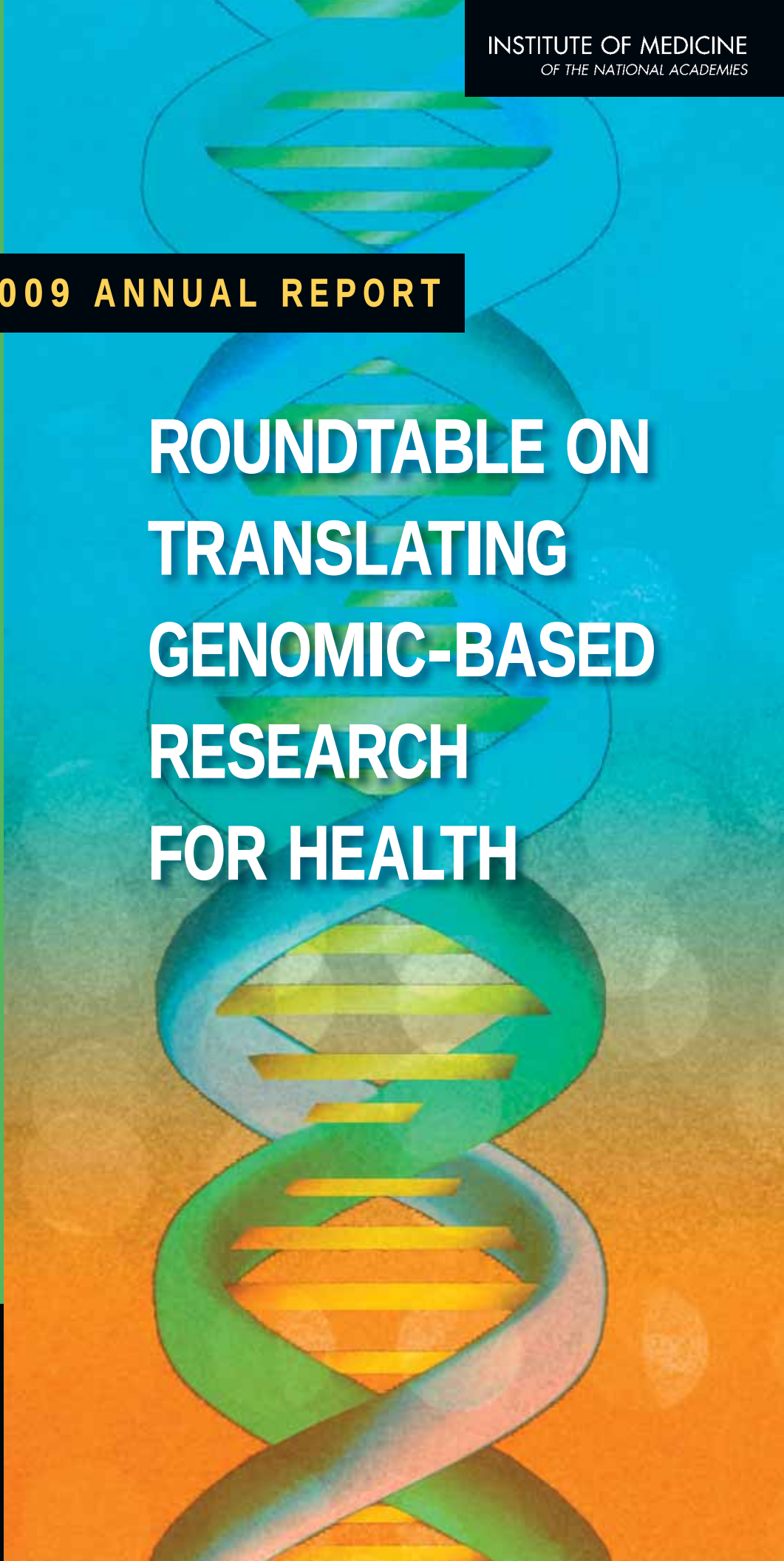
INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

