Human Genomics, Precision Medicine, and Improving Human Health

Eric Green, M.D., Ph.D.
Director, NHGRI

NIH National Human Genome Research Institute
The Origin of “Genomics”: 1987

EDITORIAL

A New Discipline, A New Name, A New Journal

Genomics (1987)

“For the newly developing discipline of [genome] mapping/sequencing (including the analysis of the information), we have adopted the term GENOMICS…"
Twenty-five years of big biology

The Human Genome Project, which launched a quarter of a century ago this week, still holds lessons for the consortium-based science it ushered in, say Eric D. Green, James D. Watson and Francis S. Collins.

A Quarter Century of Genomics

Human Genome Sequenced for First Time
by the Human Genome Project
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
A Quarter Century of Genomics

Human Genome Sequenced for First Time by the Human Genome Project

Cost of Sequencing a Human Genome Reduced Nearly ~1 Million-Fold
Human Genome Sequence

~$1,000,000,000

~$1,000

“The $1000 Genome”
The $1,000 genome

In Silicon Valley, Moore's law seems to stand on equal footing with the natural laws codified by Isaac Newton. Intel co-founder Gordon Moore's iconic observation that computing power tends to double — and that its price therefore halves — every 2 years has held true for nearly 50 years with only minor revision. But as an exemplar of rapid change, it is the target of playful abuse from...
Sequencing a Human Genome

**Human Genome Project (1st Sequence)**

- ~1-3 days
- ~$2-3K

**Today**

- ~$1B
- ~6-8 years

- ~1-3 days

A Quarter Century of Genomics

Human Genome Sequenced for First Time by the Human Genome Project

Cost of Sequencing a Human Genome Reduced Nearly ~1 Million-Fold

Tens of Thousands of Human Genomes Sequenced
ARTICLE

A global reference for human genetic variation

The 1000 Genomes Project Consortium*

A Quarter Century of Genomics

- Human Genome Sequenced for First Time by the Human Genome Project
- Cost of Sequencing a Human Genome Reduced Nearly ~1 Million-Fold
- Tens of Thousands of Human Genomes Sequenced
- Profound Advances in Understanding How the Human Genome Functions
ENCODE: Giving ‘GPS’ Views of Genomes
A Quarter Century of Genomics

Human Genome Sequenced for First Time by the Human Genome Project

Cost of Sequencing a Human Genome Reduced Nearly ~1 Million-Fold

Tens of Thousands of Human Genomes Sequenced

Profound Advances in Understanding How the Human Genome Functions

Significant Advances in Unraveling the Genomic Bases of Human Disease
Genomic Architecture of Genetic Diseases

Rare, Simple, Monogenic, Mendelian...

Common, Complex, Multigenic, Non-Mendelian...

Manolio et al., J Clin Invest (2008)
A Quarter Century of Genomics

- Human Genome Sequenced for First Time by the Human Genome Project
- Cost of Sequencing a Human Genome Reduced Nearly ~1 Million-Fold
- Tens of Thousands of Human Genomes Sequenced
- Profound Advances in Understanding How the Human Genome Functions
- Significant Advances in Unraveling the Genomic Bases of Human Disease
- Vivid Examples of Genomic Medicine in Action Now Emerging
‘Hot Areas’ in Genomic Medicine

Cancer Genomics
Cancer is a Disease of the Genome

It Takes Several Mutations to Make a Cell Malignant
Routine Cancer Diagnostic Tools

Cancer Histopathology

Cancer Genome Sequencing
Genomics and Cancer: Here and Now

www.cancercenter.com
‘Hot Areas’ in Genomic Medicine

Cancer Genomics

Pharmacogenomics
Because Everyone Responds Differently.
All of these work.

Just not for everyone.

Perlegen may be able to help you sort out which medicine helps which patient.

Working with you, we can comprehensively analyze the DNA from thousands of patients taking your drug. Out of the millions of genetic variations between patients, we may be able to help you identify the ones that are associated with strong efficacy, poor efficacy, or side effects.

Perlegen’s exceptional coverage of the genome and experienced team of analysts could help you get clinically relevant answers, not just data, in a matter of months.

We partner with the top pharmaceutical companies around the world. We also license late-stage drugs. If you have a drug that can benefit from our approach, please contact us.
IMPRECISION MEDICINE

For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).

1. ABILIFY (aripiprazole)
   Schizophrenia

2. NEXIUM (esomeprazole)
   Heartburn

3. HUMIRA (adalimumab)
   Arthritis

4. CRESTOR (rosuvastatin)
   High cholesterol

5. CYMBALTA (duloxetine)
   Depression

6. ADVAIR DISKUS (fluticasone propionate)
   Asthma

7. ENBREL (etanercept)
   Psoriasis

8. REMICADE (infliximab)
   Crohn’s disease

9. COPAXONE (glatiramer acetate)
   Multiple sclerosis

10. NEULASTA (pegfilgrastim)
    Neutropenia

Based on published number needed to treat (NNT) figures. For a full list of references, see Supplementary Information at go.nature.com/4ar78f.

Pharmacogenomics

Pharmacogenomics
The Promise of Personalized Medicine
‘Hot Areas’ in Genomic Medicine

Cancer Genomics

Pharmacogenomics

Rare Genetic Disease Diagnostics
"...disorders not readily explained by standard tests can sometimes be diagnosed through genome sequencing and analysis."

