

BUILDING STRATEGIC PARTNERSHIPS TO ADVANCE HEALTH RESEARCH



Conference Proceedings
May 3-4, 2006
Washington, D.C.



A national consortium of non-governmental
funders of health research and training



A national consortium of non-governmental funders of health research and training

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Meeting Report

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TABLE OF CONTENTS

Agenda	4
Acknowledgments	8
Preface	9
Introduction	11
Plenary Session 1: The Changing Landscape for Medical Research	12
Plenary Session 2: Federal Initiatives in Clinical and Translational Research	19
Breakout Sessions on Funding Partnerships:	
A. Translation: Models for Developing Translational Infrastructure and Capacity	23
B. Human Capital: Building Research Networks and Funding Teams	26
C. Community: Models of Community-Based Participatory Research	30
D. Translation: Disease-Oriented Models of Drug/Vaccine Development	32
E. Human Capital: Career Development of Clinical Investigators	35
F. Community: Regional Models for Influencing State Policy	40
The Importance of Science from the Perspective of a Patient Advocate	43
Plenary Session 3: Translating Research into Practice	45
Breakout Sessions on Operational Issues:	
G. Encouraging the Mentoring of Early-Career Clinical Investigators and Scientists	47
H. Managing Donor Activism in the Peer-Reviewed Science Process	49
I. Starting from Scratch: A Biomedical Funding Tutorial for New or Small Foundations	51
J. Intellectual Property and Royalty Issues: Preclinical Drug Discovery and Development	53
Closing Plenary Session: Mechanisms for Accelerating Drug Development for Orphan Diseases	56

AGENDA

WEDNESDAY, MAY 3

- 8:30 a.m.** **Opening and Welcome**
The Health Research Alliance: Substantive Collaboration Among Private Funders of Health Research
Speaker: Nancy Sung, Ph.D., Chair, Board of Directors, Health Research Alliance (HRA) and Senior Program Officer, Burroughs Wellcome Fund
- 9:00 – 10:30** **Plenary Session 1: The Changing Landscape for Medical Research**
The Funding Environment for Biomedical and Health Research
Speaker: Gail Cassell, Ph.D., Vice President, Scientific Affairs, Distinguished Lilly Research Scholar for Infectious Diseases, Eli Lilly and Company
Scientific Frontiers in Medicine
Speaker: Jeffrey Trent, Ph.D., President and Scientific Director, Translational Genomics Research Institute (TGen)
- 10:30 – 11:00** **Break**
- 11:00 – 12:30** **Plenary Session 2: Federal Initiatives in Clinical and Translational Research**
Moderator: Gail Cassell, Ph.D., Vice President, Scientific Affairs, Distinguished Lilly Research Scholar for Infectious Diseases, Eli Lilly and Company
Update on the National Institutes of Health's New Clinical and Translational Science Awards
Speaker: Barbara Alving, M.D., M.A.C.P., Acting Director, National Center for Research Resources, National Institutes of Health
Update on the Food and Drug Administration's Critical Path Initiative
Speaker: Janet Woodcock, M.D., Deputy Commissioner for Operations, and COO, U.S. Food and Drug Administration
- 12:30 – 2:00** **Lunch**
Introduction to the HRA and its working groups
- 2:00 – 3:30** **Breakout Session #1 on Funding Partnerships**
A. Translation: Models for Developing Translational Infrastructure and Capacity
Moderator: Bill Read, Ph.D., Vice President, Research and Technology, The Flinn Foundation
The Role of Novel Partnerships in the FDA's Critical Path Initiative
Ray Woosley, M.D, Ph.D., President, The Critical Path Institute

Accelerating Med-Tech Innovation: The Role of Foundations

John Linehan, Ph.D., Whitaker Foundation (retired) and Consulting Professor of Bioengineering, Program in BioDesign, Stanford University

Developing a Statewide Translational Research Network

Bill Read, Ph.D., Vice President, Research and Technology, The Flinn Foundation

B. Human Capital: Building Research Networks and Funding Teams

Moderator: David Tancredi, M.D., Scientific Director, Fondation Leducq

International Networks in Cardiovascular Research

David Tancredi, M.D., Scientific Director, Fondation Leducq

The Multiple Myeloma Research Consortium: Lessons Learned

Kathy Giusti, M.B.A., Chief Executive Officer and Founder, Multiple Myeloma Research Foundation and Multiple Myeloma Research Consortium

A New Model for an Outcome-Directed Research Collaboration

Rusty Bromley, M.S., Chief Operating Officer, Myelin Repair Foundation

The Brain Tumor Funders' Collaborative: A Virtual Organization

Rita D. Berkson, M.P.H., Executive Director, Goldhirsh Foundation, Brain Tumor Funders' Collaborative

C. Community: Models of Community-Based Participatory Research

Moderator: Marc Hurlbert, Ph.D., Senior Consultant, Grants and Partnerships, Avon Foundation

Community-Based Participatory Research: A Partnership Approach for Conducting Health Research

Barbara Israel, Dr.P.H., Professor, University of Michigan School of Public Health
Donele Wilkins, Executive Director, Detroiters Working for Environmental Justice

Community-Based Participatory Research: Moving the Field Forward

Sarena D. Seifer, M.D., Executive Director, Community-Campus Partnerships for Health

4:00 – 5:30

Breakout Session #2 on Funding Partnerships

D. Translation: Disease-oriented Models of Drug/Vaccine Development

Moderator: Michael Katz, M.D., Senior Vice President for Research and Global Programs, March of Dimes

The Medicines for Malaria Venture: A Public/Private Partnership for Drug Development

Queta Bond, Ph.D., President, Burroughs Wellcome Fund

Creating Drugs for People with Cystic Fibrosis

Suzanne R. Pattee, J.D., Vice President of Public Policy and Patient Affairs, Cystic Fibrosis Foundation

JDRF Experiences with "Cure Therapeutics"

Robert Goldstein, M.D., Ph.D., Chief Scientific Officer, Juvenile Diabetes Research Foundation (JDRF) International

E. Human Capital: Career Development of Clinical Investigators

Moderator: Scott Campbell, Ph.D., National Vice President, Research Programs, American Diabetes Association

A Private Funder's Approach to Developing Biomedical Researchers

William Galey, Ph.D., Director, Graduate & Medical Education Programs, Howard Hughes Medical Institute

NIH Career Development Awards (“K” Awards)

James F. Hyde, Ph.D., Senior Advisor, Research Training Programs, National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health

The Role of Academic Medicine in Nurturing Translational and Clinical Research

David Korn, M.D., Senior Vice President for Biomedical and Health Sciences Research, Association of American Medical Colleges

F. Community: Regional Models for Influencing State Policy

Moderator: John Murphy, M.S., President, The Flinn Foundation

State/Regional Partnerships in the Biosciences

Walter H. Plosila, Ph.D., Vice President, Technology Partnership Practice, Battelle Memorial Institute

California’s Stem Cell Research Initiative: Science, Advocacy, Politics and the Public Trust

Philip A. Pizzo, M.D., Dean, Stanford University School of Medicine

Building Strategic Partnerships to Advance Health Research

John Murphy, M.S., President, The Flinn Foundation

Show Me Partnerships! Founding the Missouri Bio-Belt

Susan M. Fitzpatrick, Ph.D., Vice President, James S. McDonnell Foundation

6:00

Reception and Dinner

The Importance of Science from the Perspective of a Patient Advocate

Speaker: Margery Perry, Chair of Research Emeritus, JDRF International

THURSDAY, MAY 4

7:00 – 8:00

Breakfast Roundtables

8:15 – 9:00

Plenary Session 3: Translating Research into Practice

Speaker: Carolyn M. Clancy, M.D., Director, Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services

9:00 – 9:30

gHRAsp: The Online Searchable Database “Grants in the Health Research Alliance Shared Portfolio”

Speaker: T.J. Koerner, Ph.D., Director of Research Information Management, American Cancer Society, and members of the gHRAsp Working Group

9:30 – 10:30

Breakout Session #1 on Operational Issues

G. Encouraging the Mentoring of Early-Career Clinical Investigators and Scientists

Moderator: Virginia Krawiec, M.P.A., Director, Health Professional Training Grants, American Cancer Society

The Health Research Alliance Mentoring Projects

Virginia Krawiec, M.P.A., Director, Health Professional Training Grants, American Cancer Society

History and Analysis of a Mentored Clinical Investigator Award for Cancer Research

Jennifer McCafferty-Cepero, Ph.D., Scientific Director, Damon Runyon Cancer Research Foundation

Mentoring: Insights Into the Satisfied Trainee

Victoria McGovern, Ph.D., Senior Program Officer, Burroughs Wellcome Fund

Mentoring Via a Consortium

Lori Conlan, Ph.D. Program Manager, Science Alliance, New York Academy of Sciences

H. Managing Donor Activism in the Peer-Reviewed Science Process

Session Organizer and Speaker: Maria Carrillo, Ph.D., Director, Medical and Scientific Relations, Alzheimer's Association National Office

10:30 – 11:00

Break

11:00 – 12:00

Breakout Session #2 on Operational Issues

I. Starting from Scratch: A Biomedical Funding Tutorial for New or Small Foundations

Session Organizer and Speaker: Sally McNagny, M.D., M.P.H., Vice President, The Medical Foundation

J. Intellectual Property and Royalty Issues: Preclinical Drug Discovery and Development

Session Organizer and Moderator: Michelle Cissell, Ph.D., Associate Director for Strategic Planning Research Department, Juvenile Diabetes Research Foundation International

NIH Policies on Intellectual Property Protection, Licensing, and Royalties

Susan Rucker, Esq., Senior Technology Licensing Specialist, National Institutes of Health Office of Technology Transfer

How Funders Can Drive the Therapeutics Pipeline and Manage IP: The CFF Experience

Suzanne R. Pattee, J.D., Vice President of Public Policy and Patient Affairs, Cystic Fibrosis Foundation

Acquiring Patent Rights To Gene Sequences: Adding to the Portfolio of Tools to Accelerate Drug Discovery

Cynthia Joyce, M.S., Executive Director, Spinal Muscular Atrophy Foundation

12:15 – 1:30

Lunch and Closing Plenary: Mechanisms for Accelerating Drug Development for Orphan Diseases

Speaker: Tom Caskey, M.D., F.A.C.P., Executive Vice President for Molecular Medicine & Genetics, The University of Texas Health Science Center at Houston

1:30

Adjourn

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PREFACE

The Health Research Alliance (HRA): Substantive Collaboration Among Non-Governmental Funders of Health Research

The private philanthropic sector in the United States is growing at a steady pace, with private foundations now numbering nearly 68,000, with an asset base of more than \$500 billion. Foundation giving has nearly tripled since 1995¹. The proportion of private funds in support of biomedical and health research has remained at about five percent for decades and is dwarfed by the contributions of both the government and for-profit industry. Yet, in light of the flattened National Institutes of Health (NIH) budget², the role of private funders is increasingly important. As a relatively small group of growing players in the biomedical and clinical research enterprise, nonprofit funders must carefully consider how to target their investments for greatest impact.

“[Foundations should] concentrate resources on problems that are not being dealt with by governments or for-profit organizations. Being constrained by neither voters nor shareholders, they can take risks to find pioneering new solutions that can then be adopted on a larger scale by governments or for-profit firms.”

*The Business of Giving: A Survey of Wealth and Philanthropy,
The Economist, 2006.*

Toward that end, the 2006 National Conference of the HRA drew participants and speakers from 50 not-for-profit, non-governmental funders of health research and training, six research institutions, several federal research agencies, and a pharmaceutical company. The conference series began in 1998 with an initial focus on opportunities for nonprofit private funders to advance health research. Biennial meetings since then have focused on the career development of clinical investigators, advances in electronic grantmaking, as well as new partnership models for funding health research and drug development.

Trends in Foundation Giving

- Number of foundations grew two percent from 2003-4:
66,398 to 67,736
- Foundation assets grew seven percent from 2003-4:
\$477B to \$510B
- Giving in science/technology and health showed largest gains

Source: *Foundation Giving Trends*,
The Foundation Center, 2006

“Health Foundations” (created by the conversion of non-profit hospitals and health systems to for-profit status):

	1997	2004
Number of foundations	81	174
Assets	\$9.0 billion	\$18.3 billion

Source: *Grantmakers in Health, Survey of Foundations Formed from Health Care Conversions*, 2004

¹ The Foundation Center, *Foundation Yearbook 2006*. www.foundationcenter.org

² Moses et al, *JAMA* 294:1333-1342, 2005, also Loscalzo, J., *NEJM* 354:1665-1667 (2006).

Grants in the Health Research Alliance Shared Portfolio (gHRAsp): The Online Searchable Database

gHRAsp, perhaps the HRA's most important undertaking to date, will consolidate award information among non-governmental funders of health research. The goal is to provide a comprehensive source of information that will be useful to large and small funders or grantmakers in strategic planning and decision-making. Public users will have access to limited information similar to the data provided by NIH to the public through its database CRISP (crisp.cit.nih.gov).

