DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

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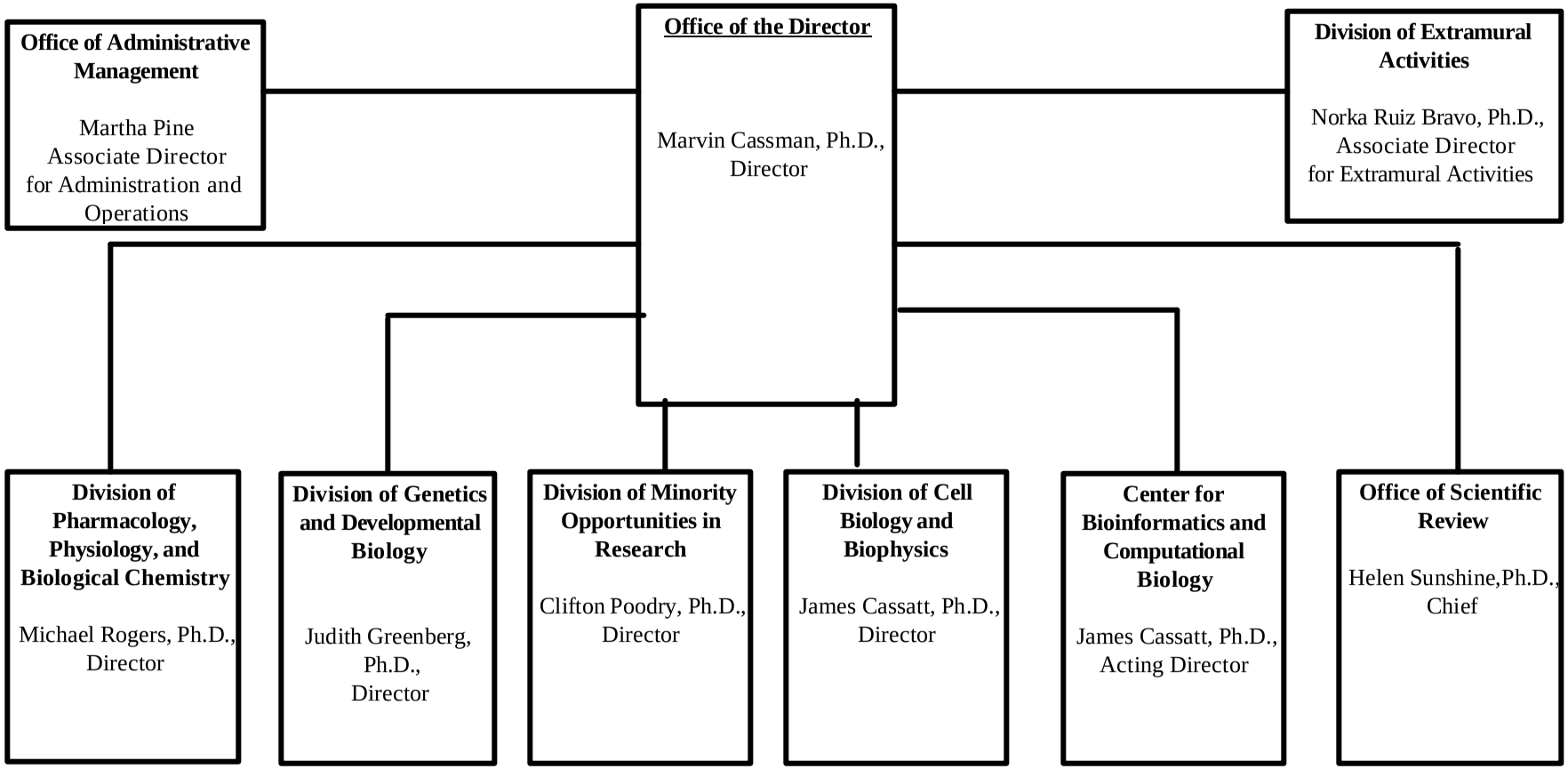
Organization Structure



NIGMS-2

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

For carrying out section 301 and title IV of the Public Health Service Act with respect to general medical sciences, [$1,725,263,000] *$1,842,404,000*.

[Departments of Labor, Health and Human Services, Education, and Related Agencies Appropriations Act, for Fiscal Year 2002 (P.L. 107-116).]

National Institutes of Health

National Institute on Aging
Amounts Available for Obligation 1/

Source of Funding	FY 2001 Actual	FY 2002 Estimate	FY 2003 Estimate
Appropriation	$786,039,000	$893,443,000	$950,150,000
Enacted Rescission	(285,000)	(313,000)	---
Subtotal, Adjusted Appropriation	785,754,000	893,130,000	950,150,000
Comparable adjustment for legislative proposal for accrued retirement costs	2,711,000	2,934,000	3,010,000
Real transfer to:			
Other HHS Agencies through Secretary's one-percent transfer authority	(149,000)	---	---
Real transfer to HHS for the Office of Human Research Protection	(164,000)	---	---
Comparative transfer from:			
Office of the Director for the Academic Research Enhancement Award program	862,000	---	---
National Cancer Institute for research activities	---	---	18,549,000
Comparative transfer to:			
National Institute of Biomedical Imaging and Bioengineering	(247,000)	---	---
Subtotal	788,767,000	896,064,000	971,709,000
Subtotal, adjusted budget authority	788,767,000	896,064,000	971,709,000
Unobligated balance, lapsing	(28,000)	---	---
Total obligations	788,739,000	896,064,000	971,709,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2001 - $1,101,000; FY 2002 - $1,101,000; FY 2003 - $1,101,000.

Excludes $395,000 in FY 2001 and $395,000 in FY 2002 for royalties.

Justification

National Institute of General Medical Sciences

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended.
Reauthorizing legislation will be submitted.

Budget Authority:

	2001 Actual	2002 Appropriation	2002 Current Estimate	2003 Estimate	Increase or Decrease
Current Law BA	$1,530,988,000	$1,725,263,000	$1,725,139,000	$1,879,984,000	$ 154,845,000
Accrued Costs	1,192,000	1,328,000	1,328,000	1,394,000	66,000
Proposed Law BA	1,532,180,000	1,726,591,000	1,726,467,000	1,881,378,000	154,911,000
FTE	170	179	179	178	(1)

This document provides justification for the Fiscal Year 2003 activities of the National Institute of General Medical Sciences (NIGMS), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2003 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

The President's appropriations request of $1,881,378,000 for this account includes current law adjusted by assuming Congressional action on the proposed Managerial Flexibility Act of 2001.

Introduction

NIGMS supports basic biomedical research that expands our knowledge about normal life processes and the diseases that arise when these processes malfunction. Its research includes cutting-edge studies on genes, proteins, cells, and gene-influenced responses to medicines. The Institute is at the vanguard of a major shift in the biological sciences from a static view of the parts of a system to an analysis of the design and operating principles of entire systems, with all of their dynamic behaviors and other complexities. This shift is generating vast amounts of data, leading to a growing reliance on the tools of bioinformatics and computational biology to mine the data and draw meaning from it.

The value of NIGMS-supported basic research was underscored in 2001 by the awarding of top scientific prizes to long-time Institute grantees. Dr. Leland Hartwell of the Fred Hutchinson Cancer Research Center received the Nobel Prize in physiology or medicine for his discovery of genes that control the cell division cycle. Since diseases like cancer and some birth defects arise when the cycle does not proceed normally, Dr. Hartwell's work is revealing new directions to pursue in developing drugs to treat these diseases.

Dr. K. Barry Sharpless of The Scripps Research Institute received the chemistry Nobel Prize for discovering molecules that enable researchers to selectively control chemical reactions. His research has made it possible to produce purer and safer forms of many important medicines, including certain antibiotics, heart medicines, and antidepressants.

The Lasker Award for Basic Medical Science, known as "America's Nobel Prize," went to Dr. Mario Capecchi of the University of Utah and Dr. Oliver Smithies of the University of North Carolina at Chapel Hill School of Medicine. The scientists were honored for developing a method for creating laboratory mice that contain genes from other organisms. If the transferred genes are involved in human diseases, the resulting mice can serve as model organisms for the study of those conditions. Scientists can use the mice to learn about a disease in a mammal that is very similar to humans, develop possible treatments, and test them with no risk to human patients. The technique, which is also useful for pinpointing the actions of specific genes, has become an indispensable tool for genetics research.

Another example of the impact of NIGMS-funded research is found in the recent contributions of two grantees to the fight against anthrax. One of the scientists studies the evolution of infectious diseases, and is using the knowledge he has gained in this area to assist in the investigation of anthrax infections by identifying the strains involved in each case. The other researcher is a chemist who has designed a molecule that neutralizes the anthrax toxin in animal experiments. The work of both grantees grew out of basic research that initially appeared to have little immediate significance for human health. Now, it is directly addressing a critical public health threat. A more detailed description of these researchers' work appears in the Science Advances section of this narrative. That section, along with the story of discovery below, illustrates the breadth of NIGMS-supported research, the fundamental new knowledge and insights it provides, and some of the ways it is being applied.

Story of Discovery: The Human Genome, Chapter Two

Many people think that scientists have--once and for all--cracked the human genetic code. Indeed, two teams of researchers published a draft sequence of our 3-billion-piece jumble of DNA "letters," chemical units called nucleotides. Yet how our bodies interpret, or "express," our cells' genetic code plays a prominent role in our everyday health. Thoroughly deciphering the code's protein-making instructions--something our bodies do with ease all the time--remains a complicated puzzle. Scientists already know that certain spelling differences in DNA cause disease. But other inheritable factors, aside from DNA, can influence how likely a person is to develop a particular disease. A compelling tale of discovery is found in researchers' quest to tease apart these so-called "epigenetic" factors that, along with diet and other environmental influences, profoundly affect our health.

The correct packaging of DNA is essential to the proper functioning of the cells that make up our bodies. Cells contain and protect their precious cargo, genes, in protein-rich complexes called chromatin. Chromatin consists of long, stringy DNA spooled around an orderly, ball-like core of proteins called histones. In a sense, chromatin acts as a gatekeeper for our genes, regulating access to DNA by cellular equipment that decodes the genetic instructions. Among other things, this arrangement permits embryos to develop the right way, and it directs precursor cells to form organs and tissues. Conversely, if access to the genes in chromatin is not stringently controlled, cancer and a variety of other diseases can be the terrible consequence.

Beads on a String

The chromatin story begins over a hundred years ago. In the late 1800s, researchers first discovered the molecules now known as histones, and there was widespread belief among scientists that these proteins--not DNA, as determined over 50 years later--were the source of heredity. In 1973, Drs. Ada and Donald Olins of the University of Tennessee, Oak Ridge and Dr. Christopher Woodcock of the University of Massachusetts, Amherst independently released preliminary reports describing electron microscopic pictures of chromatin fibers as "particles on a string." A year later, putting together the microscopy data and results from other biochemical and biophysical techniques, Dr. Roger Kornberg, then a Junior Fellow of Harvard University working at the MRC Laboratory in Cambridge, England, published a seminal paper. He proposed a model of chromatin structure as repeating units of approximately 200 nucleotide pairs of DNA and 8 histone molecules--the string and beadlike particles, respectively. Virtually every college biology student now knows this description of chromatin as "beads on a string." Beginning with these early studies, NIGMS has funded a quarter-century of groundbreaking research on chromatin--what it is, how it works, and more recently, how it is tied to cancer and other diseases.

