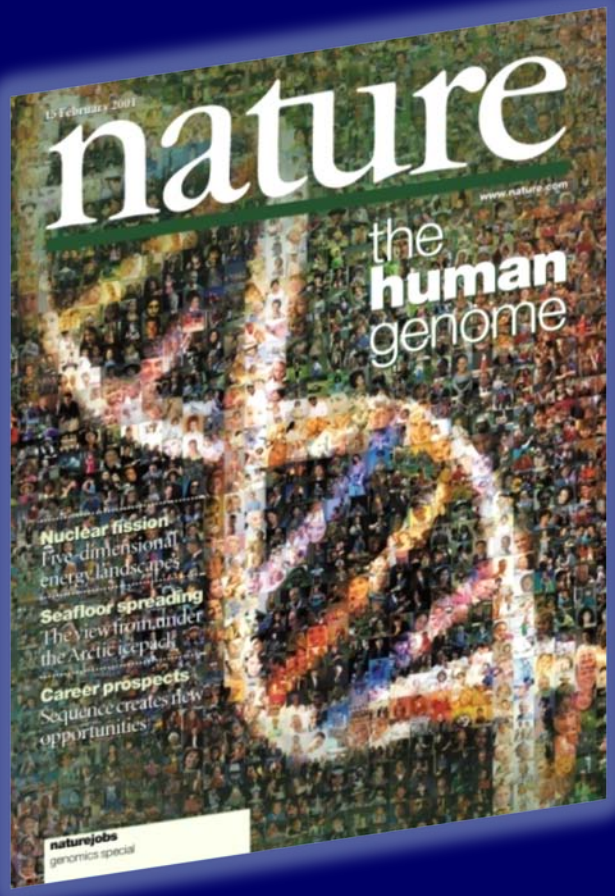
The Pace of Genomic Discovery

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

~10 Years Ago



February 2001

Draft Human Genome Sequence Published

1 April 2010 www.nature.com/nature $10

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

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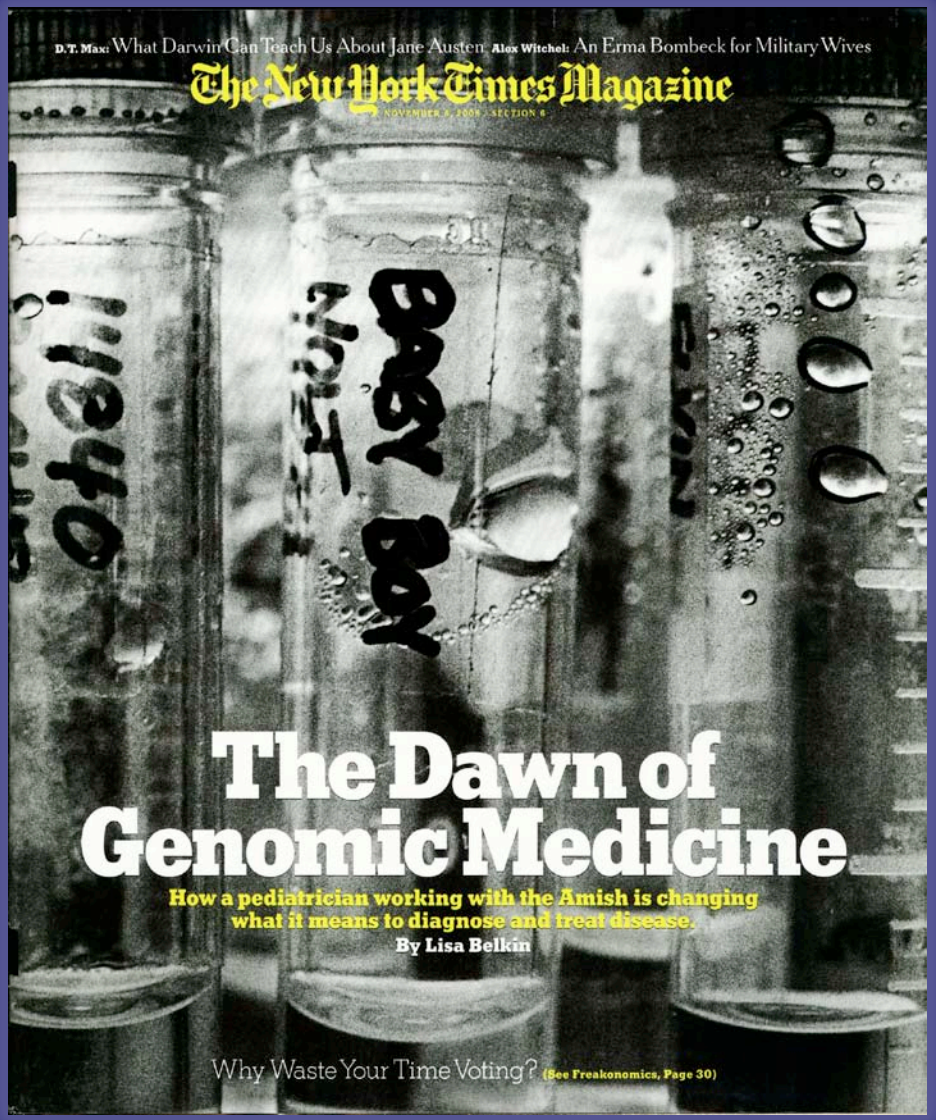
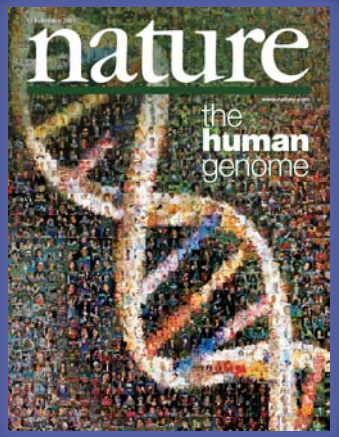

