY 2005. After across the board reductions, the final allocation is \$222,208,000. Funding for the specific programs within IDeA is—Centers of Biomedical Research Excellence (COBRE): \$134,912,000; IDeA Networks of Biomedical Research Excellence (INBRE): 80,352,000. The remaining funds of \$6,944,000 will support the second year of co-funding with other NIH Institutes and Centers for research project grants to individuals within the IDeA states.

In developing the FY 2005 budget allocations, N C R R first provided funds for construction as instructed in the Public Law. Then funds for statutory and policy increases in program evaluation assessments, small business research program awards, trans-NIH activities, and salaries and expenses were allocated. Lastly, N C R R reduced the Shared Instrumentation Grant Program by \$4,661,000, or six percent, to accommodate other Committee Report language earmarks for IDeA and General Clinical Research Centers (M01). The remaining N C R R programs: National Primate Research Centers, Biotechnology Research Resources, Research Centers in Minority Institutions, other Clinical Research Resources, Science Education Partnership Awards, and Comparative Medicine- laboratory animal resource were held to FY 2004 levels.

Item

National primate research centers- The Committee values the important role played by the eight national primate centers. In the past several years, there has been an extensive expansion of the breadth and volume of demands for primate center resources. The Committee encourages N C R R to strengthen the base support for these centers and to conduct an assessment of primate center resource needs. This assessment should be submitted to the Committee at the time of the FY 2006 budget request. (page 100)

Action taken or to be taken

The National Primate Research Centers (NPRCs), in combination with other non-human primate resources supported by N C R R , have played a key role in supporting the expanding needs for non-human primate species used for critical investigations into biomedical research ranging from A I D S to neurodegenerative diseases. In 2001, an independent contractor working with 11 scientists with varied backgrounds and experience related to non-human primate research conducted an evaluation of the N P R C program. Based on their recommendations, discussions held by various components of the N I H , and analyses from the scientific research community at large, it was suggested that continued expansions of the N C R R -funded N P R C program was appropriate. Recommendations for expansions and funding increases fall into the following areas: First, increase the availability of primate models by expanding existing and implementing new breeding programs, as well as expanding use of alternative species of primates (Primate Model Investment). Second, increase of the quality and capacity of primate housing and breeding facilities and the availability of state-of-the-art diagnostic and clinical equipment (Primate Infrastructure Investment). And third, increase the number of personnel trained in primate care and management (Primate Care and Research Personnel Investment).

N C R R recognizes the importance of increasing and expanding primate breeding programs, primate housing facilities and related equipment, and training of specialized personnel with knowledge in primate biology. In response, N C R R , with additional support provided by the N I H Office of AIDS Research, has and will continue to address these needs. Specifically, the F Y 2004 N C R R funding for the N P R C program increased by seven percent over F Y 2003. In addition, in F Y 2004, N I H 's Office of AIDS Research provided an additional \$5 million in supplemental funding to the N P R C s . The N P R C program received facility improvement and expansion support in excess of \$15.8 million in F Y 2004. N C R R also started to address the need for personnel training by providing supplemental training funds for veterinarians to the N P R C s in their F Y 2004 budgets. And lastly, in addition to the eight centers that make up the N P R C program, N C R R supports a number of other primate resources, including twelve SPF non-human primate breeding colonies, primate resources supporting both old- and new-world monkeys, and programs that focus on non-human primate models for A I D S research, among others. These resources received over \$28 million in F Y 2004.

Furthermore, through N C R R 's support of a range of primate breeding colonies and other resources related to primate research which result in improved quality of non-human primate models and availability of N P R C s and other associated biological materials, the N P R C s can focus their support on base operations and specific demands from the biomedical research community. Building a network and partnership among the N C R R -supported non-human primate biomedical research and behavioral resource communities has greatly facilitated all aspects of primate-related research.

