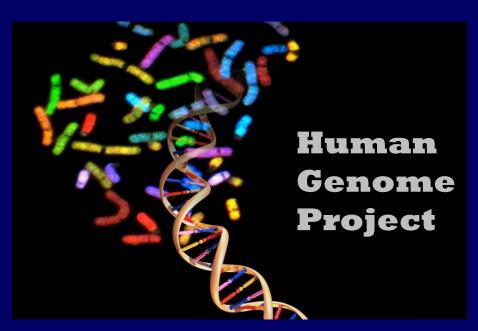
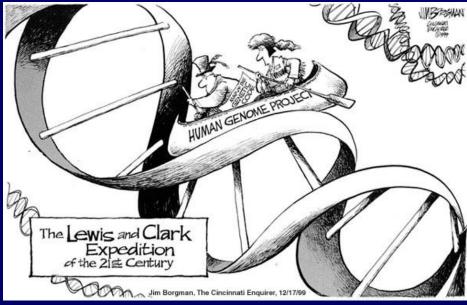


~20 Years Ago

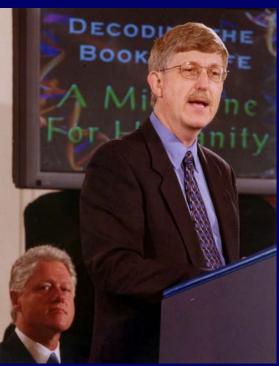


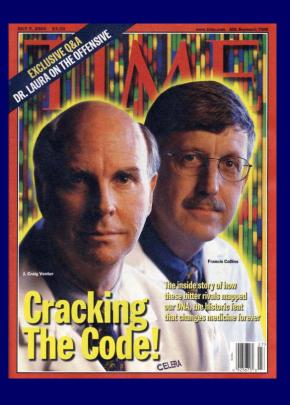


October 1990 Human Genome Project Begins

~10 Years Ago



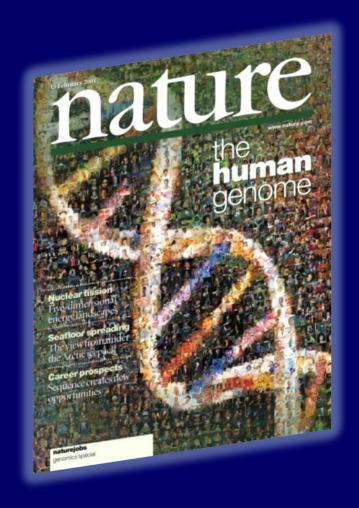




June 2000

Draft Human Genome Sequence Announced

~10 Years Ago



February 2001

Draft Human Genome Sequence Published

~1 Day Ago



PERSPECTIVE

doi:10.1038/nature09764

Charting a course for genomic medicine from base pairs to bedside

Eric D. Green¹, Mark S. Guyer¹ & National Human Genome Research Institute⁴

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.

ince 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 project3 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 cancer⁴⁻⁷, 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 disease⁸, some of which have already led to new therapies⁹⁻¹³. Other advances have already changed medical practice (for example, microarrays are now used for dinical detection of genomic imbalances16 and pharmacogenomic testing is routinely performed before administration of certain medications 15). Together, these achievements (see accompanying paper16) document that genomics is contributing to a better understanding of human biology and to improving human health.

As it did eight years ago¹⁷, the National Human Genome Research Institute (NHGRI) has engaged the scientific community (http://www. gmome.gsw/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 a griculture, energy and other areas). Like the FIQs, achieving this wision 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 the nbecomes 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 ¹⁶⁷), 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 disgnostics 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 conflience 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 bicinformatics and computational biology (Box 3), education and training (Box 4), and genomics and society (Mox 5).

Understanding the biology of genomes

Substantial progress in understanding the structure of genomes have 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 diseaserelated traits require comprehensive catalogues of genetic variation, which provideboth 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 Consortium³⁰ and the International HapMap Preject³² (http://hapmap. nch.rdm.mih.gov), and is ongoing with the 1000 Genomes Project³² (http://www.100genomes.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

¹National Human Genome Research Institute, National Institutes of Health, 31 Center Dr., Bethesda, Maryland 20892-2152, USA

"Lidts of participants and their affiliations appear at the end of the paper.