In the mid-1960s, even though researchers did not know precisely what histones did inside cells, scientists such as Dr. Vincent Allfrey, then of the Rockefeller Institute in New York City, suspected that natural chemical tags on histones could control genes by turning them on or off. Throughout the 1970s, more scientists began to appreciate and gradually accept the connection between DNA's physical environment (chromatin) and the activity of genes. Genes are turned on ("transcribed"), for the most part, by proteins called transcriptional activators that must touch DNA to exert their effects. The basic structure of chromatin, in which DNA is spooled and compacted, would appear to be a major obstacle to the transcription process by blocking the access of activator proteins to genes. Indeed, researchers have reported many examples of how chromatin can prevent genes from being read. In the late 1980s and early 1990s, scientists such as Dr. Jerry Workman of Pennsylvania State University and Dr. Robert Kingston of Massachusetts General Hospital discovered that some transcriptional activator proteins (and often combinations of them) can attach themselves to DNA in chromatin, displacing histones. This observation proved to be a major step in researchers' understanding of how genes can be read through a veil of protective chromatin.

Another Code

Groundbreaking studies by Dr. C. David Allis of the University of Virginia Health Sciences Center have begun to reveal that a key step in how cells interpret their genetic code involves actually finding genes tucked away inside chromatin. Part of a cell's gene-decoding machinery is drawn to the histone proteins in chromatin. In recent years, Dr. Allis and other NIGMS-funded scientists have defined several cellular systems that carefully balance how histones are "marked" with a variety of natural chemical tags--called acetyl, phosphate, and methyl groups--in a specifically timed order. Putting on these tags and taking them off--something Dr. Allis refers to as the "histone code"--turns out to be a critical aspect of a cell's gene-reading activities.

The past 10 years in particular have witnessed an explosion of major discoveries by Dr. Allis and other NIGMS-funded researchers that are paving the way toward a better understanding of how genes are controlled and how certain diseases result when gene access is either too lenient or too stringent. In many cancer cells, for instance, inappropriate control of certain growth genes can fuel unchecked cell division. Scientists are finding a prevalence of telltale marks on chromatin in certain cancer cells, leaving growth genes bare and prone to near-constant activation. When histone-marking enzymes are revved up in cancer cells, these molecules become important potential targets for developing future cancer drugs.

In recent years, NIGMS-supported researchers have also made links between chromatin and normal biological processes like aging. Dr. Leonard Guarente of the Massachusetts Institute of Technology discovered that a gene-silencing protein called Sir2 removes the chromatin-marking chemical tags called acetyl groups from genes. He found that Sir2 is intimately dependent on a molecule central to the body's process of metabolizing food into energy. The finding has far-reaching implications, providing a tantalizing potential explanation for the observation by other researchers that low-calorie diets in model organisms such as yeast and worms can extend lifespan.

Science Advances

Some of the major research advances made recently with NIGMS support are described below. Although only the lead scientists are named, coworkers contributed significantly to these achievements.

New Insights into Biological Processes

Molecular Structure of Key Enzyme Solved

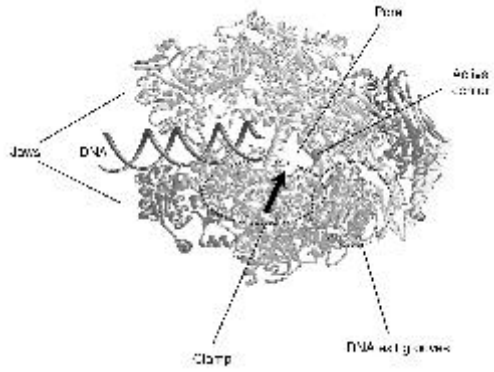
"If any enzyme does the cell's heavy lifting, it's RNA polymerase II," begins a recent scientific news article.[1] RNA polymerase II is responsible for the first step in making proteins in all organisms ranging from yeast to humans. The multisubunit enzyme copies each cell's genes into RNA, a type of genetic material that serves as an intermediary between genes and proteins. And it does this at just the right time and in just the right amounts. The article continues, "pol II, as the enzyme is called, is the heart of the machinery that controls everything that cells do--from differentiating into all the tissues of a developing embryo to responding to everyday stresses."

A group of researchers led by Dr. Roger Kornberg of the Stanford University School of Medicine has solved two detailed, three-dimensional structures of pol II--one of the enzyme alone and one with the enzyme joined to some of its molecular partners. The feat culminates nearly 20 years of

[1] Marx J. X-ray crystallography: transcription enzyme structure solved. *Science* 2001;292:411-4.

effort. It is particularly remarkable because the enzyme is rather scarce in cells and is so large--it contains 12 different subunits--that it is unwieldy for the required technique (X-ray crystallography).

The solved structure gives scientists their first close look at the enzyme in action. It suggests a role for each of the enzyme's dozen subunits and reveals how they fit together to form a molecular machine that copies genes into RNA. The work may have clinical applications as well. Researchers may be able to design new antibiotic drugs by targeting structural differences between human and bacterial forms of the enzyme. They may also be able to design anticancer drugs that prevent pol II from stimulating cell growth in tumor cells.



The structure of RNA polymerase II shows, at the molecular level, how the enzyme completes the first step in making proteins--copying genes into RNA. It reveals a pair of jaws that appear to grip genes (DNA), a clamp that holds the DNA in place, a pore through which RNA building blocks probably enter, and grooves through which the completed RNA strand may thread out of the enzyme.

Only Two Genes Needed to Form Heads in Model Organism Embryos

One of the most intriguing questions in human biology is how a single, fertilized egg can develop into a healthy baby. What tells some cells to form a liver, others to form bones, and still others to become blood vessels or nerves? And, even more basic, how does the developing embryo know right from left, up from down, and front from back so that all the organs are positioned properly?

Like many interesting biological questions, these are far too complex--and unethical--to answer by studying developing human embryos. So many researchers turn to simpler organisms that are genetically similar to humans. Zebrafish eggs are ideal for these studies because they are transparent, inexpensive, and hatch only 3 days after fertilization.

A team of Vanderbilt University geneticists led by Dr. Lilianna Solnica-Krezel discovered, to their surprise, that just two genes make the difference between a normal and a headless zebrafish embryo. The genes, called *bozozok* and *chordino*, were known to be involved in early development. When the scientists "knocked out" these two genes, the resulting embryos developed into overgrown tails--entirely devoid of heads or trunks. The work further showed that the role of these two genes is to suppress the activity of a protein called BMP, which is required for tail formation but blocks head formation.

The study reveals a stunningly simple genetic mechanism, involving just three factors (the two genes and BMP), that is key to the complex development of a single egg into a fully developed fish. Because

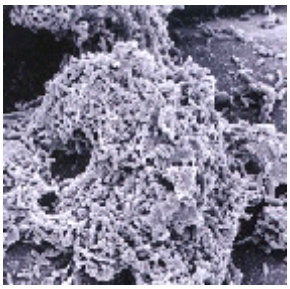
zebrafish have biochemical and genetic pathways similar to other vertebrates, the work will greatly advance our understanding of development in humans and other organisms. It will also shed light on the genetic basis of some serious birth defects.

Basic Studies Illuminate Disease Mechanisms

Bacterial Slime Clogs Cystic Fibrosis Lungs

Cystic fibrosis (CF) is one of the most common fatal genetic diseases in the United States. Approximately 30,000 Americans have the disease and an estimated 8 million are carriers of it.[2] Thick, sticky mucus clogs the lungs and intestines of those with CF, causing malnutrition, frequent lung infections, breathing difficulty, and eventually permanent lung damage. Bacteria, especially *Pseudomonas aeruginosa,* thrive in this thick mucus, causing persistent infection. Most people with CF die from respiratory failure caused by these infections--often around the age of 30.

Once these bacteria gain a foothold in CF lungs, they are invincible even to long-term antibiotic treatment. Scientists led by Dr. E. Peter Greenberg of the University of Iowa College of Medicine revealed why. The researchers showed that the bacteria encase themselves in a protective slime called a biofilm. Partial to wet surfaces, biofilms are responsible for everything from dental plaque and bathtub soap scum to bacterial colonies that corrode the bottom of ships. Within gluey pockets in the biofilm, colonies of bacteria flourish, nourished by a network of water-filled channels and shielded from the effects of antibiotics. Dr. Greenberg and his coworkers developed a sensitive lab test that detects biofilms in CF lungs, based on telltale molecules produced by the structures.



Biofilms, like this laboratory-grown specimen, form fortress-like structures that protect the bacteria from antibiotics and from the immune system of infected hosts. Because of this, biofilms are extremely difficult to treat and often persist indefinitely.

This technique could form the basis for a diagnostic test to detect the presence of biofilms in a wide range of medical conditions and industrial processes. The work might also help scientists design drugs to prevent biofilms from forming or to disrupt them after they have become established.

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[2] *Cystic Fibrosis Research Directions,* National Institute of Diabetes and Digestive and Kidney Diseases, NIH Publication No. 97-4200, July 1997.

Scientists Identify Weak Spot in a Parasite's Armor

Human African trypanosomiasis, known as sleeping sickness, is caused by infection with the parasite *Trypanosoma brucei*. Tsetse fly bites transmit this parasite to humans and livestock, where it feeds on blood. In an infected person, the parasite spreads throughout the entire body, causing at first high fever, weakness, headaches, joint pain, and itching. Over time, symptoms become more severe. People with sleeping sickness experience periods of sleeplike unconsciousness that are followed by coma and death. Although the incidence of sleeping sickness had declined dramatically by the mid-1900s, reduced screening and surveillance have led to new epidemics of the disease over the last 30 years. *T. brucei's* complicated life cycle, like that of many parasites, has limited the success of both prevention and treatment.

Recently, scientists discovered a new weak spot in the armor of the parasite *T. brucei*. Researchers already knew that enigmatic molecular processing events called "RNA editing" took place in both the life-cycle form of *T. brucei* living in tsetse flies and in the bloodstream form of this parasite. Now, Dr. Kenneth Stuart of the Seattle Biomedical Research Institute has determined that RNA editing is an essential process for survival of the bloodstream parasite. In the course of their studies, Dr. Stuart and his coworkers also found a way to thwart the growth of the bloodstream form of *T. brucei* by knocking out one of the enzymes that performs the RNA editing and that is critical to its metabolism.

Dr. Stuart's findings point to a potential new way to treat sleeping sickness by targeting the essential RNA editing function of the bloodstream form of *T. brucei*. By demonstrating that the enzyme that carries out the crucial RNA editing function is absolutely necessary for the survival of the bloodstream form of the parasite, the new work holds promise for enabling scientists to design targeted medicines to kill the parasite.

Hepatitis C Study May Lead to New Treatments

Every year, hepatitis C kills up to 10,000 Americans and costs $600 million in health care expenses and lost wages.[3] Most people who are infected develop chronic liver disease, cirrhosis, or liver cancer. Treatments for the disease usually fail, which is why finding new ways to target the virus is so important.

Dr. Joachim Frank of New York's Wadsworth Center led a research group that showed how the hepatitis C virus takes over a host cell's protein-making machinery, known as the ribosome, and forces it to churn out viral proteins for constructing more virus particles. This eventually kills the host cell and allows the spread of the new virus particles to other cells. Using a cryo-electron microscopy technique that he pioneered, Dr. Frank and his group captured the first image of viral genetic material bound to a ribosome and poised to trigger protein synthesis. The image revealed that the end of the virus' genetic material twists into a hook that snags the host's ribosomes. This viral hook forces the ribosomes to change shape dramatically, ensuring that they crank out viral proteins rather than host cell proteins.

