NHGRI's Genomic Medicine Research Portfolio

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NHGRI's Genomic Medicine Definition

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**

The Path to Genomic Medicine

Human Genome Project

→ → ? → →

Realization of Genomic Medicine

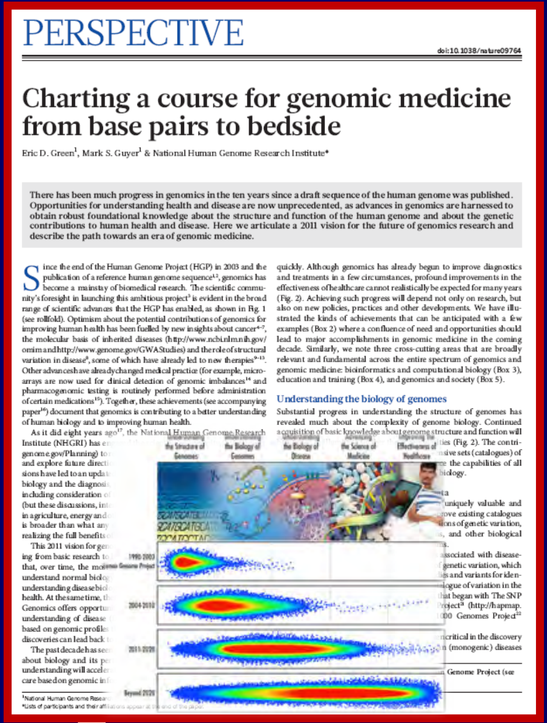

feature

A vision for the future of genomics research

A blueprint for the genomic era

Francis S. Collins, Eric D. Green, Alan E. Guttmacher and Mark S. Guyer on behalf of the US National Human Genome Research Institute

Nature


PERSPECTIVE

doi:10.1038/nature09764

Charting a course for genomic medicine from base pairs to bedside

Eric D. Green[1], Mark S. Guyer[1] & National Human Genome Research Institute*

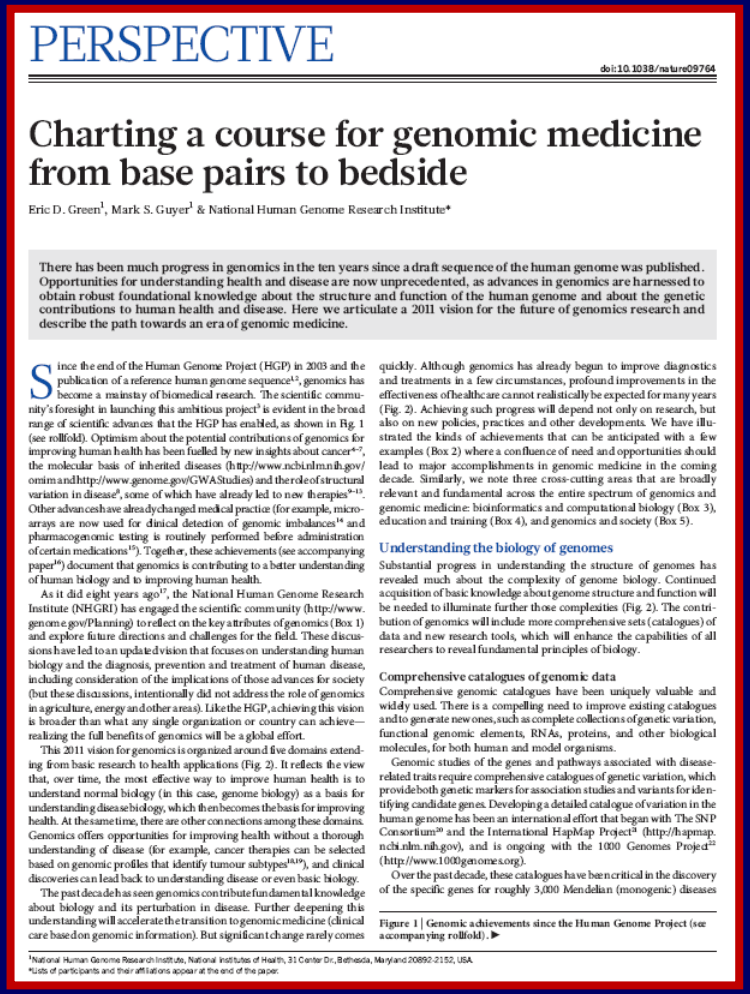
There has been much progress in genomics in the ten years since a draft sequence of the human genome was published. Opportunities for understanding health and disease are now unprecedented, as advances in genomics are harnessed to obtain robust foundational knowledge about the structure and function of the human genome and about the genetic contributions to human health and disease. Here we articulate a 2011 vision for the future of genomics research and describe the path towards an era of genomic medicine.