International collaborations resulting in increased access to non-human primate breeding facilities represents one avenue to achieve an increase in available primates. N C R R 's approach is to work through individual N P R C s , which have in the past, and continue to develop science programs in foreign countries. These programs include resource development (breeding colonies), joint research projects, education and training programs for faculty and students, and conservation of naturally occurring primate populations in the foreign countries. N C R R supports

these efforts by providing research opportunities and infrastructure support as well as logistic assistance for the continued development of these programs

Item

Research centers at minority institutions (RCMI) - The Committee continues to recognize the important role played by minority institutions at both the graduate and undergraduate level in addressing the health research and training needs of minority populations. These programs help facilitate the preparation of a new generation of scientists at these institutions. The RCMI program continues to address these problems. The Committee encourages N C R R to strengthen participation from minority institutions. The Committee also encourages N C R R to work with minority institutions with a track record of producing minority scholars in science and technology. (page 100)

Action taken or to be taken

The Research Centers in Minority Institutions (RCMI) program continues to develop the research infrastructure of predominantly underrepresented minority institutions that award doctorates in the health professions or a health-related science, and expand the capacity for clinical research by developing the appropriate infrastructure at minority institutions with affiliated medical schools through the RCMI Clinical Research Infrastructure Initiative. N C R R 's Division of Research Infrastructure has expanded two additional activities, and proposes to develop one new initiative to increase the capacity of RCMI institutions to perform basic, translational, and clinical research. The Comprehensive Centers on Health Disparities will begin implementation phases to develop sustainable, replicable and culturally appropriate prevention and/or intervention research programs targeted to minority populations designed to decrease the incidence and prevalence of diseases such as chronic kidney disease, stroke, and HIV/AIDS. The Comprehensive Centers on Health Disparities enhance opportunities for multi-disciplinary research collaborations between minority institutions and institutions with more established research programs in the identified areas and increase the role of research in maintaining a vigorous and stimulating academic environment that will inspire students and fellows to pursue careers that focus on eliminating health disparities. Similarly, the Clinical Research Education and Career Development awards, that support the development and implementation of curriculum-dependent programs in minority institutions to train doctoral and postdoctoral candidates in clinical research, have been increased from two to five institutions, and there is a consensus among N C R R and the seven other NIH institutes and centers that co-fund these awards to work toward their continuation beyond the initial five year commitment.

The newest initiative is the RCMI Translational Research Network, a cooperative research network to facilitate clinical research in health disparity areas as recommended in the N C R R 2004-2008 Strategic Plan. This Network will consist of a consortium of clinical investigators from the various RCMI programs; other NIH-supported Clinical Research Centers; relevant organizations, including community health centers, with an interest in health disparity areas; and a data and technology coordinating center. The goal is to facilitate development of multi-site clinical research in health disparity areas; distributed clinical data management, incorporating novel approaches and technologies for data management; and access to information related to health disparities for researchers, academic and practicing physicians, patients, and the lay public.

The 18 institutions receiving funding via the various R C M I programs have an outstanding track record of producing minority scholars in science and technology. Some examples include the following: Meharry Medical College was ranked #1 in the number of PhDs awarded to African Americans 1999-2003; Tuskegee University graduates account for over 75 percent of the African American Veterinarians annually; the University of Texas at San Antonio was ranked #1 in the number of BS degrees in the Biological Sciences awarded to Hispanics in 2003; the University of Hawaii was ranked #2 in the number of doctorates awarded to Asian Americans in 1999; Jackson State University was ranked #15 in the number of PhDs awarded to African Americans in all areas in 2003; and Ponce School of Medicine was ranked #1 in the number of doctorates awarded to Hispanics among private Universities in 2003.

