NHGRI’s Genomic Medicine Research Portfolio

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Perspective

Charting a course for genomic medicine from base pairs to bedside

There has been much progress in genomics in the ten years since a draft sequence of the human genome was published. Opportunities for understanding health and disease are now unprecedented, as advances in genomics are harnessed to obtain countless translational knowledge about the structure and function of the human genome and about the genetic contributions to human health and disease. Here we articulate a vision for the future of genomics research and describe the path forward for the area of genomic medicine.

Since the end of the Human Genome Project (HGP) in 2003 and the publication of a reference human genome sequence,9 genomics has become a primary focus of biomedical research. This scientific community is facing the challenge of understanding the broad range of scientific advances that the HGP has enabled, as shown in Fig. 1 (see online). Advances in the functional contributions of genomic information towards improving health have been linked to new insights about cancer10,11, the molecular basis of inherited diseases (http://www.ncbi.nlm.nih.gov/)12 and (http://www.genome.gov/20512692)13, and to the observation of normal variation in disease14, all of which have already led to new discoveries.15,16 Other advances in the disease ecology17,18 medium (for example, resear)

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An emerging medical discipline that involves using genomic information about an individual as part of their clinical care (e.g., for diagnostic or therapeutic decision-making) and the other implications of that clinical use

- **Purposefully narrow definition**

- **By ‘genomic,’ NHGRI means direct information about DNA or RNA; downstream products outside the immediate view**

- **Metaphorically viewed as a key ‘destination’ for attaining NHGRI’s mission of improving health through genomics research**
Green et al. 2011

Understanding the Structure of Genomes  Understanding the Biology of Genomes  Understanding the Biology of Disease  Advancing the Science of Medicine  Improving the Effectiveness of Healthcare

Discovery

Genomic Medicine

1990-2003 Human Genome Project

2004-2010

2011-2020

Beyond 2020
NHGRI Programs in Genomic Medicine

Cancer Genomics

Pharmacogenomics

eMERGE Network & eMERGE-PGRN
NHGRI Programs in Genomic Medicine

- Cancer Genomics
- Pharmacogenomics
- Genomic Medicine ‘Test Drive’ Programs
Moving the genome into the clinic

In the past, standard medical practice for genetic testing involved looking at one gene at a time. With new advances in our understanding of the genomic basis of health and disease and in technology, it is now possible to test all of our genes at once using tests called whole exome or whole genome sequencing. Medical uses of genome sequencing are being applied and adapted on a case-by-case basis, but research to study the optimal uses and implementation of these tests is needed.
Implementing Genomics in Practice (IGNITE)

Overview

Findings from the genomics field have slowly started to find applications in clinical care. The field of "genomic medicine" could potentially improve patient health and treatment strategies or better predict the likelihood of disease.

The Implementing Genomics in Practice (IGNITE) consortium (RFA-HG-12-006, RFA-HG-12-007 and RFA-HG-13-004) was created to enhance the use of genomic medicine by supporting the development of methods for incorporating genomic information into clinical care and exploration of the methods for effective implementation, diffusion and sustainability in diverse clinical settings.

These demonstration projects will incorporate genomic information into the electronic medical record (EMR) and provide clinical decision support (CDS) for implementation of appropriate interventions or clinical advice. The sites will work together to develop new methods and projects and disseminate their findings to the public. Dissemination of these methods and developing best practices for implementation is a key goal so that the information generated from the program will contribute to the growing knowledge base of using genomic information in patient care.
NHGRI Programs in Genomic Medicine

- Cancer Genomics
- Pharmacogenomics
- Genomic Medicine ‘Test Drive’ Programs
- Newborn Genomic Analysis
 NIH program explores the use of genomic sequencing in newborn healthcare

Bethesda, Md., Wed., Sept. 4, 2013 - Can sequencing of newborns’ genomes provide useful medical information beyond what current newborn screening already provides? Pilot projects to examine this important question are being funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Human Genome Research Institute (NHGRI), both parts of the National Institutes of Health. Awards of $5 million to four grantees have been made in fiscal year 2013 under the Genomic Sequencing and Newborn Screening Disorders research program. The program will be funded at $25 million over five years, as funds are made available.

"Genomic sequencing has potential to diagnose a vast array of disorders and conditions at the very start of life," said Alan E. Guttmacher, M.D., director of NICHD. "But the ability to decipher an individual’s genetic code rapidly also brings with it a host of clinical and ethical issues, which is why it is important that this program explores the trio of technical, clinical, and ethical aspects of genomics research in the newborn period."

The awards will fund studies on the potential for genome and exome sequencing to expand and improve newborn health care. Genomic sequencing examines the complete DNA blueprint of the cells, and exome sequencing is a strategy to selectively sequence exons, the short stretches of DNA within our genomes that code for proteins.

Sequenced from the start

Four US studies are set to explore how genomic data can best help healthy and ill newborns. They must also settle some questions of ethics.

Genetic sequencing has established itself as a powerful tool for diagnosis, but it is not yet clear how useful it will be for disease prevention or health management. A US$25–million project announced last week aims to explore that issue in perhaps the most high-stakes patient group: newborn babies.