D.T. Max: What Darwin Can Teach Us About Jane Austen Alex Witchel: An Erma Bombeck for Military Wives
The New York Times Magazine
NOVEMBER 9, 2008 · SECTION 6
The Dawn of Genomic Medicine
How a pediatrician working with the Amish is changing what it means to diagnose and treat disease.
By Lisa Belkin
Why Waste Your Time Voting? (See Freakonomics, Page 30)


Science
24 October 2003
Vol. 302 No. 5645
Pages 517–728 $10
Genomic Medicine
American Association for the Advancement of Science

Genomic Medicine

Healthcare tailored to the individual based on genomic information

The Path to Genomic Medicine



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Human Genome Project

Realization of Genomic Medicine

"Fulfilling the Promise"

✓

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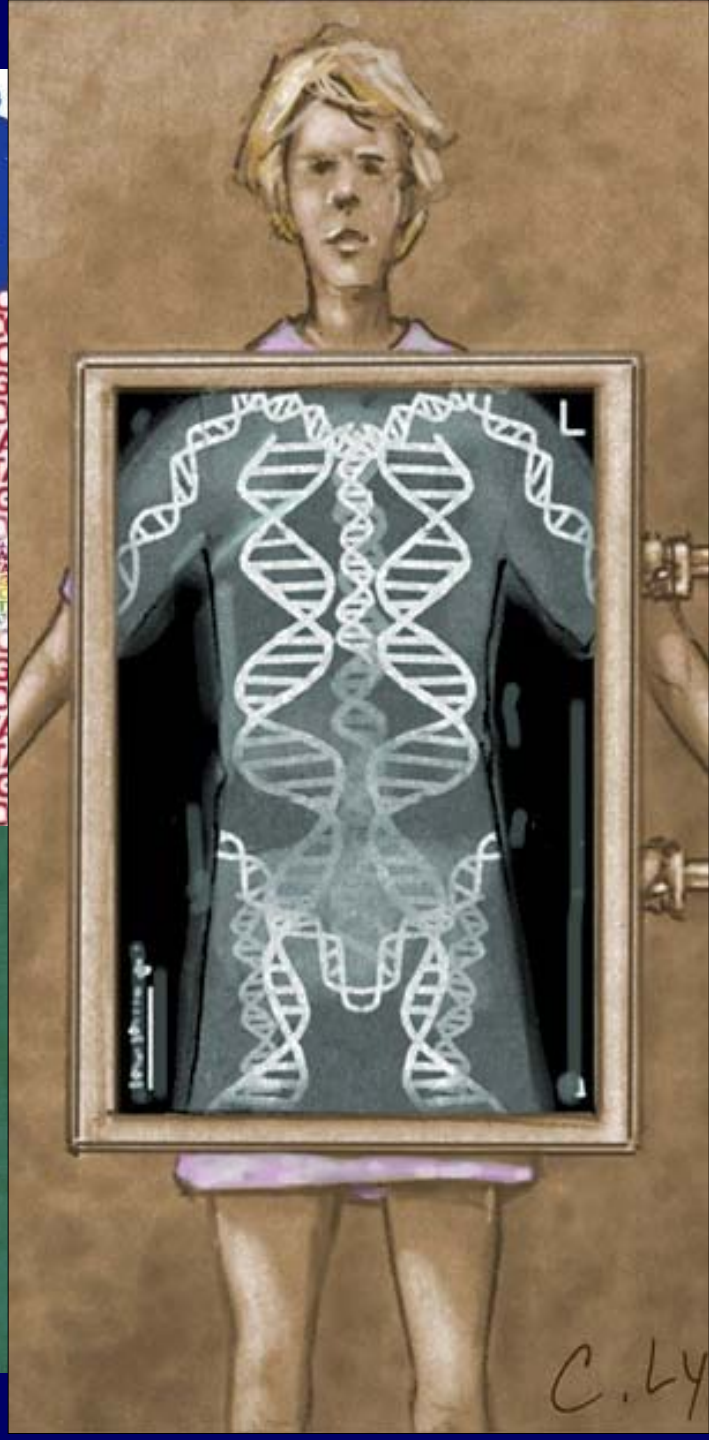
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NHGRI Strategic Planning Process

1991-1995

1993-1998

1998-2003

2003-2010

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- Contact NHGRI
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- Institute Advisors
- NHGRI Long-Range Planning
- Organizational Structure
- Reports and Publications

NHGRI Long-Range Planning

Keywords: what's this?
- long-range planning
- white papers
- topics for further exploration
- workshops

The National Human Genome Research Institute (NHGRI) has started its next long-range planning process. The Institute wants to conduct a wide-ranging assessment of the state of the art in genomics and where the field should be going in the next several years. This will help NHGRI and others plan their research investments to further the contributions of genomics to improvements in human health and other areas of society.

The NHGRI's planning process will involve a wide range of activities through which the research and medical communities, and the public, can provide their opinions and advice to the Institute. These activities will include on-line opportunities, workshops, and other forums yet to be decided, and will take place through 2010. The final such activity will be a large meeting to review a final draft.