Item

General clinical research centers (GCRCs) - The 79 NCRR-funded general clinical research centers across the country are important to NIH efforts to translate basic science discoveries into vaccines, treatments, and cures for disease. Approximately 10,000 researchers use GCRCs each year for patient-oriented research focused on a wide variety of diseases. The Committee is concerned that NCRR has in the past included activities not related to GCRCs in NCRR-reported funding totals for the GCRCs. In the future, the Committee expects NCRR to restrict its reporting to funds that go directly to GCRCs instead of including general clinical research activities in those totals. (page 100)

Action taken or to be taken

NCRR has included a program activity on page 17, which provides a better analysis of all NCRR programs, including clinical research and the General Clinical Research Centers (M01). Although Congress has expressed an interest in the funding level for the network of GCRCs paid solely through the M01 mechanism, it is important to note that NCRR also provides support for clinical research infrastructure through other means as well. For the past few years, the GCRCs have been awarded almost 80 percent of the funds that the Division for Clinical Research Resources awards for clinical research.

In 1974, NCRR initiated a clinical research career development program, the Clinical Associate Physician (CAP) program, to maintain the pool of clinical researchers. NCRR funded meritorious CAP applications through competitive supplements to the parent GCRC (M01) grant until FY 2000 when they were replaced by the new NIH "K23" award. As a result, the previous CAP supplements were "stepped out" of the core grant and moved to the "Other Research" budget mechanism in keeping with NIH practice.

NCRR continues to support complementary efforts to leverage the needs of the entire clinical research enterprise. For example, the NCRR 2004-2008 Strategic Plan *Challenges and Critical Choices*, emphasized the goal of ensuring that the clinical research community has ready access to specialized resources. One recommendation was to create a high-throughput national resource for genotyping and phenotyping. NCRR determined that this was a high priority need and in FY 2004 a new national resource was funded. This high-capacity resource, the National Center for High-Throughput Genotyping and Analysis, will allow U.S. researchers to quickly and cost-

effectively carry out large-scale studies of genetic variation in humans and animals that will advance disease gene identification. Support for this, and other non-M01 clinical research resource centers account for about 3 percent of the annual clinical research budget.

The profile of infrastructure support for clinical research has changed and will continue to evolve to take advantage of the research findings of the past several years—sequencing the human genome, better imaging techniques, isolation and characterization of human embryonic stem cells, scaleable computing, and modeling of data. Funds appropriated to support clinical research infrastructure are provided through the specific mechanisms intended for those resources. See the table below for a further breakout of specific funding in clinical research resources:

National Center for Research Resources
Funding for Clinical Research Resources
(Dollars in thousands)

	FY 2004		FY 2005		FY 2006	
	No.	Amount	No.	Amount	No.	Amount
Clinical Research Centers						
General Clinical Resource Centers (M01)	80	275,318	80	286,118	80	286,118
Other Clinical Resource Centers	28	12,157	26	12,306	26	12,306
Sub-Total, Clinical Research Centers	108	287,475	106	298,424	106	298,424
Other Clinical Research Support						
Clinical Research Career Development	147	34,407	124	35,867	130	35,867
Loan Repayment Program	60	2,927	60	2,896	60	2,896
Science Education Partnership Awards	56	16,141	56	16,141	55	16,141
Other Research Support	12	6,075	11	6,081	9	6,082
Sub-Total, Other Clinical Res Support		59,550		60,985		60,986
Total, Clinical Research Resources		347,025		359,409		359,410

Item

Islet resource centers - The Committee encourages NCRN to accelerate the efforts of the islet cell resource centers to improve the quality and yield of islets, to improve the storage and transportability of islets to enhance regional distribution of these cells, and to serve as national resource centers to support national efforts in islet transplantation by providing human islets for both basic research and clinical islet transplantation. (page 100)

Action taken or to be taken

Many type 1 diabetic patients who have received pancreatic islet transplants no longer require insulin injections. However, additional innovative clinical protocols are needed to optimize the effectiveness and clinical durability of this procedure. This requires that supplies of human islets of the highest quality be made available to clinical researchers engaged in such efforts.

Accordingly, the National Center for Research Resources (N C R R) with the support of the National Institute of Diabetes and Digestive and Kidney Diseases and the Juvenile Diabetes Research Foundation, established a consortium often Islet Cell Resources (ICRs) throughout the country to harvest, isolate and distribute islets for use in approved clinical transplantation protocols.