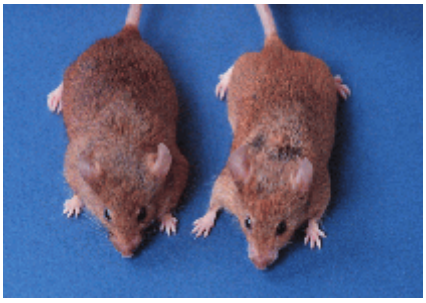
[3] Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. *MMWR* 1998;47(No. RR-19):1-33.

By providing a clear view of how hepatitis C commandeers cell machinery in an infected host, the work may point to new molecular targets for drugs to treat the disease. Other viruses--such as those that cause polio, foot-and-mouth disease, and a type of herpes--are thought to use similar infection strategies. A better understanding of how hepatitis C infects cells may also advance efforts to design drugs to treat these viruses. More generally, the work improves our understanding of how proteins are made--a cellular process essential for all life.

Designer Mice Eat More, Weigh Less

"Eat more, weigh less"--it sounds like the advertising slogan of a weight loss program. But it is a reality for a certain type of genetically engineered mouse, providing tantalizing possibilities for treating obese humans. Obesity is responsible for the deaths of 280,000 adult Americans each year,[4] making it a leading cause of preventable death in the United States. The total cost of treating overweight and obese individuals approaches $100 billion annually.[5] Excess body weight and obesity also increase the risk of a range of diseases, including diabetes, heart disease, stroke, and various cancers.

For more than 10 years, Dr. Salih Wakil of Baylor College of Medicine and his coworkers have studied an enzyme called acetyl-CoA carboxylase 2, or ACC2, which governs the body's ability to burn fat. The researchers recently discovered that mice designed to lack this enzyme eat 20 to 30 percent more food, and yet accumulate less fat and weigh about 10 percent less than normal mice. Best of all, the engineered mice are otherwise normal--"[they] seem very happy, live and breed well," says Dr. Wakil. And they have lived such lives for 2 years now, which is the average life expectancy for lab mice. Detailed biochemical studies show that the designer mice simply burn more fat than their normal counterparts.



When allowed to eat as much as they'd like, normal mice (left) tend to become overweight. Under the same conditions, mice lacking the ACC2 enzyme (right) actually eat more food but remain thinner.

If Dr. Wakil's results in mice hold true for humans, then a drug that blocks the function of ACC2 might allow people to lose weight while maintaining a normal diet. The study, which grew out of a desire to determine the different roles of ACC2 and its relative, ACC1, also sheds light on the normal pathways used to metabolize fat.

[4,5] *Statistics Related to Overweight and Obesity*. National Institute of Diabetes and Digestive and Kidney Diseases, NIH Publication No. 96-4158, July 1996.

New Approaches to Therapeutics

Answers on Anthrax

In the wake of recent bioterrorist releases of anthrax bacteria, some of the most critical questions raised are: What strain of anthrax was released? How can we treat it? and How can we vaccinate against it? Two NIGMS grantees are helping to answer those questions.

Dr. Paul Keim of Northern Arizona University developed the technique that authorities are using to identify the strain of anthrax used in each attack. The identity of the strains suggests whether different attacks were carried out by the same person or group and reveals clues about the source of the bacteria. Using Dr. Keim's technique, investigators concluded that identical strains of anthrax were mailed to Senate Majority Leader Thomas A. Daschle (D-S.D.), NBC News anchor Tom Brokaw, and American Media Inc. in South Florida.

Dr. Keim studies the evolutionary relationships among anthrax strains so that he can determine where any strain originated, even if it is subtly different from its ancestor. His technique relies on slight genetic differences between the hundreds of known strains of anthrax. His team detects these differences using a type of "DNA fingerprinting" technique related to that used in criminal and paternity cases. He has collected a library of about 1,350 different anthrax samples, and he has fingerprinted more than 900 of them.

In 2001, Dr. Keim used the technique to analyze the strain of anthrax released in 1993 by the Japanese cult Aum Shinrikyo. His work showed that the attack failed because the cult members used a veterinary vaccine strain of anthrax that is not dangerous to humans**.**

Dr. George Whitesides of Harvard University designed a molecule that might lead to a new treatment for anthrax infection. The molecule neutralizes the bacteria's deadly effects by interfering, at a molecular level, with the assembly of anthrax's toxic machinery. It prevented illness in rats exposed to 10 times the lethal dose of anthrax proteins, showing promise as the basis of a future treatment. Dr. Whitesides and his coworkers combined two separate techniques to generate their synthetic molecule. The success of their unique approach suggests it might be widely applicable to the design other useful molecules, such as anticancer drugs or laboratory reagents.

Old Drugs Learn New Tricks

Diseases caused by tropical parasites are a major worldwide health problem. According to the World Health Organization, malaria alone kills more than 1 million people per year across the globe, and a child dies of malaria every 30 seconds.[6] Other scourges caused by parasites include Chagas' disease, leishmaniasis, sleeping sickness, and the AIDS-related infections toxoplasmosis and cryptosporidiosis. Scientists have not yet succeeded in developing vaccines against these

[6] *Fact Sheet No. 94--Malaria*. World Health Organization, 1998.

parasitic infections, which collectively affect 3 billion people worldwide.[7] As a result, there is an urgent need for new, inexpensive treatments for these diseases.

Dr. Eric Oldfield, a chemist at the University of Illinois, discovered that a class of drugs called "bisphosphonates" currently approved by the Food and Drug Administration to treat osteoporosis and other bone ailments may also be useful for treating malaria, Chagas' disease, leishmaniasis, and the AIDS-related infections. Previous research by Dr. Oldfield and his colleagues had hinted that the active ingredient in medicines such as Fosamax®, Actonel®, and Aredia® blocks a key step in parasite metabolism. To test whether this was true, the researchers gave the medicines to five different parasites, each cultured in a plastic lab dish. The scientists found that low concentrations of the osteoporosis drugs killed the parasites, while sparing human cells. The researchers are now testing the drugs in animal models of the parasitic diseases and so far have obtained cures--in mice--of certain types of leishmaniasis.

Patients and doctors alike benefit when existing drugs find new uses. Since research efforts to develop vaccines against parasites have been largely unsuccessful to date, there is an urgent need for scientists to find new medicines to attack tropical parasites, which have also begun to develop resistance to currently effective medicines. If the ongoing studies demonstrate that bisphosphonate drugs work in larger animal models, the next step will be to determine if the medicines can thwart parasitic infections in humans. This could occur relatively quickly, since the medicines have already been approved for other uses, and therefore have already been tested for safety in people.

Tiny Nanotubes as New Antibiotics

One of medicine's greatest triumphs--the development of antibiotics--is steadily growing into one of medicine's greatest fears: that the infectious diseases easily vanquished decades ago will be as deadly to our grandchildren as they were to our grandparents. Within recent years, for example, hospital workers in the United States have detected strains of *Staphylococcus aureus*--"staph," the leading cause of hospital-acquired infections--that are resistant to every known antibiotic medicine. The race is on to find new types antibotic medicines.

Chemistry to the rescue! Dr. M. Reza Ghadiri of The Scripps Research Institute has devised a clever chemical scheme to create a novel class of antibiotic compounds. Dr. Ghadiri and his coworkers invented a way to get laboratory-made rings and strings of amino acids (peptides) to assemble themselves into channels and pores. With just the right mix of ingredients and conditions, the researchers coaxed the rings to stack on top of each other, forming a tube. The artificial tubes work as antibiotics by poking holes in bacterial membranes, making them too leaky to hold their contents. Dr. Ghadiri and his team found that the tiny tubes kill a variety of bacteria in laboratory experiments. The scientists went on to test the compounds in mice infected with a lethal dose of drug-resistant bacteria and discovered that all of the mice survived over the course of a 7-day study. In contrast, all the mice in the control group (which received no nanotubes) died within 48 hours.

This work holds great promise that a new class of nanotube peptides can be effective in treating potentially fatal antibiotic-resistant infections caused by staph and other dangerous microbes.

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[7] Hirst SI, Stapley LA. Parasitology: the dawn of a new millennium. *Parasitol. Today* 2000;16:1-3.

New Insights Into Why Medicines Work Differently Among People

On their journey through the body, medicines interact with many different proteins. Some of these proteins work to get rid of medicines, while others help medicines do their jobs treating or preventing illness. Small differences between people in the genes that produce these proteins can affect how people react--or don't react--to certain medicines. Very slight changes in a gene can cause its protein product to be defective, or such changes can lead to either over- or underproduction of the protein. Partly because of these gene differences, when it comes to medicines, one size clearly does not fit all.

Dr. Erin Schuetz of St. Jude Children's Research Hospital has uncovered the genetic basis for why some people do not produce sufficient levels of a drug-metabolizing protein called CYP3A5, which is believed to be capable of metabolizing nearly half of all medicines. Dr. Schuetz and her coworkers found several "single-letter" changes in the DNA spellings of the gene that produces the CYP3A5 protein that affect how much of the protein is manufactured. Moreover, the researchers discovered that racial and ethnic background play a role in determining CYP3A5 protein levels, offering a genetic explanation for why certain individuals from particular racial and ethnic groups can display such a varied response to medicines like HIV protease inhibitors, cholesterol-lowering drugs, organ rejection treatments, and cancer chemotherapy medicines. The study showed that only 25 percent of Americans of European descent and 50 percent of Asians and African Americans produce enough of the CYP3A5 protein to break down drugs properly and avoid reactions caused by the buildup of toxic breakdown products.

The new work provides an explanation for why some people react so differently to a broad range of medicines. The research may lead to genetic tests that could help doctors prescribe accurate doses of medicines based upon patients' ability to metabolize certain drugs. Correct dosing of many CYP3A5-processed medicines with potentially fatal toxicities, such as some forms of cancer chemotherapy and organ rejection treatments, will make these therapies safer and more effective.

Promising Technologies

Detecting Lead Using DNA

Lead poisoning is the number one environmental hazard to American children.[8] Nearly 1 million children in the United States have enough lead in their blood to cause irreversible damage to their brains, nervous systems, kidneys, or reproductive organs.[9] At higher levels, lead poisoning can cause coma, convulsions, and death. Most of these children absorb lead into their blood from sources in and around their own homes: old paint and contaminated dust and soil. Current methods for detecting lead require sophisticated scientific equipment or complicated sample preparation.

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[8] *Fact Sheet #8: Lead 3/97*. National Institute of Environmental Health Sciences.
[9] *Lead Fact Sheet*. Centers for Disease Control and Prevention, 1998.

Dr. Yi Lu and one of his students at the University of Illinois at Urbana-Champaign developed a simple, inexpensive method to detect and measure lead in the environment. The technique harnesses DNA as a biosensor that literally glows in the dark when it contacts the metal. The scientists designed a specific strand of DNA that twists into a pocket tailor-made to capture lead. The method is extremely sensitive and can measure quantities of the metal over a wide range of concentrations.

Because DNA is stable and can easily be used in optical fibers and microchips, the technique might be used not only to detect household lead, but also on a larger scale to monitor lead in wastewater and industrial processes. The researchers also state that by varying the DNA and other chemicals, they can modify the technique to detect other metals, including those that are toxic, such as mercury and cadmium, and those that are beneficial to humans, such as calcium and potassium. Finally, the work will teach scientists more about the sequences and shapes of DNA that normally bind metals in the body. The researchers have applied for a patent on the work.

