About NIH

Statement of the Director

It is my privilege to present to Congress the Biennial Report of the Director of the National Institutes of Health (NIH) for Fiscal Years (FYs) 2008 and 2009. Thanks to ongoing congressional support, NIH continues the pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability. Indeed, the contributions of NIH to improved health are countless and have touched the lives of not only all Americans, but also of millions of people around the world.

Unique Resources and Opportunities

It is an extraordinary time to be chosen to direct the world’s largest biomedical research enterprise. The power of the molecular approach to health and disease has steadily gained momentum over the past several decades, and is now poised to catalyze a true revolution in medicine—ultimately with profound consequences for diagnosis, prevention, and treatment of virtually all diseases. The success of the Human Genome Project and several other major projects that followed quickly afterward have provided a powerful foundation for a new level of understanding of human biology, and have opened a new window into the causes of disease. That includes the revelation of hundreds of previously unknown risk factors for cancer, diabetes, heart disease, hypertension, and a long list of other common illnesses. In the area of cancer, a new ability to achieve comprehensive understanding of the mechanisms responsible for malignancy has already provided insights into diagnostics and pointed to a whole new array of drug targets. Advances in stem cell research—now poised to move forward at an accelerated pace after the President’s signing in March 2009 of Executive Order 13505: Removing Barriers to Responsible Scientific Research Involving Human Stem Cells—hold great promise for applications to diseases such as Parkinson’s disease, type 1 diabetes, and spinal cord injury. New partnerships between academia and industry promise to revitalize the flagging drug development pipeline. An era of personalized medicine is emerging where prevention, diagnosis, and treatment of disease can be individualized, instead of using the one-size-fits-all approach that all too often falls short. Vigorous U.S. support of biomedical research in all these areas promises to save lives, reduce the burden of chronic illness, stimulate the economy, empower new and more effective prevention strategies, and reduce health care costs.

NIH Research Works!

Over the years, NIH research has contributed enormously to the remarkable increase in health and life expectancy in the United States. For example, we have gained 7.4 years of life expectancy from 1961 to 2004. Infant mortality has decreased from 26 deaths per 1,000 live births in 1960 to 6.9 in 2005. Two decades ago, the 5-year survival rate for women diagnosed with breast cancer was 84.3 percent and the annual mortality rate was 32.2 per 100,000. Due in large part to NIH research, the 5-year survival rate has risen to more than 90 percent. Breast-conserving surgery followed by local radiation therapy has replaced mastectomy as the preferred surgical treatment. New non-surgical therapies include combination chemotherapies, hormonal treatments, and new monoclonal antibodies.

In the 1990s, the discovery and development of antiretroviral drugs transformed HIV infection for many infected individuals from a death sentence into a chronic disease. Recently, researchers found that beginning antiretroviral therapy early in children infected with HIV significantly improves their immune systems. Because of this evidence, the HHS Panel on Pediatric Antiretroviral Therapy and Management Guidelines has modified recommendations on when to start HIV antiviral treatment in children.

Just a few decades ago, 30 percent of patients died within 25 years of a diagnosis of type 1 diabetes. One in four diabetics developed kidney failure, and diabetic retinopathy was responsible for 12 percent of
new cases of adult blindness. The concept of controlling blood sugar tightly to prevent diabetes-related eye disease, nerve damage, and kidney failure was untested. In 1989, enrollment of 1,441 people with type 1 diabetes was completed in the landmark Diabetes Control and Complications Trial (DCCT). The trial showed that intensive blood sugar control reduced risk for eye, kidney, and nerve complications by 50 to 75 percent. Upon completion of the DCCT, intensive therapy rapidly became the standard of care nationwide. Nearly all DCCT participants continue to be followed in an ongoing successor study. Now, based on new results from this pivotal study, we see not only continued dramatic reductions in eye, kidney, and nerve complications, but also that heart disease and stroke are cut by more than 50 percent. We also see improved long-term health outcomes: 30 years after their initial diagnosis, fewer than 1 percent of the intensively controlled DCCT participants have become blind, required kidney replacement, or had an amputation. Thus, people with type 1 diabetes are living longer, healthier lives than ever before, largely due to long-term NIH-supported research.