N C R R provides advice and grant support to accelerate I C R efforts to 1) generate and distribute the highest quality of human pancreatic islets to clinical investigators for transplantation into patients afflicted with severe Type 1 diabetes mellitus, 2) optimize techniques for isolation, purification, storage, transportability and characterization of human pancreatic islets for use in clinical protocols, 3) generate and distribute human pancreatic islets to investigators for use in laboratory-based research studies, and 4) serve as national resource centers that support efforts in islet transplantation throughout the Nation.

Currently, less than one-half of the islets present in a donor pancreas are recoverable for clinical transplantation. Consequently, N C R R has organized efforts within the I C R s to improve techniques to obtain higher yields of functional islets, preserve viability and function during storage and transport and to identify donor and recipient characteristics that are associated with the best clinical outcomes. N C R R has accomplished this by establishing common clinical isolation protocols, establishing electronic databases and sharing information among the I C R s.

Item

Cystic fibrosis - N C R R has played a leadership role in providing clinical researchers with the tools they need to conduct their research and to undertake and complete clinical trials efficiently. N C R R has supported the development of shared resources for clinical researchers, an activity that has strengthened the Nation's clinical research capabilities. The Committee commends N C R R for its support of clinical trials networks, including the cystic fibrosis clinical trials network. The Committee suggests that N C R R consider supporting a cystic fibrosis biospecimen repository, which would serve as an important resource to CF researchers and function as a model for other diseases. (page 100)

Action taken or to be taken

Cystic fibrosis is a rare genetic disease in which thick sticky secretions block passages in the lung, resulting in an increased number of respiratory infections. Similar thick secretions affect the pancreas leading to digestive problems. The Office of Rare Diseases has set up a trans-NIH planning committee to look at the issue of repositories for rare diseases. Many categorical Institutes have already established repositories for specific rare disease samples, including NIDDK, NHLBI, NICHD, and NIGMS. While N C R R's mission is to provide resources that are of value to a broad range of researchers in all areas of science and not in specific diseases, we are participating with other ICs and the Office of Rare Diseases in planning a conference to address biospecimen repositories for rare diseases.

Item

Animal Research - The Committee encourages N C R R to support research and development focused on improving methods for recognizing, assessing, and alleviating pain and distress in research animals. (page 156)

Action taken or to be taken

One of the primary tenets of the federal regulations governing research with animals is recognizing, reducing or alleviating unnecessary pain and distress. The N C R R has long recognized the impact that stress, distress and pain can have on the welfare of laboratory animals and research outcomes. Since 1988, N C R R has invited grant applications for investigations into research methods that do not use vertebrate animals, use fewer animals, or that produce less pain and distress in animals used for biomedical research. Through its Division of Comparative Medicine, N C R R supports improvement of the health and well-being of laboratory animals by providing grants to investigators to study anesthetics and analgesics to minimize or eliminate pain and distress, environmental and behavioral factors that affect the emotional component of pain perception, and animal housing conditions and psychological well-being of laboratory animals. N C R R encourages researchers to submit proposals to improve methods for evaluating and alleviating pain, distress and discomfort, development and evaluation of environmental enrichment techniques and improved housing and husbandry technology.

Fulfilling the commitment to providing the most humane and ethical care to research animals as well as maintaining research quality, N C R R also provides grants to upgrade, improve and construct new animal facilities and housing that will have a positive impact on the health and psychological well-being of animals. Additionally, N C R R has provided funding for several information resources including the National Academy of Sciences' Institute for Laboratory Animal Research which develops guidelines and disseminates information on the scientific, technological and ethical use of animals and related biological resources in research, testing and education.

Item

Cystic Fibrosis - The Committee commends N C R R for its support of clinical trials networks, including cystic fibrosis clinical trials networks. A number of research institutions and private organizations are engaged in efforts to initiate or provide ongoing support to biospecimen repositories or specimen banks. The Committee recognizes that N C R R has supported programs to provide biomaterials to researchers and recommends that N C R R continue such efforts, including collaborative efforts with private sector entities. The Committee recommends that N C R R support a cystic fibrosis biospecimen repository, which would serve as an important resource to CF researchers and function as a model for other diseases. (page 156)

Action taken or to be taken

Please refer to page N C R R - 3 2 of this document for N C R R 's response to this significant item regarding Cystic Fibrosis.