Nature

2003

2011

NHGRI Strategic Vision for Genomics



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Charting a course for genomic medicine from base pairs to bedside

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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 robust foundational knowledge about the structure and function of the human genome and about the genetic contributions to human health and disease. Here we articulate a 2011 vision for the future of genomics research and describe the path towards an era of genomic medicine.

Since the end of the Human Genome Project (HGP) in 2003 and the publication of a reference human genome sequence[1,2], genomics has become a mainstay of biomedical research. The scientific community's foresight in launching this ambitious project[3] is evident in the broad range of scientific advances that the HGP has enabled, as shown in Fig. 1 (see rollfold). Optimism about the potential contributions of genomics for improving human health has been fuelled by new insights about cancer[4–7], the molecular basis of inherited diseases (http://www.ncbi.nlm.nih.gov/omim and http://www.genome.gov/GWAStudies) and the role of structural variation in disease[8], some of which have already led to new therapies[9–13]. Other advances have already changed medical practice (for example, microarrays are now used for clinical detection of genomic imbalances[14] and pharmacogenomic testing is routinely performed before administration of certain medications[15]). Together, these achievements (see accompanying paper[16]) document that genomics is contributing to a better understanding of human biology and to improving human health.

As it did eight years ago[17], the National Human Genome Research Institute (NHGRI) has engaged the scientific community (http://www.genome.gov/Planning) to reflect on the key attributes of genomics (Box 1) and explore future directions and challenges for the field. These discussions have led to an updated vision that focuses on understanding human biology and the diagnosis, prevention and treatment of human disease, including consideration of the implications of those advances for society (but these discussions, intentionally did not address the role of genomics in agriculture, energy and other areas). Like the HGP, achieving this vision is broader than what any single organization or country can achieve—realizing the full benefits of genomics will be a global effort.

This 2011 vision for genomics is organized around five domains extending from basic research to health applications (Fig. 2). It reflects the view that, over time, the most effective way to improve human health is to understand normal biology (in this case, genome biology) as a basis for understanding disease biology, which then becomes the basis for improving health. At the same time, there are other connections among these domains. Genomics offers opportunities for improving health without a thorough understanding of disease (for example, cancer therapies can be selected based on genomic profiles that identify tumour subtypes[18,19]), and clinical discoveries can lead back to understanding disease or even basic biology.

The past decade has seen genomics contribute fundamental knowledge about biology and its perturbation in disease. Further deepening this understanding will accelerate the transition to genomic medicine (clinical care based on genomic information). But significant change rarely comes quickly. Although genomics has already begun to improve diagnostics and treatments in a few circumstances, profound improvements in the effectiveness of healthcare cannot realistically be expected for many years (Fig. 2). Achieving such progress will depend not only on research, but also on new policies, practices and other developments. We have illustrated the kinds of achievements that can be anticipated with a few examples (Box 2) where a confluence of need and opportunities should lead to major accomplishments in genomic medicine in the coming decade. Similarly, we note three cross-cutting areas that are broadly relevant and fundamental across the entire spectrum of genomics and genomic medicine: bioinformatics and computational biology (Box 3), education and training (Box 4), and genomics and society (Box 5).

Understanding the biology of genomes

Substantial progress in understanding the structure of genomes has revealed much about the complexity of genome biology. Continued acquisition of basic knowledge about genome structure and function will be needed to illuminate further those complexities (Fig. 2). The contribution of genomics will include more comprehensive sets (catalogues) of data and new research tools, which will enhance the capabilities of all researchers to reveal fundamental principles of biology.

Comprehensive catalogues of genomic data

Comprehensive genomic catalogues have been uniquely valuable and widely used. There is a compelling need to improve existing catalogues and to generate new ones, such as complete collections of genetic variation, functional genomic elements, RNAs, proteins, and other biological molecules, for both human and model organisms.

Genomic studies of the genes and pathways associated with disease-related traits require comprehensive catalogues of genetic variation, which provide both genetic markers for association studies and variants for identifying candidate genes. Developing a detailed catalogue of variation in the human genome has been an international effort that began with The SNP Consortium[20] and the International HapMap Project[21] (http://hapmap.ncbi.nlm.nih.gov), and is ongoing with the 1000 Genomes Project[22] (http://www.1000genomes.org).