Led by T. J. Koerner, Ph.D., director of research information management at the American Cancer Society, the work began as a collaboration between a volunteer software architect and representatives from HRA member agencies. Contract staff are preparing the database to receive agency data beginning in 2007. Key development issues have included management of duplicate entries, protecting confidential information, building a reporting function, and deciding on an appropriate taxonomy of funded research topics. Once operational, gHRAsp will be a valuable tool to help member organizations identify funding opportunities, areas of common interest, and effective methods of award program evaluation.

Following the 2004 conference, participants decided to formalize their partnership as the HRA, with the mission of improving communication and collaboration among private, non-governmental funders; by making available more comprehensive information on research funded by private funders; and by increasing the overall effectiveness of private grantmakers.

In addition to the national conference, representatives from HRA member organizations meet several times a year on a smaller scale, for the consideration of issues relevant to the work of its members. Examples include examining new programs launched by NIH, public access to the medical research literature, drug development for neglected diseases, mentoring and career development of clinical investigators, and the role of donors and investors in achieving a funding agency's scientific agenda. HRA provides a forum where private foundations, voluntary health agencies, and disease-specific funders can address issues of mutual concern and interest.

A major early project of the HRA is to construct a searchable database of privately funded grant awards—in order to know the extent of private investment in particular disease areas or in certain types of investigators. All HRA members will be required to include their award data in the database, which will be useful for both program development and policymaking by funding agencies. Implementation of the database, Grants in the Health Research Alliance Shared Portfolio (gHRAsp), is forecast for 2007, and the intent is eventually to make the data publicly available (see sidebar).

Finally, the HRA aims to enhance the overall effectiveness of grantmakers in supporting biomedical and health research through the sharing of information and best practices. HRA working groups have considered the topics of how to conduct peer review, how to manage conflict of interest, how to provide the mentoring that keeps young investigators on track, and how to measure the results of funded programs.

One of the strengths of the nonprofit sector in the U.S. is the distinctiveness of its many members—as well as the healthy competition among them for donors, which drives them toward excellence in finding innovative solutions to important problems. New models for funding health research must be tried, shared with peers, and evaluated, as the lessons learned in one disease area are bound to accelerate progress in other areas.

INTRODUCTION

The plenary sessions at the 2006 National Conference were designed to provide a broad overview of the current funding and scientific landscapes, as well as to highlight recent initiatives from the National Institutes of Health, the Food and Drug Administration, and the Agency for Healthcare Research and Quality. The work of these federal agencies covers the whole range of health research—from basic biomedical research, through drug discovery and development, into outcomes and effectiveness research.

The breakout sessions on the first day of the meeting focused on programmatic issues relevant to funders, including models for developing translational infrastructure and capacity, building research networks and funding teams, as well as models of community-based participatory research.

On the second day of the meeting, the focus was on internal operational issues that funders face; namely how to begin funding biomedical research, managing donor expectations, dealing with intellectual property issues associated with funded projects, and opportunities for funders to encourage the mentoring of supported investigators.

The following summary captures the main points of the discussions and also provides references to other relevant sources of information on the topics addressed.

PLENARY SESSION 1: THE CHANGING LANDSCAPE FOR MEDICAL RESEARCH

The Funding Environment for Biomedical and Health Research

The purpose of this plenary session was to address the following questions:

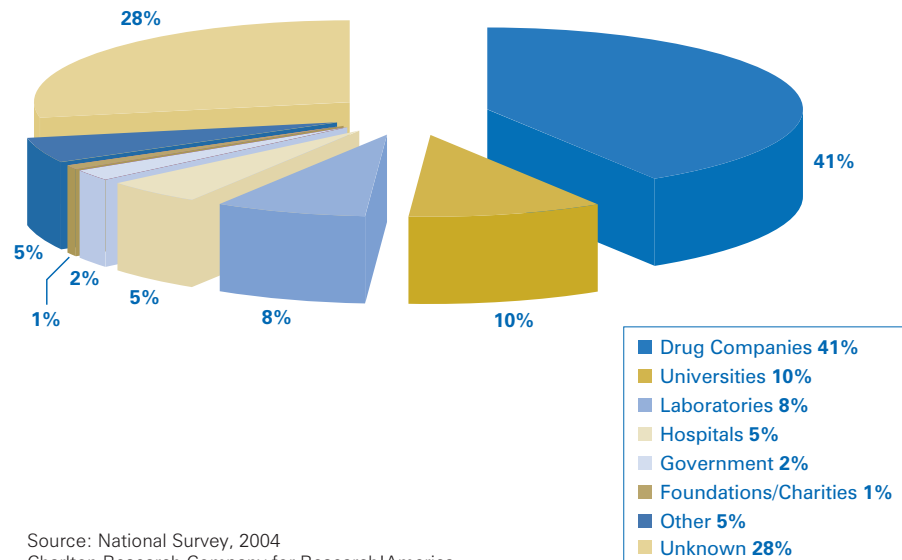
- How do federal deficits, investment in bioterrorism research, global disparities, and other factors affect the federal funding environment for biomedical and health research?
- Where are the opportunities for private sector investment?

Gail Cassell, Ph.D., vice president for scientific affairs and Distinguished Lilly Research Scholar for Infectious Diseases at Eli Lilly and Company, reviewed some of the realities in drug and vaccine development.

Basic research is the key to innovation, but development—turning discovery into a product—is the time-limiting step in research and development, and by far the more expensive. Traditionally, public agencies have paid for basic research and training, while industry has shouldered the investment in applied and translational research. The total public and private investment in biomedical research increased from \$37 billion in 1994 to \$94 billion in 2003, but industry still accounts for 57 percent of total investment, and the prospects for continuing increases in federal research dollars appear grim.

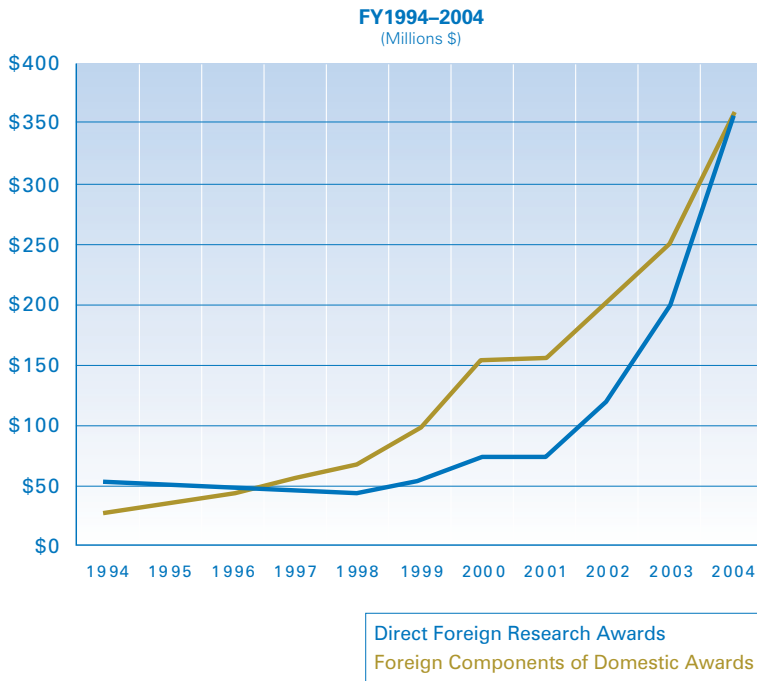
Where are New Drugs Developed in the U.S.?

At what type of institutions or organizations do you think most drug development takes place in this country?



Source: National Survey, 2004
Charlton Research Company for Research!America

NIH International Research Expenditures



Source: Fogarty International Center, Nov. 2005

The National Institutes of Health (NIH) has enjoyed a doubling of its budget over five years and currently funds 28 percent of all biomedical research and development, but NIH is looking at flat or declining budgets in coming years. Biomedical research budgets are down at the Centers for Disease Control and Prevention (CDC), the Department of Defense (DOD), and the U.S. Agency for International Development (AID) as well. The recently announced American Competitiveness Initiative (ACI) will put new funds into the National Science Foundation (NSF) and Department of Energy (DOE), but most of those dollars will be invested in the physical sciences and engineering. The Food and Drug Administration (FDA), whose regulatory activities influence a quarter of the U.S. economy, has had no funding increase beyond inflation in decades. In the future, this loss of federal investment may disrupt the delicate balance between fundamental research and advanced development, with an overall negative impact on the productivity of the research enterprise.

Biomedical research in the 21st century is still influenced considerably by the Bayh-Dole Act of 1980, which made it easier to transfer and commercialize technologies developed by federal agencies. During the 1990s, the rise of genomics as well as the reemergence of infectious diseases greatly increased public interest in and expectations for biomedical research.

The first decade of the new century has highlighted the increasing importance of global health in terms of not only relevance to domestic health problems, but also to economic development and political stability. Major events included the emergence of severe acute respiratory syndrome (SARS) and avian flu, as well as the September 11, 2001 attacks and the threat of bioterrorism, which rocketed to a national priority and now consumes 50 percent of the budget of the National Institute of Allergy and Infectious Diseases (NIAID). The NIAID portfolio now includes grants for work in more than 95 countries. The NIAID profile is indicative of an NIH-wide increase in internationally-targeted research grants, which more than doubled from 2001 to 2004. While absolute dollars have increased, still only about 10 percent of the U.S. biomedical research budget goes to address 90 percent of the world's health problems¹, thus the global health disparity remains.

Closely related to the global health issue is a growing national concern regarding U.S. ability to compete in a global economy given the decreased numbers of U.S. citizens pursuing degrees in science and engineering, compared to those in developing nations such as China and India. The National Academy of Sciences report, "Rising above the Gathering Storm: Energizing and Employing America for a Brighter Economic Future," recommended actions that federal policymakers could take to reverse current trends and ensure that the U.S. will be able to compete, prosper, and be secure in the 21st century.

National Academy of Sciences Report: *Rising Above the Gathering Storm: Energizing and Employing America for a Brighter Economic Future*

Four broad recommendations for the future:

1. Increase America's talent pool by vastly improving K-12 science and mathematics education and providing scholarships for undergraduate majors in science and engineering.
2. Sustain and strengthen the nation's financial commitment to long-term basic research that has the potential to be transformational, in order to maintain the flow of new ideas that fuel the economy, provide security, and enhance quality of life.
3. Make the U.S. the most attractive setting in which to study and perform research so that we can develop, recruit, and retain the best and brightest students, scientists, and engineers from within the U.S. and throughout the world.
4. Ensure that the U.S. is the premier place in the world to innovate; invest in downstream activities such as manufacturing and marketing; and create high-paying jobs based on innovation by such actions as modernizing the patent system, realigning tax policies to encourage innovation, and ensuring affordable broadband access.

www.nap.edu/catalog/11463.html

¹ Global Forum for Health Research. The 10/90 report on health research 2001-2002. Available at: www.globalforumhealth.org/filesupld/1090_report_01-02/01_02_front_matt.pdf

While this report is aimed broadly across many industry sectors, the trends and recommendations do have bearing on the progress of biomedical and health research, particularly their emphasis on funding for science education at all levels and for high-risk/high payoff research. Another goal of the report is to enhance intellectual property protection while allowing research, and developing financial incentives for innovation-related investments.

Response to report

- **President's American Competitiveness Initiative in State of the Union and FY 2007 Budget** www.whitehouse.gov/stateoftheunion/2006/aci
- **Protecting America's Competitive Edge Bills** on Energy (S. 2197), Education (S. 2198), and Finance (S.2199) (Senators Domenici, Bingaman, Alexander, Mikulski)
– 65 cosponsors (34R, 31D)
- **ARPA-E Bill** (S. 2196) (Senators Clinton, Reid, Bingaman)
- **Three House Bills** introduced by Congressman Bart Gordon on Education (HR 4434), ARPA-E (HR 4435), and Research (HR 4596) (Minority, House Science)
- **Democrats' Innovation Agenda** (Pelosi)

On the domestic front, the first years of the new century have seen the emergence of several new state government programs, such as California's Stem Cell Initiative and the California Institute for Quantitative Biology (QB3). Meanwhile academic health centers face increasing challenges in maintaining the supply of physician-researchers and meeting public expectations for cures, while facing rising research costs and the need to partner with industry. Initiatives such as NIH's Roadmap and FDA's Critical Path promise to put new emphasis on translational research in partnership with universities and drug companies.

Where are the opportunities for private sector investment?

In the area of global health, groups like the Rockefeller and Bill & Melinda Gates foundations have been shifting the focus to health disparities as a new architecture of global health by funding public-private partnerships intended to address huge global problems such as HIV/AIDS, malaria, and tuberculosis. By taking on the risk that would normally be borne by industry, since 2000 these groups have tripled the number of products in the development pipeline for these neglected diseases compared to the number developed during the preceding 25 years².

In both the U.S. and international arenas, HRA members have a unique opportunity to influence the way forward by encouraging partnerships between the public and private sectors. Examples include supporting a fellowship program that would place young researchers within the FDA, programs that place researchers within developing countries, as well as developing new models for investigator training in translating basic science insights into clinical application. The HRA can serve a useful role as a neutral convener of various stakeholders to identify opportunities for collaboration and to prevent duplication of projects and grants.