Glowing "Quantum Dots" May Speed Diagnosis, DNA Testing

A new technology enables scientists to "see" the molecules they study with more ease and clarity than ever before. The technology--called quantum dots--may one day be used for speedy disease diagnosis, DNA testing, or analysis of biological samples.

Dr. Shuming Nie and coworkers at Indiana University adapted quantum dot technology to label proteins, genes, and other biological molecules. Quantum dots are crystals made of semiconducting compounds and are so small (far less than a millionth of an inch in diameter) that they are referred to as "nanocrystals." Under ultraviolet light, each quantum dot radiates a brilliant color, depending on its size. For example, larger dots radiate red and smaller dots shine blue.

To use quantum dots as molecular labels, the researchers coax the nanocrystals into the pores of tiny, plastic beads that are tagged with a molecular probe--a protein or DNA sequence that binds strongly to the molecule of interest. After the probe binds to its molecular target in a cell or other biological sample, scientists can visualize the location or abundance of the molecule by lighting up the quantum dots with ultraviolet light.

By mixing quantum dots in different colors and intensities as an artist would mix paints, the scientists predict they can create 10,000 to 40,000 distinguishable quantum dot labels. With each label corresponding to a particular gene or protein, the researchers can detect tens of thousands of molecules all at once.

Quantum dots offer many technical advantages over traditional fluorescent dyes and newer DNA chip technologies, which are commonly used to detect and track biological molecules. They are brighter and easier to visualize than organic dyes. They are also more flexible and yield faster results than other current technologies, such as DNA chips.

In addition to their usefulness in identifying and tracking molecules in basic biomedical studies, quantum dots promise faster, more flexible, and less costly tests for on-the-spot clinical analyses such as screening for illegal drugs and diagnosing conditions ranging from HIV infection to allergies.

New Initiatives

NIGMS Creates Center for Bioinformatics and Computational Biology

Recognizing that the future of biomedical science will be driven by advances in bioinformatics and computational biology, NIGMS established a new Center for Bioinformatics and Computational Biology (CBCB) in May 2001. CBCB will support research and training in areas that join biology with the computer sciences, engineering, mathematics, and physics. NIGMS formally announced its interest in nurturing this interdisciplinary research area in 1998, but created the Center to provide a stronger focus for the Institute's efforts.

A key goal of computational biologists and bioinformatics scientists is to use computer technologies to solve enormously complex biomedical problems, such as how cells communicate and how organs or embryos develop. CBCB will encourage biomedical scientists and so-called quantitative (mathematically based) researchers to work together to generate mathematical models of biological networks, create modeling and simulation tools, conduct basic theoretical studies related to the organization of biological networks, and develop bioinformatics tools for integrating and interpreting data. In addition, the Center will fund training and fellowship grants and will sponsor workshops, courses, and meetings.

The Center will also oversee NIH's Biomedical Information Science and Technology Initiative (BISTI) through its management of the BISTIC Consortium (BISTIC). The goal of this initiative is to make optimal use of computer science and technology to address problems in biology and medicine. BISTIC is composed of senior-level representatives from NIH institutes and centers as well as representatives of other Federal agencies concerned with bioinformatics and computer-based applications.

New Synchrotron Beamlines Will Advance Studies of Molecular Structures

Synchrotrons are enormous machines that produce powerful X-ray beams used by researchers to tease apart the three-dimensional structures of molecules. The use of synchrotrons by biological scientists has exploded in recent years, but the availability of synchrotron resources has been limited, leading to long waits for scarce synchrotron "beam time."

To improve access to synchrotron beamlines and advance structural studies of biological molecules, NIGMS and the National Cancer Institute are supporting the design and construction of a facility with three new beamlines at Argonne National Laboratory's Advanced Photon Source, the newest and most advanced synchrotron in the country. The institutes estimate that the beamlines will be fully operational in 3 years.

Glue Grants Address Major, Unsolved Biological Mysteries

As reported last year, in response to advice from leaders in the scientific community, NIGMS established a program of grants to "glue" together large, multifaceted groups of scientists pursuing some of the biggest unsolved mysteries in biomedicine today. In September 2000, NIGMS made the first "glue" grant award to a consortium of basic scientists who are studying cellular communication. The consortium is led by Dr. Alfred Gilman of the University of Texas Southwestern Medical Center, who won the Nobel Prize in 1994 for work on signaling molecules called G proteins.

In the fall of 2001, NIGMS awarded three more large glue grants. One is to a consortium of scientists who will work to unlock the secrets of cell movement, a process that plays a role in embryonic development, immune response, and wound healing, as well as in diseases like cancer, arthritis, and osteoporosis. Despite many years of intensive study, biologists still do not have a good understanding of the mechanics of cell movement. The "Cell Migration Consortium" will be led by two scientists at the University of Virginia School of Medicine, Dr. Alan F. "Rick" Horwitz and Dr. J. Thomas Parsons.

The second new glue grant is to a team of clinical and basic scientists that will attempt to tease apart the complex set of events culminating in the immune system's reaction to a traumatic injury. Researchers know that inflammation is one common thread in the body's response to a burn or other traumatic injury. While inflammation is a necessary defense mechanism, excessive inflammation can lead to a body-wide, often fatal infection called sepsis. The scientists, led by Dr. Ronald G. Tompkins, a surgeon and biomedical engineer at Massachusetts General Hospital, hopeto find ways to guide physicians in predicting patient outcomes and choosing the best treatments. This could increase the likelihood of survival, reduce the length of hospitalization and the cost of treatment, and improve the quality of life for patients who have suffered burns and other traumatic injuries.

The third new glue grant looks at the roles that carbohydrates--sugar molecules that blanket every cell in our bodies--play in cellular communication. Carbohydrates and proteins associated with them permit cells to transmit and receive chemical, electrical, and mechanical messages that underlie everything from growth to movement to thought. Unlike proteins, which are produced for the most part from a single template--an individual gene--carbohydrates are made by a cascade of chemical reactions in the body. Many of these reactions are extremely hard to reproduce in the lab. In addition, the complex, branched structures of carbohydrates have stymied the development of efficient and routine methods to study them. Because immune cells rely on carbohydrates to travel to sites of inflammation and prompt responses to foreign invaders, the scientists expect that many of their findings will improve understanding of the immune system. This grant will be led by Dr. James Paulson of The Scripps Research Institute.

Protein Structure Initiative Expands

NIGMS is the world's single largest funder of research in structural genomics, a field dedicated to piecing together the three-dimensional structures of proteins using computational analyses of genome sequence data. Determining the structures of proteins can help scientists understand how these workhorses of our bodies function. Visualizing protein structures also helps researchers tailor the design of new drugs to treat a host of diseases. The NIGMS Protein Structure Initiative (PSI) aims to streamline and automate structural determination methods.

NIGMS expanded its support of structural genomics research in 2001 by awarding two new PSI grants. These awards bring the number of PSI grants to nine; the first seven awards were made in 2000. One of the new grants is to Dr. Wim G.J. Hol of the University of Washington, who will lead the "Structural Genomics of Pathogenic Protozoa Consortium" to develop new methods and technologies for obtaining protein structures from protozoa, many species of which cause deadly diseases. The other new grant is to Dr. John L. Markley of the University of Wisconsin, Madison, whose "Center for Eukaryotic Structural Genomics" will develop high-throughput methods for protein production, characterization, and structure determination. The scientists will work with *Arabidopsis thaliana*, a plant that is frequently used as a model organism for laboratory research, in part because it has many genes in common with humans and animals, including genes linked to diseases.

Also in 2001, a Protein Structure Initiative Advisory Committee was established as a working group of the National Advisory General Medical Sciences Council, the advisory body to NIGMS. The committee will advise NIGMS on the management of the PSI pilot structural genomics research centers and the subsequent establishment of the production phase of this project.

Pharmacogenetics Research Network Adds New Members

In September 2001, NIGMS and the National Heart, Lung, and Blood Institute (NHLBI) awarded grants to four new members of the NIH Pharmacogenetics Research Network. The Institute also extended the funding of one existing network investigator after the successful completion of a one year pilot project. The new grants will look at the role of gene variation in people's response to drugs to treat heart disease, depression, and stomach and intestinal cancers.

The Pharmacogenetics Research Network, established in April 2000 with the awarding of the first nine grants, aims to understand how a person's genetic makeup determines the way a medicine works in his or her body. In addition to NIGMS and NHLBI, other NIH components funding this nationwide research effort are the National Cancer Institute, the National Human Genome Research Institute, the National Institute of Environmental Health Sciences, and the National Library of Medicine. The network held its first annual meeting in April 2001.

The network has also formed an Industry Liaison Group to promote a dialogue with the pharmaceutical industry and identify areas of high priority and interest to both network members and pharmaceutical companies. The group held its inaugural meeting in January 2001.

Other Areas of Interest

Research Grants

During FY 2001, NIGMS continued its efforts to stimulate "high-risk/high-impact" research proposals and support new investigators. It also announced its special interest in supporting research in several areas, ranging from the organization and dynamic behaviors of complex biological systems to the study of single molecules. Examining single molecules can yield information on dynamic processes in living cells that cannot be obtained by using less sensitive techniques that look at the average behavior of large numbers of molecules. Another way to dramatically advance our understanding of important biological molecules and events is through the use of instruments called nuclear magnetic resonance (NMR) spectrometers. NIGMS plans to support shared access to extremely powerful NMR machines by groups of grantees who are studying significant and challenging biological problems that can uniquely benefit from this technology.

Additional areas of interest include a joint initiative in mathematical biology with the National Science Foundation; improved understanding of the role of metals in cells, which could lead to the identification of targets for new medicines; and the development of methods for designing, synthesizing, analyzing, and handling libraries of molecules that can be screened for physiological effects and possible therapeutic use.

Research Training

NIGMS maintains its leading role at NIH in research training by supporting nearly 44 percent of the predoctoral trainees and approximately 29 percent of all of the trainees who receive assistance from NIH. In recognition of the interdisciplinary nature of biomedical research today, the Institute's research training programs stress approaches to biological problems that cut across disciplinary and departmental lines. Such experience prepares trainees to pursue creative research in a wide variety of areas. The Institute also requires its institutional training programs to document how they plan to recruit minority students and report on the success of their efforts. To promote the sharing of best practices in this area, NIGMS sponsored a workshop in May 2001 at which institutions presented effective programs and strategies for the recruitment and retention of minority science students.

A new NIGMS program provides opportunities for undergraduate students in the quantitative and physical sciences to take part in summer biomedical research experiences mentored by NIH-supported investigators. NIGMS recently made the first 10 awards in this program.

Two ongoing special training programs are the Medical Scientist Training Program (MSTP) and the Pharmacology Research Associate (PRAT) Program. The MSTP supports research training leading to the combined M.D.-Ph.D. degree and produces investigators who can bridge the critical gap between basic and clinical research. In response to the pressing need for more investigators with such training,

NIGMS has expanded the number of trainees in this program by nearly 100 between FY 1998 (828 trainees) and FY 2001 (925 trainees). The PRAT Program is NIGMS' only intramural activity. PRAT fellows conduct 2 years of postdoctoral research in NIH intramural laboratories, working in such cutting-edge areas as neurobiology, tumor biology, and cell signaling.

AIDS Program

NIGMS support related to AIDS falls into three areas: program project grants that fund structure-based drug design, AIDS-related research training in molecular biophysics, and investigator-initiated research grants focused on improving the understanding of AIDS and its associated opportunistic infections.

