1

Strategy of the National Institutes of Health (NIH) of the US to Accelerate Biomedical Research (NIH Roadmap)

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1 Introduction

The National Institutes of Health (NIH)[1] is an agency of the Department of Health and Human Services of the US. The mission of the NIH is to "expand fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life, and conduct and support research in the diagnosis, treatment and prevention of human diseases." The NIH consists of the Office of the Director and 27 Institutes and Centers. The Office of the Director is responsible for setting policies for the NIH and for planning, managing, and coordinating the programs and activities of all of its institutes and centers. The 27 institutes and centers include the National Cancer Institute, the National Heart, Lung and Blood Institute, and the National Human Genome Research Institute. The NIH conducts research through these institutes and centers, and fosters research work at universities and research institutes both in the US and abroad by providing grants and funding opportunities.

NIH announced on September 30, 2003 the "NIH Roadmap" that outlines its "strategy to accelerate biomedical research progress." The NIH Roadmap provides a framework of the priorities the NIH must address in order to improve its research capabilities and speed the movement of research discoveries from the bench to the bedside.

This article outlines an overall picture of the NIH Roadmap by illustrating its objective, crafting process, pressing issues, and other major features.

2 NIH R&D Budget

Congress has not yet approved the NIH R&D budget bill for FY 2004[2]. The bill, which had been passed by the Lower House on December 8, 2003, is expected to be approved by the Upper House in January 2004. If approved, the bill would provide the NIH with $27.1 billion in FY 2004 (up 3.2% from FY 2003). The nation's R&D budget totals $127 billion, of which $56 billion are directed to non-defense programs. This means that the NIH budget accounts for nearly 50% of the nation's non-defense budget[3].

The NIH R&D budget continued to mark a 7 to 8% annual increase until FY 1998. Upon the launch of the "doubling of NIH budget" under the initiative of President Clinton in FY 1999, the NIH budget continued to mark outstanding annual growth of 14 to 15% (see Table 1). The NIH budget request for FY 2004, however, shows that such a rapid increase has come to an end, as it proposes a 3.2% increase from FY 2003[2,4].

The NIH budget doubling campaign effectively increased the budget for all NIH institutes. For

Table 1 :Change in the NIH R&D Budget [2,4]

Fiscal year	Budget (million $)	Comparison with previous year (%)
1998	13,110	7.3
1999	14,995	14.4
2000	17,234	14.9
2001	19,807	14.9
2002	22,714	14.7
2003*	26,245	15.5
2004**	27,093	3.2

* Figure for the final NIH budget for FY 2003
** Figure for the NIH budget as of December 8, 2003

Source: Author's compilation based on Reference[2,4].

example, "Human Genome Research" saw a substantial increase in its R&D budget from FY 1999 to FY 2000 due to the strengthened effort to map the human genome. The Human Genome Project made a major breakthrough when the human genome was finally sequenced in 2001. There has also been a rapid increase in the R&D budget for "Allergy and Infectious Diseases" since FY 2002[5-9].

3 Background to the Creation of the NIH Roadmap

There are two major factors that prompted the NIH to chart the priority initiatives entitled the "NIH Roadmap."

Firstly, the NIH intends to continue using its research potentials recognized during the doubling of NIH budget, which lasted five years from FY 1999 to FY 2003. Secondly, Dr. Elias A. Zerhouni was appointed the new NIH director in May 2002.

4 Overview of the "NIH Roadmap"

This chapter outlines the NIH Roadmap based on official information on the NIH website[10, 11].

4-1 Purpose

The purpose of the NIH Roadmap was to "identify major opportunities and gaps in biomedhical research that no single institute at NIH could tackle alone but that agency as a whole must address to make the biggest impact on the progress of medical research." Traditionally, the NIH conducts research through its 27 institutes and centers to facilitate its own research programs and offer funding opportunities. The NIH Roadmap, however, highlights the "priorities the NIH must address by transcending traditional departmental boundaries."