² Mary Moran, London School of Economics, "The New Landscape of Neglected Disease Drug Development" 8 Sept. 2005
www.lse.ac.uk/collections/pressAndInformationOffice/PDF/Neglected_Diseases_05.pdf

Scientific Frontiers in Medicine

Jeffrey Trent, Ph.D., president and scientific director at the Translational Genomics Research Institute (TGen), was charged with identifying the current frontiers in medicine, and how genomics has impacted research and practice. He characterized the completion of the Human Genome Project (HGP) in 2004 as a transforming event on the scale of Mendel's discovery of genetic inheritance in 1865 or Watson and Crick's discovery of the structure of DNA in 1953. Genomics have already contributed to the identification and diagnosis of disease, and in the future genomics will also speed the development of therapeutics.

As human genome data is exploited in the interest of improving human health, the social, ethical, and legal implications must be thoughtfully considered. The National Human Genome Research Institute is the only institute of the 22 at the NIH mandated by Congress to spend a portion of its budget on bioethical issues.

An area of particular concern is enhancing protection against genetic discrimination and defining the boundaries for appropriate applications of genetic procedures. For example, genetic testing must operate within a framework that safeguards against a patient losing access to health insurance and potentially employment based upon the results.

The availability of genomic data for clinical use has outstripped the 'genomic literacy' of practicing physicians. A test conducted in 1996 and again 10 years later showed that only a small fraction of physicians considered themselves very well informed about the genetic basis of disease and less than one in 10 has the confidence to deliver genetic counseling. Patients should be able to ask their physicians three important questions based on genetic information: What do I have? What's my prognosis? What can I do about it? Educational strategies need to be developed to assure that both physicians and patients are able to understand how to incorporate genomic data into diagnostic interpretations and treatment decisions.

Genotyping is an important tool in genetic research. Humans share 99.9 percent of their DNA sequence in common. Thus only 0.1 percent of the 3 billion total base pairs accounts for all that distinguishes unique human beings from each other, including their susceptibility to diseases and responses to therapies. Where the genetic sequence varies by a single base, these differences are called single nucleotide polymorphisms (SNPs). The collection of all the SNPs in an individual's genome is that person's genotype. Some SNPs occur in clusters and are thought to be related to disease.

Related links:

- Hap Map Project: www.hapmap.org
- National Human Genome Research Institute: www.genome.gov

TGen, a nonprofit research institute based in Phoenix, examines 50,000 samples per year looking for single nucleotide polymorphisms (SNPs) that are already known to be associated with diseases such as autism, cancer, and short-term episodic memory deficits (related to Alzheimer's), among other conditions. This approach requires a lot of genomic data, between 100,000 and 500,000 data points per individual, and the currently available tools miss a lot of possible "hits," meaning clear associations between a genotype and a disease phenotype, or responsiveness to a particular therapy.

In the future, as the available tools for this analysis become more advanced, it may be possible to identify SNPs associated with equally complex but more common conditions, such as diabetes, and to provide genome-directed therapy to customize the best treatment for a particular patient and disease. HIV-AIDS may be a perfect test for this approach, using genomic approaches to profile subtle differences among strains of the virus and how they respond to the current formulary of antiretroviral drugs.

“HRA can help by finding collaborators to help with translation, preserving precious NIH dollars for fundamental research.”

Jeffrey Trent

In response to questions, Trent cautioned that NIH's funding of basic research is critical to the entire biomedical research enterprise. Several institutes are already moving further and further—perhaps too far—from basic research. It will continue to be important to determine whether funding for the “NIH Roadmap” comes at the expense of investigator-initiated research. The goal of investing in the researcher—not the “project”—has been a critical aspect of the success of the NIH system. HRA could serve a useful function by finding collaborators to help with translation, preserving precious NIH dollars for fundamental research.

PLENARY SESSION 2: FEDERAL INITIATIVES IN CLINICAL AND TRANSLATIONAL RESEARCH

This session was designed to address the following questions:

- How will the NIH Roadmap, the new Clinical and Translational Science Awards and FDA's Critical Path Initiative "re-engineer the clinical research enterprise?"
- What is new, what changes are still needed, and what is the role of private funders?

Related links:

- NIH Roadmap: nihroadmap.nih.gov
- FDA's Critical Path Initiative: www.fda.gov/oc/initiatives/criticalpath

Update on NIH Clinical and Translational Science Awards

Barbara Alving, M.D., acting director of the National Center for Research Resources at the National Institutes of Health (NIH), characterized the NIH Roadmap Initiative as a means to accelerate the pace of discoveries in the life sciences; provide their rapid translation into practice for health improvement; and provide opportunities to build an integrated research system that is far more effective than current approaches. The background realities creating this heightened urgency include an aging U.S. population whose health is characterized by chronic rather than acute conditions, widening health disparities between different socioeconomic groups, the emergence of new infectious diseases, as well as the need to develop the biodefense capabilities of the U.S. All of these problems are interdisciplinary in nature, and will require team approaches if discoveries are to be translated into therapies. Yet the current system of academic advancement favors the independent investigator, whose incentives are structured within a discrete academic department. Despite the growing necessity for interdisciplinary approaches to emerging public health problems, such teams take time to assemble and require a different type of infrastructure and resources.

Pathway to Independence Award (K99/R00)

NIH has put “money on the table” for this Trans-NIH initiative that provides an opportunity for promising postdoctoral scientists to receive both mentored and independent research support from the same award.

- Five years of support consisting of two phases: Mentored (K99) and Independent Investigator (R00)
- Phase I provides 1-2 years of mentored support for advanced fellows, funds up to \$90,000 per year including eight percent F&A
- Phase II provides up to 3 years of independent research support contingent upon securing an independent research position and administrative review, funds up to \$249,000 per year including full F&A
- U.S. citizens and non-citizens are eligible to apply
- First round of applications received April 7, 2006
- 150 to 200 awards expected in FY 2007

One of the NIH’s key Roadmap initiatives is the integration of clinical research networks into an interoperable ‘network of networks.’ Depending heavily on advances in clinical research informatics, the National Electronic Clinical Trials/Research Network (NECTAR) will link existing networks to more rapidly address questions beyond their traditional scope with the goal of forming true ‘communities of research’ among patients, physicians, and scientists. Ideally, nodes in the networks will share software applications for protocol preparation, IRB management, and adverse event reporting, as well as common data standards and coordinating centers. The data will be held in a public database. The result will be a reduction in the cost, startup time, overall duration, and duplication of clinical research. Additionally, greater community involvement will increase public awareness, trust, and participation in clinical research.

The NIH recognized that major changes were needed in the structure of clinical research within academic health centers. The explosion in clinical service demands and reduction in financial margins had sidelined the training of clinician scientists. Yet the complexity of knowledge needed to be an effective translational scientist is not easily acquired, and young clinical faculty have trouble finding a real academic ‘home’ for their aspirations. The NIH’s Clinical and Translational Science Awards (CTSA) program was designed to provide the academic home and integrated resources that can advance the disciplines of clinical and translational sciences. The CTSA’s aim to not only develop well-trained investigators, but also increase the efficiency of translation of research into practice. In the current fiscal year the CTSA’s will provide 12 full grants and about 50 planning grants of up to \$6 million over five years. By 2012, this program should expand to 60 awards with an aggregate budget of \$500 million. In addition to providing an academic home for clinical research by offering advanced degrees in this area, institutions seeking to be part of the CTSA program are expected to provide core support for protocol preparation, regulatory compliance, data management, recruitment of research participants, safety monitoring, and other specialized cores and services needed to facilitate translational research.

Partnership approaches are encouraged, and HRA members are encouraged to seek out opportunities to support these grants through supplemental training grants and through sponsorship of initial pilot studies.

Opportunities for partnerships between HRA member organizations and NIH

- Build public trust
- Fund training of new investigators
- Fund initial pilot projects
- Advocate for mission of NIH, and the role of the Roadmap in providing cross-cutting infrastructure.

In response to questions, Alving added that money for CTSA grants will come from other Roadmap initiatives. This program will require cultural changes at academic health centers, as well as NIH. A first step in this direction will be the awarding of multiple-principal investigator grants. Another would be to provide support for investigators—men and women alike—who are trying to start careers and families at the same time. The first round of CTSA grants was announced in the fall of 2006.

CTSA awarded institutions: www.nih.gov/news/pr/oct2006/ncrr-03.htm

Update on the FDA's Critical Path Initiative

Janet Woodcock, M.D., deputy commissioner for operations at the Food and Drug Administration, described the Critical Path as the unfunded sister initiative to NIH's Roadmap. Its goal will be to move innovative new drugs and devices into clinical practice in a more timely fashion, with greater confidence and lower costs. She noted that significant increases in biomedical research and development spending have not led to the expected increase in the number of new medical therapies; on the contrary, 2004 marked a 20-year low in the number of these introductions.

The reasons for this translational failure are unclear. Development costs have increased, creating disincentives for high-risk approaches, but success rates have also fallen. At present, a new drug in a Phase I trial has about an eight percent chance of making it to market, down from 14 percent just 15 years ago; even a drug in a Phase III trial has a 50 percent chance of failing, compared with only 20 percent a decade ago. Other contributing factors include the long lag time that is expected before genomics and other new technologies can be exploited, a feeling that the easy targets have all been taken (rare and chronic diseases are more difficult to address), and a wave of mergers in the pharmaceutical industry that has resulted in a winnowing of development projects. Some also blame the structure and function of the FDA itself.

The Critical Path Initiative is designed as a serial examination of the science used at each step of the drug development process, with a special focus on safety, efficacy, and reproducibility. For too long this process has been the province of industry, with no academic base in product development. FDA does not have the money to invest in such a base, but encourages collaborative partnerships that will strengthen the relevant academic disciplines and infrastructure, such as bioinformatics. Other opportunities for improvement include biomarker qualification, clinical trial modernization, manufacturing modernization, improved development of pediatric therapies, and better responses to public health emergencies.

“There are opportunities for collaborations and consortia (with the FDA) in areas such as biomarker qualification, clinical trial design, manufacturing modernization, and development of pediatric therapies.”

Janet Woodcock

In the area of biomarkers, for example, it would be useful to have several consortia to identify and validate the clinical correlates of biomarkers in different diseases, which would allow FDA to use them in evaluating new drugs. Just such a consortium was announced in January 2006 in oncology biomarkers, and similar consortia are under development for AIDS and other diseases. In the area of clinical trial modernization, opportunities include improved analytic methodology, greater automation in reporting and oversight, and rational and adaptive designs that generate more information from fewer patients and with fewer adverse events.

FDA expects nonprofit groups to play a major role in the Critical Path Initiative, for example by publishing the results of preclinical assays and assisting in the priority research projects outlined by the FDA to speed the development and approval of medical products.

In response to questions, Dr. Woodcock said that the FDA and NIH initiatives might eventually be more closely coordinated but this would merely increase the potential role for nonprofits. Public education, in particular, is an area where the government needs help; public perception (along with the indifference of community-based physicians) is the principal barrier to increased participation in clinical trials, which currently hovers around three percent.

BREAKOUT SESSIONS ON FUNDING PARTNERSHIPS

A. Translation: Models for Developing Translational Infrastructure and Capacity

The Role of Novel Partnerships in the Food and Drug Administration's (FDA) Critical Path Initiative

Ray Woosley, M.D., Ph.D., president of the Critical Path Institute (CPath), expressed confidence that the FDA's Critical Path initiative can remove roadblocks that keep basic scientific research from reaching the clinic. These roadblocks are huge: in 2004, only 11 percent of the drugs in clinical trials eventually reached the market, and cancer drugs (where more money is invested than in any other field) had the lowest success rate. In other words, most of the money invested in translational research is spent on drugs that fail. One important reason for this is that the pharmaceutical industry is conservative—it tends to develop new drugs the same way others successfully developed similar drugs before.

CPath, a non-profit institute with funding from the state of Arizona and from private funders like the Flinn Foundation, tries to address these issues by creating a "neutral ground" where scientists from the FDA, academia, and the pharmaceutical industry can come together, not to develop specific drugs, but instead to evaluate the tools that are needed to accelerate the development of safe medical products. He notes that development can be safely accelerated and cites the example of new AIDS drugs reaching the market in only three years, because FDA was at the table with the pharmaceutical industry and agreed to accept CD4 counts as a surrogate endpoint for clinical trials. CPath will now look for this kind of biomarker for Alzheimer's and other diseases as well. Another strategy is to simulate clinical trials to reduce the number of drugs that fail using data from improved electronic medical records.

CPath and FDA are currently working with rare disease foundations to create improved disease registries, living electronic records that reflect each disease not as it was described in the literature many years ago, but as it exists in the community today. Pilot projects include collaborations with the Ara Parseghian Medical Research Foundation to create a registry for Niemann Pick Type C disease, an inherited metabolic disorder, and with the T. Richards Foundation to create a registry for adrenocortical carcinoma. Similar registries are planned for other diseases. Another project is the Predictive Safety Test Consortium, where drug companies share and test each other's safety tests for drugs, with the FDA at the table to weed out the tests that fail to predict drug safety. Currently, 15 companies are part of the consortium and more are considering joining.

