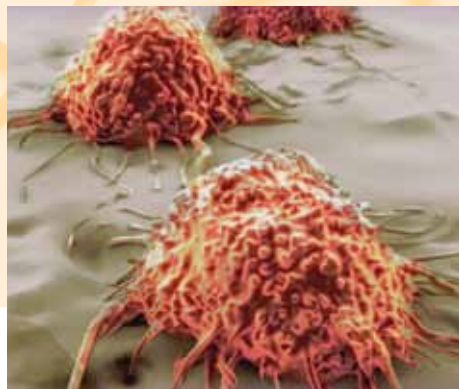


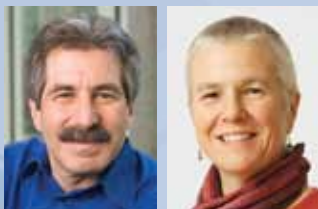
Roundtable on Translating Genomic-Based Research for Health

2013 Annual Report



INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

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Message from the Co-Chairs

The promise of genomics to improve health care is now becoming a reality.

Decreasing genome sequencing costs and innovative science have placed genomics and related molecular tools at the center of biomedical research. New molecular tools are being used to diagnose disease, predict the potential for adverse events, reduce

the use of unnecessary medical services, and tailor therapeutic regimens. As genomic medicine advances, it holds the tremendous potential to enable the health care system to provide improved and more accessible care at a lower cost.

However, translation into health care applications remains challenging due to a currently underdeveloped evidence base, a misalignment between basic research and clinical needs, and the lack of a robust knowledge generating system that incorporates genomic information from both basic and clinical research. Many important questions must be addressed to ensure that this new technology is appropriately adopted, but overcoming these obstacles is not an easy task.

The Roundtable on Translating Genomic-Based Research for Health provides an opportunity for strategic thinking and action to solve these paramount issues. Since its establishment in 2007, the Roundtable has organized and hosted 21 meetings and 17 public workshops and published 13 workshop summary reports. During these meetings, the Roundtable has explored areas including challenges for genomics, such as return of incidental findings from genome sequencing; improving the efficiency of translation of genomic applications; impediments to bringing basic research discoveries into clinical trials; integration of genomic information into health information technology systems; systems approaches to developing evidence for genomic applications and their evaluation; economic issues associated with precision medicine; genome-based strategies for drug and diagnostic discovery and development; and ethical considerations in conducting genomics research.

As a forum for academia, industry, advocacy and provider groups, government, and others, we stimulate discussion, press to clarify complex concepts, and seek pathways to solutions. In 2013, the Roundtable sponsored workshops and meetings on the co-development of molecular diagnostics and targeted therapeutics, conflict of interest and medical innovation, and drug repurposing. Essential to our process is discourse that allows all perspectives to be voiced, with special attention given to clarifying competing views and identifying actions and strategies for resolving issues.

Our agenda for 2014 will include further exploration of grand challenges for genomics—identifying key issues in the evidence evaluation process for genomic technologies, examining pragmatic approaches to educating health care providers about genomics, working with vendors and end users on integrating genomic information into the electronic health record, and developing a framework for investigators and industry to acquire DNA routinely as part of clinical trials.

The Roundtable recently welcomed new sponsoring members from the American Academy of Nursing, the Association for Molecular Pathology, the International Society for Cardiovascular Translational Research, the National Institute of Nursing Research, and PhRMA. We welcome our new members and look forward to a productive year with the participation of all stakeholders.

Sincerely,

A handwritten signature in black ink, appearing to read 'Geoffrey Ginsburg'.

Geoffrey S. Ginsburg, M.D., Ph.D.

Director, Center for Genomic Medicine
Institute for Genomic Sciences & Policy
Duke University

A handwritten signature in black ink, appearing to read 'Sharon F. Terry'.

Sharon F. Terry, M.A.

President & CEO
Genetic Alliance

Reflecting Back

Roundtable Activities in 2013

Roundtable Meetings

Roundtable members met four times in 2013 to continue their discussions on emerging and enduring issues in advancing the field of genomics. Meeting topics that were discussed included development of a knowledgeable health care system for precision medicine; evidentiary issues; education, engagement, and cultural change needed to implement genomic medicine; governance and ethical issues; research strategies to identify therapeutic targets based on genetic factors influencing human life span and health span; and integration of genomic information into health information technology systems.