2008-2009 ANNUAL REPORT

ROUNDTABLE ON TRANSLATING GENOMIC-BASED RESEARCH FOR HEALTH



BOARD ON HEALTH SCIENCES POLICY

MESSAGE FROM THE CHAIR

WYLIE BURKE

When the Human Genome Project began in 1990, the idea of predicting, diagnosing, and treating disease based on genetic sequences was merely a vision. Now, nearly 20 years later, DNA analysis is being used to help guide treatment decisions for breast and colon cancer, predict drug responses, and diagnose a growing array of genetic conditions. In addition, private companies have begun offering genetic testing for everything from ancestry to dating compatibility to disease risk. Each day, new associations are found that could result in advanced capabilities to screen, treat, and perhaps even prevent common diseases. However, many questions remain about these discoveries: What levels of evidence are necessary in order to introduce new technologies into the clinical setting? What are the ethical, legal, and social implications? How will new genomic technologies fit into an already overburdened health care system?

With these issues in mind, the National Academies created the Roundtable on Translating Genomic-Based Research for Health in 2007. The Roundtable brings together experts from academia, industry, patient and provider groups, government, and others to hold a conversation of how to advance the field of genomics, and in particular, how to improve the translation of research findings into applications that result in real health benefit. One key function of the Roundtable is to identify topics and hold public discussions in order to educate and to engage the public on key issues in the field.

The Roundtable has held several public workshops and discussions in 2008-2009, including a workshop that explored novel ways of delivering genomic services, and a workshop that examined systems designed to facilitate the collection and analysis of genomic data. We have formed several working groups to probe more deeply into topics such as population health, issues in drug and test development, and models for evidence collection.

As the pace of genomic discoveries quickens, and concerns and questions increase in tandem, the Roundtable has the unique opportunity to bring stakeholders and the public together for dialogue and debate about areas of uncertainty and the opportunities and challenges that lay ahead.

Sincerely,

Wylie Burke, M.D., Ph.D.
Professor and Chair
Department of Bioethics & Humanities
University of Washington

MEMBERSHIP

Membership of the Roundtable includes a diverse range of stakeholders, including government, the pharmaceutical industry, academic health centers, researchers, associations, patient advocates, and others.

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Duke University

SHARON TERRY
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STEVEN TEUTSCH, M.D., Ph.D.
Secretary's Advisory Committee on Genetics, Health and Society

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MICHAEL S. WATSON, Ph.D.
American College of Medical Genetics

CATHERINE A. WICKLUND, M.S., CGC
National Society of Genetic Counselors

JANET WOODCOCK, M.D.
Food and Drug Administration

ROUNDTABLE ACTIVITIES IN 2008

MEETINGS AND WORKSHOPS

Case Studies of Translation Pathways — April 1-2, 2008

The Roundtable held a public meeting using four case studies for an in-depth exploration of the translation of genomic innovations from the initial research to clinical application. The workshop particularly focused on identifying barriers and facilitators to translating research findings and assuring an adequate evidence base for clinical decision making. Speakers were invited to share their experiences with the four case studies: HLA B*5701 testing for abacavir, array comparative genomic hybridization, thrombophilia screening, and cytochrome P450 testing for serotonin-specific reuptake inhibitor (SSRI) use. Some specific questions addressed were:

- How did the manufacturers decide what variants would be measured and how results were to be interpreted?
- What was the business model for the test?
- What obstacles have the manufacturers or distributors experienced? Are other obstacles foreseen?
- What regulatory issues had to be addressed in bringing the test to market?
- What evidence base was needed at different stages of translation? What were the barriers or facilitators to developing the needed evidence?
- Has post-market research been performed? Are there data on outcomes of testing in clinical settings? Has use of test changed with experience?