Undiagnosed Diseases
‘Hot Areas’ in Genomic Medicine

- Cancer Genomics
- Pharmacogenomics
- Rare Genetic Disease Diagnostics
- Genomics of Pregnancy
Since late 2011, clinicians have been able to screen mothers’ blood for fetal chromosome problems using circulating DNA.

Newborn Genome Sequencing

In 2025, Everyone Will Get DNA Mapped At Birth

Scientists have scoured trends in research grants, patents and more to come up with these 10 innovations that will be reality in 10 years (or so they think)

Everybody likes to blue-sky it when it comes to technology. Driverless cars! Fat-burning pills! Telepathic butlers! But the folks at Thomson Reuters Intellectual Property & Science do it for a living—and they do it with data.

Time (2014)
Newborn Sequencing In Genomic medicine and public Health (NSIGHT)
Genome Sequencing of Acutely Sick Newborns

Fast sequencing saves newborns

Rapid analysis of infant genomes is aiding diagnosis and treatment of inexplicably ill babies.

Nature (2014)
‘Hot Areas’ in Genomic Medicine

- Cancer Genomics
- Pharmacogenomics
- Rare Genetic Disease Diagnostics
- Genomics of Pregnancy
- Clinical Genomics Information Systems
Generating a Human Genome Sequence is (Almost) Trivial
Clinical Genome Resource (ClinGen)


Technological advances are quickly allowing genome-wide analysis to become commonplace in the care of patients. However, the ability to detect DNA variants has greatly surpassed the ability to interpret their clinical impact, limiting patient benefit. Improving genomic interpretation will require a coordinated effort from both the clinical and research communities. Learn more »

clinicalgenome.org
The Relevance of Genomics

Biomedical Researchers

Healthcare Professionals

Patients (and Friends & Relatives of Patients)
President Obama:
Long-Standing Interest in Genomics

Senator Obama, 2006
Precision Medicine

A broader context for ‘individualizing’ medical care to advance human health
Today: most medical care based on expected response of the average patient

Tomorrow: medical care based on individual genomic, environmental, and lifestyle differences that enable more precise ways to prevent and treat disease

How do we get from today to tomorrow?
President Obama’s State of the Union Address: January 20, 2015
“…[the] new Precision Medicine Initiative [will bring] America closer to curing diseases like cancer and diabetes, and gives all of us access, potentially, to the personalized information that we need to keep ourselves and our families healthier.”

President Barack Obama
January 30, 2015
A New Initiative on Precision Medicine

Francis S. Collins, M.D., Ph.D., and Harold Varmus, M.D.

“Tonight, I’m launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes — and to give all of us access to the personalized information we need to keep ourselves and our families healthier.”

— President Barack Obama, State of the Union Address, January 20, 2015

The proposed initiative has two main components: a near-term focus on cancers and a longer-term aim to generate knowledge applicable to the whole range of health and disease. Both components are now within our reach because of advances in basic research, including molecular biology, genomics, and bioinformatics. Furthermore, the initiative
U.S. National Research Cohort

- >1 million U.S. volunteers
- Participants to share genomic data, lifestyle information, biological samples – all linked to their EHRs
- Forge new model for ‘doing science’ that emphasizes:
  - Engaged participants
  - Open, responsible data sharing
  - Strong privacy protections
The case for a US prospective cohort study of genes and environment

Francis S. Collins

National Human Genome Research Institute, National Institutes of Health, Building 31, Room 4B09, MSC 2152, 31 Center Drive, Bethesda, Maryland 20892-2152, USA (e-mail: fc23a@nih.gov)

Information from the Human Genome Project will be vital for defining the genetic and environmental factors that contribute to health and disease. Well-designed case–control studies of people with and without a particular disease are essential for this, but rigorous and unbiased conclusions about the causes of diseases and their population-wide impact will require a representative population to be monitored over time (a prospective cohort study). The time is right for the United States to consider such a project.

NIH framework points the way forward for building national, large-scale research cohort, a key component of the President’s Precision Medicine Initiative

For Immediate Release: Thursday, September 17, 2015

The National Institutes of Health Advisory Committee to the Director (ACD) today presented to NIH Director Francis S. Collins, M.D., Ph.D., a detailed design framework for building a national research participant group, called a cohort, of 1 million or more Americans to expand our knowledge and practice of precision medicine. Dr. Collins embraced the design recommendations made by the ACD, noting the need to remain nimble and adaptable as the Initiative progresses. He also thanked the Committee for their recommendations on policy issues and welcomed the opportunity to review them. NIH plans to move quickly to build the infrastructure so that participants can begin enrolling in the cohort in 2016, with a goal of enrolling at least 1 million participants in three to four years.
About the Precision Medicine Initiative

Far too many diseases do not have a proven means of prevention or effective treatments. We must gain better insights into the biology of these diseases to make a difference for the millions of Americans who suffer from them. Precision medicine is an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person. While significant advances in precision medicine have been made for select cancers, the practice is not currently in use for most diseases. Many efforts are underway to help make precision medicine the norm rather than the exception. To accelerate the pace, President Obama unveiled the Precision Medicine Initiative (PMI) — a bold new enterprise to revolutionize medicine and generate the scientific evidence needed to move the concept of precision medicine into everyday clinical practice.

www.nih.gov/precisionmedicine
Déjà Vu, All Over Again?

Human Genome Project
Circa Fall/Winter 1990

Precision Medicine Initiative
Circa Fall/Winter 2015
Advancing human health through genomics research