Item

Extramural Facilities Construction at Minority Institutions - The Committee encourages N C R R to give priority consideration to supporting extramural facilities construction projects at historically minority institutions which have developed a comprehensive plan to address the disproportionate impact of cancer in minority communities. (page 156)

Action taken or to be taken

N C R R has supported a number of extramural facilities construction projects at historically minority institutions. In FY 2004, construction awards were made to Meharry Medical College, Morehouse School of Medicine, and Howard University School of Pharmacy which are historically minority institutions that are conducting cancer research projects. The awards will provide support for the following projects: (1) consolidation of research on health issues that disproportionately affect women of color conducted by investigators in the departments of obstetrics and gynecology and psychiatry; the studies focus on breast cancer, reproductive health, and socio-behavioral dimensions of HIV / A I D S (Meharry); (2) upgrades to the animal care and use program, that will benefit breast cancer and cardiovascular disease research in African Americans (Morehouse); and (3) construction of a state-of-the-art research laboratory facility that will house the Center for Drug Research and Development that will benefit prostate and breast cancer research projects (Howard).

In FY 2002 and FY 2003 construction awards were made to the Charles R. Drew University of Medicine and Science Biomedical Research Unit to provide state-of-the-art research facilities for complex metabolic disorders (diabetes, hypertension, and obesity), HIV, drug addiction, cardiovascular and related diseases, and cancer research projects. Drew serves the needs of disadvantaged and largely uninsured constituents who are located in South Central Los Angeles.

N C R R will continue to encourage historically minority institutions to apply for extramural construction projects in conjunction with developing plans to address the disproportionate impact of cancer and other diseases in the minority community.

Item

General Clinical Research Centers—The 79 N C R R -funded General Clinical Research Centers across the country are critical to N I H efforts to translate basic science discoveries into vaccines, treatments, and cures for disease. Approximately 10,000 researchers use G C R C s each year for patient-oriented research focused on a wide variety of diseases. A recent publication by the members of the Institute of Medicine Clinical Research Roundtable described the G C R C s as "an extraordinarily important model for how clinical research can be done" within academic health centers and recommended an expansion of the program. To enhance the capacity of these Centers to support patient-oriented research, the Committee has provided \$300,000,000 for G C R C Grants (M01), an increase of \$14,800,000 over fiscal year 2004. To clarify its intentions, the Committee emphasizes that this funding should be allocated directly to N C R R -funded G C R C s through or as a supplement to the M01 mechanism to support clinical research infrastructure such as inpatient and outpatient beds, laboratory services, research nutrition services, and statistical support for publicly and privately funded clinical investigators. The

Committee asks to be informed in advance of any new initiatives within the G C R C program that entail expenditure or reallocation of funds. (page 156)

Action taken or to be taken

Please refer to page N C R R - 3 0 of this document for N C R R ' s response to this significant item on General Clinical Research Centers.

Item

General Clinical Research Centers - The Committee encourages the N C R R to upgrade G C R C facilities with the sophisticated technologies needed to apply the mapping of the human genome to the study of human disease and respond to the threat of bioterrorism; expand staffing as recently mandated by N C R R to assure patient safety; and support local G C R C pilot projects as approved by the N C R R Advisory Council. (page 157)

Action taken or to be taken

N C R R continues to seek to upgrade G C R C facilities with the sophisticated technologies needed to apply the mapping of the human genome to the study of human disease and respond to the threat of bioterrorism. We also support complementary efforts to leverage the needs of the entire clinical research enterprise. To meet these needs, the N C R R 2004-2008 Strategic Plan, *Challenges and Critical Choices*, emphasized the goal of ensuring that the clinical research community has ready access to specialized resources. One recommendation was to create a high-throughput national resource for genotyping and phenotyping. N C R R determined that this was a high priority need and in FY 2004 a new national resource was funded. This high-capacity resource, the National Center for High-Throughput Genotyping and Analysis, will allow U.S. researchers to quickly and cost-effectively carry out large-scale studies of genetic variation in humans and animals that will advance disease gene identification.