Innovations in Service Delivery in the Age of Genomics — July 28-29, 2008

The Roundtable on Translating Genomic-Based Research for Health held a public workshop regarding service delivery in the age of genomics. The current system for delivering genetic services is based on a model of intensive counseling for rare diseases. As the use of genomic technology becomes more prevalent, providers and patients will need new ways of communicating about genetic information and how it may change health care options. Old practice models that rely on extensive education and counseling may not be suitable when patients and payers demand the inclusion of genomic information in making everyday health care decisions. New practice models of service delivery will have to be developed to contend with the rising tide of genomic innovations.

The workshop featured presentations and discussion focused on three goals:

- To understand the current status of genetic and genomic service delivery.
- To explore how needs will change as genomic innovation progresses.
- To examine what types of alternative practice models will be needed.

A workshop summary was prepared and published in 2009.

Discussion of Evidentiary Issues in the Translation of Genomic Innovations — October 6-7, 2008

New links between disease and genetics are being discovered at a rapid pace. However, questions remain about the appropriate time to move a discovery from the research stage into the clinical setting. The Roundtable held a public meeting to discuss issues of evidence in genomic innovations, exploring questions such as:

- What kind of evidence is necessary to move an innovation into practice?
- How does the evidence bar change at the different stages of translation?
- Is the amount of evidence required the same for all stakeholders?
- Where are the biggest gaps in evidence?
- Can one overarching process or set of standards be developed?
- Do evidence standards need to be different by disease? By stakeholder?
- Who should take the lead in compiling evidence, identifying gaps, filling gaps?

The Roundtable heard presentations on various strategies for gathering and evaluating evidence, examined the current landscape of evidence, and discussed the challenges and possible solutions to the issue of setting standards for evidence to bring genomic innovations to market.

SPONSORSHIP

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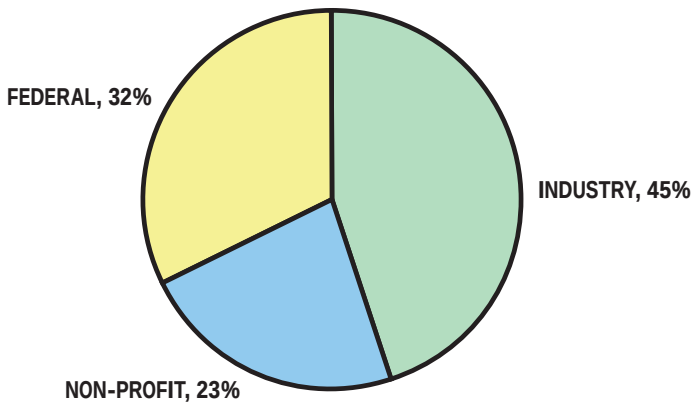
Pfizer, Inc.
Secretary's Advisory Committee on Genetics, Health and Society

ROUNDTABLE 2008-2009 FUNDING



ROUNDTABLE ACTIVITIES IN 2009

WORK GROUPS

In late 2008, the Roundtable formed small sub-groups in order to concentrate on specific issues important to Roundtable members. These groups meet in monthly conference calls, as well as in person at Roundtable meetings. The members discuss the issue at hand, develop a list of priorities, and decide on activities to pursue—a workshop, a commissioned paper, or other activity. There are four work groups:

- Diagnostic Applications
- Drug Development Informed by Genetics and Genomics
- Clinical Practice and Public Health
- Overview

The Drug Development group is considering issues such as alignment of stakeholders and sample collection for testing interventions. The Diagnostic Applications group is considering various models for demonstrating clinical benefit of innovations. The Clinical Practice and Public Health group is examining the value of genetic and genomic innovations and how value is defined for different stakeholders. The Overview group will assemble and analyze the output of the various groups and develop an overall strategic plan to move the work of the Roundtable forward.

MEETINGS AND WORKSHOPS

Systems for Research and Evaluation for Translating Genome-Based Discoveries for Health — February 12-13, 2009

The rapidly advancing field of genomics has stirred great interest in "personalized" health care from both the public and private sectors. A variety of genetically-based health care innovations have already reached the marketplace, but information about the clinical utility of these treatments and diagnostics is limited. Initiatives such as the National Institutes of Health's Genome Wide Association Studies database seek to identify genetic factors that influence health and disease. Identifying an association between a gene and a trait or disease does not, however, provide information about how this understanding could impact clinical care and patient health outcomes.