Woosley also described work on the need for an active drug surveillance system, such as the Community Pharmacy Safety network, which is being tested in Arizona with the goal of picking up adverse drug reactions in weeks to months instead of the average of 6.6 years it takes today. Patients who get a new prescription drug at the pharmacy are asked to contact a call center (actually a poison control center) to enter their complete drug history in a registry, and then call back if they have any side effects within 30 days. The registry, if successful, hopes to be electronically networked with the FDA. Currently, 55 pharmacies are participating in Arizona, and nationally, 34,000 pharmacies are ready to participate. However, C-Path needs to find funding to make a nationwide network possible.

“In the past I have heard scientists from company after company say, ‘let’s not take a chance on trying anything new, because the FDA may not accept it. That reluctance to be innovative breeds stagnation and is a model for eventual failure.’”

Ray Woosley

Developing a Statewide Translational Research Network

Bill Read, Ph.D., vice president of research and technology at the Flinn Foundation, explained that in addition to funding part of the CPath Institute, Flinn has been involved in developing the Arizona Biosciences Roadmap, whose goal is to make Arizona more economically robust by advancing its role in research. Work on the roadmap began in 2002 with the identification of near-term opportunities where Arizona is already strong (such as cancer therapeutics, neuroscience, and bioengineering) and mid-term opportunities in other fields (such as asthma and infectious diseases) where Arizona could become competitive. The roadmap will also start consortia in technological areas that cut across and support research in all of these areas. For example, the University of Arizona and Arizona State University are collaborating to develop bioimaging resources. Another collaboration, among all of the state’s institutions that collect tissue samples from patients, aims to pool those samples in a standardized way and make them available for scientific research.

Funding for the roadmap includes \$440 million from the state for the construction of university research facilities, including translational research centers. The state’s tobacco tax consortium—called the Arizona Biomedical Research Consortium (ABRC)—will contribute another \$10 million per year. The Flinn Foundation provides additional funds for specific translational research projects, such as the development of a statewide Institutional Review Board to share costs and enable smaller institutions to participate in medical research.

Draft Recommended Actions

Strategic Priority: Building Statewide Collaborative Capacity

- Institutional Review Board (IRB) Networking Forum to create a sense of community and shared activities across IRBs, which are a linchpin in advancing clinical research activities
- Technical Policy Development Retreat to advance common policies and practices for IRBs in the state
- Statement of principles and practice guidelines to remove barriers to broader translational research collaborations for Arizona institutions
- Arizona Clinical Research Consortium to advance a range of cooperative activities to increase the scale of clinical trial activities in the state
- Establishing an Arizona-based Community IRB to serve the needs of the broad range of smaller hospital and non-profit research institutions found in Arizona seeking to participate in clinical research. The advantages will be bringing local knowledge, cost-efficiency, and expertise to these smaller institutions and perhaps a resource for more active solicitation of multi-site, industry-based clinical trials
- Advancing policies and practices for community-based participatory research with special population groups in the state
- Establishing a Biosciences Research Network as a web-based directory tool to advance teaming and collaborations, along with Site Managers across institutions to facilitate communications among investigators and to identify opportunities for advancing translational research

Accelerating Med-Tech Innovation: The Role of Foundations

John Linehan, Ph.D., consulting professor of bioengineering in the Program in BioDesign at Stanford University, told the audience how the Whitaker Foundation transformed the biomedical engineering research and education landscape with an investment of \$800 million. Founded in 1975 to support medical research and training, Whitaker initially provided grants to young faculty members who were establishing interdisciplinary research programs in bioengineering. Despite these grants, however, the number of undergrad programs in biomedical engineering remained flat. In the early 1990s, the foundation decided to invest its total endowment in order to catalyze efforts to create teaching curricula in bioengineering, to form entire departments, to hire faculty and Ph.D. students, and even to build facilities. As a result, the number of undergrad biomedical engineering programs increased from the mid-twenties to roughly 90 programs today. One reason for this success was that foundation representatives visited their major awardees every year for five years.

“The foundation said ‘all in’—we’re not going to spend five percent a year, [we’ll] spend all of it to get the job done. And it worked very nicely.”

John Linehan

The last Whitaker check was written in 2005, but other initiatives have emerged to continue what Whitaker started. NIH has formed the National Institute of Biomedical Imaging and Bioengineering, where bioengineers can apply for grants. Howard Hughes Medical Institute has created a program that awards \$1 million grants to initiate changes in interdisciplinary Ph.D. scientist training at the interface between biomedical, physical, and computational sciences. The Coulter Foundation started a grant program to accelerate translational research, funding biomedical engineering departments with \$580,000 per year, providing five year grants that have two principal investigators—a clinician and a biomedical engineering faculty member—for each project. Coulter also offers early career translation-research awards to help young investigators establish research careers involving translational research. The Alfred E. Mann Foundation will eventually invest between \$1 and \$2 billion in several universities with strong biomedical engineering programs.

Finally, Linehan described the Stanford program in biodesign, which he is currently leading. The program trains students to become leaders in innovation in the medical device industry. Each year, four fellows with Ph.D.s or M.D.s from different disciplines, such as chemical engineering, mechanical engineering, or surgery, are mentored by physician and engineering inventors and immersed into the clinic for three months to identify clinical needs. Selected needs become the substrate for a biodesign innovation graduate course with medical, engineering and business students working in teams to come up with prototypes. And the program works: “One [semester], at the end of the class 30 provisional patents were filed.”

B. Human Capital: Building Research Networks and Funding Teams

International Networks in Cardiovascular Research

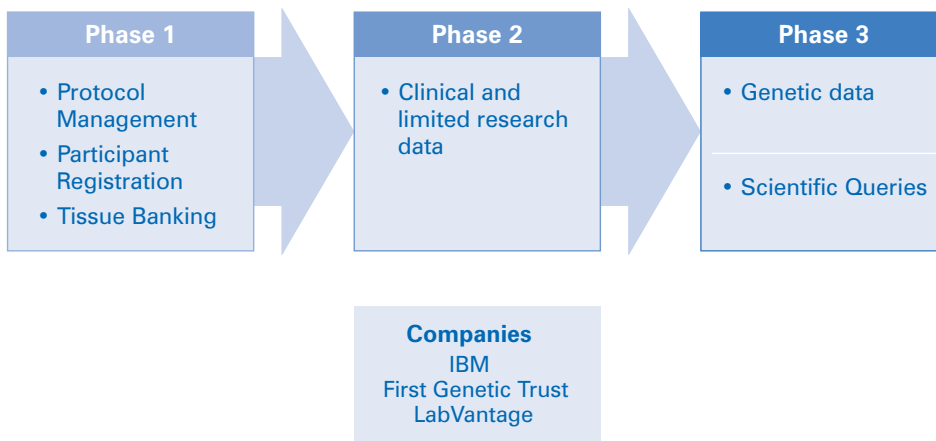
David Tancredi, M.D., scientific director at the Fondation Leducq, suggested that, although collaboration may seem like a recent buzzword in the foundation community, scientific collaborations have been taking place for a long time. Like anything else, collaborations have their fair share of success and failure. There can also be a fair amount of resistance to collaboration, which is not always a natural impulse in academic settings. Historically, discovery and invention have been seen as individual pursuits, but successful collaborations share a number of potential benefits. For example, collaboration and networks create a large pool of additional resources for those involved. By reducing duplication and focusing more on the core problem at hand, collaboration creates an enormous amount of efficiency. Lastly, collaboration assembles a critical mass of talent. Collaboration is not without its challenges, of course—questions of oversight, incentives, evaluation, and management must all be addressed.

The Multiple Myeloma Research Consortium: Lessons Learned

Kathy Giusti, M.B.A., chief executive officer and founder of the Multiple Myeloma Research Foundation (MMRF) and Multiple Myeloma Research Consortium, explained that MMRF was created in 1998 to stimulate research funding for myeloma treatment and to raise awareness for this so-called orphan cancer. Myeloma—an incurable but treatable cancer of the plasma cells in bone marrow—has a frequency of five to six new cases per 100,000 persons per year, or an estimated 15,980 new cases in the United States each year. An estimated 50,000 Americans are living with multiple myeloma. MMRF focused initially on research grants, trial recruitment, and drug development, but soon found that collaboration among academic centers was difficult, not because of a lack of interest but because of a lack of time and systems. In response, the foundation created the Multiple Myeloma Research Consortium (MMRC) in 2004 to focus on rapidly identifying and validating new molecular targets for multiple myeloma, screening new drugs against these targets, and expediting Phase I/II clinical trials of the new drugs. Today, MMRC has 11 member institutions who support a shared data bank that follows a three-phased design and implementation process [see graphic]. The data bank now contains more than 800 tissue samples.

MMRC Data Bank

The MMRC integrates the member institutions through a shared Data Bank. The Data Bank follows a three-phased design and implementation process. CRO audits confirm quality of data.



Lessons learned from MMRC:

- Development of the model was the most difficult aspect.
- Industry and scientific input was critical as was benchmarking.
- Well-respected leadership provides extraordinary insights and credibility.
- The Steering Committee and Project Review Committee do not work for the MMRC.
- Reward systems must be addressed early.
- All institutions must bring ideas to the table.
- All ideas must be quickly vetted through a simple but peer-reviewed process.
- The Steering Committee and Project Review Committee do not want/need to know the “behind the scenes” efforts such as project management, contracting, communications, expansion, audits, and fundraising.
- Outsourced technical support is critical.
- Philanthropists should get used to expecting clear deliverable and timelines.
- Philanthropists should expect communication of the key learnings to other disease groups.
- Internal and external communications are critical.

Myelin Repair Foundation critical success factors—

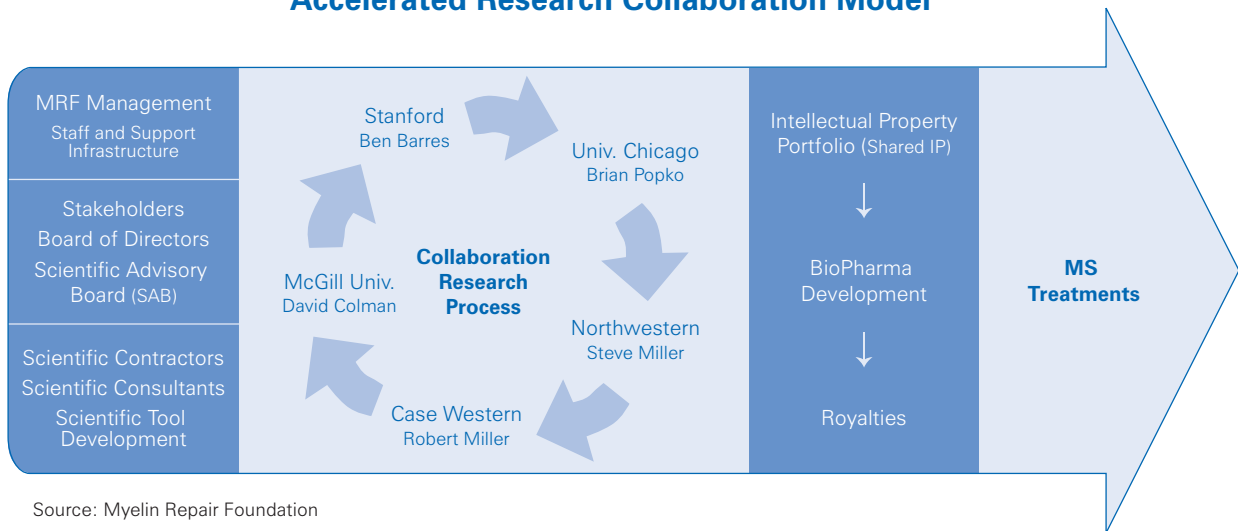
- Interdisciplinary research team
- “Best-in-Class” principal investigators and scientific advisory board
- Jointly-developed research process
- Jointly-developed research plan
- Full-time professional “management” and coordination
- Partner with biopharma for rapid drug development
- Accountability

Effective collaboration requires structure, management, and leadership

A New Model for an Outcome-Directed Research Collaboration

Rusty Bromley, chief operating officer of the Myelin Repair Foundation (MRF) told participants that the professional backgrounds of his foundation’s leaders are deeply rooted in business, so it is no surprise that the foundation’s model borrows strategies from the business world to produce results. Acknowledging the large gap between discovery and treatment, MRF’s goals are succinct: to identify and validate new myelin repair drug targets by 2009. To accomplish this, MRF has developed an Accelerated Research Collaboration (ARC) model, providing scientific and business oversight to co-principal investigators from five universities (Case Western, Chicago, McGill, Northwestern, and Stanford) who jointly developed a five-year research plan and will later share the resulting patents and royalties. This collaboration discovered nine novel targets between July 2004 and March 2006, with MRF seeking partners in the biopharmaceutical industry to move the resulting drugs from laboratory to clinic. MRF has already raised \$14 million towards its goal of \$25 million to fund the initiative. Bromley admitted, however, that academic research does not equal drug discovery. Among the shortcomings he has noticed in typical academic proposals and peer review: incrementalism in proposals to NIH; competition and lack of coordination between scientific disciplines; and basic science isolated from consideration of clinical application. Among the biggest needs: explicit disease-based research roadmaps and better protection of intellectual property rights.