February 2011 NHGRI Published New Vision for Genomics

Understanding Our Genetic Inheritance

The U.S. Human Genome Project:

The First Five Years FY 1991-1995

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service National Institutes of Health

U.S. DEPARTMENT OF ENERGY Office of Energy Research **Environmental Research**

1991-1995

POLICY FORUM

The U.S. Human Genome Project

of an international effort to develop

netic and physical maps and determin

DNA sequence of the human genom

the genomes of several model organ

Thanks to advances in technology

tightly focused effort, the project track with respect to its initial 5-year Because 3 years have elapsed since goals were set, and because a much

sophisticated and detailed understand what needs to be done and how to d

now available, the goals have been re

and extended to cover the first 8

(through September 1998) of the 1

In 1990, the Human Genome pro of the National Institutes of Health

and the Department of Energy (DOE veloped a joint research plan with sp goals for the first 5 years [fiscal year

1991-95] of the U.S. Human Ge

Project (1). It has served as a va-

guide for both the research communit the agencies' administrative staff in o

oping and executing the genome p

and assessing its progress for the

years. Great strides have been made t

the achievement of the initial set of

particularly with respect to constructing

tailed human genetic maps, impr

physical maps of the human genom

the genomes of certain model organ

developing improved technology for

sequencing and information handling

defining the most urgent set of ethic

gal, and social issues associated with t

quisition and use of large amounts

goals for the genome project appears

on schedule or, in some instances,

ahead of schedule. Furthermore, t

logical improvements that could not

been anticipated in 1990 have in son

eas changed the scope of the project as

lowed more ambitious approaches. E

this year, it was therefore decided to a

and extend the initial goals to addre

scope of genome research beyond

F. Collins is the director of the National Ce

Progress toward achieving the first

netic information.

genome initiative.

A New Five-Year Plan for the U.S. **Human Genome Project**

Francis Collins and David Galas*

physical maps; (iii) the definition of the sequence tagged site (STS) (5) as a common unit of physical mapping; and (iv) improved technology and automation for DNA sequencing. Further substantial im-provements in technology are needed in all 1993-1998

SPECIAL SECTION

- G. An, B. D. Watson, C. C. Chiang. Plant Physiol. 81, 301 (1986); A. M. Lloyd et al., Science 234, 464 (1986); K. A. Feldmann and M. D. Marks, Mol. Gen. Genet. 208, 1
- (1987). i. E. M. Meyerowitz and R. E. Pruitt, Science 229, 1214 (1985).
- E. M. Meyerowitt and K. E. Fruitt, Science 229, 1214 (1995).
 G. R. Fink, Camskir 149, 473 (1996).
 C. Konz, N.-H. Chua, J. Schell, Eds., Method: in Arabidopsis Research (World Scientific, River Edge, N. 1992). J. M. Martins-Zapazer and J. Sallmaz, Eds., Arabidopsis Protocols, vol. 82 of Methods in Molecular Siology (Humana, Totowa, N.J.
- 9. For example, see S. A. Kempin et al., Nature 38 10. N. Bechtold, J. Ellis, G. Pelletier, C. R. Acad. Sci.
- et al., Plant j. 5, 551 (1994). 11. V. Sundaresan, Trends Plant Sci. 1, 184 (1996).
- D. Meinke and M. Koomneef, Flant J. 12, 247 (13. P. Fransz et al., Ibid. 13. 867 (1998). 14. C. Lister and C. Dean, Ibid. 4, 745 (1993); C. A
- (1996).
 I. Finnegan, R. K. Genger, W. J. Peacock, E. S. Der Mol. Biol. 49, 223 (1996).
 D. Preuss, S. Y. Rhee, R. W. Davis, Science 264, 14
- Browne, D. Preuss, Proc. Natl. Acad., Sci. U.S.A. 17. For recent examples of identifying knockouts in al., Plant, J. 8, E13 [1995]; P. J. Krysan, J. C. Youn Acad., Sci. U.S.A. 93, 8145 (1996).
- or information, contact http://www.bio.net/hyp). Meinke et al., Eds., "Multinational coordina research project, progress report, year sk." 97-131, Arlington, VA. 1997). M. Bevan et al., Flant Cell 9, 476 (1997).
- 21. H. Hofte et al., Flant J. 4, 1051 (1993); T. Ne

New Goal

Francis S. Collins,* Ari Patrir

The Human Genome Project has suo the major goals in its current 5-year of 1993-98. A new plan, for 1998-2003 human DNA sequencing will be the n bitious schedule has been set to com by the end of 2003, 2 years ahead of the course of completing the sequence the human sequence will be produced plan also includes goals for sequenci ment; for studying human genome developing technology for functional ing the sequence of Caenorhabditis melanogaster and starting the mous the ethical, legal, and social implication for bioinformatics and computational of genome scientists.