Importantly, as the Nation is in the midst of debating ways to reduce increasing health care costs dramatically, NIH research has resulted in remarkable U.S. gains in health and longevity, often with surprisingly modest investments and often accompanied by significant cost savings. A recent analysis of the trajectory of U.S. population health\(^1\) shows substantial correlation of NIH funding with improved life expectancy, reduced disability rates, and economic benefits. For example, deaths from coronary heart disease have declined by 63 percent in the last 30 years, thanks to a host of new insights about prevention and treatment. These dramatic advances have come about with an investment of just $3.70 per American per year in NIH research support. Another example of savings we have seen over time is the development of a vaccine against *Haemophilus influenzae* type b (Hib), which has resulted in a 99 percent decline in the incidence of this leading cause of bacterial meningitis in children under age 5. This has achieved an estimated medical cost savings of $950 million per year, as well as another $1.14 billion per year in avoidance of lost earnings due to disability of the patient and uncompensated caregivers.\(^2\)

ARRA: Jumpstarting a New Era

It was because of this remarkable synergy between the health and economic impacts of NIH-supported research that Congress directed an extraordinary $10.4 billion to NIH as part of the American Recovery and Reinvestment Act (ARRA). Annually, about 85 percent of the NIH budget is dispersed by grants and contracts through the 50 states and territories, with a significant impact on the local economies. Economic input-output studies found that through a multiplier effect each Federal dollar of NIH funding generates more than twice as much in state economic output.\(^3\) Moreover, estimates for FY 2007 indicated that NIH grants and contracts supported more than 350,000 jobs, in full or in part.\(^4\) Due to the ARRA funding, we estimate that approximately 50,000 jobs (full or in part) will be created or retained. It is important to note that 2-year ARRA funds will provide job creation and retention as well as longer-lasting impacts from advances in health science. Therefore, this unprecedented infusion of funds has been an excellent opportunity for sustaining our critical investment in medical research while creating jobs, stimulating related economic activity, and also buttressing the competitiveness of the Nation’s biomedical research enterprise. The astounding number of applications that we received for ARRA funding (more than 20,000 Challenge Grant applications and 2,000 Grand Opportunity Grant applications)\(^5\) revealed an untapped pool of innovative research ideas and projects with the potential for future breakthroughs and discoveries that address some of the Nation’s and world’s most pressing health problems. Clearly, NIH serves a unique role as the critical stimulus for the entire U.S. biomedical R&D enterprise.

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\(^4\) Ibid.

\(^5\) Data as of October 26, 2009.
Five Exceptional Opportunities for Biomedical Research at NIH

The investment in NIH research has certainly paid off. However, we are continuously faced with serious challenges in the fight against disease and disability. I see five major thematic areas that build on NIH’s recent advances and that could reap substantial downstream benefits for the diagnosis, prevention, and treatment of a long list of diseases, both rare and common.

First Thematic Area: Applying the unprecedented opportunities in genomics and other high-throughput technologies to understand fundamental biology, and to uncover the causes of specific diseases

In the past, most basic science projects in biomedicine required investigators to limit the scope of their studies to some single aspect of cell biology or physiology. The revolution now sweeping biomedical science is an emphasis on comprehensive approaches that identify all of the genes, all of the proteins, and all of the pathways involved in a disease process. Technologies contributing to these advances, many of which only recently have become practical to use on a routine basis, include DNA sequencing, microarray technology, nanotechnology, small molecule screening capabilities, new imaging modalities, and computational biology.

Cancer is a prime example of the potential of high-throughput approaches. Although a lot of information has been gleaned in the past from targeted efforts with certain tumors, the first complete cancer genomes are now becoming available (for leukemia and brain tumor). Stunning revelations are emerging about the genetic lesions that are involved in malignancies. Due partly to ARRA funding, The Cancer Genome Atlas is poised to derive comprehensive information about the causes of 20 major tumor types. It is virtually certain that this information will force a complete revision of diagnostic categories in cancer, and will usher in an era when every cancer will be evaluated in this comprehensive way, allowing an individualized matchup of the abnormal pathways in that specific tumor with the specific drug or therapeutic known to target that pathway.