NIGMS initiated its AIDS-related program project grants in 1987 to bring together crystallographers, chemists, and biologists to determine the detailed, three-dimensional structures of potential drug targets in HIV. In 2001, one of the program's grantees, Dr. Ian Wilson at The Scripps Research Institute, determined the structure of an antibody that neutralizes HIV. This research could provide the basis for designing a vaccine against the virus.

The NIGMS research training program in molecular biophysics, which was established in 1988, prepares scientists to apply the techniques of physics and computer modeling to biological problems, chief among them HIV infection. Graduates of this program are trained to use structural biology in the design of drugs to fight HIV.

Minority Opportunities in Research

NIGMS has a long-standing commitment to increasing the number and capabilities of underrepresented minorities engaged in biomedical research. The focal point for this effort is the Division of Minority Opportunities in Research (MORE). The goal of the MORE Division is to encourage minority students to pursue training for scientific careers and to enhance the science curricula and faculty research capabilities at institutions with substantial minority enrollments. Support is available at the undergraduate, graduate, postdoctoral, and faculty levels.

The MORE Division has three components: the Minority Biomedical Research Support (MBRS) Branch, the Minority Access to Research Careers (MARC) Branch, and a section that handles special initiatives. Through MORE's programs, NIGMS takes a leading role at NIH in research and research training activities targeted to underrepresented minorities.

Minority Biomedical Research Support Branch

MBRS awards grants to minority-serving institutions (MSIs) through three programs: Support of Continuous Research Excellence (SCORE), the Research Initiative for Scientific Enhancement (RISE), and the Initiative for Minority Student Development (IMSD).

The purpose of the SCORE Program is to assist biomedical research faculty at MSIs in developing competitive research programs and to increase the number of underrepresented minorities professionally engaged in biomedical research. The RISE Program seeks to enhance the research environment and increase the interest, skills, and competitiveness of students and faculty in pursuit of biomedical research careers. The IMSD encourages public and private educational institutions with fully developed and funded research programs to initiate and/or expand innovative efforts to improve the academic and research capabilities of underrepresented minority students and to facilitate their progress toward careers in biomedical research.

MBRS awards also support student and faculty developmental activities identified by applicant institutions, including attendance at scientific meetings and workshops, novel classes and curriculum changes, and participation in research at on- and off-campus laboratories. In FY 2001, 683 faculty members at 113 institutions worked on 407 MBRS research projects, and 1,195 undergraduate and 765 graduate students participated in these projects as research assistants. The number of MBRS student participants has nearly doubled since 1997.

Minority Access to Research Careers Branch

MARC supports special research training opportunities for students and faculty at educational institutions with substantial minority enrollments. MARC programs also enable grantee institutions to develop and strengthen their biomedical research training capabilities. As a result, these schools are able to interest students in, and prepare them for, pursuing doctoral study and biomedical research careers.

MARC accomplishes these goals through Undergraduate Student Training in Academic Research (U*STAR) institutional grants, predoctoral fellowships, faculty predoctoral and senior fellowships, a visiting scientist program, and grants for ancillary training activities. MARC also manages a program of NIH predoctoral fellowships for minorities.

MARC support in FY 2001 went to 647 students at 63 institutions that participated in the undergraduate program; 45 students who received MARC predoctoral fellowships; 2 faculty members who received training and/or degrees through the faculty fellowship program; and 75 NIH predoctoral fellowships, 25 of which were new in FY 2001.

Special Initiatives

MORE supports several special initiatives that strive to develop new approaches for the recruitment and retention of minority biomedical scientists. One such activity is the Bridges to the Future Program, which is co-sponsored by NIGMS and the NIH National Center on Minority Health and Health Disparities. This program encourages students in associate's or master's degree programs to make the transition to the next level of training (the bachelor's or Ph.D. degree, respectively) toward careers in biomedical research. Since the inception of the Bridges Program in 1992, NIGMS has supported 130 programs, 12 of which received initial funding in FY 2001.

The division also supports two innovative awards to foster the development of new skills. The MORE Faculty Development Award enables eligible faculty members to update or enhance their research skills by spending a summer (or one academic term) every year for 2 to 5 years in full-time research in a research-intensive laboratory outside their home institutions. The Institutional Research and Academic Career Development Award combines a traditional mentored postdoctoral research experience with an opportunity to develop teaching skills through mentored assignments at an MSI. The goals of the program are to provide a resource to motivate the next generation of scientists at MSIs and to promote linkages between research-intensive institutions and MSIs that can lead to further collaborations in research and teaching.

In September 2001, NIGMS and the Indian Health Service made the first eight awards in a program designed to promote, develop, and support centers that link the Native American community with organizations that conduct health research. The program, Native American Research Centers for Health (NARCH), encourages research on diseases and health conditions of importance to American Indians and Alaska Natives, and seeks to develop a cadre of Native American biomedical and behavioral scientists and health professionals who are able to compete successfully for NIH funding. At the same time, the program aims to increase the capacity of both the research-intensive organizations and the Native American organizations to work in partnership to produce competitive research proposals.

An activity that has continued to be a success is the MORE Division's support of technical assistance workshops and mini-courses in a number of areas, including grant writing and program evaluation. In addition, staff from the MORE Division conducted seven technical assistance workshops at sites across the country to assist current and potential grantees in writing more effective grants for student development activities.

Success Stories

MORE program directors who have recently received national recognition for their achievements include:

- Dr. Carlos G. Gutierrez, a chemistry professor and director of the MARC and MBRS programs at California State University, Los Angeles, received the 2001 American Chemical Society Award for Encouraging Disadvantaged Students into Careers in the Chemical Sciences.

- Dr. Edward R. Garrison, an MBRS investigator at the Shiprock campus of Diné College in New Mexico, was honored as the recipient of the Community College/Tribal College Mentor award from the Society for Advancement of Chicanos and Native Americans in Science.

- Dr. Maria Elena Zavala, a professor of biology and the MARC and Bridges to the Future program director at California State University, Northridge, received the Wang Family Excellence Award from the California State University system for her mentoring efforts.

Many participants in MORE programs go on to productive academic careers and professions in research or research administration. This provides evidence that the educational strategy of involving students in hands-on research experiences is one that works. Among this year's success stories are:

- Dr. Liz Reynoso Paz, a former MARC trainee at San Jose State University, is currently doing postdoctoral research in biochemistry at the University of California, Davis, School of Medicine.

- Henry Rodriguez, a former MBRS program participant at Florida International University, is now a molecular and cell biologist at the National Institute of Standards and Technology.

- Dr. Paul Lamont Bryant, a former Bridges to the Future program participant at North Carolina Central University, is now a researcher with the Procter & Gamble company.

Innovations in Management and Administration

NIGMS promotes a culture of continuous improvement in the areas of management and administration. Several of the Institute's efforts in these areas are described below.

Administrative Best Practices

NIGMS maintains its partnership with the National Heart, Lung, and Blood Institute and the National Institute of Neurological Disorders and Stroke to share administrative best practices, form collaborations to undertake common problem solving, and discuss strategies for overcoming administrative barriers. Early in 2002, administrative leaders from the three institutes will again assemble to address a pressing current topic. These information-sharing sessions have had a number of positive outcomes, including the establishment of an NIH-wide Management Analyst Working Group, the development of creative approaches for recruiting and retaining a highly qualified and diverse workforce, and the identification of shared opportunities for using information technology to streamline administrative processes.

Information Technology Resource Management

The NIGMS Information Resources Management Committee sets the Institute's priorities for information technology-related initiatives and serves as a forum for discussions between the Institute's Information Resources Management Branch and end users. This committee ensures that the Institute's technology needs are adequately addressed and that its information technology plans and activities meet the shared vision of the NIGMS staff.

The Institute has already implemented or has begun efforts to implement a number of the recommendations from an external study of its information technology operations. This included recruiting a Chief Information Officer, increasing the role of the Information Resources Management Committee, and documenting all of the Institute's major business processes.

Council Information Web Site

NIGMS continues to operate a Web site that provides its National Advisory General Medical Sciences Council members with orientation information and the latest information on meeting agendas and Institute activities. The site allows Council members to easily access up-to-date information at their desktops and eliminates the need for mailing large volumes of paper materials.

E-IMPACT Committee

The E-IMPACT Committee is an NIGMS workgroup charged with discussing ways to position the Institute for anticipated changes due to reinvention initiatives, such as Electronic Research Administration and IMPAC II. The group discusses how these impending initiatives may impact work processes and staffing, and it offers recommendations to better position the Institute to deal with and plan for the anticipated changes. The committee suggested the creation of a database that will allow the Institute to keep track of and relate specific NIGMS staff members' job responsibilities to IMPAC II module capabilities. The tracking and mapping capabilities of the database will help the Institute make informed choices about assigning job responsibilities and overall staffing. In addition, the database will serve as a management tool for supervisors when dealing with IMPAC II-related workload issues, as well as determining staff training needs in these areas.

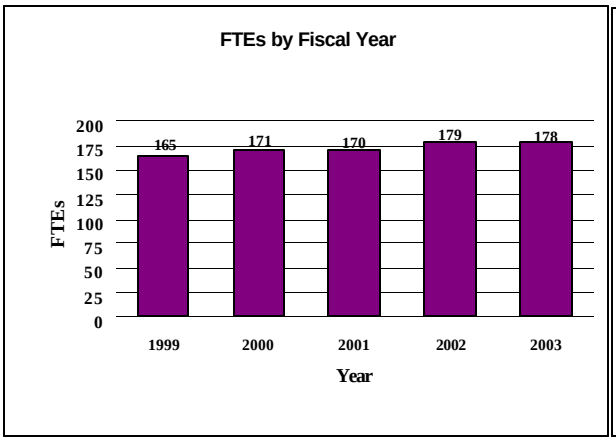
NIH Competitive Service Center Participation

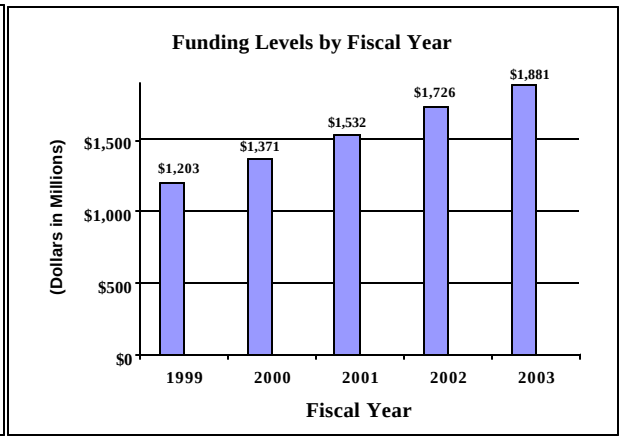
NIGMS currently participates in three NIH competitive service centers. The Institute is a user of the Center for Scientific Review's Scientific Review Evaluation Award Check Writing Competitive Service Center, the National Institute of Child Health and Human Development's Committee Management Service Center, and the NIH Office of Extramural Research's National Research Service Awards Payback Service Center.

Budget Policy

The Fiscal Year 2003 budget request for the NIGMS is $1,881,378,000 including AIDS, an increase of $154,911,000 and 9 percent over the FY 2002 level.

A five year history of FTEs and Funding Levels for NIGMS are shown in the graphs below. Note that Fiscal Years 2000 and 1999 are not comparable for the Managerial Flexibility Act of 2001 legislative proposal.