The Human Genome Project (HGP) is f single most important project in biology es—one that will permanently change bio

S. Collins and E. Jordan are with the National F National Institutes of Health, Bethesda, MD 20892, of Biological and Environmental Research, Depart 20585 USA A Chakravarti is with the Departmen Genetics, Case Western Reserve University and U Cleveland, OH 44106, USA, R. Gesteland is at the F University of Utah, Salt Lake City, UT 84112, USA Institute of Ethics, Georgetown University, Washin *To whom correspondence should be addresse

- 22. S. Choi, R. A. Creelman, J. E. Mullet, R. A. Wing, Mant Mol., Blol, Rep. 13, 124 (1995): E Crousof et al. Hant J 8 763 (1995)
- F. Creszot et al., Mart J. 8, 75 (1995).

 2. R. Schmidt et al., Gricera 270, 460 (1995); E. A. Zachgo et al., Genome Rez. 6, 19 (1995); S. Schmidt, E. Lore, J. West, Z. Liesshan, C. Desar, Mient J. 11, 563 (1997).

 24. N. Bersan et al., Grick and J. Schwidt and J. 11, 563 (1997).

 25. Safot et al., Grick Rez. 4, 215 (1997).

 26. C. Chang, S. F., Nowick, A. B. Blecckar, E. H. Mey erowitz, Johnson 262, 539 (1995); G. E. Schüller and A. B. Blecckar, Grick 270, 1989 (1995).

 1. U. F. Haspolt, Visitan T. C. McMorell, C. Chan 36, 75, 759 (1996); H. Szelanze.

1998-2003

2003-2010

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

The completion of a high-quality, comprehensive sequence of the human genome, in this fiftieth anniversary year of the discovery of the double-helical structure of DNA, is a landmark event. The genomic era is now a reality.

In contemplating a vision for the uture of genomics research, it is appropriate to consider the remarkable path that has brought us here. The rollfold (Figure 1) shows a timeline of landmark accomplishments in genetics and genomics, beginning with Gregor Mendel's discovery of the laws of heredity and their rediscovery in the early days of the wentiethcentury. Recognition of DNA as the hereditary material², determination of its structure⁵, elucidation of the genetic code⁴ development of recombinant DNA technologies 56, and establishment of increasingly utomatable methods for DNA sequen cing⁷⁻¹⁰ set the stage for the Human Genome Project (HGP) to begin in 1990 (see also www.nature.com/nature/DNA50). Thanks to the vision of the original planners, and the creativity and determination of a legion of talented scientists who decided to make this project their overarching focus, all of the initial objectives of the HGP have now peen achieved at least two years ahead of expectation, and a revolution in biological

esearch has begun. The project's new research strategies and experimental technologies have generated a teady stream of ever-larger and more complex genomic data sets that have poured into oublic databases and have transformed the study of virtually all life processes. The genomic approach of technology development and large-scale generation of community resource data sets has introduced an important new dimension into biological and piomedical research. Interwoven advances in genetics, comparative genomics, high-throughput biochemistry and bioinformatics

Wile Burke, Ronald W. Davis, William M. Gelbart, Eric T. Itsenus ronya I. Kasts, Raju Kucherla pati, Richaed F. Lifton, Kim J. lickerson, Mayaard V. Olson, Janet D. Rowley, Robert Topper obert H. Valterston and Tachtala Yarrada.

in a few weeks by a single graduate student with access to DNA samples and associated phenotypes, an Internet connection to the public genome databases, a thermal cycler and a DNA-sequencing machine. With the recent publication of a draft sequence of

of interesting mouse phenotypes has similarly been greatly simplified. Comparison of the human and mouse sequences shows that the proportion of the mammalian genome under evolutionary selection is more than twice that

Our ability to explore genome function is increasing in specificity as each subsequent

genome is sequenced. Microarray technologies have catapulted many laboratories from studying the expression of one or two genes in a month to studying the expression of tens of thousands of genes in a single afternoon12. Clinical opportunities for gene-based pre-symptomatic prediction of illness and adverse drug response are emerging at a rapid pace, and the therapeutic promise of genomics has ushered in an exciting phase of expansion and exploration in the commercial sector13. The investment of the HGP in

studying the ethical, legal and social implications of these scientific advances has created a talented cohort of scholars in ethics, law, social science, clinical research theology and public policy, and has already resulted in substantial increases in public awareness and the introduction of significant (but still incomplete) protections against misuses such as genetic discrimination (see www.genome.gov/PolicyEthics).

These accomplishments fulfil the expan sive vision articulated in the 1988 report of the National Research Council, Mapping and Sequencing the Human Genome14. The successful completion of the HGP this year thus represents an opportunity to look forward and offer a blueprint for the future of genomics research over the next several years.