The NIH decided to craft the NIH Roadmap due, in part, to a change in the nature of biomedical research. This change was initiated by the completion of the human genome sequence, which dramatically increased the speed of new discoveries in the last few years. However, the complexity of biology remains a daunting challenge for the NIH, which aims at transforming scientific knowledge into tangible benefits for people. To meet that challenge, the NIH had to review its strategy to conduct biomedical research and bring research discoveries from the bench to the bedside.

4-2 Crafting Psrocess

Soon after becoming the director of the National Institutes of Health (NIH) in May 2002, Dr. Elias A. Zerhouni convened a series of meetings and consultations to chart the NIH Roadmap.

The initial step in crafting the Roadmap process involved a series of five meetings. More than 300 nationally recognized leaders in academia, industry, government, and the public discussed about the most compelling initiatives that the NIH should pursue over the next 10 years. Participants were asked to address three key questions. "What are today's most pressing scientific challenges?," "What are the roadblocks to progress, and what must be done to overcome them?," and "What is the responsibility of the NIH as a whole?" Through discussions, three major areas (themes) emerged.

Later, a series of Institute Director-chaired Working Groups of NIH staff were formed to make final selections of key initiatives on the advice of the NIH Council and the NIH Advisory Committee.

The NIH leadership weighed all initiatives in the context of several broad criteria to make final selections that deserve funding. These criteria include: "Is the initiative truly transforming - will it dramatically change the content or the process of medical research in the next decade?," "Would outcomes from the initiative be used by, and synergize the work of, many institutes?," "Will the initiative be compelling to NIH stakeholders, especially the public?," and "Does the initiative position the NIH to do something that no other entity can or will do?"

The Roadmap working groups were then grouped into several Implementation Groups to devise and examine detailed implementation plans, and short- and long-term objectives for the next stage of the Roadmap for FY 2004.

4-3 Major NIH Roadmap Areas Themes

(1) New Pathways to Discovery

This theme addresses the need "to understand complex biological systems." Having completed the sequencing of the human genome, further progress in medicine will require quantitative knowledge about the many interconnected networks of molecules that comprise cells and tissues, along with improved insights into how these networks are regulated and interact with each other. Implementing groups in this area will address several initiatives, including "Structural Biology," "Proteomics (research to determine the amounts, locations, and interactions of the large numbers of individual proteins within a single cell)," and "Metabolomics (research to determine the metabolic components and networks within the cell)."

In this set of initiatives, researchers will also build a better "toolbox" for today's biomedical research. To fully capitalize on the recent sequencing of the human genome and many new discoveries in molecular and cell biology, these initiatives address the research community's need for database access and analytical technologies.

With this theme, the Roadmap addresses the following five initiatives.

(i) Building Blocks, Pathways, and Networks

- The National Technology Centers for Networks and Pathways will be established to promote the development of new technologies to describe the dynamics of protein interactions. The center will also develop instruments, methods and reagents for quantitative measurements and for measurements at very short timescales.
- New technologies will be developed to study metabolomics. Knowledge gained from these studies will be used to understand the role of metabolites in the context of cellular pathways and networks.
- Workshops will be convened to study proteomics and metabolomics in order to establish data standards for research in proteomics and metabolomics, and investigate ways for establishing an evaluation index for future research in proteomics.

(ii) Molecular Libraries and Molecular Imaging

- The NIH Bioactive Small Molecule Library and the Screening Centers will be established to develop new screening methods and provide a public molecule library.
- A database of chemical structures, properties, and activities will be established. A competitive research fund will also be established to promote the development of tools and technologies for chemiformatics.
- Compounds as basic research tools will be developed. Bottlenecks in the development of compounds as drugs will be targeted.
- An imaging probe with strong detection sensitivity and specificity will be developed. A 1,000-fold improvement in imaging probe detection sensitivity is targeted, ultimately, for basic research and clinical applications. The initial step is to achieve a 10 to 100-fold improvement within five years.
- A database of specificities, activities and applications of an imaging probe will be established.
- The core facility will be established to provide imaging proves and generate novel imaging probes.