Over the past decade, these catalogues have been critical in the discovery of the specific genes for roughly 3,000 Mendelian (monogenic) diseases

Figure 1 | Genomic achievements since the Human Genome Project (see accompanying rollfold). ▶

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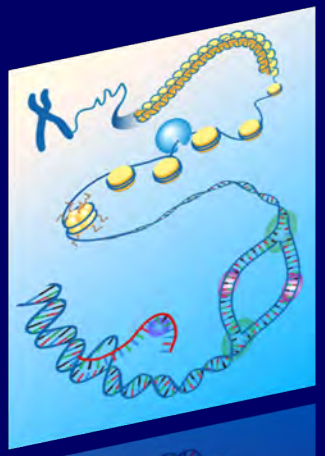
*Lists of participants and their affiliations appear at the end of the paper.

February 2011

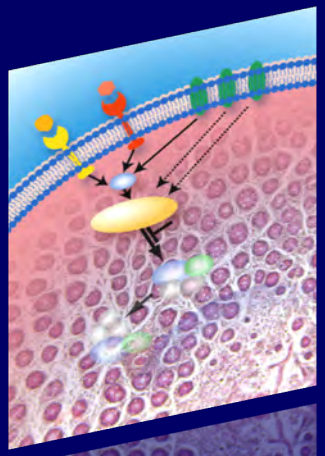
Five Domains of Genomics Research

Understanding the Structure of Genomes

Understanding the Biology of Genomes

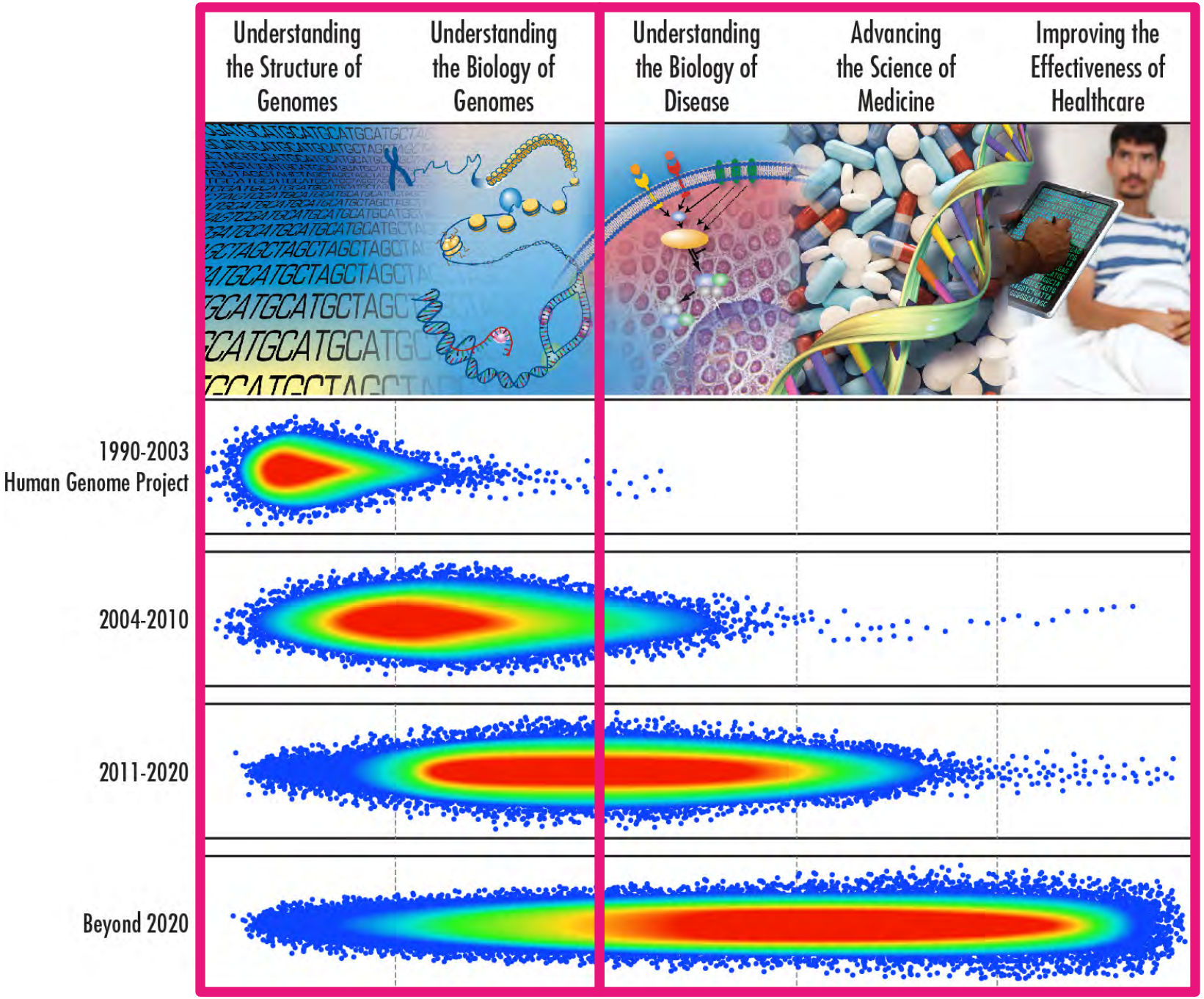


Understanding the Biology of Disease



Advancing the Science of Medicine

Improving the Effectiveness of Healthcare



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Disease-Related Genomics Research

Domain 3
Discovery Research

Establish genotype-phenotype associations for human diseases

- Identify persons at increased risk of disease based on their genomic variants
- Find all variants related to a given phenotype or disease
- Characterize variants known to be related to disease or treatment response

Domain 4
Clinical Validation

Assess outcomes from using genomic information for clinical care

- Assess impact on health outcomes and care utilizati
- causes of rare or undiagnosed diseases
- Validate drug targets and develop improved therapeutics

Domain 5
Clinical Implementation

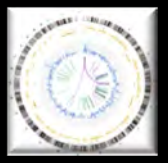
Develop processes for using genomic information for clinical care

- Dev
- nformation