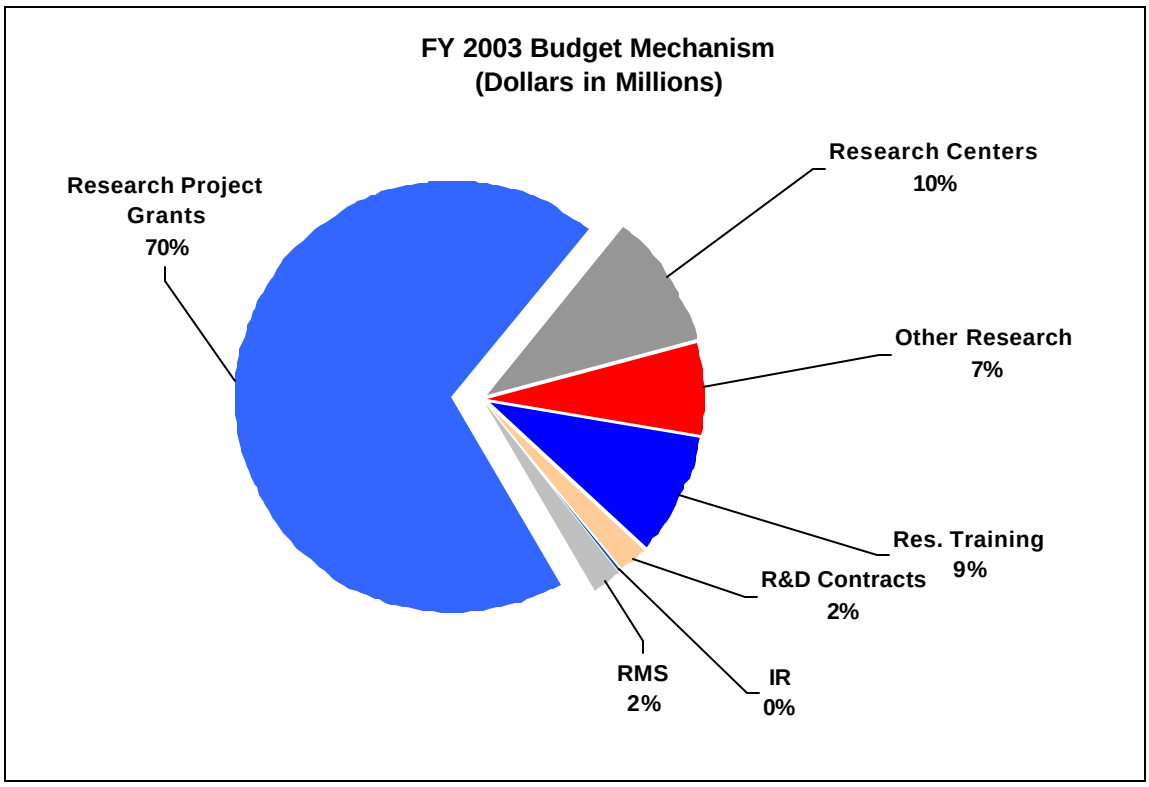


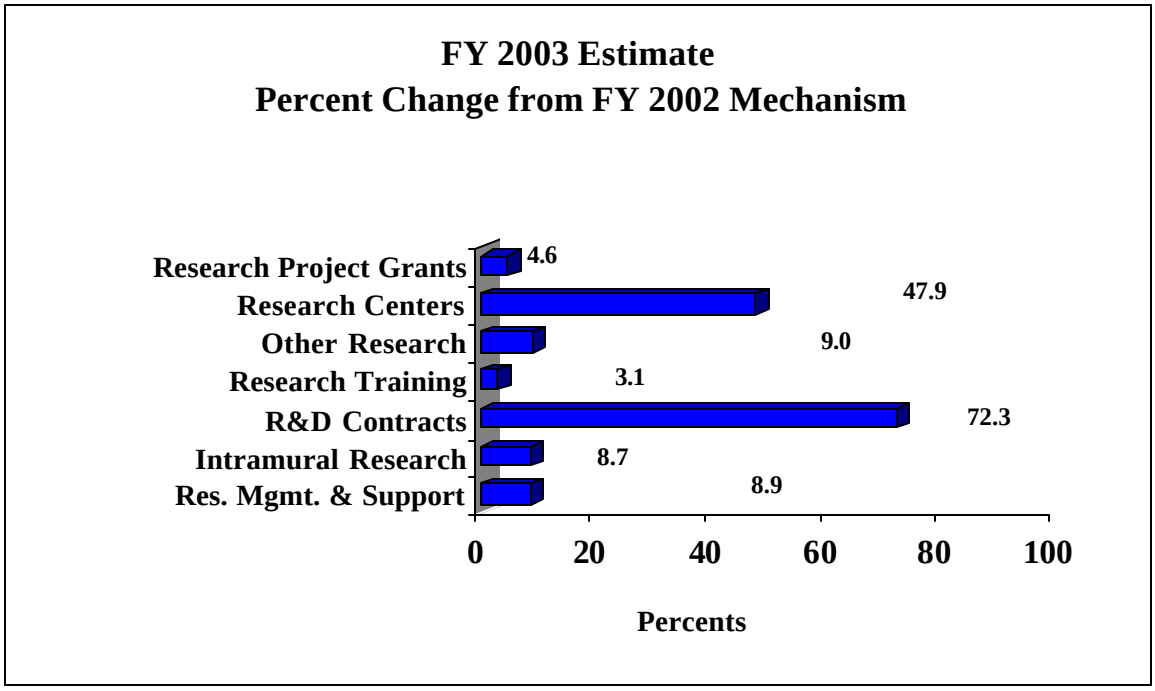
One of NIH's highest priorities is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities. The Fiscal Year 2003 request provides average cost increases for competing RPGs equal to the Biomedical Research and Development Price Index (BRDPI), estimated at 4.0 percent. Noncompeting RPGs will be funded at committed levels which include increases of 3 percent on average for recurring direct costs.

Promises for advancement in medical research are dependent on maintaining the supply of new investigators with new ideas. In the Fiscal Year 2003 request, NIGMS will support 4,482 pre- and postdoctoral trainees in full-time training positions, the same number as in FY 2002. Stipend levels for NRSA trainees will increase by 4 percent over Fiscal Year 2002 levels.

The Fiscal Year 2003 request includes funding for 49 research centers, 286 other research grants, including 42 career awards, and 24 R&D contracts. Within the increase for contracts, $11,270,000 is directed toward support of laser debridment for burned tissue. Intramural Research and Research Management and Support receive increases of 9 percent over FY 2002.

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





NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
TOTAL - Current Law
Budget Mechanism

MECHANISM	FY 2001 Actual		FY 2002 Appropriation		FY 2002 Current Estimate		FY 2003 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	2873	$790,081,000	3024	$890,512,000	3024	$890,512,000	2975	$907,969,000
Administrative supplements	(266)	14,530,000	(264)	14,966,000	(264)	14,966,000	(264)	15,415,000
Competing:								
Renewal	508	162,677,000	494	165,614,000	494	165,614,000	565	197,021,000
New	491	123,998,000	510	135,044,000	510	135,044,000	511	138,535,000
Supplements	7	790,000	8	945,000	8	945,000	10	1,181,000
Subtotal, competing	1006	287,465,000	1012	301,603,000	1012	301,603,000	1086	336,737,000
Subtotal, RPGs	3879	1,092,076,000	4036	1,207,081,000	4036	1,207,081,000	4061	1,260,121,000
SBIR/STTR	153	33,632,000	172	37,811,000	172	37,811,000	189	41,463,000
Subtotal, RPGs	4032	1,125,708,000	4208	1,244,892,000	4208	1,244,892,000	4250	1,301,584,000
Research Centers:								
Specialized/comprehensive	25	88,390,000	41	126,536,000	41	126,536,000	49	187,128,000
Clinical research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative medicine	0	0	0	0	0	0	0	0
Research Centers in Minority Institution	0	0	0	0	0	0	0	0
Subtotal, Centers	25	88,390,000	41	126,536,000	41	126,536,000	49	187,128,000
Other Research:								
Research careers	30	6,278,000	37	7,982,000	37	7,982,000	42	8,700,000
Cancer education	0	0	0	0	0	0	0	0
Cooperative clinical research	0	0	0	0	0	0	0	0
Biomedical research support	0	0	0	0	0	0	0	0
Minority biomedical research support	146	81,444,000	156	91,787,000	156	91,787,000	165	100,048,000
Other	53	15,353,000	71	22,884,000	71	22,884,000	79	24,944,000
Subtotal, Other Research	229	103,075,000	264	122,653,000	264	122,653,000	286	133,692,000
Total Research Grants	4286	1,317,173,000	4513	1,494,081,000	4513	1,494,081,000	4585	1,622,404,000
Training:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual awards	528	18,393,000	543	21,142,000	543	21,142,000	543	21,852,000
Institutional awards	3920	134,705,000	3939	144,438,000	3939	144,438,000	3939	148,824,000
Total, Training	4448	153,098,000	4482	165,580,000	4482	165,580,000	4482	170,676,000
Research & development contracts	17	24,534,000	16	24,534,000	16	24,534,000	24	42,276,000
(SBIR/STTR)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	FTEs		FTEs		FTEs		FTEs	
Intramural research	14	1,622,000	18	1,841,000	18	1,841,000	18	2,006,000
Research management and support	156	34,561,000	161	39,227,000	161	39,103,000	160	42,622,000
Cancer prevention & control	0	0	0	0	0	0	0	0
Construction		0		0		0		0
Total, NIGMS	170	1,530,988,000	179	1,725,263,000	179	1,725,139,000	178	1,879,984,000
(Clinical Trials)		(0)		(0)		(0)		(0)

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
TOTAL - Accrued Costs for Retirement and Health Benefits
Budget Mechanism

MECHANISM	FY 2001 Actual		FY 2002 Appropriation		FY 2002 Current Estimate		FY 2003 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting								
Administrative supplements								
Competing:								
Renewal								
New								
Supplements								
Subtotal, competing								
Subtotal, RPGs								
SBIR/STTR								
Subtotal, RPGs								
Research Centers:								
Specialized/comprehensive								
Clinical research								
Biotechnology								
Comparative medicine								
Research Centers in Minority Institutions								
Subtotal, Centers								
Other Research:								
Research careers								
Cancer education								
Cooperative clinical research								
Biomedical research support								
Minority biomedical research support								
Other								
Subtotal, Other Research								
Total Research Grants								
Training:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual awards								
Institutional awards								
Total, Training								
Research & development contracts (SBIR/STTR)								
	FTEs		FTEs		FTEs		FTEs	
Intramural research	0	119,000	0	133,000	0	133,000	0	139,000
Research management and support	0	1,073,000	0	1,195,000	0	1,195,000	0	1,255,000
Cancer prevention & control	0	0	0	0	0	0	0	0
Construction								
Total, NIGMS	0	1,192,000	0	1,328,000	0	1,328,000	0	1,394,000
(Clinical Trials)		(0)		(0)		(0)		(0)

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
TOTAL - Proposed Law
Budget Mechanism