(iii) Structural Biology

- Methods will be developed to produce protein samples that scientists can use to determine the three-dimensional structure of a protein, and apply obtained knowledge to determine the structure of membrane protein.

(iv) Bioinformatics and Computational Biology

- The National Centers for Biomedical Computing will be developed. This initiative will also create a national software engineering system in which researchers will be able to tap into a supercomputing network from anywhere in the country to share and analyze data.

(v) Nanomedicine

- A series of workshops will be convened in FY 2004 to prepare for the launch of the Nanomedicine Centers in FY 2005. These Centers will focus on quantitative

measurement of biological processes at the nanoscale and the engineering of new tools to intervene at the nanoscale. This research will help scientists construct miniature pumps for drug delivery or tiny sensors to determine the cause of a disease.

(2) Research Teams of the Future

This theme is intended to address the issue of research system by implementing three initiatives: "Introduction of a new funding system," "Interdisciplinary Research," and "Public-Private Partnerships."

(i) High-Risk Research

A new funding system (NIH Director's Innovator Awards) will be introduced to provide support for "high-risk medical research that may achieve a major breakthrough." Historically, the NIH has almost exclusively supported low-risk research projects, because more detailed research proposals were selected over creative but high-risk proposals under its existing peer review system. The new award evaluates individual scientists in terms of their creative abilities, originalities, evidence of focused skillful habits of mind that predict perseverance and thorough exploration of his/her ideas, and prospects for making seminal biomedical research advances. In other words, originality or the potential of individual scientists weigh more than research proposals.

(ii) Interdisciplinary Research

There is a growing need for researchers to transcend the traditional departmental boundaries and to work with researchers in other areas of scientific interest, as today's biomedical research becomes increasingly diverse and complex. For instance, radiologists, physicists, biologists, and computer programmers may need to work together to solve a problem of image analysis. To keep pace with the changing nature of biomedical research, these initiatives will encourage researchers to "integrate different scientific disciplines." With this theme, the Roadmap seeks to address the following initiatives.

- Grants will be awarded to interdisciplinary research programs that use new approaches. A total of 15 grants will be awarded in FY 2004.
- Training will be provided to scientists in interdisciplinary research programs. This new model of funding will be introduced in FY 2004.
- Technologies and methods will be developed to facilitate interdisciplinary research.
- Structural barriers will be removed to facilitate interdisciplinary research.
- A model program for interdisciplinary research will be established within the NIH to provide training to scientists in interdisciplinary research and establish an interdisciplinary research team. The feasibility and benefits of the program will also be examined.
- The NIH and National Science Foundation (NSF) will hold the first interagency conference in FY 2004 to discuss "what needs to be done to encourage progress in the physical science that will provide support and underpinning in the future for advances in the life sciences."

(iii) Public-Private Partnerships

"Novel partnerships between the public and private sectors" will be encouraged to accelerate the movement of scientific discoveries from the bench to the bedside. There are two initiatives to encourage Public-Private Partnerships.

- The Public-Private Sector Liaison will serve as a resource to NIH staff on partnerships to set up an internal Public-Private Partnerships Coordinating Committee.
- Partnership Meetings will provide the NIH and potential partner organizations with opportunities to meet to discuss potential partnerships.

(3) Re-engineering the Clinical Research Enterprise

With this theme, the Roadmap addresses the need for "Re-engineering the Clinical Research Enterprise."

Ideally, basic research discoveries are quickly transformed into diagnostics, drugs, treatments or methods for prevention. Such translation lies

at the very heart of the NIH's mission. The NIH has succeeded in fulfilling that mission. If such efforts are to remain as successful as they have been in the past, the NIH must renew its effort to improve the health of the people.