To begin the work, NHGRI has produced four white papers that address specific issues that have already been identified as needing broad input. These will be the first to use a novel feedback system on this Web site to allow unprecedented input into the planning process. The Institute has also identified a number of workshops that will be held over the next year. Finally, we are asking for advice as to other issues that the planning process should address and for other avenues that interested people could use to provide us their thoughts.

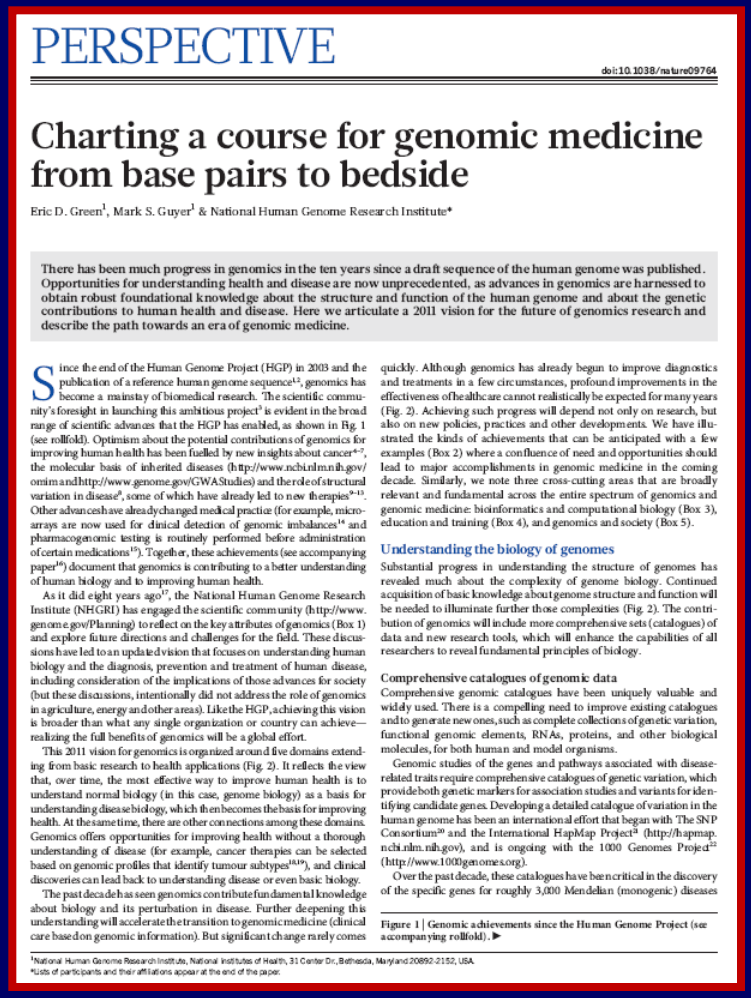
NHGRI's goal, at this stage, is to gather as many ideas as possible, so please comment on anything and everything. There is additional information on the following topics:

- **Go to**: About the NHGRI Long-Range Planning Process to read an overview of the current planning process and overall issues.
- **Go to**: NHGRI White Papers for the Planning Process to read the **revised** white papers and the community papers.
- **Go to**: NHGRI Planning Process Topics for Further Exploration to read about the issues being considered or to suggest other topics.
- **Go to**: NHGRI Planning Process Workshops to read about the planning meetings NHGRI is currently considering.

genome.gov/Planning


Planning the Future of Genomics:
Foundational Research and Applications in Genomic Medicine
Airlie Center, Warrenton, Virginia
July 6-8, 2010

~2 Months Ago



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.

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 update division 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). ▶

[1]National Human Genome Research Institute, National Institutes of Health, 31 Center Dr, Bethesda, Maryland 20892-2152, USA.
*Lists of participants and their affiliations appear at the end of the paper.