Another example is the exciting new opportunity to understand how interactions between our bodies and the hundreds of trillions of microbes that live on us and in us (the so-called “microbiome”) can influence health and disease. The inability to culture most of the species that make up the human microbiome severely limited earlier investigations. But all of these organisms have DNA and/or RNA—and so it is now possible to categorize the vast array of species that are present in various body sites, in both healthy and ill individuals. The consequences for our understanding and treatment of a long list of diseases are likely to be profound. Currently, Human Microbiome Project investigators are studying microbial involvement in a range of diseases including psoriasis, Crohn’s disease, ulcerative colitis, and obesity.

Second Thematic Area: Translating basic science discoveries into new and better treatments

Often the path from molecular insight to therapeutic benefit has not been easily or quickly discernible for many disorders. That is changing now. The major factors propelling this change include the discovery of the fundamental molecular defect in hundreds of diseases, new resources that allow the screening of hundreds of thousands of compounds for drugs that target the defective molecule or molecular pathway, and the partnering of academia and industry to bring the strengths of each to the drug development pipeline.

The NIH Therapeutics for Rare and Neglected Diseases (TRND) program, established in FY 2009, is an example of a critical step in the direction of a truly integrated partnership for drug development between NIH and the private sector. TRND will combine experienced, high-level experts from pharmaceutical and biotechnology organizations and academic researchers. These scientists will work together to translate basic research findings into candidate drugs for patients with rare and neglected diseases. This program will allow promising compounds to be taken to the preclinical phase—often referred to as the “Valley of Death” because it is the place where good ideas often die—by modeling its infrastructure and staffing on best practices in the pharmaceutical and biotechnology industries while also capitalizing on the many
human, intellectual, and technological resources available at NIH that are not easily accessed by industry.

Another major area that is ripe for major translational advances is the application of various types of stem cells to treatment of human disease. FDA recently approved the first human protocol (for spinal cord injury) involving human embryonic stem cells (hESCs), and the potential for increased Federal support for human embryonic stem cell research will bring into this field many investigators who have been reluctant to participate due to uncertainties regarding Federal funding of research in this area. The recent revelation that skin fibroblasts can be transformed into induced pluripotent stem cells (iPSCs) opens up a powerful new strategy for therapeutic replacement of damaged or abnormal tissues, without the risk of transplant rejection. While much work remains to be done to investigate the possible risks of this approach, there is much excitement about the potential. The development of the iPSC approach stands as one of the most breathtaking advances in basic science in the last several years, and NIH will be making every effort to pursue with maximum speed the therapeutic consequences of iPSCs, hESCs, and adult stem cells.

**Third Thematic Area: Putting science to work for the benefit of health care reform**

NIH can make substantial contributions to health care reform. For example, in comparative effectiveness research (CER), NIH has supported clinical studies for many years that rigorously evaluate the outcomes of different medical treatment options. Examples include the Diabetes Prevention Program, which demonstrated substantially better benefits of exercise and lifestyle changes over medication in preventing the onset of diabetes, and the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, which compared older, cheaper antipsychotic drugs with newer ones, demonstrating that the older drugs worked just as well and had a better side-effect profile.

Prevention and personalized medicine is another area where NIH can widely contribute to health care reform. Advances in pinpointing individual genetic and environmental risk factors for disease now make it possible to focus prevention strategies more effectively on those who need them most. For example, including newly derived information about individual genetic risks for colon cancer or prostate cancer in determining the timing of colonoscopy or PSA screening could save lives and save money. Behavioral research focusing on how personalized information about disease risk actually alters health behaviors and clinical outcomes will be a critical component of this program.

Pharmacogenomics is another important area where research can inform health care. Already there is compelling evidence of a correlation between genotype and drug response for more than a dozen drugs, and that number is growing. But prospective studies will be needed for many of these applications, such as the one for warfarin (a widely prescribed anticoagulant), currently underway at NIH. The opportunity to choose the right drug at the right dose for the right person holds great promise for better health, both by avoiding treatments that are not going to work, and by reducing the incidence of adverse drug reactions.