- Educate clinicians and patients about use of genomic information
- Define and disseminate information on actionable clinical variants and relevant evidence base

Genomic Medicine

NHGRI Programs in Genomic Medicine

Cancer Genomics

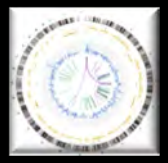


Pharmacogenomics

eMERGE Network
& eMERGE-PGRN
Dan Roden

NHGRI Programs in Genomic Medicine

Cancer Genomics



Pharmacogenomics

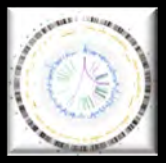
Genomic Medicine
'Test Drive' Programs

Clinical Sequencing Exploratory Research (CSER)
Lucia Hindorff

Implementing Genomics in Practice (IGNITE)
Geoff Ginsburg

NHGRI Programs in Genomic Medicine

Cancer Genomics



Pharmacogenomics

Genomic Medicine
'Test Drive' Programs

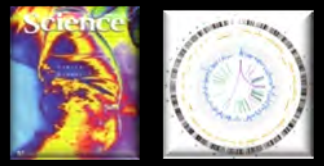
Newborn Genomic
Analysis

Newborn Sequencing Program

Anastasia Wise

NHGRI Programs in Genomic Medicine

- Cancer Genomics



- Pharmacogenomics

- Genomic Medicine ‘Test Drive’ Programs

- Newborn Genomic Analysis

- Clinical Genomics Information Systems

Clinical Genomics Information Systems

Clinical Genome Resource (ClinGen)

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.

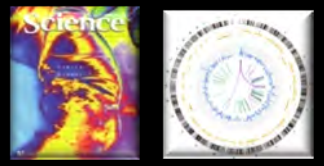
More and more medical and research centers are sequencing the DNA of whole genomes (the body's entire genetic blueprint) or exomes (the genome's protein-coding region) of patients. Each time, millions of DNA differences in genes and the regions between the genes are detected. But doctors struggle to 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.