February 2011

NHGRI Published New Vision for Genomics

Five Domains of Genomics Research

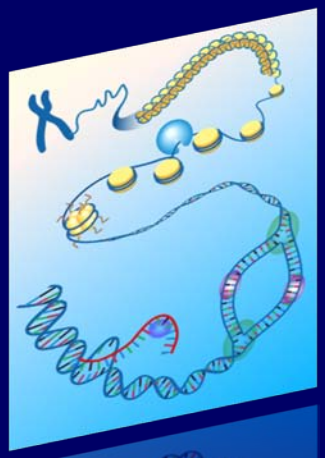
Understanding the Structure of Genomes

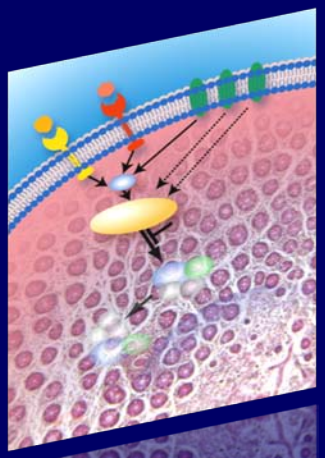
Understanding the Biology of Genomes

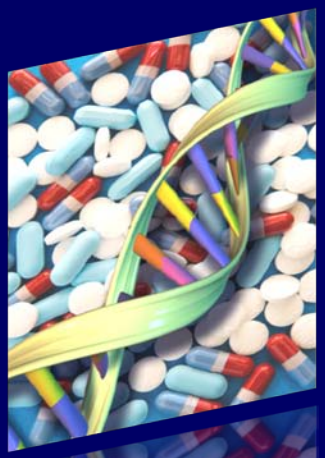
Understanding the Biology of Disease

Advancing the Science of Medicine

Improving the Effectiveness of Healthcare



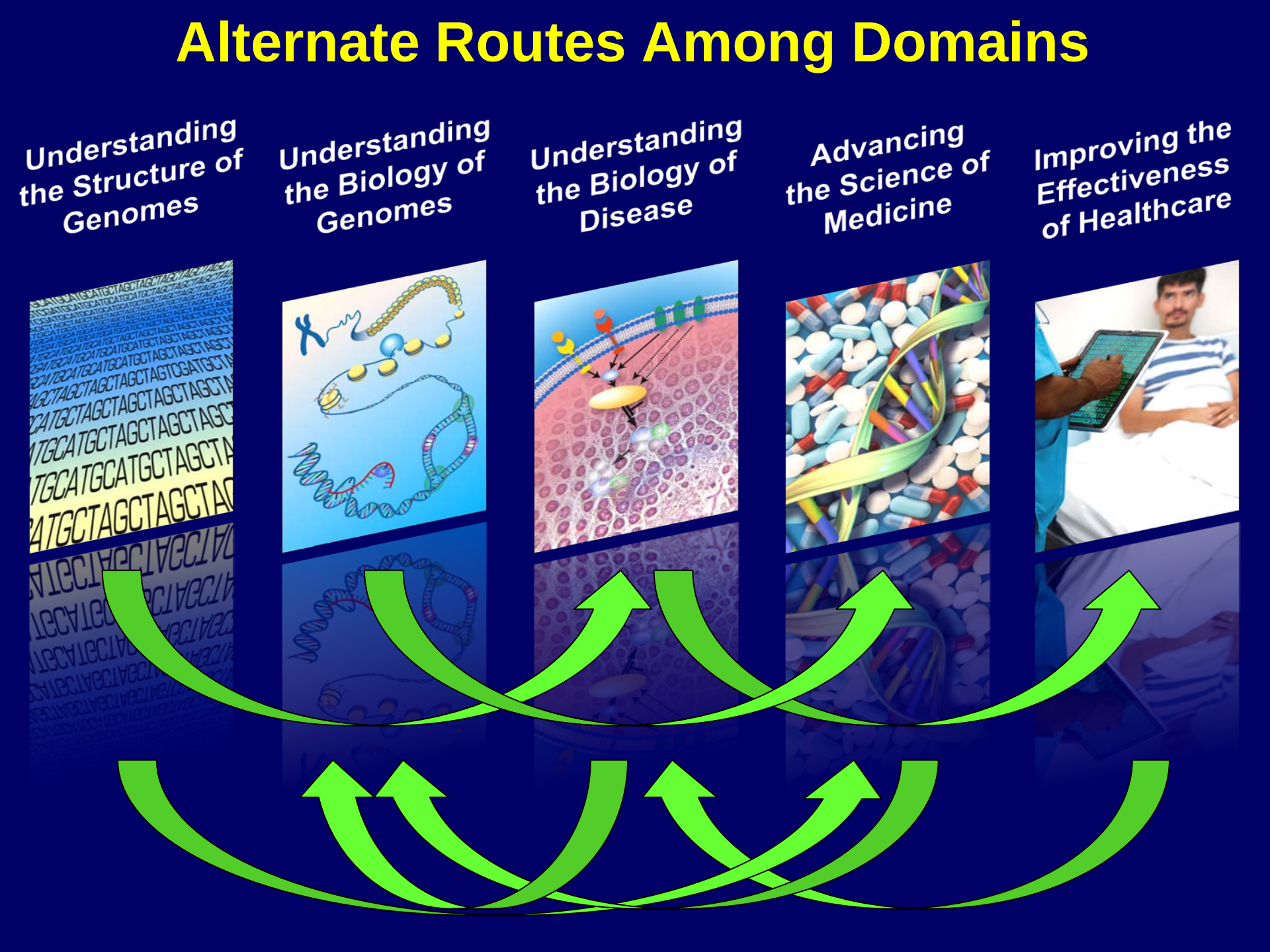




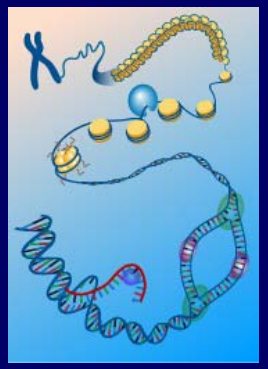
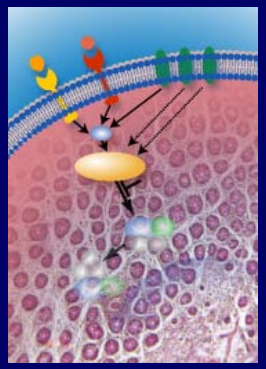
Base Pairs to Bedside

Helix to Health

Alternate Routes Among Domains



Cross-Cutting Elements in Genomics

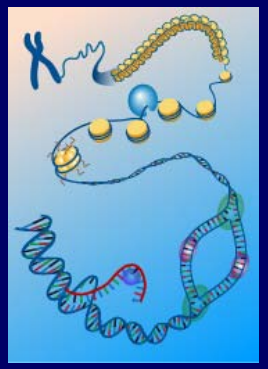
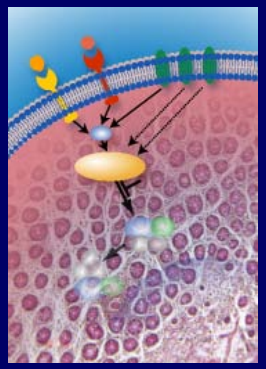
Understanding the Structure of Genomes	Understanding the Biology of Genomes	Understanding the Biology of Disease	Advancing the Science of Medicine	Improving the Effectiveness of Healthcare
				