MECHANISM	FY 2001 Actual		FY 2002 Appropriation		FY 2002 Current Estimate		FY 2003 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	2873	$790,081,000	3024	$890,512,000	3024	$890,512,000	2975	$907,969,000
Administrative supplements	(266)	14,530,000	(264)	14,966,000	(264)	14,966,000	(264)	15,415,000
Competing:								
Renewal	508	162,677,000	494	165,614,000	494	165,614,000	565	197,021,000
New	491	123,998,000	510	135,044,000	510	135,044,000	511	138,535,000
Supplements	7	790,000	8	945,000	8	945,000	10	1,181,000
Subtotal, competing	1006	287,465,000	1012	301,603,000	1012	301,603,000	1086	336,737,000
Subtotal, RPGs	3879	1,092,076,000	4036	1,207,081,000	4036	1,207,081,000	4061	1,260,121,000
SBIR/STTR	153	33,632,000	172	37,811,000	172	37,811,000	189	41,463,000
Subtotal, RPGs	4032	1,125,708,000	4208	1,244,892,000	4208	1,244,892,000	4250	1,301,584,000
Research Centers:								
Specialized/comprehensive	25	88,390,000	41	126,536,000	41	126,536,000	49	187,128,000
Clinical research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative medicine	0	0	0	0	0	0	0	0
Research Centers in Minority Institution	0	0	0	0	0	0	0	0
Subtotal, Centers	25	88,390,000	41	126,536,000	41	126,536,000	49	187,128,000
Other Research:								
Research careers	30	6,278,000	37	7,982,000	37	7,982,000	42	8,700,000
Cancer education	0	0	0	0	0	0	0	0
Cooperative clinical research	0	0	0	0	0	0	0	0
Biomedical research support	0	0	0	0	0	0	0	0
Minority biomedical research support	146	81,444,000	156	91,787,000	156	91,787,000	165	100,048,000
Other	53	15,353,000	71	22,884,000	71	22,884,000	79	24,944,000
Subtotal, Other Research	229	103,075,000	264	122,653,000	264	122,653,000	286	133,692,000
Total Research Grants	4286	1,317,173,000	4513	1,494,081,000	4513	1,494,081,000	4585	1,622,404,000
Training:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual awards	528	18,393,000	543	21,142,000	543	21,142,000	543	21,852,000
Institutional awards	3920	134,705,000	3939	144,438,000	3939	144,438,000	3939	148,824,000
Total, Training	4448	153,098,000	4482	165,580,000	4482	165,580,000	4482	170,676,000
Research & development contracts	17	24,534,000	16	24,534,000	16	24,534,000	24	42,276,000
(SBIR/STTR)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	FTEs		FTEs		FTEs		FTEs	
Intramural research	14	1,741,000	18	1,974,000	18	1,974,000	18	2,145,000
Research management and support	156	35,634,000	161	40,422,000	161	40,298,000	160	43,877,000
Cancer prevention & control	0	0	0	0	0	0	0	0
Construction		0		0		0		0
Total, NIGMS	170	1,532,180,000	179	1,726,591,000	179	1,726,467,000	178	1,881,378,000
(Clinical Trials)		(0)		(0)		(0)		(0)

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
Budget Authority by Activity 1/
(dollars in thousands)

ACTIVITY	FY 2001 Actual		FY 2002 Estimate		FY 2003 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural Research:								
Biomedical Research		1,341,707		1,518,615		1,664,680		146,065
Biomedical Research Training		153,098		165,580		170,676		5,096
Subtotal, extramural research		1,494,805		1,684,195		1,835,356		151,161
Intramural research	14	1,741	18	1,974	18	2,145	0	171
Research managament and support	156	35,634	161	40,298	160	43,877	(1)	3,579
Total	170	1,532,180	179	1,726,467	178	1,881,378	(1)	154,911

1/ Please see the following tables for the crosswalk from current law to proposed law to reflect the administration's proposal for full accrued retirement and health benefits.

National Institutes of Health

National Institute of General Medical Sciences

2001 Crosswalk for Accrued Retirement and Health Benefit Costs
(Dollars in thousands)

	2001 Actual Current Law	2001 Additional Accrual Costs	2001 Actual Proposed Law
Extramural Research:	$1,494,805	$0	$1,494,805
Subtotal, extramural resarch	1,494,805	0	1,494,805
Intramural Research	1,622	119	1,741
Research management and support	34,561	1,073	35,634
Total	1,530,988	1,192	1,532,180

National Institutes of Health

National Institute of General Medical Sciences

2002 Crosswalk for Accrued Retirement and Health Benefit Costs
(Dollars in thousands)

	2002 Appropriation Current Law	2002 Additional Accrual Costs	2002 Appropriation Proposed Law
Extramural Research:	$1,684,195	$0	$1,684,195
Subtotal, extramural resarch	1,684,195	0	1,684,195
Intramural Research	1,841	133	1,974
Research management and support	39,103	1,195	40,298
Total	1,725,139	1,328	1,726,467

National Institutes of Health

National Institute of General Medical Sciences

2003 Crosswalk for Accrued Retirement and Health Benefit Costs
(Dollars in thousands)

	2003 Estimate Current Law	2003 Additional Accrual Costs	2003 Estimate Proposed Law
Extramural Research:			
	$1,835,356	$0	$1,835,356
Subtotal, extramural research	1,835,356	0	1,835,356
Intramural Research	2,006	139	2,145
Research management and support	42,622	1,255	43,877
Total	1,879,984	1,394	1,881,378

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
Summary of Changes

2002 Estimated budget authority				$1,726,467,000
2003 Estimated budget authority				1,881,378,000
Net change				154,911,000
	2002 Current Estimate Base		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:	18			
a. Within grade increase		$1,429,000		$26,000
b. Annualization of January 2002 pay increase		1,429,000		18,000
c. January 2003 pay increase		1,429,000		29,000
d. Payment for centrally furnished services		253,000		23,000
e. Increased cost of laboratory supplies, materials, and other expenses		214,000		4,000
f. Accrued costs for retirement and health benefits		133,000		6,000
Subtotal				106,000
2. Research Management and Support:	161			
a. Within grade increase		14,926,000		259,000
b. Annualization of January 2002 pay increase		14,926,000		188,000
c. January 2003 pay increase		14,926,000		305,000
d. Payment for centrally furnished services		7,258,000		653,000
e. Increased cost of laboratory supplies, materials, and other expenses		17,412,000		856,000
f. Accrued costs for retirement and health benefits		1,195,000		60,000
Subtotal				2,321,000
Subtotal, Built-in				2,427,000

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
Summary of Changes--continued

CHANGES	2002 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	3,024	905,478,000	(49)	17,906,000
b. Competing	1,012	301,603,000	74	35,134,000
c. SBIR/STTR	172	37,811,000	17	3,652,000
Total	4,208	1,244,892,000	42	56,692,000
2. Centers	41	126,536,000	8	60,592,000
3. Other research	264	122,653,000	22	11,039,000
4. Research training	4,482	165,580,000	0	5,096,000
5. Research and development contracts	16	24,534,000	8	17,742,000
Subtotal, extramural		1,684,195,000		151,161,000
	FTEs		FTEs	
6. Intramural research	18	1,974,000	0	65,000
7. Research management and support	161	40,298,000	(1)	1,258,000
8. Construction		0	0	0
Subtotal, program		1,726,467,000		152,484,000
Total changes	179		(1)	154,911,000

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
Budget Authority by Object

	FY 2002 Appropriation	FY 2002 Current Estimate	FY 2003 Estimate	Increase or Decrease
Total compensable workyears:				
Full-time employment	179	179	178	(1)
Full-time equivalent of overtime and holiday hours	1	1	1	0
Average ES salary	$138,125	$138,125	$142,495	$4,370
Average GM/GS grade	10.6	10.6	10.6	0.0
Average GM/GS salary	$66,561	$66,561	$68,666	$2,105
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)	$0	$0	$0	$0
Average salary of ungraded positions	$88,713	$88,713	$91,519	$2,806

	OBJECT CLASSES	FY 2002 Appropriation	FY 2002 Estimate	FY 2003 Estimate	Increase or Decrease
	Personnel Compensation:				
11.1	Full-Time Permanent	$11,010,000	$11,010,000	$11,578,000	$568,000
11.3	Other than Full-Time Permanent	1,824,000	1,824,000	1,918,000	94,000
11.5	Other Personnel Compensation	444,000	444,000	467,000	23,000
11.8	Special Personnel Services Payments	0	0	0	0
11.9	**Total Personnel Compensation**	**13,278,000**	**13,278,000**	**13,963,000**	**685,000**
12.1	Personnel Benefits	3,077,000	3,077,000	3,235,000	158,000
12.1	Personnel Benefits, Accrued Retirement Costs	780,000	780,000	812,000	32,000
13.0	Benefits for Former Personnel	0	0	0	0
	Subtotal, Pay Cost, Current Law	**16,355,000**	**16,355,000**	**17,198,000**	843,000
	Subtotal, Pay Cost, Proposed Law	**17,135,000**	**17,135,000**	**18,010,000**	**875,000**
21.0	Travel and Transportation of Persons	483,000	483,000	559,000	76,000
22.0	Transportation of Things	87,000	87,000	93,000	6,000
23.1	Rental Payments to GSA	0	0	0	0
23.2	Rental Payments to Others	16,000	16,000	17,000	1,000
23.3	Communications, Utilities and Miscellaneous Charges	191,000	191,000	220,000	29,000
24.0	Printing and Reproduction	719,000	719,000	784,000	65,000
25.1	Consulting Services	77,000	77,000	83,000	6,000
25.2	Other Services	4,021,000	3,897,000	4,423,000	526,000
25.3	Purchase of Goods and Services from Government Accounts	60,209,000	60,209,000	84,204,000	23,995,000
25.3	Accrued Retirement Costs	548,000	548,000	582,000	34,000
25.4	Operation and Maintenance of Facilities	21,000	21,000	23,000	2,000
25.5	Research and Development Contracts	4,721,000	4,721,000	5,004,000	283,000
25.6	Medical Care	0	0	0	0
25.7	Operation and Maintenance of Equipment	261,000	261,000	285,000	24,000
25.8	Subsistence and Support of Persons	0	0	0	0
25.0	**Subtotal, Other Contractual Services, Current Law**	**69,310,000**	**69,186,000**	**94,022,000**	**24,836,000**
25.0	**Subtotal, Other Contractual Services, Proposed Law**	**69,858,000**	**69,734,000**	**94,604,000**	**24,870,000**
26.0	Supplies and Materials	413,000	413,000	450,000	37,000
31.0	Equipment	1,300,000	1,300,000	1,417,000	117,000
32.0	Land and Structures	0	0	0	0
33.0	Investments and Loans	0	0	0	0
41.0	Grants, Subsidies and Contributions	1,636,389,000	1,636,389,000	1,765,224,000	128,835,000
42.0	Insurance Claims and Indemnities	0	0	0	0
43.0	Interest and Dividends	0	0	0	0
44.0	Refunds	0	0	0	0
	Subtotal, Non-Pay Costs, Current Law	**1,708,908,000**	**1,708,784,000**	**1,862,786,000**	**154,002,000**
	Subtotal, Non-Pay Costs, Proposed Law	**1,709,456,000**	**1,709,332,000**	**1,863,368,000**	**154,036,000**
	Total Budget Authority by Object, Current	**1,725,263,000**	**1,725,139,000**	**1,879,984,000**	**154,845,000**
	Total Budget Authority by Object, Proposed	**1,726,591,000**	**1,726,467,000**	**1,881,378,000**	**154,911,000**
	Total Accrued Retirement Costs	**1,328,000**	**1,328,000**	**1,394,000**	**66,000**