Accelerated Research Collaboration Model



Source: Myelin Repair Foundation

The Brain Tumor Funders' Collaborative: A Virtual Organization

Rita Berkson, M.P.H., executive director of the Goldhirsh Foundation, posed the following question: Is it easier to propose a collaboration among funders than it is among scientists? For the dozen or more U.S. foundations that fund research on brain tumors, the answer may be the Brain Tumor Funders Collaborative, a virtual organization with a website but no staff. The Goldhirsh Foundation had recognized that the research it was funding tended to result in more research, instead of moving forward to new and more effective therapies. Meeting informally in 2002, Goldhirsh and three other brain tumor funders hoped to organize learning workshops where researchers could share their experience with the broader funding community. The goal was to identify research opportunities in brain tumor research, choose a funding target or niche, and launch a coordinated funding approach by 2004. These workshops did not produce the hoped-for scientific results, in large part because the researchers remained aligned within their disciplines and could not create a clear business plan. In 2005, however, eight philanthropic and advocacy organizations signed on to jointly commit money for a program of grants to support collaborative, interdisciplinary, interinstitutional teams of scientists and clinicians who would focus on translating preclinical results into novel clinical therapies. In the end, they raised \$6 million to pay for three multiyear grants, with each contributor having an equal vote in selecting the grantees regardless of their monetary contribution. The final grants were announced in March 2006, and evaluations will be based on the success of grantees in meeting their project milestones—what amounts to a business plan. In this way, funders of relatively modest means have pooled their resources for greater impact, without sacrificing their involvement in the selection process.

BTFC Lessons learned:

- Collaboration is difficult, but the ripple effect it creates is good.
- Everyone must be committed to the goal.
- Careful selection of the scientific advisory committee is critical.
- Face-to-face meetings are needed to create personal, as well as professional, relationships.

Community-based participatory research (CBPR) blurs the traditional distinction between academic “researcher” and community “subject,” because all parties are engaged in the research.

C. Community: Models of Community-Based Participatory Research

Community-Based Participatory Research: A Partnership Approach for Conducting Health Research

Barbara Israel, Dr.P.H., professor at University of Michigan School of Public Health, suggested that research rarely benefits the community in which it takes place, and in some cases it has done actual harm. This has led to an understandable distrust of research and a reluctance to participate, especially within communities of color. Community-based participatory research (CBPR), by contrast, actively involves community members and organizations in every phase of the research process, identifying the research questions, shaping research design to fit local conditions, and translating the results into interventions that benefit public health. An example is the Detroit Community-Academic Urban Research Center (URC)—a partnership involving representatives from public health and health care agencies, community-based organizations, and academia. There are a number of CBPR projects affiliated with the URC which involve different types of research (e.g., intervention research, randomized trials, etiologic research) that address a number of different issues (e.g., diabetes management and prevention, access to quality care, environmental triggers of childhood asthma, social and environmental determinants of cardiovascular disease). The overarching goal is to reduce and eventually eliminate health disparities which exist within the city’s Latino and African American communities. Nearly all of the URC-affiliated projects involve some kind of intervention component, which is something the community partners have insisted upon. Since 1995, the URC has hired more than 200 local residents as full- or part-time employees in studies that have involved 20 University of Michigan faculty and more than 100 graduate students, resulting in about 70 peer-reviewed publications and more than 100 presentations and posters.

Donele Wilkins, executive director for Detroiters Working for Environmental Justice, described Community Action Against Asthma (CAAA), one of the URC-affiliated CBPR projects. CAAA sought to identify and reduce environmental triggers for childhood asthma, using questionnaires, air-quality monitoring, individual backpack monitors, and a variety of customized interventions to remove known triggers. The results showed that more than 30 percent of the children with moderate to severe asthma (identified through a screening questionnaire) had not received a diagnosis by a health care provider.

The results of the intervention, which involved home visits by community health workers, concluded that it was effective in improving measures of lung function, reducing the frequency of asthma symptoms, reducing the proportion of children requiring unscheduled medical visits and reporting inadequate use of asthma controller medication, and reducing caregiver report of depressive symptoms. Based on this and numerous other projects, Israel and Wilkins recommended that community-based participatory research efforts need to involve the community, build trust, balance the goals of research and interventions, establish clear procedures for dissemination of results, and plan for a long-term relationship with community residents.

Community-Based Participatory Research: Moving the Field Forward

Sarena D. Seifer, M.D., executive director of the Community-Campus Partnerships for Health (CCPH), noted that few organizations have been practicing CBPR for as long as URC, but her organization has been working since 1997 to build the capacity of communities and universities to work together in the U.S. and 12 other countries. Growing evidence points to the validity and efficacy of this approach, including a 2004 metastudy by the Agency for Health Research and Quality (AHRQ) and the growing increase in NIH and foundation support for CBPR-based studies, totaling \$45 million in 2002 alone. NIH's National Center for Minority Health Disparities has endorsed the CBPR approach and is currently funding 25 joint research interventions. Based on her own experience in training community and university participants, Seifer believes that CBPR needs a broader base of funding mechanisms, including grantmakers who "don't do research" but do support community action, as well as a better pipeline of training, fellowships, and faculty development for CBPR specialists. It would be particularly helpful for RFAs from NIH and CDC, as well as nonprofits, to ask about community benefits (i.e., community impact statement) or even to require CBPR approaches. The AHRQ report contains several model RFPs of this sort¹.

In the discussion that followed, the speakers acknowledged that there is continuing skepticism about the scientific validity of CBPR studies, as well as lingering prejudice in tenure and promotion for university practitioners. CCPH is working with nine different universities to consider CBPR in their tenure decisions. It's important for grantmakers to understand that they are investing in a partnership, not just testing a hypothesis. Sometimes this will take the project in unexpected directions, as happened in one study on an Indian reservation that started out to study diabetes but found that kidney cancer was a far bigger concern for the community. In addition, the community is not interested in waiting years for full statistical analysis—they want to know what disease they have and what they should do to prevent and treat it. The sense of data ownership can be very strong, and investigators are well advised to publish their results sooner rather than later, and in local newspapers as well as professional journals.

¹ Community-Based Participatory Research: Assessing the Evidence, August 2004
<http://www.ahrq.gov/downloads/pub/evidence/pdf/cbpr/cbpr.pdf>

D. Translation: Disease-Oriented Models of Drug/Vaccine Development

Translational researchers and drug developers in the U.S. have traditionally neglected the so-called “orphan diseases” that afflict a small number of people or a population too poor to generate a revenue stream for the drug developer. Grantmakers and advocacy groups can sometimes fill this gap.

JDRF Experiences with “Cure Therapeutics”

Robert Goldstein, M.D., Ph.D., chief scientific officer at the Juvenile Diabetes Research Foundation International (JDRF), said that his foundation is most interested in translating basic scientific results into clinical applications, such as sources of islet cells, an artificial pancreas or 24-hour glucose monitors. Because JDRF is committed to funding only the best research regardless of geographic location, 40 percent of its grants in 2006 were awarded to institutions and individuals outside the U.S. JDRF will collaborate with any entity willing to accept its research agenda, including the National Institutes of Health (NIH), the Center for Disease Control and Prevention (CDC) and National Aeronautics and Space Administration (NASA). JDRF also partners with numerous international organizations, such as the U.K.-based International Stem Cell Forum.

“To take the mouse work through a preclinical phase to a phase I/II trial, that’s where the action is. . . .If we come up with something spectacular, we believe industry will pick it up.”

Robert Goldstein

JDRF is also one of the sponsors of the Immune Tolerance Network (ITN), which has been set up by the NIH to implement clinical trials of potential therapies for kidney, liver, and islet transplantation and autoimmune diseases including type I diabetes. JDRF supports these ITN studies because they are affordable for a foundation, but also because they are a valuable way to get drug companies interested. One example is a study that uses anti-CD3 monoclonal antibodies to block the T-cell autoimmune response to islet and insulin-secreting cells. Companies with patents on anti-CD3 antibodies have not used them to develop treatments for type I diabetes, focusing instead on diseases like inflammatory bowel disease or ulcerative colitis, which require a lifetime of medication; drugs would only have to be given for a short time to treat type I diabetes.

Virtual companies are another way for a foundation to translate research into early clinical studies. A few years ago, JDRF partnered with the Australian government to create the Diabetes Vaccine Development Centre (DVDC), a virtual company that develops vaccines to delay the early onset of type I diabetes. DVDC has a board of directors and a CEO, but everything else is outsourced. It organizes studies up to a proof of concept stage within three to five years, closer to a stage where an industrial partner could take over.

Creating Drugs for People with Cystic Fibrosis

Suzanne R. Pattee, J.D., vice president of public policy and patient affairs at the Cystic Fibrosis Foundation (CFF), described similar challenges in getting drug companies interested in cystic fibrosis, which affects fewer than 30,000 patients in the U.S. and only 70,000 worldwide. CFF created its Therapeutics Development Program in 1997 to provide financial support to biopharmaceutical companies to encourage development of new drugs for CF. The program awards funds for preclinical research and for Phase I and II clinical trials; in return, CFF gets financial returns based either on multiples of its investment or royalty on net sales. In 1998, CFF established a non-profit Therapeutics Development Network to facilitate conduct of early phase clinical trials for new therapies, with funding from CFF, NIH, and industry sponsors. CFF's collaborations with about 18 or more industry allies have resulted in more than 24 compounds at different stages of development, including several in Phase III clinical trials and some drugs that are already available to patients.

“Most companies would be delighted to have a portfolio so heavy in late-stage projects. [MMV now has the] largest jointly managed antimalarial R&D portfolio in history.”

Queta Bond

The Medicines for Malaria Venture: A Public/Private Partnership for Drug Development

Queta Bond, Ph.D., president of the Burroughs Wellcome Fund and board member of the Medicines for Malaria Venture (MMV), pointed out that malaria is the most prevalent disease in the world, accounting for up to 3 million deaths per year, 90 percent of them preventable. Malaria affects patients in 107 countries and accounts for 15 to 35 percent of the hospital deaths in Sub-Saharan Africa. Nevertheless, drug companies have been not sufficiently interested to invest in developing drugs for malaria. MMV, founded in 1999, is a Public Private Partnership (PPP)—“like a like virtual multinational company,” according to Bond, integrating drug development across multiple partners and finding philanthropic and public funds to develop drugs for neglected diseases. In the case of MMV, this means discovering, developing, and delivering affordable new antimalarial drugs. Bond called this model a “win/win proposition”—MMV puts in money and intellectual property rights and in return gets rights in the developing world; industry puts in expertise and accepts liability for the development risk but gets rights in the developed world and a public relations benefit. MMV’s international partners now include more than 50 research entities including universities, non-profit organizations, and companies in the U.S., Europe, India, and South Korea. The current MMV portfolio has about 20 projects, including 11 in the discovery phase, three in the preclinical phase, seven in clinical development, and several in late stage clinical trials.

Overall View

Future Success Depends on MMV Navigating a Number of Challenging Transitions

Yesterday		Today
Mission focused on “Discover” and “Develop”	→	Additional emphasis on “Delivery”—still through partnerships; funding needed
Independence from global public health groups	→	Active engagement and partnership
Clear division of markets: MMV gets the public market, its partners the private market	→	An active role for MMV in shaping private market dynamics for public health impact
R&D spending focused largely on late-stage development projects	→	Shift in investment mix needed toward early-stage programs and delivery
Informal management processes, learning by doing	→	Greater codification and transparency—portfolio and investment management
Projects	→	Health outcomes

Source: The Boston Consulting Group

E. Human Capital: Career Development of Clinical Investigators

A Private Funder's Approach to Developing Biomedical Researchers

William Galey, Ph.D., director of the graduate and medical education programs at the Howard Hughes Medical Institute (HHMI), described several HHMI training programs that support biomedical researchers in cooperation with the National Institutes of Health (NIH).

- In the Research Scholars Program, for example, medical student fellows (“cloister scholars”) live in HHMI-furnished housing on the NIH campus as a “community of scholars.” Each fellow selects a research project with guidance from an NIH advisor and HHMI staff; more than 1,200 NIH investigators are available as mentors. The program stages Monday night science dinners, with a lecture by a renowned HHMI or NIH investigator as well as informal interaction with the speaker before and after dinner. A second, less formal dinner each week allows two scholars to present their work to their peers, broadening the group’s exposure to other fields, as well as developing important presentation skills.
- The HHMI Medical Fellows Program is open to medical students to spend a year conducting research at any academic or nonprofit research institution other than NIH. At the beginning and end of their fellowship term, fellows attend annual conferences to learn about the latest scientific advances or to present their own research. Network opportunities with the Cloister Scholars, other student researchers, and senior scientists result, which can be beneficial to their future success as physician-scientists.
- The HHMI Alumni Network provides a venue for career development, collaboration, networking, and social interaction. Events are held regionally and at selected scientific meetings.
- Early Career Awards for HHMI physician-scientist trainees are available to HHMI Medical Research Fellow and HHMI-NIH Research Scholar alumni. Qualified applicants may apply during the last year of training or in the first two years of their first tenure-track faculty position. The awards—13 per year—distribute \$150,000 over three years to each of the recipients, strictly for research, with the home institution providing salary, space and time for research.

Why do Ph.D.s need knowledge of medicine?

- To understand the core issues faced by clinical practitioners.
- To participate in the translation of current knowledge into medicine.
- To direct their own future research to address important medical problems.
- To be better partners of clinical scientists in efforts to accomplish the translation of biology into medical practice.