Bioinformatics & Computational Biology

Education & Training

Genomics & Society

Genomic Accomplishments Across Domains

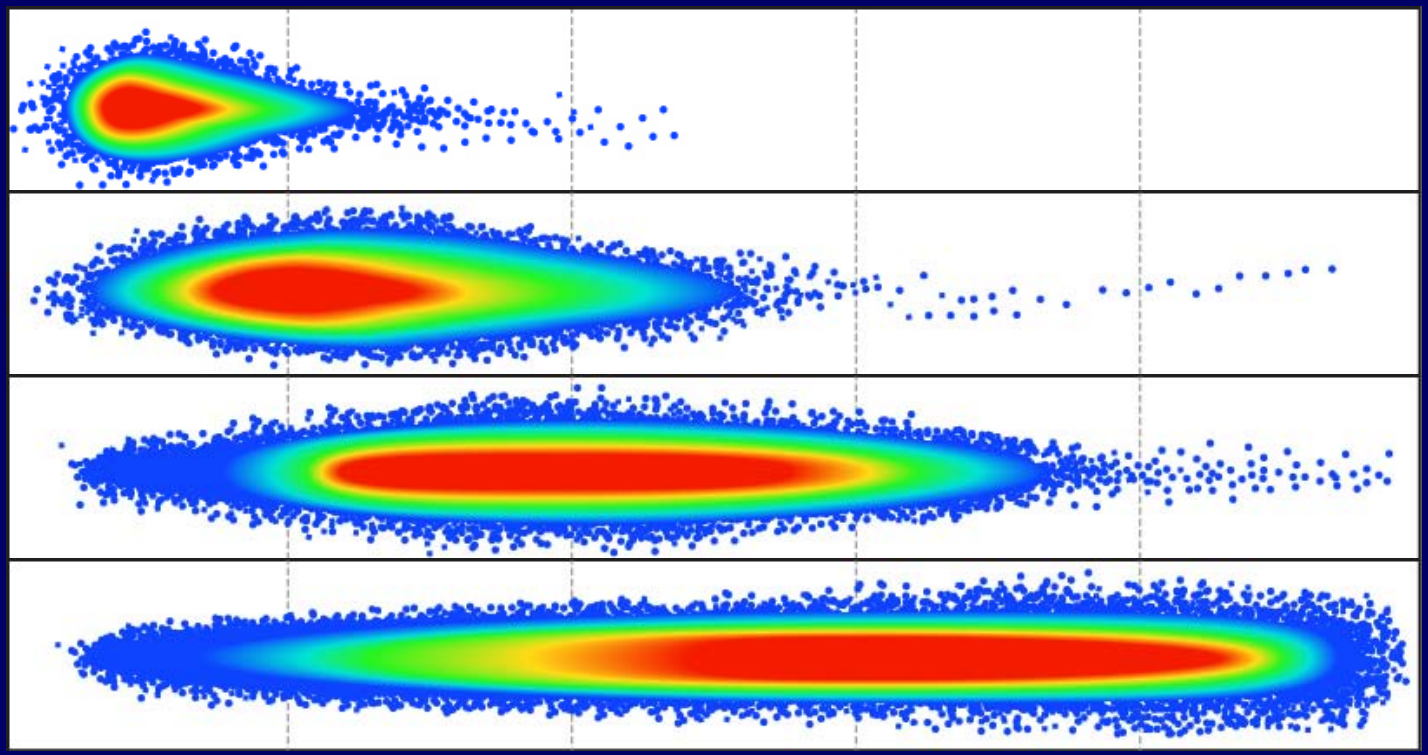
Understanding the Structure of Genomes	Understanding the Biology of Genomes	Understanding the Biology of Disease	Advancing the Science of Medicine	Improving the Effectiveness of Healthcare
				