In the past, all research for a clinical trail could be conducted in one academic center. Clinical research, however, has become more difficult to conduct over the years. Today, it is necessary to develop new partnerships among organized patient communities, community-based physicians, and academic researchers in order to conduct clinical research. To address such need, the NIH will promote the creation of better integrated networks of academic centers to speed clinical applications of basic research discoveries and enhance clinical research capabilities. This theme is intended to address this crucial area by implementing the following initiatives.

- A clinical research process will be coordinated, standardized and streamlined.
- The efficiency and productivity of the nation's clinical research enterprise will be enhanced through the creation of clinical research networks.
- Specialized training will be offered to clinical researchers.
- The National Electronic Clinical Trials and Research Network will be established as the standard data system that enables clinical researchers to share data and resources.
- The translation of basic discoveries to early phase clinical testing (translational research) will be promoted.
- The Regional Translational Research Centers will be established to increase interactions between basic and clinical scientists. The essential core infrastructure will be consolidated into these centers.
- Technologies will be developed to better quantify clinically important symptoms and outcomes, including pain and fatigue and to determine the severities of illnesses.

5 Conclusion

The NIH plans to set up a common pool of resources to facilitate the effort to implement the NIH Roadmap initiatives across the NIH as a whole. In FY 2004, $130 million will be committed to the Roadmap initiatives, with a total of $2.1 billion for five years to come[12]. This is a new attempt for the NIH, as it has always distributed a budget to all of its institutes and centers. The NIH will play a central role in shaping a budget and observing the progress of implementation, with each implementing group translating a plan into action on behalf of the NIH as a whole.

Presently, the NIH is inviting scientists to submit research proposals for obtaining competitive research funds on website, which are intended to support the NIH Roadmap initiatives. The NIH will begin to implement most of the initiatives in FY 2004 (from October 2003 to September 2004). At the beginning of FY 2004, applications were being received for several Roadmap-related competitive research funds. A gradual rise in the number of Roadmap related funding opportunities shows that the NIH is committed to moving towards a full-scale implementation of the Roadmap initiatives.

It is believed that the announcement of the NIH Roadmap at the beginning of FY 2004 was prompted by the need to present a new policy for the NIH as a whole, following the appointment of the new NIH director and the completion of the doubling of NIH budget in FY 2003.

The "NIH Roadmap" does not set a clear milestone for its initiatives. Rather, it lays out the direction for future research. In the area of basic research, post-genome research, development of post-genome analytical tools, and interdisciplinary research are made the priority initiatives. This shows that the NIH gives the utmost priority to the facilitation of clinical research in consideration of its mission.

We will watch the future development of the NIH Roadmap closely to report on how the President's Budget proposals for FY 2005 weigh on the NIH initiatives and how Congress alters and agrees the budget for final approval.

Reference

[1] National Institutes of Health (NIH), http://www.nih.gov/

[2] AAAS, "NIH Wins 3 Percent Increase in Final FY 2004," Dec. 9, 2003.

[3] AAAS, "FY 2004 Federal R&D Climbs to Record High of $127 Billion," Dec. 8, 2003.
[4] AAAS, "Historical Data on Federal R&D, FY 1976-2004," March 7, 2003.
[5] AAAS, "FY 2003 Omnibus Bill Completes NIH Doubling Plan; Large Increases for Bioterrorism R&D and Facilities," Feb. 25, 2003.
[6] AAAS, "NIH Budget Climbs $3.2 Billion or 15.7 Percent," Jan. 4, 2002.
[7] AAAS, "Congress and President Clinton Agree on 14 Percent Boost for NIH," Jan. 4, 2001.
[8] AAAS, "Congress Agree on $2.2 Billion Boost for NIH, But Withholds $3 Billion Until Next September," Nov. 24, 1999.
[9] AAAS, "NIH Wins $2 Billion Increase in FY 1999," Nov. 13, 1998.
[10] NIH Roadmap, http://nihroadmap.nih.gov/
[11] Elias Zerhouni, The NIH Roadmap, Science, 302 (5642): 63 - 72.
[12] Chemical & Engineering News, 81 (40): 10.

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