- The HHMI Med into Grad Initiative is composed of institutional grants to stimulate the learning and use of medical and pathobiological knowledge by tomorrow's biomedical science Ph.D.s. These programs have been awarded to 13 universities across the U.S.
- Finally, HHMI and the National Institute for Biomedical Imaging and Bioengineering provide funding for a new Interfaces Initiative. This effort supports interdisciplinary biomedical science graduate research training that incorporates physical science and/or mathematical disciplines. So far, 10 institutions have been awarded \$1 million by HHMI over three years to build their programs. Successful grantees who reach the established goals will also be awarded five year training-grant support from NIH, potentially extending the life of the programs to eight years.

How Successful Have the Two HHMI Medical Student Research Training Programs Been?

	Fellows	Scholars
Currently Doing Research	59%	58%
Hold Academic Appointment	52%	51%
Pursued Ph.D.Degree	8%	7%

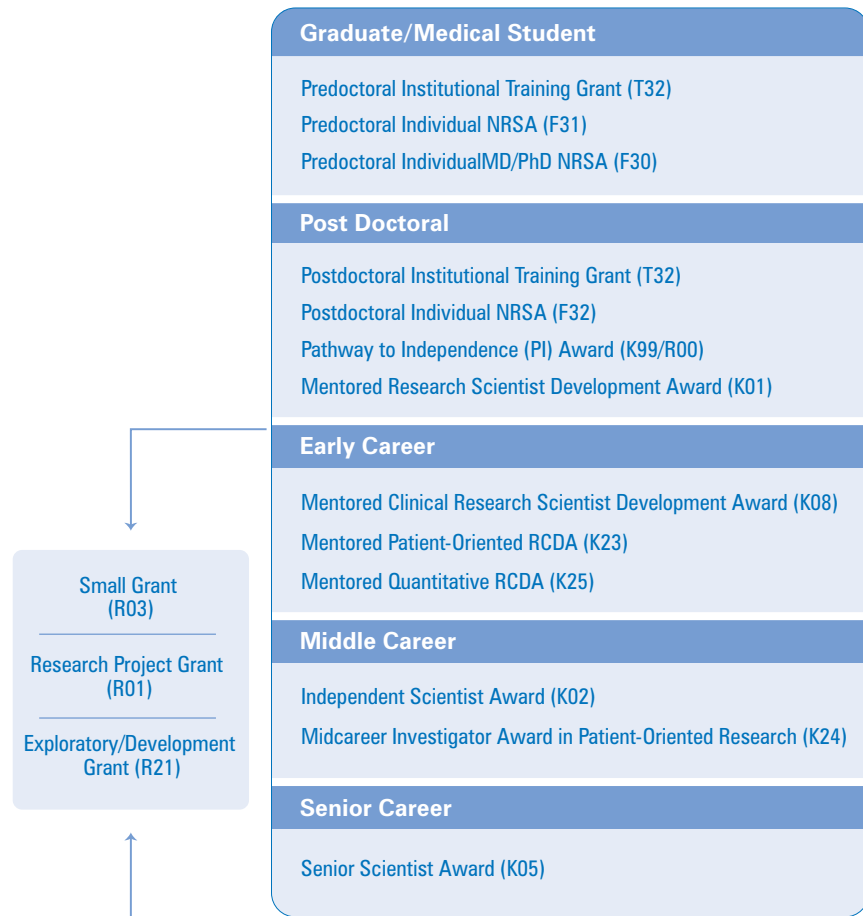
99% Reporting, Classes 1989–1992

NIH Career Development Awards (“K” Awards)

James F. Hyde, Ph.D., senior advisor of research training programs at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), described new developments in the NIH Research Training and Career Development Programs, which help ensure that highly trained scientists are available, in adequate numbers and in appropriate research areas, to address the nation’s biomedical, behavioral and clinical research needs. Most Career Development Awards (so-called “K” grants) are designed to enhance the expertise and capabilities of early-career (post-doctoral) investigators by supporting research experiences that will lead to independent and productive research careers. The duration of the awards is generally from three to five years.

- The Mentored Research Scientist Development Award (K01), Mentored Clinical Scientist Development Award (K08) and Mentored Patient-Oriented Research Career Development Award (K23) all require a mentor, a full-time appointment with the applicant organization, and a commitment of at least 75 percent time devoted to research and career development activities. Applicants must submit both a research plan and a career development plan. Recipients are encouraged to apply for independent support during the project period, and they can reduce their effort on mentored awards to 50 percent during the last two years if they become a principal investigator or subproject program director of an independent research grant.
- The Independent Researcher Award (K02) is designed for newly independent researchers who need additional experience to enhance their careers. It requires a 75 percent commitment to conducting research and relevant career development activities. Awards may be competitively renewed at the discretion of the participating NIH Institutes and Centers.
- The Pathway to Independence Award (K99/R00) combines features of the above categories, providing one or two years of mentored support followed by up to three years of independent support, contingent on securing an independent research position. Recipients are expected to submit a grant application for independent R01 support from the NIH during the R00 award period.
- The Mid-Career Investigator Awards in Patient-Oriented Research (K24) provides protected time for more experienced clinician investigators to act as research mentors for clinical residents, clinical fellows, and/or junior clinical faculty. It requires a commitment to research of 25 to 50 percent of the recipient’s time and may be renewed one-time.

NIH Research Training and Career Development Timetable



Eligibility

Applicants must hold a doctoral degree, and some awards (K08, K23, K24) require a clinical degree. Candidates must be U.S. citizens, noncitizen (i.e., territorial) nationals or permanent residents for nearly all K awards. Researchers who have already received R01 grants or served as principal investigators on other NIH-funded research projects are generally ineligible, although previous recipients of unsolicited small grants (R03) and exploratory or developmental research grants (R21) may still apply. Individual K awards are usually portable, although changing institutions or mentors requires prior approval of the NIH awarding component.

The Role of Academic Medicine in Nurturing Translational and Clinical Research

David Korn, M.D., senior vice president at the Association of American Medical Colleges (AAMC), suggested that medical schools and teaching hospitals must work to increase the number of physician-scientists available to follow up on recent scientific advances. To do this, they need to develop a culture that is supportive of clinical research and that transmits the excitement of clinical research to medical students, residents and fellows. Clinical research training programs must define a rigorous set of competencies and skills, and medical schools and teaching hospitals should develop model training and credentialing programs for clinicians who wish to participate in clinical trials. A new report from the AAMC, "Promoting Translational and Clinical Science: The Critical Role of Medical Schools and Teaching Hospitals," makes specific recommendations on how academic medical institutions can attract, nurture, and support more translational and clinical physician-scientists. Among the key recommendations:

- Require medical schools and residency programs to educate all students and residents in the fundamental principles of translational and clinical science. Ensuring that physicians can effectively interpret and evaluate the significance of new discoveries published in the medical literature will better enable them to improve their practices, explain research findings to their patients, and refer them to clinical trials when appropriate. Exposing medical students to this research early in their education will also help stimulate them to consider careers in these disciplines.
- Accelerate the preparation of physician scientists by revising the structure of research training in undergraduate, graduate, and fellowship education. Modifying the structure of medical school and residency programs to accommodate research tracks, and requiring a more rigorous, mentored postdoctoral graduate training experience will help researchers be better prepared to secure independent research funding earlier in their careers and be more successful junior faculty members.
- Implement institutional changes to ensure that translational and clinical research and training is a cornerstone of the core mission of academic medicine. Academic institutions, journals, the federal government, and other research sponsors should work together to recognize, appropriately credit, and reward the contributions of researchers to team science, thereby facilitating their career advancement.

F. Community: Regional Models for Influencing State Policy

This panel reviewed state funding of health research and highlighted recent models/case studies for influencing state policy and involvement in health research. State support of health research is substantial, estimated to be about \$2.0 to \$2.4 billion annually; however, data on support is limited and is not collected by any single national organization. Over the past 10 years, increased state support for health research has resulted from, among other issues: (i) the tobacco settlement of 1998; (ii) policy discrepancies between federal and state governments, particularly related to the issue of stem cell research; and (iii) an increase in community members' desire to be involved with health research issues related to their communities.

State/Regional Partnerships in the Biosciences

Walter H. Plosila, Ph.D., vice president of Technology Partnership Practice at the Battelle Memorial Institute, reported that the biosciences sector now comprises 40,000 establishments employing 1.2 million people and providing products and services in fields as diverse as agriculture, drugs, medical devices, and laboratory testing. The absolute prerequisite for technology-based economic development is a strong research base, and many states have or are planning to focus their efforts on building the infrastructure for biosciences and filling the pipeline of trained scientists and engineers. The National Science Foundation (NSF) has documented university and medical center spending of \$7.6 billion on biotechnology capital initiatives during the two-year period 2002-2003, most of it for research and development buildings and facilities. Most states are concentrating on their own niches and strengths, and are not just trying to replicate Silicon Valley. Experience shows that best practice includes engaged universities, an entrepreneurial culture, venture capital, and skilled human capital.

In recent years, one of the factors encouraging these state initiatives has been the 1998 tobacco settlement, which will provide the states with \$246 billion over 20 years. Many states have cashed in their share of this money or are using it to build roads or balance budgets, but to date between two and four percent has been spent on health research. Nineteen states have announced such investments, and while Michigan and Missouri have already reduced or modified their programs, states such as Ohio and Pennsylvania are still making major investments in health research from their tobacco settlement funds.

While all 50 states have made some investment in health research, only five have committed money to stem cell research. Foundations are playing a growing role in changing and guiding state policies on health research, and they can also play an important role in filling investment gaps and mobilizing other resources.

For example in Indiana, the Lilly Endowment provided the “glue money” to ensure that the state’s Genomics Initiative went forward, and five foundations in Pennsylvania have matched the state’s investment in the Pittsburgh Life Sciences Greenhouse. In Arizona it has been the leadership of the Flinn Foundation that has spurred a major private and public partnership since 2002 in the biosciences, starting with a Strategic Roadmap.

California and the Stem Cell Research Initiative

Philip A. Pizzo, M.D., dean of Stanford University’s School of Medicine, described California’s decision to invest in a \$3 billion stem cell initiative. Policymakers recognized that stem cell biology is a promising, even transforming area of science, and California universities were already performing much of the NIH-funded research in this area. California has a long tradition of using public bonds to fund socioeconomic initiatives, and it is already home to 2,600 biotechnology companies. The driving force behind Proposition 71 was a patient advocate named Robert Klein, whose son has type I diabetes, but the initiative was backed by 60 percent of the voters and is already galvanizing the research community. It creates a California Institute of Regenerative Medicine (CIRM), an autonomous organization with its own policies, scientific oversight committee, and grant-making authority. CIRM has already raised \$50 million in donations in anticipation of the first bond issue, of which \$14 million has been put out in training grants for non-profit California research institutes and universities who will later apply for research grants. While he is pleased that CIRM and other state initiatives are moving forward, Pizzo cautioned that—in stem cell research as in all other cutting-edge health research—these state-level efforts are no substitute for the fundamental role of NIH, and they should not become the models for an abdication of the traditional federal role in supporting basic biomedical research.

Building Strategic Partnerships to Advance Health Research

John Murphy, M.S., president of The Flinn Foundation, presented a case study of the role of foundations in mobilizing resources in support of state health research initiatives. The Flinn Foundation, originally founded by a Phoenix physician and his wife, was already involved in health-related philanthropy and saw the need for additional investments to provide the infrastructure—in buildings, dollars and advocates—that would support investigators as part of a larger research enterprise in Arizona. Partnering with other foundations, Flinn was able to target its funds to projects that would leverage additional funds from other sources. The result has been a \$440 million investment in research facilities, a city-sponsored science park, new science and math courses in high schools and junior colleges, and \$150 million in state funds (matched by \$150 million from business sources) to fund research grants. Murphy warned, however, that success will require a strong vision (what he called a “big hairy ambitious goal”) and a long-term commitment of at least 15 years. Over time, changes are inevitable, and participants do well to stay flexible and nimble.

Show Me Partnerships! Founding the Missouri Bio-Belt

Susan M. Fitzpatrick, Ph.D., vice president of the James S. McDonnell Foundation, agreed that, at a time of tight federal budgets, states must step forward to support health research. She cautioned, however, that states are motivated to make these investments to stimulate economic development, not scientific discovery, and the initiatives can become entangled in the political “culture wars” over topics such as stem cell research, cloning and abortion. Nevertheless, foundations can play an important role in influencing the direction of state investments. For example, Missouri recently announced the \$425 million Lewis & Clark Discovery Initiative, mostly for capital improvements at state universities, and \$38.5 million for the Missouri Life Sciences Trust Fund, despite a state ban on stem cell research that has effectively halted all state grants for biomedical research. Missouri also receives \$245 million per year from tobacco settlement funds but spends none of this money on prevention or other health research. On the other hand, the Danforth Foundation has committed \$117 million to promote St. Louis as a center for biotechnology, and a Missouri Coalition for Life-Saving Cures has emerged to support legislation that would keep stem cell research legal in the state. In the end, foundations need to decide how much money is required to fund all meritorious research, and whether economic development is an appropriate goal for foundations.