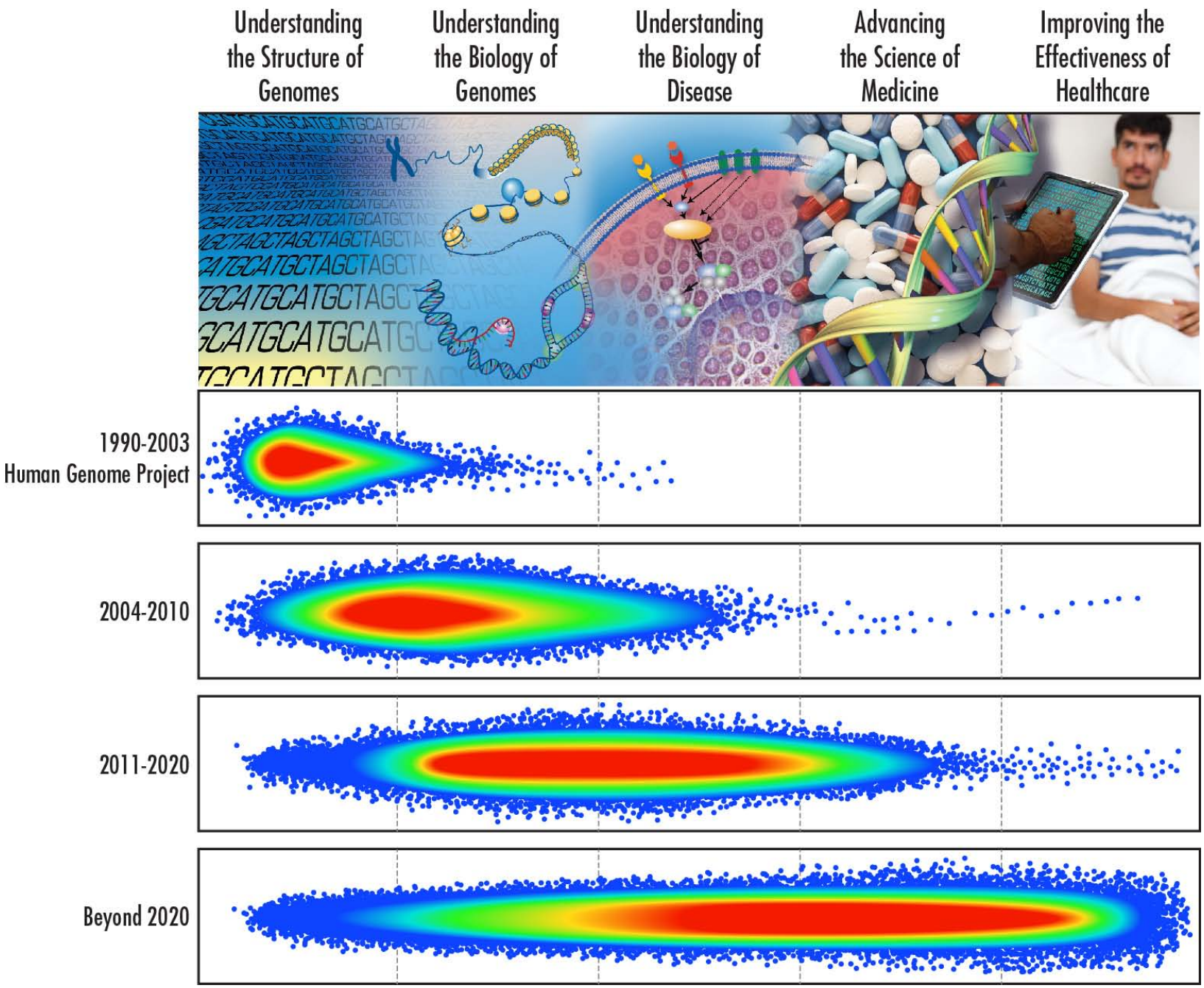
1990-2003
Human Genome Project

2004-2010

2011-2020

Beyond 2020





Green et al. 2011

Genomics: A Disappointment???

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POLICYFORUM

GENOMICS

Deflating the Genomic Bubble

James P. Evans,[1]* Eric M. Meslin,[2] Theresa M. Marteau,[3] Timothy Caulfield[4]

Unrealistic expectations and uncritical translation of genetic discoveries may undermine other promising approaches to preventing disease and improving health.

By
Te
me

Jonathan Latham

guardian.co.uk, Sunday 17 April 2011 20.30 BST
Article history

"Right now there are three depressing aspects to the current course of the U.S. economy. First, the growth of health care spending, if it continues, will put a stranglehold on employers and taxpayers. Second, the apparent inability of the private sector to generate well-paying jobs for college grads, if it continues, will put a squeeze on young workers.