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
Salaries and Expenses

OBJECT CLASSES	FY 2002 Appropriation	FY 2002 Current Estimate	FY 2003 Estimate	Increase or Decrease
Personnel Compensation:				
Full-Time Permanent (11.1)	$11,010,000	$11,010,000	$11,578,000	$568,000
Other Than Full-Time Permanent (11.3)	1,824,000	1,824,000	1,918,000	94,000
Other Personnel Compensation (11.5)	444,000	444,000	467,000	23,000
Special Personnel Services Payments (11.8)	0	0	0	0
Total Personnel Compensation (11.9)	**13,278,000**	**13,278,000**	**13,963,000**	**685,000**
Civilian Personnel Benefits (12.1)	3,077,000	3,077,000	3,235,000	158,000
Accrued Costs of Retirement Benefits (12.1)	780,000	780,000	812,000	32,000
Benefits to Former Personnel (13.0)	0	0	0	0
Subtotal, Pay Costs, Current Law	**16,355,000**	**16,355,000**	**17,198,000**	**843,000**
Subtotal, Pay Costs, Proposed Law	**17,135,000**	**17,135,000**	**18,010,000**	**875,000**
Travel (21.0)	483,000	483,000	559,000	76,000
Transportation of Things (22.0)	87,000	87,000	93,000	6,000
Rental Payments to Others (23.2)	16,000	16,000	17,000	1,000
Communications, Utilities and Miscellaneous Charges (23.3)	191,000	191,000	220,000	29,000
Printing and Reproduction (24.0)	719,000	719,000	784,000	65,000
Other Contractual Services:				
Advisory and Assistance Services (25.1)	67,000	67,000	73,000	6,000
Other Services (25.2)	4,021,000	3,897,000	4,423,000	526,000
Purchases from Govt. Accounts (25.3)	6,588,000	6,588,000	7,178,000	590,000
Accrued Retirement Costs (25.3)	548,000	548,000	582,000	34,000
Operation & Maintenance of Facilities (25.4)	21,000	21,000	23,000	2,000
Operation & Maintenance of Equipment (25.7)	261,000	261,000	285,000	24,000
Subsistence & Support of Persons (25.8)	0	0	0	0
Subtotal, Other Contractual Services, Current Law	**10,958,000**	**10,834,000**	**11,982,000**	**1,148,000**
Subtotal, Other Contractual Services, Proposed Law	**11,506,000**	**11,382,000**	**12,564,000**	**1,182,000**
Supplies and Materials (26.0)	413,000	413,000	450,000	37,000
Subtotal, Non-Pay Costs, Current Law	**11,371,000**	**11,247,000**	**13,928,000**	**2,681,000**
Subtotal, Non-Pay Costs, Proposed Law	**11,919,000**	**11,795,000**	**14,510,000**	**2,715,000**
Total, Administrative Costs, Current Law	**27,726,000**	**27,602,000**	**31,126,000**	**3,524,000**
Total, Accrued Costs	**1,328,000**	**1,328,000**	**1,394,000**	**66,000**
Total, Administrative Costs, Proposed Law	**29,054,000**	**28,930,000**	**32,520,000**	**3,590,000**

National Institute of General Medical Sciences

SIGNIFICANT ITEMS IN HOUSE AND SENATE APPROPRIATIONS COMMITTEE REPORTS

FY2002 House Appropriations Committee Report Language (H. Rpt. 107-229)

Item

Minority Scientist Training Programs **-** The Committee continues to be pleased with the quality of NIGMS's training programs, particularly those that have a special focus on increasing the number of minority scientists such as Minority Access to Research Careers (MARC) and Minority Biomedical Research Support (MBRS). The Committee urges NIGMS to continue to support these training programs. The Committee commends NIGMS for its support of biomedical research career opportunities programs for high school and undergraduate college students in conjunction with minority institutions. (p.14)

Action to be Taken

The Minority Access to Research Careers (MARC) and Minority Biomedical Research Support (MBRS) Programs, have a distinguished forty year history of offering opportunities to underrepresented minorities to prepare for careers in biomedical research, both at minority-serving and other institutions. The Institute remains committed to these long-standing programs, along with other more recent efforts, such as the Bridges to the Future Program. As the FY2003 budget shows, NIGMS will steadfastly support these and other mechanisms, such as the Minority Supplements, to increase the number of minority scientists engaged in biomedical research.

FY2002 Senate Appropriations Committee Report Language (S. Rpt. 107-84)

Item

Behavioral science research and training **-** The Committee is concerned that NIGMS does not support behavioral science research training. As the only Institute mandated to support research not targeted to specific diseases or disorders, there is a range of basic behavioral research and training that NIGMS could be supporting. The Committee urges NIGMS, in consultation with the Office of Behavioral and Social Sciences, to develop a plan for pursuing the most promising research topics in this area. (p.27)

Action to be Taken

The Institute's research training programs mirror the areas of science that fall within the mission of the National Institute of General Medical Sciences (NIGMS). Except for a few fields of inquiry, behavioral studies largely fall outside of the Institute's research mission, and are instead deemed to be within the missions of other institutes at the National Institutes of Health.

The National Institute of Mental Health (NIMH), as well as a number of others with missions focused on diseases, support both basic behavioral research and behavioral research in humans, since many disease states have behavioral dimensions. As is customary at the NIH, behavioral research training programs are mounted by those institutes with sizable behavioral research programs. A major new research or research training effort in basic behavioral sciences by NIGMS would be duplicative and inappropriate. A few of the institutions supported through NIGMS' Systems and Integrative Biology (SIB) training grant program offer participants opportunities to pursue training in the basic behavioral sciences. NIGMS intends to highlight this option of including behavioral science departments in SIB training programs when it reannounces its training programs in the coming months. In addition, individuals supported under the Institute's Medical Scientist Training Program (which leads to the M.D.-Ph.D. degree) may pursue research training in behavioral sciences if their institution offers that option. In both cases, the grantee institution chooses to offer this option as part of the multidisciplinary training mandated for all of NIGMS' training programs. NIGMS's individual fellowship support extends to fellows working on the molecular and genetic basis of behavior. In the past, some fellows have studied movement, sensation, and perception.

With regard to research, NIGMS supports studies, primarily in model systems, to examine the genetic and biochemical mechanisms underlying behavior. This includes research on the mechanisms underlying specific behaviors related to circadian rhythms, learning and memory, sensation and perception, pain and its management, and analgesia and anesthesia.

NIGMS is exploring new areas of opportunity. Together with the Office of Behavioral and Social Sciences Research (OBSSR), NIGMS will soon host a workshop to explore whether it is an opportune time to study how allostatic load (that is, the cumulative "wear and tear" on the body's adaptive responses to stress) influences an individual's reaction to traumatic or surgical injury. Also in a joint effort with OBSSR, NIGMS is exploring the feasibility of supporting Ph. D. biomedical scientists who wish to receive a Masters degree in the behavioral sciences enhancing their ability to conduct research in that field or in relevant interdisciplinary fields.

Item

Training **-** The Committee continues to be pleased with the quality of NIGMS's training programs, particularly those that have a special focus on increasing the number of minority scientists, such as the Minority Access to Research Careers (MARC) and Minority Biomedical Research Support (MBRS) programs. The Committee expects NIGMS to continue to support these important initiatives, and is particularly pleased that NIGMS has supported biomedical research career opportunity programs for high school

and undergraduate college students in conjunction with minority institutions. The Committee

urges continued, long-term support of this program. (p.28)

Action to be Taken

The Minority Access to Research Careers (MARC) and Minority Biomedical Research Support (MBRS) Programs have a distinguished forty year history of offering opportunities to underrepresented minorities to prepare for careers in biomedical research, both at minority-serving and other institutions. The Institute remains committed to these long-standing programs, along with other more recent efforts, such as the Bridges to the Future Program. As the FY2003 budget shows, NIGMS will steadfastly support these and other mechanisms, such as the Minority Supplements, to increase the number of minority scientists engaged in biomedical research.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2001 Amount Authorized	2002 Estimate	2003 Amount Authorized	2003 Budget Estimate 1/
Research and Investigation	Section 301	42§241	Indefinite	$1,560,887,000	Indefinite	$1,710,702,000
National Institute of General Medical Sciences	Section 417B	42§285	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	165,580,000	b/	170,676,000
Total, Budget Authority				1,726,467,000		1,881,378,000

a/ Funding provided under the Departments of Labor, Health and Human Services, Education, and Related Agencies Appropriations Act, 2002 (P.L. 107-116).
b/ Reauthorizing legislation will be submitted.

1/ Reflects proposed transfer from the National Cancer Institute

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
Appropriation History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1994	$833,064,000	$875,511,000	$875,511,000	$875,511,000
1995 2/	882,189,000	877,113,000	877,113,000	876,889,000 3/
1996	907,674,000 2/	946,971,000	897,465,000 2/	946,971,000
Rescission				(75,000)
1997	936,573,000 2/	1,003,772,000	953,214,000 2/	998,387,000 4/
1998	992,032,000 2/	1,047,963,000	1,058,969,000	1,065,947,000
1999	1,111,439,000 2/5	1,150,840,000	1,197,825,000	1,197,825,000
Rescission				(799,000)
2000	1,194,068,000 2/	1,298,551,000	1,352,843,000	1,361,668,000
Rescission				(7,248,000)
2001	1,389,492,000 2/	1,548,313,000	1,554,176,000	1,535,823,000
Rescission				(125,000)
2002	1,720,206,000 2/	1,706,968,000	1,753,465,000	1,725,263,000
Rescission				(124,000)
2003	1,881,378,000			

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 reductions of $227,000
4/ Excludes enacted administrative reductions of $83,000
5/ Reflects a decrease of $3,447,000 for the budget amendment for bioterrorism.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2001 Actual	FY 2002 Estimate	FY 2003 Estimate
Office of the Director	17	17	17
Office of Scientific Review	14	15	15
Office of Administrative Mangagement	35	35	34
Division of Extramural Activities	43	43	43
Genetic and Developmental Biology Division	13	15	15
Pharmacology, Physiology, and Biological chemistry Division	28	32	32
Cell Biology and Biophysics Division	12	12	12
Bioinformatics and Computational Biology Center	--	2	2
Minority Opportunities in Reseach Division	8	8	8
Total, NIGMS	170	179	178
Funds to support these FTEs are provided by Cooperative Research and Development	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
1999	10.6
2000	11.2
2001	10.7
2002	10.6
2003	10.6

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences
Detail of Positions

GRADE	FY 2001 Actual	FY 2002 Estimate	FY 2003 Estimate
ES-6	0	0	0
ES-5	0	0	0
ES-4	5	3	3
ES-3	0	1	1
ES-2	1	0	0
ES-1	0	0	0
Subtotal	**6**	**4**	**4**
Total - ES Salary	$794,382	$552,501	$569,978
GM/GS-15	21	12	12
GM/GS-14	18	20	20
GM/GS-13	20	23	23
GS-12	10	12	11
GS-11	6	6	6
GS-10	1	1	1
GS-9	9	9	9
GS-8	11	11	11
GS-7	15	15	15
GS-6	7	7	7
GS-5	5	5	5
GS-4	3	3	3
GS-3	3	3	3
GS-2			
GS-1			
Subtotal	**129**	**127**	**126**
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			
Subtotal	0	0	0
Ungraded	43	61	61
Total permanent positions	129	127	126
Total positions, end of year	178	192	190
Total full-time equivalent (FTE) employment,end of year	170	179	178
Average ES level	ES-4	ES-4	ES-4
Average ES salary	$132,397	$138,125	$142,495
Average GM/GS grade	10.7	10.6	10.6
Average GM/GS salary	$63,656	$66,561	$68,666