Discussion

In response to questions for the panel, Plosila noted that the National Science Foundation and NIH do not measure the economic return on their investments in health research, but he agreed that citation analysis would be an inadequate measure of the return on foundation-funded research grants. Murphy noted that private foundations do not typically fund economic development, but they must take economic development into consideration when they partner with politicians. Pizzo reported that California’s analysis shows a very small return on investment if measured in terms of royalties, but a much larger return if measured in terms of new therapies that reduce the cost of care and the burden of disease.

KEYNOTE SPEECH

The Importance of Science from the Perspective of a Patient Advocate

Margery Perry, chair of research emeritus of the Juvenile Diabetes Research Foundation International (JDRF) discussed the role of lay volunteers in research funding decisions. JDRF was founded in 1970 by parents of children with diabetes. The foundation is now the world's leading non-governmental funding organization of type I diabetes research, raising and spending some \$120 million this year alone. By design, there is no endowment. Perry, herself a lay volunteer, first got in touch with the foundation in 1989, when her daughter Adriana was diagnosed with juvenile diabetes at the age of seven.

“You have probably two choices: you either go into denial or you try to fight like crazy and learn as much as you can. I chose the second route.”

Margery Perry

JDRF has a two-step grant selection process. The first step involves a scientific review committee, and the second involves a lay review committee that decides whether proposals accepted by the scientific review committee will be funded. The lay review committee tries to support grants that are critical to JDRF's mission, even if they are not hypothesis-driven research. The main goal is to fund research that will lead to therapeutics and to focus on moving discoveries to the clinic as quickly as possible. In rare cases the lay committee recommends funding grants that would not have passed the scientific peer review alone.

One such grant suggested the establishment of islet cell distribution centers. The grant's authors argued that such centers were necessary because many scientists who create islet cells only give them to their friends, leaving many promising research projects without the necessary cells. Initially, the scientific review committee did not even want to score the islet cell center grant, because it was really an infrastructure project as opposed to a research project. But the lay review committee forced the scientific committee to score it, and decided that it should be funded. As a result, the JDRF funded 10 centers in the U.S. and Europe that distribute islet cells to basic researchers. This eventually spurred NIH to establish 10 additional centers across the U.S. in 2001. JDRF is still funding some of the international centers.



In another example of volunteer involvement, a lay volunteer suggested a project to develop an artificial pancreas. The volunteer had identified a gap in JDRF's research portfolio that could close the loop between monitoring glucose and delivering insulin. Here again a JDRF grant spurred a federal agency to take action: in March 2006, FDA named the development of an artificial pancreas as a component in its Critical Path Opportunities List.

While many scientific funding agencies have traditionally involved only scientists in the grant selection process, more agencies are adding this step of involving lay reviewers—who have their eye on a cure, as opposed to having an eye on the potential citation impact factor of a funded research publication. The impatience for results and passionate involvement has strengthened the portfolio of many voluntary health agencies.

PLENARY SESSION 3: TRANSLATING RESEARCH INTO PRACTICE

This plenary session focused on the gap between what is known to be effective clinically, and what is actually made available to patients. It requires a very different type of research than what is needed to discover and develop new therapies.

Carolyn M. Clancy, M.D., director of the Agency for Healthcare Research and Quality (AHRQ) at the U.S. Department of Health and Human Services (HHS), suggested that if we do not fix the health care delivery system, research will not make any difference. She urged participants to think of the delivery system as a platform for discovery, not only of what works (or does not work) but also of why what works for one patient does not work for another. One AHRQ study found that half of all diabetes patients are not taking medication, not because they are noncompliant but because they cannot afford the co-payment. Another showed that AIDS drugs, as expensive as they are, can more than pay for themselves by reducing the need for costly hospitalizations.

AHRQ supports a network of Centers for Education and Research on Therapeutics (CERTs) that looks for potential harms, such as drug interactions, as well as benefits of medications and therapeutics, and disseminates the results widely to physicians, pharmacists and patients. Another AHRQ program is Effective Health Care, which looks at the bottom-line question of what works, and for whom, in Medicare, Medicaid and the state child health insurance program. The comparative effectiveness reviews developed under this program synthesize current knowledge, identify gaps in that knowledge that can be filled by research, and disseminate that information to doctors and patients who are making treatment decisions. Initial studies have focused on cholesterol control, gastric reflux, and biopsies following mammograms; future studies will address prostate cancer, asthma, depression, and osteoporosis.

None of this research will be possible without electronic patient databases and the other fruits of health information technology (HIT). HIT is an important tool to move the latest research and evidence into clinical practice more quickly and effectively. The best results to date have come from homegrown IT systems, which grow out of the needs and abilities of actual users. Evidence on commercially marketed systems is less conclusive, since they are designed primarily with billing, rather than research, in mind. The transition to a paperless system will not be easy or painless, but it will provide opportunities for improvement. The key is to focus on designing and operating computer systems to serve and improve patient care, rather than allowing system requirements to dictate their use and potentially negatively affect the patient care.

FDA's Critical Path and NIH's Roadmap will work only if the U.S. has an intact and effective health care delivery system that can make use of its discoveries and improve on innovations. At present, the U.S. spends about six cents of every health care dollar on research, but only a one-tenth of penny on the kind of health services research funded by AHRQ. Clancy closed by inviting participants and their organizations to attend an AHRQ-sponsored research conference, "Translating Research into Practice," that was to be held in Washington D.C. in July 2006.

BREAKOUT SESSIONS ON OPERATIONAL ISSUES

G. Encouraging the Mentoring of Early-Career Clinical Investigators and Scientists

HRA Mentoring Projects

Virginia Krawiec, M.P.A., director of Health Professional Training Grants at the American Cancer Society, noted that HRA identified mentoring as a priority issue in 2004 and that many HRA member organizations offer awards with mentoring components. The Grants Administration Working Group is compiling a list of mentoring awards programs, strategies, and resources that currently exist within HRA member organizations. The goal of this current breakout session was to arrive at consensus on the qualities of good mentoring and how to evaluate mentoring programs.

Mentoring: Insights Into the Satisfied Trainee

Victoria McGovern, Ph.D., senior program officer at the Burroughs Wellcome Fund, reported that foundations include mentoring components in their award programs both to attract and launch young scientists on careers in research and to help develop the next generation of scientific leaders. As a result, some of these components focus on basic or advanced career skills, while others focus on personal development, community building and leadership qualities. Metrics for success can be subjective (how satisfied is the postdoc with himself or his advisor?) or objective (productivity or absence of misconduct). A study by Geoff Davis, Ph.D. at Sigma Xi revealed that the strongest correlates of postdoc satisfaction and productivity are structured oversight and a wide range of professional development opportunities. Salary and other compensation-related factors appear to have less influence on productivity or satisfaction, possibly because postdoc salaries are much higher than they were five to 10 years ago.

Dr. McGovern left the audience to ponder an idea paraphrased from the U.S. Army War College—teaching, coaching, and leading by example are things that should be expected in leadership development and not lumped together under the term mentoring.

Related link:

Davis, G. 2005. Doctors without orders. *American Scientist* 93 (3, supplement). postdoc.sigmaxi.org/results

Mentoring Via a Consortium

Lori Conlan, Ph.D., program manager at Science Alliance of the New York Academy of Sciences, reported on a different model of mentoring, namely a consortium approach that began in New York City but now includes 26 universities, medical schools, and research institutes in the United States and abroad. This program began with the discovery that 80 percent of mentored postdocs desire tenure-track faculty positions, but only 20 percent will find them. The rest go into industry or other non-academic careers, thus they need to be exposed to a broader range of career alternatives and opportunities during their training. The Science Alliance has attracted more than 6,000 young scientists, most of them paid for by their home institutions, to attend e-briefings and on-site programs in career opportunities, job hunting, grant and article writing, tax and immigration issues, and business management skills. Success has been assessed by the number of event attendees, event exit surveys, the number of institutions waiting to join, and website hits.

History and Analysis of a Mentored Clinical Investigator Award for Cancer Research

Jennifer McCafferty-Cepero, Ph.D., scientific director at the Damon Runyon Cancer Research Foundation, described her foundation's experience with two different approaches to supporting mentoring. The Clinical Investigator Award, launched in 2000 with support from the Eli Lilly and Company, was a five year, \$1 million fellowship that included up to \$30,000 per year in compensation for a tenured faculty mentor who would devote 15 percent of his/her time to the supported investigator. A program evaluation in 2005 discovered that although 94 percent of awardees were satisfied with the level of mentoring they received, many felt that the financial reward for the mentor was too large, and 67 percent of faculty mentors felt that the stipend was unnecessary, as mentoring was part of their job and the stipend could be better spent on the awardee's research. Accordingly, as part of the overall reconfiguration of the award, the mentor stipend was eliminated and the award amount and duration were reduced.

Other information gathered by Damon Runyon suggests that good mentoring means different things at different stages in a clinical investigator's career, and that sometimes a team approach is more effective. The most important goal is to develop career independence, but this involves both scientific and career issues—communication skills, networking, and how to obtain and succeed in the first independent position. The best mentoring programs are well structured, try to match mentors and mentees, and offer a wide exposure to career skills and career alternatives. Many allow or even require awardees to attend scientific and professional meetings.

H. Managing Donor Activism in the Peer-Reviewed Science Process

Maria Carrillo, Ph.D., director of medical and scientific relations at the Alzheimer's Association National Office, moderated an interactive session on how to manage donors who have an active interest in setting the scientific agenda for a funding agency, or who wish to be involved in the selection of grantees. Not all donors want to get involved, she said, and those who do may want to become active in many different ways. Participants provided examples of how six foundations handle their donors:

1. At the Alzheimer's Association, donors can sponsor certain studies that have already passed the peer review process. They can also partially sponsor a study in a certain geographic area. If no studies in that area are being conducted, the Alzheimer's Association will hold the donated money in a trust until a project emerges within the desired geographic area.
2. The March of Dimes also allows donors to target their support to certain types of studies or geographic areas, for example cardiovascular diseases, or prematurity research, or research conducted within the state of California, said Dr. Michael Katz, senior vice president for Research and Global Programs at the March of Dimes, adding that there are limits. The donor cannot select a particular institution or grant recipient, under any circumstances. Donors do not participate in the review of the applications or are they made privy to these confidential processes. "We [once] had a request for funding, which, it turned out, was aimed for the nephew of the donor in San Diego," Katz said. "We said we cannot do that." The March of Dimes also allows stock donations or gifts as small as \$5.
3. The American Heart Association encourages donors to fund AHA-approved studies. However, when asking for such major gift support, the AHA generally asks for a multi-year commitment for at least one full award. All the studies AHA funds are original research studies, and the AHA will honor a donor's request to fund research in a particular area of cardiovascular disease or stroke or in a particular geographic area. If a donor wants to fund a specific unfunded AHA proposal, and if that study is considered highly meritorious by AHA standards—top 30 percent of applications—the AHA will accept donor sponsorship for that study. But again, to support a specific science area, AHA needs a commitment from the donor to fund the full amount of the award over its multi-year lifecycle. When donors contribute smaller amounts restricted to AHA research, such contributions are used to support AHA affiliate and national research programs in general—75% of the contribution to affiliate research program where donor resides; 25% to national research program.

4. Juvenile Diabetes Research Foundation International allows donors to direct funds to a very specific research area and will even name a grant after the donor if at least half of the award comes from that specific donor and if the award is at least as high as \$200,000. It also accepts donations of automobiles.
5. At the Damon Runyon Cancer Research Foundation, 100 percent of donations are used to fund research. Its general and fundraising overhead are paid for by its Broadway Tickets Service and endowment. Donors may fund individual postdoctoral fellows or clinical investigators who have been selected by the Foundation through its peer review process, but may not designate scientists to fund outside of this process.
6. The Foundation Fighting Blindness lets the donor, the foundation, and the scientist work together to write certain grants, a process that can take up to a year. But these grants must be then submitted and be considered meritorious in peer review before funding is awarded.

“Donor activism is a positive thing, but sometimes it can get overwhelming.”

Maria Carrillo

Dr. Carillo said that sending out research reports is important to keep in touch with donors. At the Alzheimer’s Association, some officials questioned the usefulness of having science writers translate reports into lay language, due to the expense involved. But when Dr. Carillo asked colleagues in other organizations about their practices, she found that most of them do this translation and have found the expense to be justified. This illustrated why the ‘sharing of intelligence’ at meetings such as this is of great practical value in our daily work.

Other aspects of donors’ expectations are also an issue—including communicating that they should not necessarily expect to fund the one grant that leads to a cure of the disease. Donors need to understand that the key difference between private and public funding is that private foundations can make riskier investments—which means that some of the funded research projects will fail. If a donor asks to fund a potentially high-impact project, the Alzheimer’s Association will look for projects that will yield more rapid results; for example, an imaging study as opposed to a mouse model research study.

In the discussion that followed, Russell Bromley, chief operating officer of the Myelin Repair Foundation said that the donor pool is changing. “People who donated based on trust are a dying breed,” Bromley said. “The new donors are more activist, and if your programs aren’t evolving to take that into account, then it will become more difficult to raise the same kind of money as in the past.”

One thing has to be avoided to keep the donations coming: “We have to be careful about overpromising,” one person in the audience said. “It can come back and bite you if you say the cure is tomorrow and then 10 years later the cure is still not there.”