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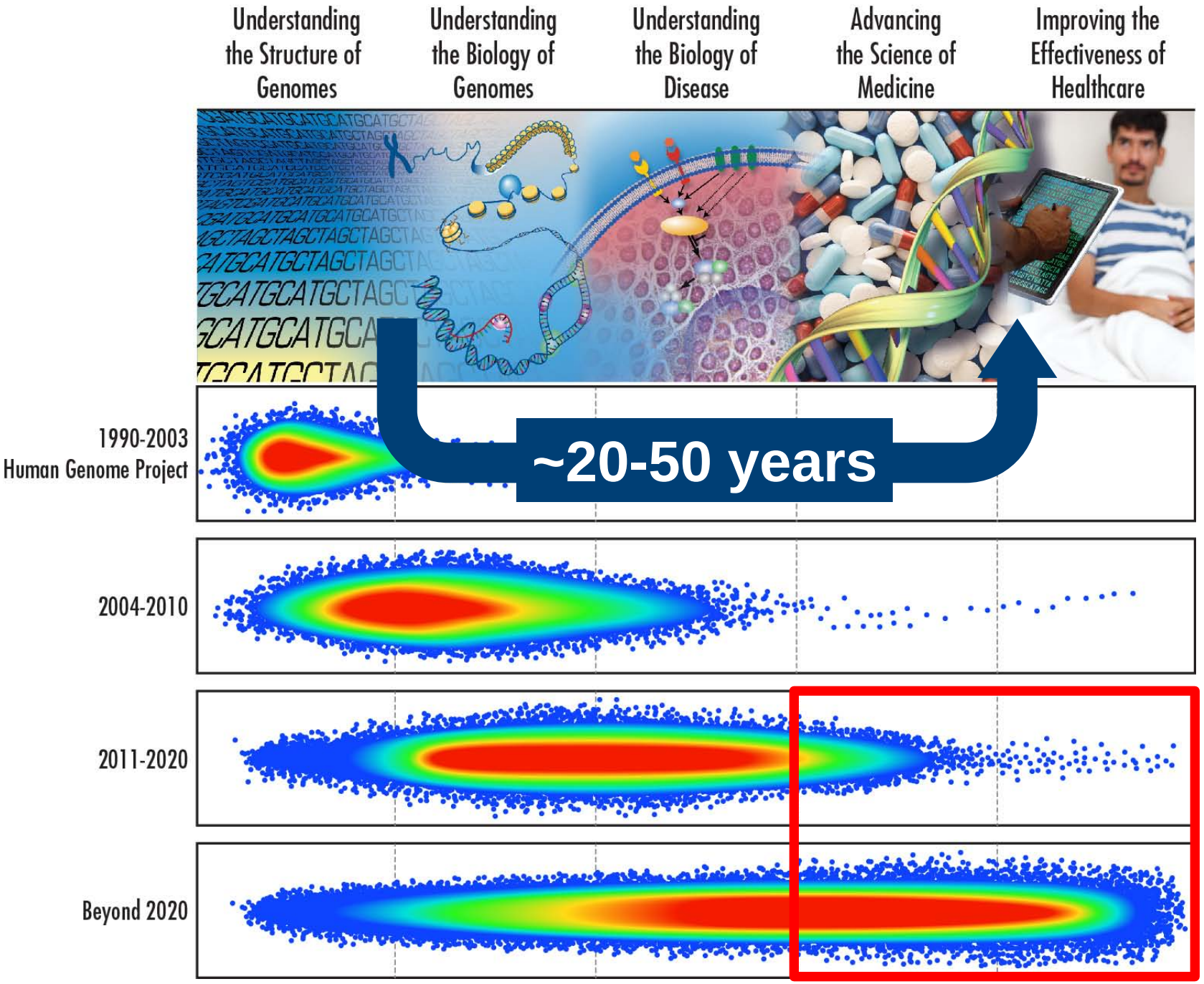
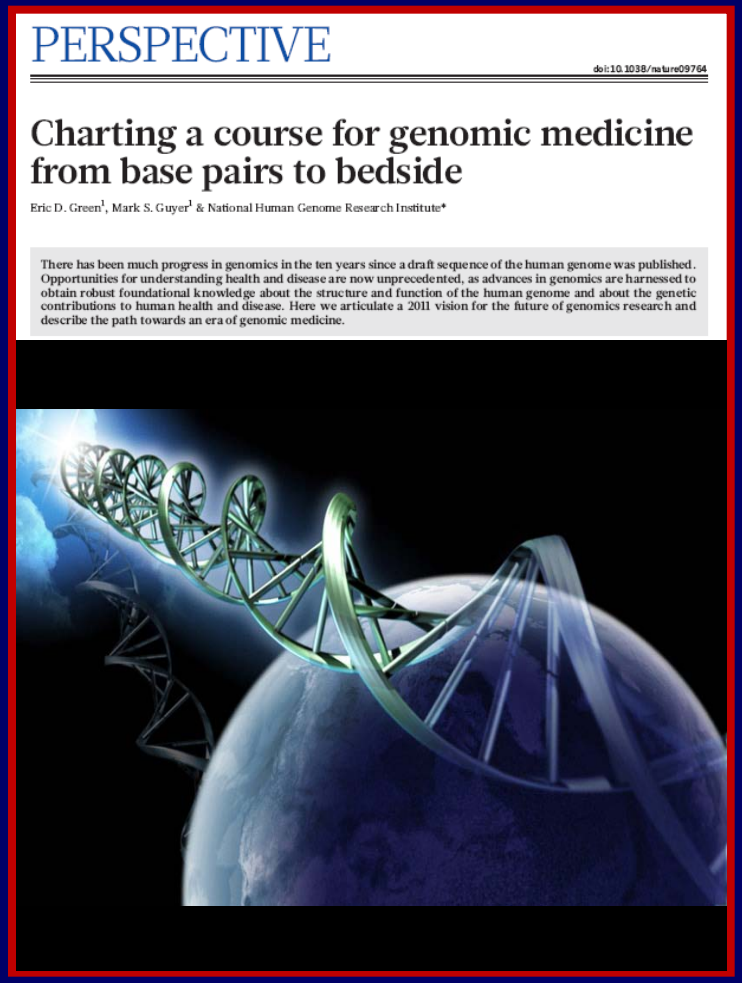

Understanding the Structure of Genomes
Understanding the Biology of Genomes
Understanding the Biology of Disease
Advancing the Science of Medicine
Improving the Effectiveness of Healthcare
~20-50 years
1990-2003 Human Genome Project
2004-2010
2011-2020
Beyond 2020

2011 NHGRI Strategic Plan for Genomics



PERSPECTIVE

doi:10.1038/nature09764

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>>>

NHGRI

Dissemination of Genomics

BOX 2

Imperatives for genomic medicine

Opportunities for genomic medicine will come from simultaneously acquiring foundational knowledge of genome function, insights into disease biology and powerful genomic tools. The following imperatives will capitalize on these opportunities in the coming decade.

Making genomics-based diagnostics routine. Genomic technology development so far has been driven by the research market. In the next decade, technology advances could enable a clinician to acquire a complete genomic diagnostic panel (including genomic, epigenomic, transcriptomic and microbiomic analyses) as routinely as a blood chemistry panel.

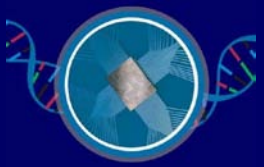
Defining the genetic components of disease. All diseases involve a genetic component. Genome sequencing could be used to determine the genetic variation underlying the full spectrum of diseases, from rare Mendelian to common complex disorders, through the study of upwards of a million patients; efforts should begin now to organize the necessary sample collections.