One of the most tragic aspects of our health care system is the widespread presence of disparities in health. The health of racial and ethnic minorities, people living in poverty, people living in rural and remote locations, and other disadvantaged groups in the United States is worse than the health of the overall population. National concerns for these health disparities repeatedly have been expressed as a high priority in national health status reviews (including Healthy People 2010), and attention to this issue will be a critical component of any successful reform of the U.S. health care system. Now, new opportunities are emerging to define the causes and potential solutions for many health disparities, and these call for integration of research on the multifactorial nature of health disparities, including biological and nonbiological factors, and an understanding of the causes of disparities in access to and delivery of health care.

**Fourth Thematic Area: Encouraging a greater focus on global health**

NIH has a long tradition of supporting research on global health, and recent seminal scientific advances
position NIH to make even more important contributions. Examples already in hand include the development of a vaccine against Ebola virus (proven effective in primates) and the recent discovery by NIH researchers of the first new potential drug in 50 years to treat the parasitic disease schistosomiasis.

Much of recent global health research justifiably has been focused on AIDS, tuberculosis, and malaria, given the enormous human toll from these common and life-threatening disorders. NIH is ideally positioned to play a major role in ramping up the discovery phase for these infections, by applying new technologies such as RNAi, high-throughput screening, proteomics, and metabolomics, and tapping into the talents of highly motivated young researchers with a deep understanding of pathogen-host interactions. Combining these technological and human resources will inform future vaccine development and potentially open a vast new range of targets in pathogens and hosts for prevention, diagnostics, and therapeutics. It also is critical to go beyond the focus on the "big three" diseases to apply some of these same strategies to neglected diseases of low-income countries (e.g., roundworm, hookworm, leprosy, African sleeping sickness).

Importantly, we also must respond to the growing challenge of chronic noncommunicable diseases and injuries, which are now responsible for more than half of deaths in the developing world. Studying the causes of diseases such as diabetes and cancer in countries with limited resources can shed important light on pathogenesis and suggest interventions that can be implemented in low-resource settings.

Fifth Thematic Area: Reinvigorating and empowering the biomedical research community

The lifeblood of biomedical research in the United States rests on the talent and dedication of its scientists and an emphasis on innovation—both factors are considered in NIH's peer review system. The two-level peer review process is much admired and copied by other research agencies around the world. However, the increasing breadth, complexity, and interdisciplinary nature of modern research pose challenges to the traditional review process. To enhance peer review, NIH recently undertook an extensive examination of its review process, and in June 2008, announced a series of concrete steps for improvement. Those include recruiting the best reviewers; shortening proposals to reduce the burden on both applicants and reviewers; adapting the review process to make it as thorough, reliable, fair, and transparent as possible; and focusing more on impact than on methodological details. The effects of these new steps will be closely monitored, and additional reforms that encourage innovation will be undertaken as needed.

NIH-wide innovation now is fostered by the NIH Common Fund, which is designed to support crosscutting innovative projects that require participation of at least two or more Institutes or Centers. Established in law by the NIH Reform Act of 2006, the Common Fund provides a unique opportunity to support research that otherwise might not find a natural home at NIH.

Finally, the success of biomedical research rests squarely on the robustness of NIH training programs for the next generation of basic, translational, and clinical scientists. Multiple issues must be explored including adequacy of support, our role in training foreign scientists, and how best to diversify the scientific workforce. We need to provide the most exciting and positive environment for new scientists possible, where their enthusiasm and creativity will be nurtured in a way that optimizes their scientific creativity and independence.

Conclusion

There are unprecedented opportunities in front of us. The current acceleration in the pace of discovery was unimaginable only a decade ago. We need to capitalize on this moment of great opportunities for biomedical science in order to tackle the maladies that afflict millions of Americans and people around the world. Strong leadership by NIH, in collaboration with the many research organizations in the country and
around the world, is a precious asset to the global community to move forward and secure better health and better lives for all.