Roundtable Workshops

Refining Processes for the Co-Development of Genome-Based Therapeutics and Companion Diagnostic Tests (February 27, 2013)

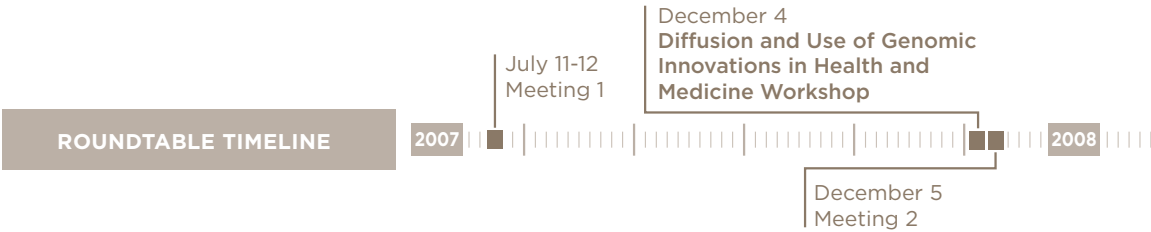
Genome information can identify new drug targets for both common and rare diseases, can identify patients predicted to respond to a specific treatment, and has the potential to significantly reduce the cost of clinical trials by reducing the number of patients that must be enrolled to demonstrate safety and efficacy. Recently, benefits such as these have led to the development and approval of a number of targeted therapeutics for diseases such as non-small-cell lung cancer, metastatic melanoma, and cystic fibrosis. A key component of each of these new drug approvals is the ability to identify the population of patients who will benefit from treatment, which has largely hinged on the co-development and co-submission to the U.S. Food and Drug Administration (FDA) of a companion molecular test. This has led to a major alteration in the way that drugs are being developed, with traditionally separate entities— pharmaceutical and diagnostic companies— now working in close collaboration.

Although these early co-development successes have bolstered the industry and demonstrated to some extent the efficacy of a genomics-based approach to drug discovery and development, this convergence has not occurred without issue. Questions remain regarding the economic viability of co-development for diagnostics, payer reimbursement for companion tests and off-label use of these drugs, the substitution of non-FDA approved tests, the challenges in changing technologies for an existing companion diagnostic, the need for multiple tests for limited amounts of diagnostic tissue specimens, and many others. The Roundtable hosted a workshop to examine the challenges of and potential solutions for co-development of molecular tests and targeted therapeutics.

Conflict of Interest and Medical Innovation: Ensuring Integrity While Facilitating Innovation in Medical Research (June 5, 2013)

New scientific innovations, such as the sequencing of the human genome, hold the promise for improving human health through greater understanding of disease biology and the development of new drugs, diagnostics, and preventive services. However, few basic research discoveries from these advancements have been translated into appreciable clinical applications, partly because of the complexity of the underlying biology, a lack of resources to validate the discoveries, and the cost and time it takes to develop a product. Business models are adapting to this new reality by placing increasing emphasis on the use of alliances, joint development efforts, early phase research partnerships, and public-private partnerships that have many potential benefits for the parties involved as well as the public.

Although the potential benefit of collaboration is great, scientific integrity and public trust must also be ensured by identifying, disclosing, and managing conflicts of interest (COI) that could create bias in the research being performed. The Roundtable hosted a workshop to examine and discuss the effect of current COI policies—both public and private—on medical innovation. The goals of the workshop were to articulate and clarify COI policies in the context of the current landscape for medical advancement, examine the impact of COI policies on innovation, and identify best practices to facilitate innovation under the current COI policies while still ensuring scientific integrity and public trust. Stakeholders, including government officials, pharmaceutical company representatives, academic administrators and





researchers, health care providers, medical ethicists, and consumers presented their perspectives and participated in discussions during the workshop.