The Roundtable identified the need for a workshop to examine existing systems that create the kinds of resources and structure that facilitate evaluation of genome-based health care. More specifically, the workshop addressed the practical realities of creating such systems; the different models that could be used; the strengths and weaknesses of each model; and the effectiveness of such systems in addressing health outcomes.

On February 12, 2009, the Roundtable convened a workshop designed to address four central questions related to the development of systems to evaluate health care innovations that stem from genome-based research:

- What are the practical realities of creating such systems?
- What are the different models that could be used?
- What are the strengths and weaknesses of each model?
- How effectively can such systems address questions about health outcomes?

A summary of the workshop presentations was published in fall 2009.

Strategic Plan and Goal Setting, Part 1 — June 10-11, 2009

At this meeting, members discussed and developed a strategic plan for the future activities of the Roundtable. Underlying the Roundtable's plan are the assumptions that:

- Health-related research and research funding are driven by important health questions.
- Research spans the translational pathway.
- There is a lack of evidence concerning the clinical utility of genomic health care applications and their optimal delivery.
- Clinical utility has multiple components.

In addition, the Roundtable set two goals for near-term work. Through the use of workshops, seminars, or commissioned papers:

- Discuss approaches to filling evidence gaps in the use of genetic diagnostics or the use of genomics in drug development.
- Explore measures, including further research, to improve or facilitate implementation of genomic health applications that could improve health outcomes.

After developing this strategic plan, the Roundtable small groups identified workshop topics that would help fulfill these goals (see "Future Activities" for details).

Strategic Plan and Goal Setting, Part 2 — November 16-17, 2009

To help guide future activities of the Roundtable, members will invite speakers to discuss a number of issues including pre-competitive collaboration, innovative services, and levels of evidence necessary for different stakeholders.

PUBLICATIONS

Diffusion and Use of Genomic Innovations in Health and Medicine — 2008

Until fairly recently, genetic information was used primarily in the diagnosis of relatively rare genetic diseases, such as cystic fibrosis and Huntington's Disease, but a transformation in the use of genetic and genomic information is under way. While many predictions have been made that genomics will transform medicine, to date few of these promising discoveries have resulted in actual applications in medicine and health.

The Institute of Medicine's Roundtable on Translating Genomic-Based Research for Health held its first workshop on December 4, 2007, to address the following questions:

- Are there different pathways by which new scientific findings move from the research setting into health care?
- If so, what are the implications of those different pathways for genomics?
- What can we learn from the translation of other new technologies as we seek to understand the translation of genome science into health care?

Information obtained from the workshop was then used to further discussion and exploration of the answers to these questions. This workshop report summarizes speaker presentations and discussions.

Innovations in Service Delivery in the Age of Genomics — 2009

On July 28, 2008, the Roundtable held a public workshop that focused on the future of genomic service delivery. New discoveries in genomics are changing how we diagnose and treat diseases. Whereas previously, genetic testing could only screen for rare genetic disorders, increasingly, patients and their physicians are able to use genetic information to predict the risk of common diseases such as diabetes and breast cancer and to help determine prevention and treatment options. Genetic specialists have long been the main providers of genetic services, through an intensive counseling model. However, as the shift occurs from testing for rare genetic disorders to screening for common diseases, it will become necessary for general practitioners, pediatricians, obstetricians/gynecologists, and other providers to be knowledgeable about and comfortable with using genetic information to better their patients' health.

This report summarizes the workshop presentations and discussions that described the current system of genetic service delivery, described some pioneering current practice models, and proposed new models for integrating genetic and genomic innovations into education, training, and clinical practice.