genome.gov

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

Chee-S

Clinical application of exome sequencing in undiagnosed genetic conditions

Anna C
Kevin V

Next-Generation Sequencing for Clinical Diagnostics

Clinical Whole-Exome Sequencing for the Diagnosis of Mendelian Disorders

Ya
Matt
Alici
Matth
Magalie

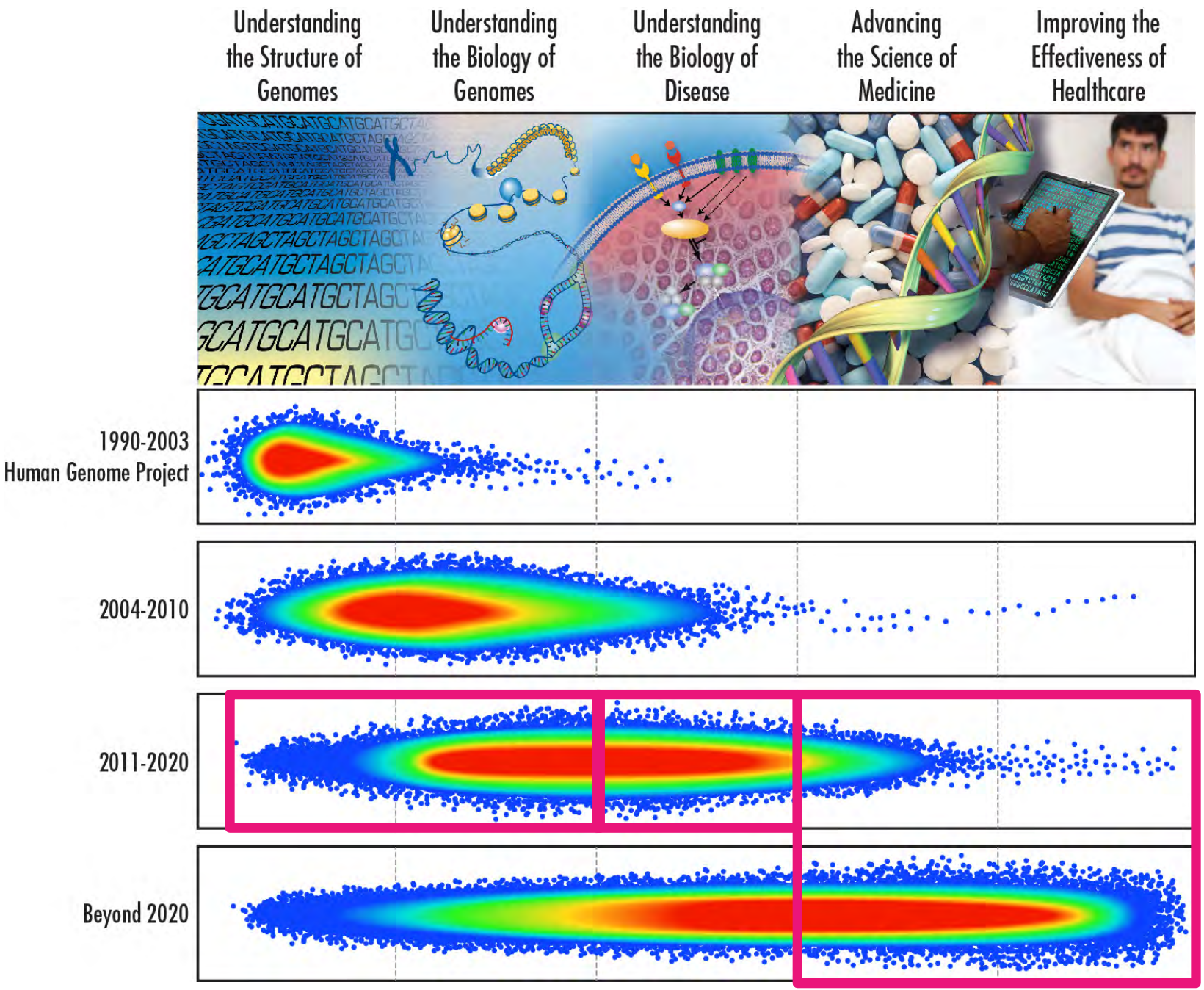
Genomics in Clinical Practice: Lessons from the Front Lines

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. Worthey[1,5,9]

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

October 21, 2013

I am pleased to debut a new means of communicating information from the National Human Genome Research Institute (NHGRI) — *The Genomics Landscape*. In response to encouragement that I have received from various stakeholders to provide more regular personal updates about topics of interest, I am starting a monthly email message that aims to disseminate information from the NHGRI Director to the broader genomics community and other interested recipients. Each month, I will endeavor to highlight two to four topics, typically featuring one in greater detail.

To subscribe, follow link from:

genome.gov/Director

NHGRI-Smithsonian Genome Exhibition

NIH National Human Genome Research Institute

Smithsonian *National Museum of Natural History*

- **Opened June 14, 2013**
- **~4400 square foot exhibition**
- **Hall 23 (adjacent to Hope Diamond)**
- **Resident in Smithsonian NMNH for ~1 year**
- **Subsequently will tour North America for 4-5 years**

NHGRI-Smithsonian Exhibition: Website

unlockinglifescode.org


National Human Genome
Research Institute
Advancing human health
through genomics research