Comprehensive characterization of cancer genomes. A comprehensive genomic view of all cancers[4–7] will reveal molecular taxonomies and altered pathways for each cancer subtype. Such information should lead to more robust diagnostic and therapeutic strategies and a roadmap for developing new treatments[74,75].

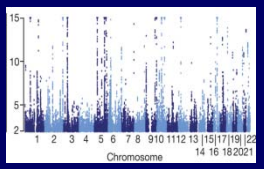
Practical systems for clinical genomic informatics. Thousands of genomic variants associated with disease risk and treatment response are known, and many more will be discovered. New models for capturing and displaying these variants and their phenotypic consequences should be developed and incorporated into practical systems that make information available to patients and their healthcare providers, so that they can interpret and reinterpret the data as knowledge evolves.

The role of the human microbiome in health and disease. Many diseases are influenced by the microbial communities that inhabit our bodies (the microbiome)[101]. Recent initiatives[102,103] (http://www.human-microbiome.org) are using new sequencing technologies to catalogue the resident microflora at distinct body sites, and studying correlations between specific diseases and the composition of the microbiome[104]. More extensive studies are needed to build on these first revelations and to investigate approaches for manipulating the microbiome as a new therapeutic approach.

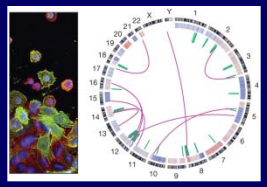
Technologies for genomic-based diagnostics



Genetic components of disease

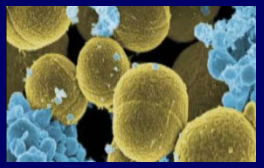


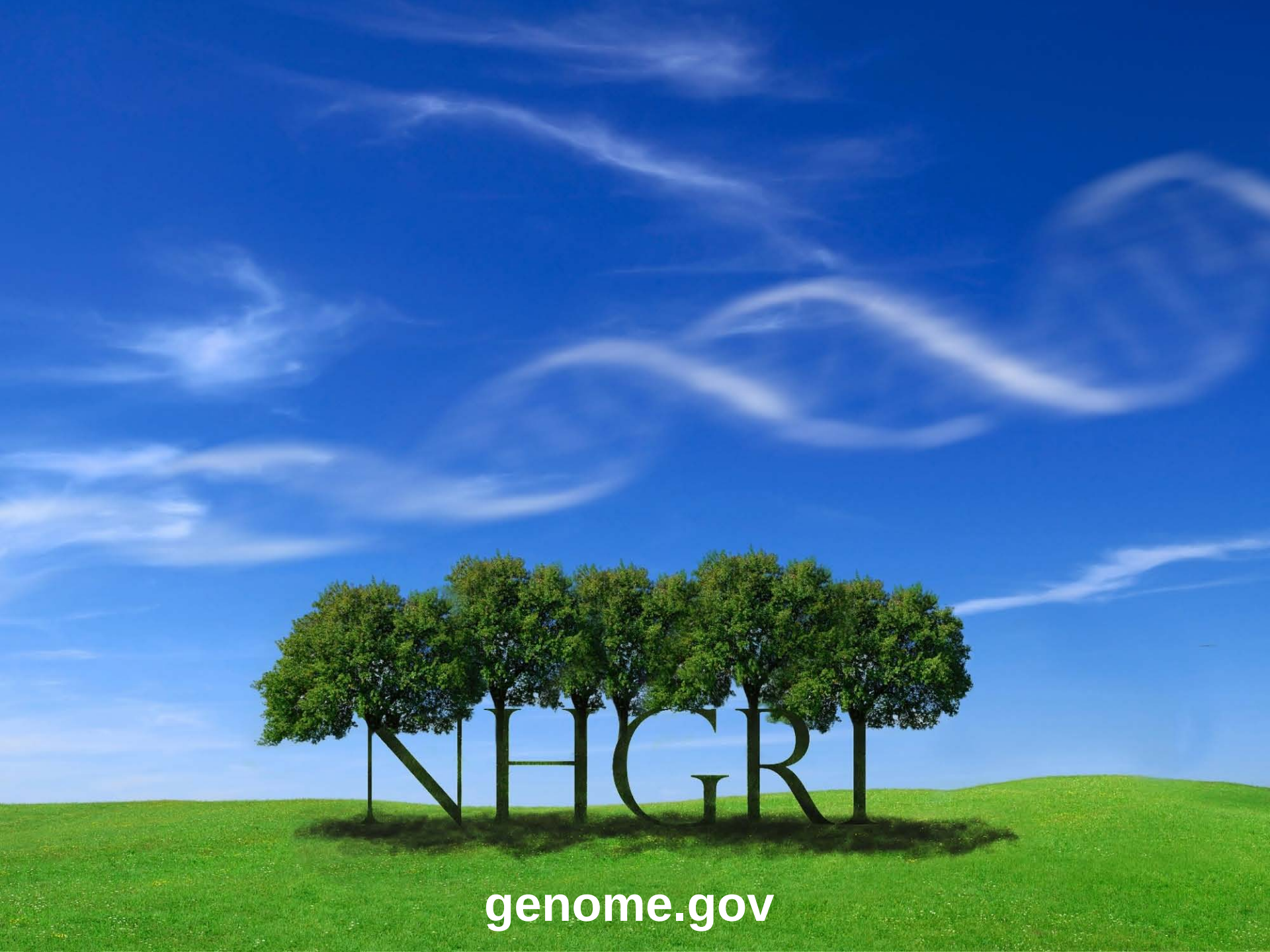
Characterization of cancer genomes



Clinical genomic information systems

Human microbiome in health and disease

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