Genomics-Enabled Drug Repurposing and Repositioning (June 24, 2013)

The path of drug development can be expensive and time-consuming. Recent estimates predict, on average, an expenditure of at least \$1 billion and a time frame of ten years to bring a drug to market. Although spending on drug research has increased, the number of drugs approved by FDA has not. In response, pharmaceutical companies are examining options to either give non-commercially available drugs a new chance at approval or to search for new indications for existing drugs. Technological advances and the increasing availability of genomic data and computational systems have resulted in new methods to systematically identify both drug targets and pathways for detecting drugs with a secondary, often seemingly unrelated, indication. The Roundtable hosted a workshop to assess the current landscape of drug repurposing activities in industry, academia, and government; examine enabling tools and technology; and evaluate the business models and economic incentives for drug repurposing programs. Stakeholders, including government officials, pharmaceutical company representatives, academic researchers, regulators, funders, and patients were invited to present their perspectives and participate in discussions during the workshop.



Looking Forward

Roundtable Activities in 2014

Roundtable Meetings

The Roundtable members will meet three times in 2014 to discuss various issues for the field of genomics. Roundtable members will discuss the challenges and opportunities for integrating genomic information into the electronic medical record, strategies for sharing clinical trial data, international efforts in genomic medicine, and focused genomic screening of companion genes for complex diseases.

Roundtable Workshops

Assessing Genomic Sequencing Information for Health Care Decision Making (February 3, 2014)

The sequencing of the human genome has led to tremendous advances in research and development, increasing our understanding of the basis of disease and hastening genetic-based targeted therapeutic development. Over the past ten years, these advances have been buoyed by the equally significant advances in technologies that have increased accuracy and lowered genome sequencing costs from \$2.7 billion in 2003 to \$1,000 today. As a result of these scientific and technological advances, large-scale genome sequencing is beginning to move into clinical practice for determining patient treatment options. The clinical use of sequencing relies on the



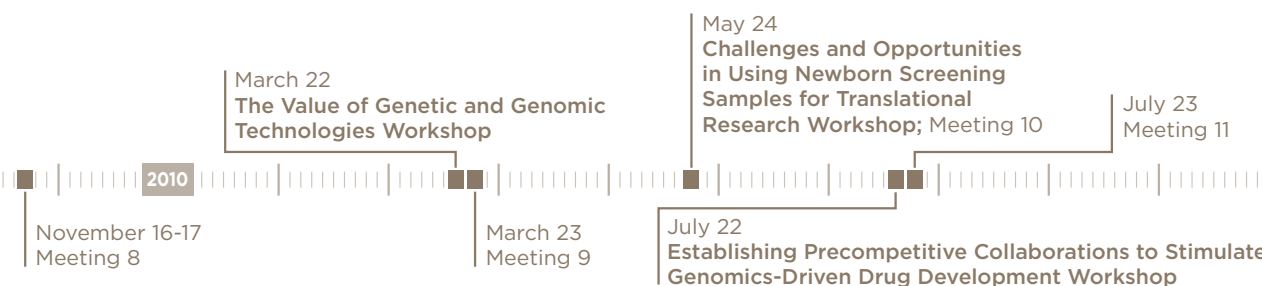


identification of linkages between genetic variants or groups of variants and disease. These findings may enhance patient care, but most associations have not been rigorously confirmed and may only play a minor role in disease. Until ideal information is developed, best practices for gathering and evaluating the available evidence are needed. The Roundtable will host a workshop to examine how evidence for genomic applications is gathered

and assessed for clinical and reimbursement decision making, guideline development, and patient care and health decisions in the absence of an ideal evidence base.

Facilitating the Integration of Genomic Information into the Electronic Health Record (December 8, 2014)

The sequencing of the human genome has facilitated a tremendous increase in our understanding of disease. This greater understanding, combined with the technological advances that have significantly improved genome sequencing accuracy while decreasing its cost, has led to large-scale sequencing now being used in clinical practice to aid in diagnosis and to identify treatment options for patients. With the expanded use of electronic health records (EHRs) by hospitals and physicians, EHRs offer vast potential to derive knowledge of disease, treatment efficacy, outcomes, and drug safety. However, the current health care system is largely unprepared to handle genomic data. There is a lack of standards for the data, and interoperability, scalability, privacy, security, and storage issues need to be resolved. The Roundtable is planning to host a workshop to examine how genomic information could be effectively integrated into EHRs. Stakeholder groups may include EHR developers and health information technology professionals, clinical providers and other institutional end users of these platforms, academic researchers, patient groups, and government representatives, who will be asked to present their perspectives and participate in discussions during the workshop.