In the Genomic Sequencing and Newborn Screening Disorders (GSNSD) programme, four teams will sequence the exomes — the protein-coding portions of the genome — or the whole genomes of more than 1,500 babies, including not only infants who are ill, whether or not the disease has been diagnosed, but also healthy babies. The programme is funded by the US National Human Genome Research Institute and the Eunice Shriver Kennedy National Institute of Child Health and Human Development (NICHD). The studies will examine how useful sequencing information is for families and doctors, and whether it is superior to data gathered through conventional newborn-screening methods, which check for about 60 genetic disorders.

plans to give the raw genetic data to the children’s families, even though that could allow the children to benefit from it throughout their lives. Finally, should the data be shared with other researchers? This would be the best way for scientists to help tackle the tough question of how genes contribute to disease. But it is increasingly difficult to guarantee the privacy of genetic data (see Nature 493, 45; 2013), and this is an important issue for babies, whose information will be known for their entire lives even though they themselves have not consented to the disclosure. One of the GSNSD projects will share data with the NICHD’s Newborn Screening Translational Research Network, and another with the National Center for Biotechnology Information’s Database of Genotypes and Phenotypes. The other two are still deciding.

As researchers explore these questions, sequencing costs continue...

Nature (2013)
NHGRI Programs in Genomic Medicine

- Cancer Genomics
- Pharmacogenomics
- Genomic Medicine ‘Test Drive’ Programs
- Newborn Genomic Analysis
- Clinical Genomics Information Systems
Clinical Genomics Information Systems
New NIH-funded resource focuses on use of genomic variants in medical care

Bethesda, Md., Wed., Sept. 25, 2013 - Three grants totaling more than $25 million over four years will help three research groups to develop authoritative information on the millions of genomic variants relevant to human disease and the hundreds that are expected to be useful for clinical practice. The awards are from the National Institutes of Health.

More and more medical and research centers are sequencing the DNA of whole genomes (the body's entire genetic blueprint) or exomes (the genome's protein-coding region) of patients. Each time, millions of DNA differences in genes and the regions between the genes are detected. But doctors struggle to know which of those differences, called variants, are relevant to disease and for a patient's medical care. As a result, information on few genomic variants is used in clinical practice.

The grants will support a consortium of research groups to develop the Clinical Genome Resource (ClinGen). The investigators will design and implement a framework for evaluating which variants play a role in disease and those that are relevant to patient care, and will work closely with the National Center for Biotechnology Information (NCBI) of the National Library of Medicine (NLM), which will distribute this information through its ClinVar database. The grants are funded by the National Human Genome Research Institute (NHGRI) and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), which, along with NCBI and NLM, are part of NIH. ClinGen was developed from NHGRI's Clinically Relevant Variants Resource program.
NHGRI Programs in Genomic Medicine

- Cancer Genomics
- Pharmacogenomics
- Genomic Medicine ‘Test Drive’ Programs
- Newborn Genomic Analysis
- Clinical Genomics Information Systems
- Ultra-Rare Genetic Disease Diagnostics
Ultra-Rare Genetic Disease Diagnostics

Exome Sequencing: Dual Role as a Discovery and Diagnostic Tool

Clinical application of exome sequencing in undiagnosed genetic conditions

Next-Generation Sequencing for Clinical Diagnostics

Clinical Whole-Exome Sequencing for the Diagnosis of Mendelian Disorders

Genomics in Clinical Practice:
Lessons from the Front Lines

Howard J. Jacob,1,5,6* Kelly Abrams,12 David P. Bick,1,5,10 Kent Brodie,1 David P. Dimmock,1,5,10 Michael Farrell,3 Jennifer Geurts,1,7 Jeremy Harris,1,5 Daniel Helbling,1,5 Barbara J. Joers,12 Robert Kliegman,5 George Kowalski,1 Jozef Lazar,1,2 David A. Margolis,5 Paula North,4,9,11 Jill Northup,1 Altheia Roquemore-Goins,11 Gunter Scharer,1,5,10 Mary Shimoyama,1,7 Kimberly Strong,1,8 Bradley Taylor,1 Shirng-Wern Tsaih,1 Michael R. Tschannen,1 Regan L. Veith,1,10 Jaime Wendt-Andrae,1 Brandon Wilk,1,5 Elizabeth A. Worthey1,5,9

Sci Transl Med (2013)
Undiagnosed Diseases Network (UDN)

- Build upon the successful experience with the NIH Undiagnosed Diseases Program to improve the diagnosis and care of patients with undiagnosed diseases
- Facilitate research into the etiology of undiagnosed diseases
- Create a highly collaborative research community to identify best practices for the diagnosis and management of undiagnosed diseases
Green et al. 2011

Understanding the Structure of Genomes
Understanding the Biology of Disease
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Beyond 2020
January 7, 2014

Happy New Year!

I start 2014 with mixed feelings. I continue to marvel at the spectacular advances seen in genomics each and every year, to struggle with the ongoing difficult budgetary circumstances for NIH and NHGRI, and to latch on to a few optimistic signs suggesting that our budgetary problems might be finally ‘bottoming out’ and that things will soon start to improve. I suspect the stories we feature in *The Genomics Landscape* during 2014 will capture elements of these mixed feelings.
Advancing human health through genomics research