Systems for Research and Evaluation for Translating Genome-Based Discoveries for Health — 2009

The Roundtable held a workshop on February 12, 2009, to examine existing systems that could be adapted to evaluate the use and impact of genetically-based innovations in patient care.

The report summarizes the presentations by the expert panelists and the open discussions moderated by Roundtable Chair, Wylie Burke. Chapter 2 provides an overview describing how the evidence needed for decision making may vary according to the particular application of the genome-based intervention. Chapters 3 though 5 summarize the three panel sessions: creating evidence systems; current practices in moving from evidence to decision; and gaps in the system for evaluation of genome-based health care. Concluding remarks are provided in Chapter 6, and the workshop agenda and biographical sketches of the panelists are available in the appendixes.

FUTURE ACTIVITIES

The Roundtable small groups are planning three workshops for 2010-2011:

Clinical Practice and Public Health

This workshop will define the set of challenges in accomplishing widespread implementation of genomic technologies to the population, using specific examples to discuss educational materials, professional guidelines, and workforce issues. Presenters will be asked to answer the question: Once stakeholders agree there is sufficient information to help clinicians and patients make decisions, what are the tasks and challenges involved in diffusing the test into practice? Workshop participants will learn from experiences in non-genetic arenas, such as the American Heart Association's "Get with the Guidelines" program, or preventive clinical services such as immunization programs. Presenters will discuss what interventions have been effective in changing health care systems or provider behavior to increase implementation of recommended clinical preventive and chronic disease management services, and identify which interventions might be most suitable for increasing implementation of recommended genomic services.

Drug Development

This workshop will examine the issue of pre-competitive collaboration for genome-based drug development. The drug-development industry has tools and knowledge that could be of benefit to others, and at the same time, the industry lacks access to samples that the government holds. The workshop will aim to:

- Elucidate a conceptual framework for the sharing of resources from many different stakeholders—academia, industry, government, and others;
- Define the rules of engagement for such collaboration;
- Look at best practices that make collaboration work; and
- Identify specific examples from other industries that have engaged in pre-competitive collaboration.

Representatives from each constituency will describe their needs, the resources they could share, and the issues they foresee in participating in collaborative activities.

Diagnostic Applications

This workshop will define the types of studies needed to generate sufficient evidence to support claims for different types of diagnostics. The Diagnostic Applications group will develop a matrix to look at the type and level of evidence required by different stakeholders, and this matrix will be presented and discussed at the workshop. Presenters and participants will then discuss the development of an incentive-based process that allows for the efficient translation of genomic tests and biomarkers into effective clinical practice, examining what types of incentives would be sufficient and necessary for different stakeholders.

ABOUT THE ROUNDTABLE

The Institute of Medicine Roundtable on Translating Genomic-Based Research for Health brings together leaders from academia, industry, government, foundations, and associations who have a mutual interest in addressing the issues surrounding the translation of genomic-based research. The mission of the Roundtable is to advance the field of genomics and improve the translation of research findings to health care, education, and policy.

Translating genomic innovations involves many disciplines, and takes place within different economic, social, and cultural contexts, generating a need for increased communication and understanding across these fields. Furthermore, these innovations have produced a diversity of new issues to be addressed, including issues such as evidence of utility, economic implications, equal access, and public perspectives. As a convening mechanism for interested parties from different perspectives to meet and discuss complex issues of mutual concern in a neutral setting, the Roundtable fosters dialogue across sectors and institutions and fosters collaboration among stakeholders.

To achieve its objectives, the Roundtable conducts structured discussions, workshops, and symposia, and publishes workshop summaries. Specific issues and agenda topics are determined by the Roundtable membership and span a broad range of issues relevant to the translation process.

The Institute of Medicine serves as adviser to the nation to improve health. Established in 1970 under the charter of the National Academy of Sciences, the Institute of Medicine provides independent, objective, evidence-based advice to policy makers, health professionals, the private sector, and the public. The mission of the Institute of Medicine embraces the health of people everywhere.

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www.iom.edu/genomicroundtable

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