Working Groups

Four working groups have been established within the Roundtable to examine various topics and aspects of translating genomic information into appreciable health care applications. Each group meets regularly by teleconference as well as in person at Roundtable meetings. Together, they discuss issues of mutual interest to the group as well as suggest, plan, and complete Roundtable workshops, seminars, and commissioned papers.

Education, Engagement, and Cultural Change

Many factors influence the adoption of new technologies across a health care system. Market forces, profit/loss ratios, and competitive advantage are several aspects that may be evaluated by institutional administrators when considering the implementation of a new program. The Education, Engagement, and Cultural Change (EECC) group is working to gain a better understanding of the major drivers of decision making at the institutional level with regard to adopting genomic medicine programs. In addition, the EECC group will be evaluating pragmatic approaches to improving genetics education for health care providers and the cultural barriers and change needed to facilitate this education.

Evidence

Over the last ten years, there has been an exponential increase in the number of single base changes that have been associated with diseases, including Alzheimer's disease and type 2 diabetes. This information can potentially be used to greatly enhance the care that patients receive. However, the evidence base for the majority of these associations is not developed enough for many stakeholders to use for decision making purposes—in particular, clinical care and patient management, reimbursement policies, and guideline development. Members of the Evidence group are working to examine how non-ideal evidence can be used in health care decision making.



Knowledgeable Health Care System for Precision Medicine

Genomic data are increasingly being generated in the clinical practice of medicine with genome sequencing being used to direct therapeutic prescribing as well as patient management. Significant questions exist regarding how to incorporate this genomic information into the electronic health record, the standards for doing so, and the readiness and interoperability of the current system to accept these data to be usable over a lifetime for directing care. The Knowledgeable Health Care System for Precision Medicine group is working with electronic health record vendors and clinical end users on issues related to the integration of genomic information into the electronic health record in a manner that is useful for both clinical practice as well as research.

Overview Group

The Overview group examines cross-cutting issues for all members and working groups and responds to emerging issues within the genetics and genomics field. Currently, this group is focusing its efforts on DNA collection and data generation in clinical trial designs.

Reports Released in 2013



The Economics of Genomic Medicine: Workshop Summary



Sharing Clinical Research Data: Workshop Summary



Genome Based Diagnostics: Demonstrating Clinical Utility in Oncology: Workshop Summary

November 15
Facilitating Development and Utilization of Genome-Based Diagnostic Technologies Workshop

2012

November 16
Meeting 15

March 21
New Paradigms in Drug Discovery: How Genomic Data Are Being Used to Revolutionize the Drug Discovery and Development Process Workshop

March 22
Meeting 16

May 24
Evidence for Clinical Utility of Molecular Diagnostics in Oncology Workshop

July 17-18
Assessing the Economics of Genomic Medicine Workshop

October 4-5
Sharing Clinical Research Data Workshop

July 18
Meeting 17

Roundtable Members

(as of December 2013)

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(Co-Chair)