As clinical research becomes more complex, the risk of adverse reactions in study subjects increases. To help address the public's concern about patient safety, N C R R established support for Research Subject Advocates or Ombudsmen (R S A or R S O) to assure appropriate safety monitoring of research subjects for G C R C - based studies. N C R R initiated the R S A program in 2001, but only for studies conducted on G C R C s across the country. The R S A s serve as advocates for research subjects and also work closely with clinical investigators to be certain they are aware of their responsibilities to research subjects as articulated within federal and state regulations, laws and guidelines that protect human subjects participating in clinical research studies. In view of the positive impact of the R S A program, N C R R plans to gradually extend the R S A program as a complement to existing institutional activities for human subject protection within the entire G C R C host institution.

Progress has also been made to increase the number of pilot projects, which have grown from 44 awards in FY 2003 to 95 in FY 2004.

Item

IDeA Grants—The Committee has provided \$224,000,000 for the Institutional Development Award [IDeA] Program authorized by section 402(g) of the Public Health Service Act. This is a \$10,000,000 increase over fiscal year 2004 and the same as the fiscal year 2005 budget request.

Within the total provided, \$81,000,000 is for the Idea Networks of Biomedical Research Excellence [INBRE] and \$136,000,000 is for the Centers of Biomedical Research Excellence [COBRE] initiative. (page 157)

Action taken or to be taken

Please refer to page N C R R - 27 of this document for N C R R 's response to this significant item regarding the Institutional Development Award [IDeA] Program.

Item

Positron Emission Tomography - The Committee continues to urge N C R R to support research resource centers for the development and refinement of positron emission tomography [PET] as a unique imaging technology to diagnose and stage diseases of the brain, including Alzheimer's disease. (Page 157)

Action taken or to be taken

In FY 2004 N C R R provided funds to acquire PET scanners and imaging research centers at Johns Hopkins University and Yale University and a cyclotron to generate PET isotopes at Massachusetts General Hospital. The PET scanners at these resources support research on new radiotracers, optimization of PET for technical assessment of response to therapy, gene expression, malignant transformation, cerebral plasticity, forebrain development, antipsychotic drug mechanisms of action, cerebral neurotransmitter interactions, and hallucination drugs.

PET scans of the brain are also being performed in several General Clinical Research Centers (GCRCs) to study, for example, depression, alcohol dependence, sleep, stroke rehabilitation, compulsive behavior, schizophrenia, post-traumatic stress disorder, trauma, and deafness. GCRC resources for PET scanning were also significantly strengthened in 2003, with the award of supplementary funding to the Brookhaven National Laboratory to support isotope generation for those isotopes that have a very short half-life and must be generated on site. In addition, several NCCR-supported National Primate Research Resources are hosting more neuroscience research using PET scans.

Item

Prader-Willi Syndrome - The Committee recognizes the commitment to establish a Rare Diseases Clinical Research Center as part of the Rare Diseases Clinical Research Network for the study of Prader-Willi Syndrome and other rare disorders. The Committee recommends that the R D C R C program be expanded to increase the level of research being conducted. (page 157)

Action taken or to be taken

N C R R is collaborating closely with the Office of Rare Diseases to develop and utilize novel informatics resources within the Rare Diseases Clinical Research Network. The Rare Diseases Clinical Research Network is composed of 10 consortia and a Data and Technology Center. Each Consortium focuses on a subset of rare diseases. One of the consortia is studying Prader-Willi Syndrome where a longitudinal study is being developed to answer important clinical questions about this disease. The Prader-Willi Syndrome Association, as well as the wider Prader-Willi community, is a partner in this effort. While N C R R 's mission is not to support disease specific resources, but those that are of value to a broad range of researchers, the

informatics and standards based tools we are developing in the Rare Diseases Clinical Research Network should serve as models for expansion of these tools to all diseases and communities.

