Human Genomics a Decade after the Human Genome Project: Opportunities and Challenges

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Past  Present  Future

October, 1990
Human Genome Project Begins

April, 2003
Human Genome Project Ends

Myriad Applications of Genomics
Health, Disease, & Medicine

Turning discovery into health
Advancing human health through genomics research

NIH

Advancing human health

NHGRI Director
Genomic Medicine

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.

The Path to Genomic Medicine

- Human Genome Project
- Realization of Genomic Medicine

“Fulfilling the Promise”

NHGRI Strategic Vision for Genomics

Nature 2003
Base Pairs to Bedside
February 2011

Five Domains of Genomics Research

- 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

Five Domains of Genomics Research

- Understanding the Structure of Genomes
- Understanding the Biology of Genomes
- UNDERWAY
Five Domains of Genomics Research
- 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

Genomic Architecture of Genetic Diseases
- Rare, Simple, Monogenic, Mendelian...
- Common, Complex, Multigenic, Non-Mendelian...

Manolio et al., J Clin Invest (2008)

Monogenic Diseases/Traits

Genomic Basis Known (~4800)
Genomic Basis Unknown (~1800)
Suspected Mendelian Disease/Trait (~1900)

Source: Online Mendelian Inheritance in Man (www.omim.org)

Genome-Wide Association Studies (GWAS)

Mostly Coding Mutations
Mostly Non-Coding Mutations

Genomic Architecture of Genetic Diseases
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Mostly Coding Mutations
Mostly Non-Coding Mutations
The Future: Genome Sequencing

Mendelian Diseases/Traits

Genomic Accomplishments Across Domains

1990-2003
Human Genome Project

2004-2010

2011-2020

Beyond 2020

The Future: Genome Sequencing

Complex Diseases/Traits

Cancer is a Disease of the Genome

Normal

Tumor

It Takes Several Mutations To Make a Cell Malignant

The Future: Genome Sequencing

Mendelian Diseases/Traits

The Future: Genome Sequencing

Centers for Mendelian Genomics

The Future: Genome Sequencing

http://www.mendelian.org


The Centers for Mendelian Genomics: A New Large-Scale Initiative to Identify the Genes Underlying Rare Mendelian Conditions

Michael J. Birdsey,1,2,5,6 Jay S. Shreffler,5,6 David Klove,7 M. M. Rennick,7 James R. Lyman,7,8,9 Richard A. Danks,7,8 Jay Shreffler,5,6,7,8 Richard F. Libers,7 Mark Germain,1,2,5,6,8,9 Sherbent Wars,7 and Deneen A. Nicholson7

on behalf of the Centers for Mendelian Genomics

1Department of Pediatrics, 2Department of Biochemistry, 3Department of Genetics, 4Department of Medicine, and 5Medical Genetics, 6Washington University School of Medicine, 7Centers for Mendelian Genomics, 8Genome Research Institute, and 9Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, Minnesota, USA

The Future: Genome Sequencing

Cancer Genomics

Genomic Accomplishments Across Domains

1990-2003
Human Genome Project

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Beyond 2020

Routine Clinical Diagnostic Tools

Radiographic Imaging

Cancer Genome Sequencing

‘Hot Areas’ in Genomic Medicine

Cancer Genomics

Pharmacogenomics

Cancer Genomics: Here and Now

www.cancercenter.com

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Beyond 2020

Routine Clinical Diagnostic Tools

Radiographic Imaging

Cancer Genome Sequencing

‘Hot Areas’ in Genomic Medicine

Cancer Genomics

Pharmacogenomics

Cancer Genomics: Here and Now

www.cancercenter.com
All patients with same disease

Good response without any side effects

No response

Bad side effects

Clinical Sequencing Exploratory Research (CSER)

Moving the genome into the clinic

50 years ago, standard medical practice for genetics was a one-gene-at-a-time approach. With new advances in our understanding of the genetic basis of health and disease and in technology, it is now possible to test all of our genes at once using tests called whole genome or whole genome sequencing. Medical use of genome sequencing is being applied and adapted on a case-by-case basis, but research to study the optimal use and implementation of these tests is needed.

cser-consortium.org

Implementing Genomics into Clinical Practice Network (IGNITE)

Overview

Harnessing the genomic field to improve care: the implementation of genomic medicine into clinical care has the potential to provide patient-specific treatment strategies and better predict the likelihood of disease.

The Implementing Genomics in Practice (IGNITE) consortium (NHLBI 15, 17, 18, 19, 20, 22, 23) was created to enhance the use of genomics by supporting the development of effective and efficient strategies for implementation of genomic medicine in clinical care and practice.

The IGNITE consortium has a research agenda focused on the implementation of the methods for effective implementation, diffusion and sustainability in diverse clinical settings.

The sites will work together to develop new methods and projects and disseminate these findings to the public. Dissemination of these methods and developing best practices for implementation is a key goal so that the information generated from this program will contribute to the growing knowledge base of using genomic information in patient care.

genome.gov/27554264

'Hot Areas' in Genomic Medicine
**‘Hot Areas’ in Genomic Medicine**

- Cancer Genomics
- Pharmacogenomics
- Genomic Medicine ‘Test Drive’ Programs
- Prenatal & 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, M.D., Kelly Abrams, M.D., David P. Bick, M.D., Kent Brodie, M.D., David R. Dinnock, M.D., Richard Farrel, M.D., Jennifer Geerts, M.D., Jeremy Harris, M.D., Daniel Hellwing, M.D., Barbara J. Jero, M.D., Robert Klempner, George Kowicki, M.D., Joseph Later, M.D., David A. Margolis, M.D., Paula North, M.D., Jill Northings, M.D., Althea Requena-Gaines, M.D., Esther Scherf, M.D., Mary Shimoyama, M.D., Kimberly Strong, M.D., Bradley Taylor, M.D., Jirong-Wenn Tsai, M.D., Michael R. Tsukahara, M.D., Ragan L. Veith, M.D., Jane Wendi-Andras, M.D., Brandon Wilhite, M.D., Elizabeth A. Welling, M.D.

**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

**Bringing Genomic Medicine into Focus**

~1990 ~2003 ~2011 ~2020

**The Relevance of Genomics**

- Biomedical Researchers
- Healthcare Professionals
- Patients (and Friends & Relatives of Patients)

**Genomics and Society**
NHGRI-Smithsonian Genome Exhibition

• Opened June 14, 2013
• Hall 23 (adjacent to Hope Diamond)
• Resident in Smithsonian NMNH for ~1 year
• Subsequently will tour North America for 4-5 years

Smithsonian Exhibition: Website

unlockinglifescode.org

To subscribe, follow link from:

genome.gov/Director

Advancing human health through genomics research