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Sharon F. Terry, M.A. (Co-Chair)
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Sarah H. Beachy, Ph.D.
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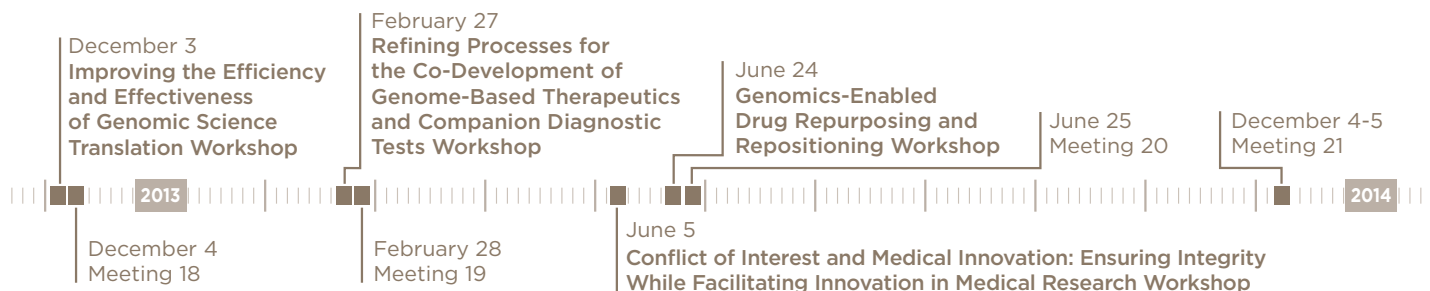
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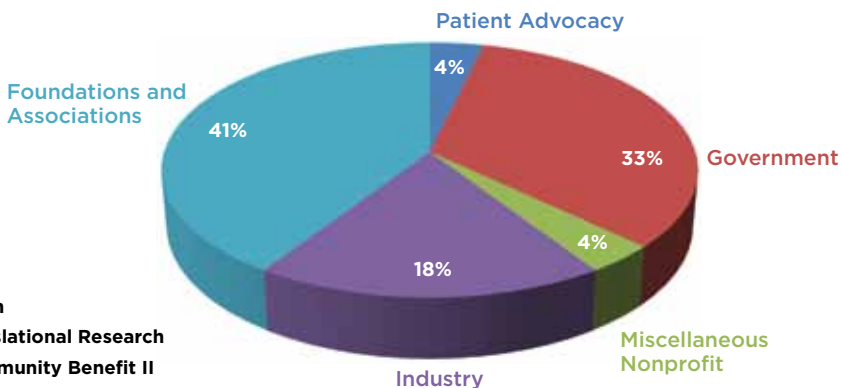
Andrew M. Pope, Ph.D.
Director



Roundtable Sponsors

(as of December 2013)

American Academy of Nursing
 American College of Medical Genetics and Genomics
 American Heart Association
 American Medical Association
 American Society of Human Genetics
 Association for Molecular Pathology
 Blue Cross and Blue Shield Association
 Centers for Disease Control and Prevention
 College of American Pathologists
 Department of Veterans Affairs
 Eli Lilly and Company
 Genetic Alliance
 Health Resources and Services Administration
 International Society for Cardiovascular Translational Research
 The Kaiser Permanente Program Offices Community Benefit II
 at the East Bay Community Foundation
 Life Technologies Corporation
 National Cancer Institute
 National Coalition for Health Professional Education in Genetics
 National Human Genome Research Institute
 National Institute on Aging
 National Institute of Mental Health
 National Institute of Nursing Research
 National Society of Genetic Counselors
 Northrop Grumman
 Pfizer Inc.
 PhRMA
 United States Air Force



February 3
 Assessing Genomic Sequencing
 Information for Health Care
 Decision Making Workshop

August 18
 Improving Genetics
 Education for Health Care
 Providers Workshop

December 8
 Facilitating the Integration
 of Genomic Information
 into the Electronic Health
 Record Workshop

2015

February 4
 Meeting 22

August 19
 Meeting 23

December 9
 Meeting 24

About the Genomics Roundtable

The Institute of Medicine of The National Academies established a Roundtable on Translating Genomic-Based Research for Health to provide both a mechanism and a venue for interested parties from government, academia, industry, and other stakeholder groups to meet and discuss global issues of mutual interest and concern regarding the translation of genomics research findings in a neutral setting. The primary purpose of the Roundtable is to foster dialogue across sectors and among interested parties and institutions, and to illuminate and scrutinize critical scientific and policy issues.

The Roundtable explores and implements strategies for improving health through the translation of genomics and genetics research findings into medicine, public health, education, and policy. During the two to three meetings the Roundtable holds each year, specific scientific and policy issues will be identified and discussed that will help further the field of genomics and enable the translation of genomics into health care applications.

For more information about the Roundtable on Translating Genomic-Based Research for Health, please visit our website at www.iom.edu/genomicroundtable or call Adam Berger at (202) 334-3756.



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