This should facilitate research in many other diseases, as well as Prader-Willi Syndrome.

Item

Research Resource Centers -The Committee continues to urge N C R R to support research resource centers for the development and refinement of positron emission tomography (PET) as a unique imaging technology to diagnose and state diseases of the brain, including Alzheimer's disease. (page 157)

Action taken or to be taken

Please refer to page N C R R - 3 6 of this document for N C R R ' s response to this significant item regarding positron emission tomography.

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2005 Amount Authorized	FY 2005 Appropriation	2006 Amount Authorized	2006 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	\$1,079,141,000	Indefinite	\$1,094,156,000
National Center for Research Resources	Section 4 IB	42§285b	Indefinite		Indefinite	
Biomedical and Behavioral Research Facilities	Section 481A Section 48 IB			\$29,760,000		\$0
National Research Service Awards	Section 487(d)	42§288	a/	6,189,000	hi	6,047,000
Total, Budget Authority				1,115,090,000		1,100,203,000

2

a. Amounts authorized by Section 301 and Title IV of the Public Health Act.

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1997	309,344,000 2/	416,523,000	324,844,000 2/	415,095,000 3/
1998	333,868,000 2/	436,961,000	455,805,000	453,883,000
1999	421,721,000 2/4/	513,948,000	554,819,000	554,819,000
Rescission				(373,000)
2000	469,684,000 2/	642,311,000	625,988,000	680,176,000
Rescission				(3,619,000)
2001	602,728,000 2/	832,027,000	775,212,000	817,475,000
Rescission				(52,000)
2002	974,038,000	966,541,000	1,014,044,000	1,012,627,000
Rescission				(89,000)
2003	1,090,217,000	1,090,217,000	1,161,272,000	1,146,272,000
Rescission				(7,451,000)
2004	1,053,926,000	1,053,926,000	1,186,483,000	1,186,183,000
Rescission				(7,125,000)
2005	1,094,141,000	1,094,141,000	1,213,400,000	1,124,141,000
Rescission				(9,051,000)
2006	1,100,203,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.

3/ Excludes enacted administrative reduction of \$50,000.

4/ Reflects a decrease of \$1,274,000 for the budget amendment for Bioterrorism.

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	F Y 2004 Actual	F Y 2005 Appropriation	F Y 2006 Estimate
Office of the Director	8	8	8
Office of Extramural Activities	20	24	24
Office of Administrative Management	17	17	17
Office of Science Policy & Public Liaison	8	8	8
Division for Clinical Research Resources	8	8	8
Division for Biomedical Technology Research and Research Resources	8	8	8
Division of Comparative Medicine	7	7	7
Division of Research Infrastructure	12	12	12
Total	88	92	92
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)
FISCAL YEAR	Average G M / G S Grade		
2002	11.4		
2003	11.4		
2004	11.7		
2005	12.8		
2006	12.8		

Detail of Positions

GRADE	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Total - ES Positions	4	5	5
Total - ES Salary	\$578,196	\$749,485	\$766,723
GM/GS-15	12	16	16
GM/GS-14	27	29	29
GM/GS-13	11	13	13
GS-12	17	19	19
GS-11	4	4	4
GS-10	1	1	1
GS-9	6	6	6
GS-8	1	1	1
GS-7	1	1	1
GS-6	1	1	1
GS-5	1	1	1
GS-4	0	0	0
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	82	92	92
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General Director Grade Senior Grade Full Grade Senior Assistant Grade Assistant Grade			
Subtotal	0	0	0
Ungraded	22	22	22
Total permanent positions	86	97	97
Total positions, end of year	109	120	120
Total full-time equivalent (FTE) employment, end of year	88	92	92
Average ES salary	\$144,549	\$149,897	\$153,345
Average GM/ GS grade	11.7	12.8	12.8
Average GM/ GS salary	\$76,562	\$77,556	\$79,340