I. Starting from Scratch: A Biomedical Funding Tutorial for New or Small Foundations

Sally McNagny, M.D., M.P.H., vice president of The Medical Foundation, moderated an interactive session on how to start and run a medical research grants program. Her own foundation is unique in that it specializes in creating medical research grants programs for other organizations. She commented, “we work with clients—family foundations, bank trust departments, and private individuals—to create customized grant programs that identify and fund outstanding scientists.” Her eight clients are all very different, providing ideal case studies to illustrate different approaches to funding.

When starting a grant program, for example, it is important to work with senior researchers in the field to determine the most effective point along the continuum of biomedical research in which to fund. This can be anywhere from basic biomedical research to late stage clinical trials or improving health care delivery. Limiting administrative costs is critical, especially for small foundations. Focusing on a particular institution, specific types of research or a limited geographic area can keep the number of applications down, and with it administrative costs. Also, trainee grants require fewer resources than large \$1 or \$2 million awards for established scientists. Interviewing finalists can be very costly, especially for a small foundation, because finalists have to be flown in from all over the country.

Careful attention must be paid when designing the eligibility criteria. For example, because the National Institutes of Health (NIH) generally funds only U.S. citizens and permanent residents, one opportunity for private foundations is to fund non-U.S. citizens who conduct much of the basic research at the postdoctoral level in the U.S. The King Trust, one of the Medical Foundation’s clients, is doing just that. From the researcher’s perspective, it is also vital to receive multiyear awards, as McNagny learned from her own experience as a researcher. Medical research takes time to yield results and multiyear grants free investigators from spending their time writing grants. Funders must also consider whether to allow indirect costs. In some cases, not paying them can disadvantage a grantee if the recipient institution can’t come up with the money to cover these costs.

“It is so painful if you [the researcher] have a one-year grant and the moment you get the money you have to start writing more grants. Try to set the duration as long as possible.”

Sally McNagny

The integrity of the scientific review committee and process is also important. One way to ensure integrity is to avoid any financial or professional conflict of interest or bias. The Medical Foundation asks committee members to sign its conflict of interest policy, which is very similar to the policy adopted by the NIH. Committee members should come from a mix of different backgrounds, such as academia as well as the pharmaceutical and biotech industries. One common problem is that the chair might recruit close colleagues to the committee, which should be avoided in order to assure diversity of scientific opinion. Compensation for reviewers can vary, depending on how prestigious it is to be a committee member. If the foundation is not well known, honorariums have to compete with the pay levels for consulting for the pharmaceutical industry, which can be as high as \$2,000 to \$3,000 per day.

Once the committee members are chosen, incoming applications need to be scored and ranked, and this can be “unbelievably complicated,” according to McNagny. First, the committee members consider the Foundation’s mission while scoring the best science. Then there is the issue of discordant scores. One approach to resolve them is to bring in a third reviewer, something the Medical Foundation does for some of its programs. The Alzheimer’s Association runs online chat rooms where reviewers can discuss their scores. Most of the time, this helps bring the scores closer together once the committee meets. The scoring process is not straightforward either: ranking by average score can be a problem if there is an outlier that skews the mean; removing the outlier can solve that problem, as can using the median. The Medical Foundation does both, and McNagny recommends giving the committee all the information, including the rank order by mean, by median, and providing the outlier scores, so the committee can make an informed decision.

A poll by the Center for Effective Philanthropy (www.effectivephilanthropy.com) found that most grantees consider a consistent foundation message and the approachability of staff most important to them. Also important are downloadable applications, clearly stated deadlines and a list of successful applications and funded grantees. Also, rejected applicants should receive honest and detailed feedback from the committee. For further information and guidance on the issues discussed in the session, McNagny referred participants to the websites of the NIH Office of Extramural Research and Center for Scientific Review, as well as the HRA website.

Related links:

- NIH Office of Extramural Research: grants.nih.gov/grants/oer.htm
- Center for Scientific Review: www.csr.nih.gov

J. Intellectual Property and Royalty Issues: Preclinical Drug Discovery and Development

Definitions of key terms

Patents: Provides the right to exclude others from making, using, selling, offering for sale, or importing the patented invention for the term of the patent, usually 20 years from the filing date. A patent is, in effect, a limited property right that the government offers to inventors in exchange for their agreement to share the details of their inventions with the public. Like any other property right, it may be sold, licensed, mortgaged, assigned or transferred, given away, or simply abandoned.

License: May be granted by a party (“licensor”) to another party (“licensee”) as an element of an agreement between those parties.

Royalty or royalties: Typically the sum of money paid to the proprietor or Licensor of Intellectual Property (IP) Rights for the benefits derived, or sought to be derived, by the user (the Licensee) through the exercise of such rights. Royalties may be paid for the use of copyright, patent, registered design, knowhow or trademark, or a combination of them.

Technology transfer: The process of developing practical applications for the results of scientific research.

Reach-through rights: An attempt by the owner of an enabling technology to acquire some right or interest in the results of the research undertaken by the recipient using the technology. The end product concerned may or may not be within ‘reach-through’ claims of a patent licensed as part of the enabling technology.

Definitions were compiled from Wikipedia.com, Pharmalicensing.com, and other sources.

Michelle Cissell, Ph.D., associate director for strategic planning research department, at the Juvenile Diabetes Research Foundation International, opened the session by suggesting that, as foundations become more involved in translational research and drug development, they may find it necessary to secure intellectual property (IP) rights in order to ensure continued development. This session was developed to explain the following questions:

- How can funding agencies protect access to IP rights or licenses for technologies that are critical for drug development?
- When it is appropriate or desirable for funding agencies to ask for royalties on IP developed with their grant support?
- How do IP and royalty issues differ when grants are made to academic or industry grantees?

NIH Policies on Intellectual Property Protection, Licensing, and Royalties

Susan Rucker, Esq., senior technology licensing specialist at the NIH Office of Technology Transfer, reported that NIH manages its portfolio of 2,300 current or pending patents to benefit public health, attract new R&D resources, and encourage the commercial development of drugs and devices discovered by intramural researchers. To stimulate commercial development, NIH has 239 active Cooperative Research and Development Agreements (CRADAs) designed to move discoveries toward market, and more than 1300 active licenses (mostly nonexclusive) to produce patented drugs and devices. The goal of these arrangements is to maximize commercialization that will secure an appropriate return on public investment, but like most research institutions, NIH doesn't show much of a profit from technology transfer. In FY 2005, NIH received royalties of \$98.2 million, compared with a total NIH budget of \$29 billion. NIH is also exploring ways to patent and license products overseas, with an emphasis on affordable antiretrovirals and other antibiotics for developing countries. These efforts must be balanced against the costs: it takes at least \$10,000 to write a patent application in the biotechnology and pharmaceutical related arts, with additional costs in multiples of \$10,000 to prosecute the application and at least another \$5,000 per application to file in the five major international markets, again with additional costs in the multiples of \$10,000 to prosecute each of those applications.

How Funders Can Drive the Therapeutics Pipeline and Manage IP

Suzanne R. Pattee, J.D., vice president of public policy and patient affairs at the Cystic Fibrosis Foundation (CFF), described the foundation's experience in driving products through the development pipeline. In 2000, the foundation created CFF Therapeutics Inc., a nonprofit drug development affiliate that now coordinates 18 clinical trial centers in 12 states, with more than 24 compounds in some stage of development. To move promising products through the pipeline, CFF awards funds of \$100,000/yr for two years to cover preclinical testing, and \$750,000/yr for two years for Phase I and II clinical trials. This support can be withdrawn at any time for failed milestones, but, if this is done, CFF retains the rights to develop the product. In general, however, CFF does not seek to obtain IP rights, but strives to ensure that the resulting information is placed in the public domain in order to advance CF research. Because a patent filing can delay progress, CFF has established a consortium for specific CF research, in which CFF forgoes the IP rights for non-CF applications of technology in exchange for a paid-up license for CF applications. This has proven to be an effective incentive for the CFTR consortium, which consists of numerous universities and research institutes, but it is being used only for this project, not across the board.

Acquiring Patent Rights to Gene Sequences: Adding to the Portfolio of Tools to Accelerate Drug Discovery

Cynthia Joyce, executive director at the Spinal Muscular Atrophy (SMA) Foundation, described a similar effort to acquire IP rights to gene sequences and other tools in order to accelerate drug discovery and development. Founded in 2003 by parents of an affected toddler, the SMA Foundation discovered that other organizations were sponsoring or conducting early-stage research on the disease, but there was little support for drug development. Researchers in France had patented the gene sequences associated with the disease and using those discoveries, several labs developed transgenic mouse models of the disease. However, concern about “reach-through” rights asserted by the discovery institutions had essentially halted development efforts dependent on these valuable research tools. The SMA Foundation took on the challenge of reducing these barriers to progress by negotiating nonexclusive licenses with the institutions, with the sublicensing options for commercial development, which essentially opened the door to all investigators interested in working in the area of therapeutics development.

Keys to success for the SMA Foundation were willingness and persistence in addressing these barriers and the compelling urgency of their cause to prevent children from dying. It was also important to understand the motivations of their negotiating partners; a priority for one partner was the interest in sharing public recognition that came from this innovative arrangement. Joyce feels that this licensing agreement provides a precedent and model for other foundations, which are well advised to invest the time and effort needed to gain expertise in the IP field. In response to questions, she and the other speakers agreed that IP licensing belongs in every foundation’s toolbox. Clearly there are other unused research tools and abandoned compounds that could benefit from the marketing efforts of foundations or consortia. But they also counseled patience—a research tool is only the first step toward a new drug, and it can take six to 10 years before it leads to new therapies that will justify the foundation’s initial investment.

CLOSING PLENARY SESSION: MECHANISMS FOR ACCELERATING DRUG DEVELOPMENT FOR ORPHAN DISEASES

Tom Caskey, M.D., executive vice president for molecular medicine and genetics at the University of Texas Health Science Center at Houston, pointed out that the recent doubling of the National Institutes of Health (NIH) budget brought a lot of new investigators into health research, and that flat or declining NIH budgets in the coming years may provide the opportunity for foundations to become the primary drivers in shaping the careers of these young investigators. There will be a need for more domestic talent, because homeland security efforts have harmed foreign recruitment resulting in many young investigators being lost to overseas opportunities.

Translational research does not work without basic research, Dr. Caskey noted, but the costs are easily 10 times as great, and the chances of success only one in 20. On average, it takes 15 years to develop a new drug, at cost estimates ranging from more than \$800 million to nearly \$2 billion—most of it for Phase II and III clinical trials. Little wonder, then, that some drug companies prefer to focus on “copy-cat” drugs or new applications for drugs already approved by FDA. In some cases, however, a new purpose for an old drug is just what is needed in an orphan disease, which do not affect enough patients to become a major source of revenue for a company.

For example, researchers at Johns Hopkins University recently discovered that losartan, an established drug for treating high blood pressure, is also highly effective in slowing the progression of Marfan syndrome, an inherited disease of the connective tissues. The fact is that most of the drugs on the market today may have multiple uses that could be discovered by intelligent screening. Pharmaceutical companies are always looking for ways to extend their patent coverage, and many also have philanthropic foundations; a clever advocate might be able to convince them of the wisdom of paying for this screening of their own drugs.

Different approaches might be needed for working with biotechnology companies and academic health centers. Biotechnology companies, for their part, seek nondiluting investments, but they welcome contract work and could be a very efficient partner in drug development. Negotiations with small biotech companies proceed far more rapidly than those with big pharmaceutical companies. Academic health centers, on the other hand, will respond more strongly to programs that focus on developing young investigators and delivering solutions to patients.

The point is that this is an excellent time for non-profit funders to play a leadership role in translational research. Foundations should pick their partners carefully and plan for the long term, establishing milestones along the way. If milestones are not met—if the drug fails toxicology, or if it does not look promising at the end of Phase I or Phase II studies—the foundation should be ready to pull the plug and move on to the next candidate. Phase III trials will inevitably involve commercial partners, in which role small biotech companies are cheaper and more nimble than large drug companies. In addition, several states recognize the economic development benefits of grantmaker investment in new therapeutics and will partially match those contributions out of public funds.

In summary, Caskey encouraged nonprofits to “step up for science,” but he also cautioned them to ask themselves whether they are ready to accept the “opportunity cost” of investing in these more expensive translational projects. If the answer is yes, then they should decide whether they want to focus on a single target or take a more distributed approach that supports the discovery process. Above all, they must learn to take the long view—choose a partner carefully, and then establish milestones that will evaluate progress over the eight to 15 years required to move from basic discovery to marketable drug. The greatest cost for pharmaceutical companies, who do this for a living, aren't the drugs that have a small market, but rather the drugs that never make it to market.



A national consortium of non-governmental funders of health research and training

The Health Research Alliance fosters collaboration among not-for-profit, non-governmental funders to support the continuum of health research and training from biomedical science to applications that advance health, by:

- Improving communication and collaboration among all grantmakers that fund health research, as well as between grantmakers and the broader health research and policymaking communities;
- Providing information about the research supported by not-for-profit, non-governmental funders of health research and training; and
- Enhancing the overall effectiveness of grantmakers in supporting biomedical and health research and training through the sharing of information and best practices.

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