The vision presented here addresses a different world from that reflected in earlier plans published in 1990-1993 and 1998 (refs 15-17). Those documents addressed the goals of the 1988 report, defining detailed paths towards the development of genome-

the mouse genome11, identification of the mutations underlying a vast number previously assumed

are providing biologists with a markedly improved repertoire of research tools that will allow the functioning of organisms in health and disease to be analysed and comprehended at an unprecedented level of molecular detail. Genome sequences, the bounded sets of information that guide biological development and function, lie at the heart of this revolution. In short, genomics has become a central and cohesive discipline of biomedical research.

The practical consequences of the emergence of this new field are widely apparent. Identification of the genes responsible for human mendelian diseases once a herculean task requiring large research teams, many years of hard work, and an uncertain outcome, can now be routinely accomplished

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Charting a course for genomic medicine from base pa REVIEW

Eric D. Green¹, Mark S. Guyer¹ & Natio

There has been much progress in g Opportunities for understanding h obtain robust foundational knowle contributions to human health andescribe the path towards an era o

ince the end of the Human Genome Pi publication of a reference human genor secome a mainstay of biomedical rese nity's foresight in launching this ambitious pr range of scientific advances that the HGP ha (see rollfold). Optimism about the potential of improving human health has been fuelled by the molecular basis of inherited diseases (h omimandhttp://www.genome.gov/GWAStuc variation in disease⁸, some of which have alm Other advances have already changed medical arrays are now used for dinical detection o of human biology and to improving human I

Institute (NHGRI) has engaged the scientif data from the public HGP.

ing from basic research to health application yet having cured most diseases. Genomics offers opportunities for improvin medicine, evolution and history? What is the road al about the geography of our genetic landscape

¹National Human Genome Research Institute, National Insti *Lists of participants and their affiliations appear at the end

Initial impact of the sequencing of the human genome **PERSPECTIVE**

doi:10.1038/nature09796

The sequence of the human genome has dr decade since its publication, on our unders basis of inherited diseases and cancer, and o in fulfilling the promise of genomics for m

n 15 February 2001, a decade ago this week, ? 62-page paper entitled Initial sequencing a human genome', reporting a first global look pharmacogenomic testing is routinely perfor the human genetic code. The paper marked a mile of certain medications 15). Together, these achi national Human Genome Project (HGP), a discovery paper¹⁶) document that genomics is contribut ceived in the mid-1980s and launched in 1990. The s published a paper2 from the company Celera Genc As it did eight years ago17, the National draft human sequence based on their own prodigio

genome.gov/Planning) to reflect on the key a: The human genome has had a certain tendency to and explore future directions and challenge excess: from early jeremiads that the HGP would st sions have led to an updated vision that focus consuming the NIH budget (it never rose to more than biology and the diagnosis, prevention and t coverage of a late-breaking genome race between p including consideration of the implications opportugionists; to a White House announcement of (but these discussions, intentionally did not: sequence in June 2000, 8 months before scientific po in agriculture, energy and other areas). Liketh been written, peer-reviewed and published; to breathl realizing the full benefits of genomics will be and genome-based panaceas; to a front-page news s

health. At the same time, there are other conne the human sequence propelled our understanding c

understanding of disease (for example, cance The past decade has shown the power of genomic m example, RNA transcripts to be assayed with arrays revised components have been added as required.

A decade's perspective on DNA sequencing technology

The decade since the Human Genome Project ended has witnessed a remarkable sequencing technology explosion that has permitted a multitude of questions about the genome to be asked and answered, at unprecedented speed and resolution. Here I present examples of how the resulting information has both enhanced our knowledge and expanded the impact of the genome on biomedical research. New sequencing technologies also have introduced exciting new areas of biological endeavour. The continuing upward trajectory of sequencing technology development is enabling clinical applications that are aimed at improving medical diagnosis and treatment

he sequencing of the Human Reference Genome, announced ten years ago, provided a roadmap that is the foundation for modern biomedical research. This monumental accomplishment was is broader than what any single organizatic Wall Street and the press about the imminence of ge enabled by developments in DNA sequencing technology that allowed data production to far exceed the original description of Sanger sequen-This 2011 vision for genomics is organized anniversary of the announcement that chided genom cing. Moving forward in the genomic era in which we now find ourselves, new (or 'next generation') DNA sequencing technology is enabling that, over time, the most effective way to i The goal of this review is to step back and assess the revolutionary advances in our understanding of health and disease. In understand normal biology (in this case, get from a scientific standpoint, addressing three questit essence, sequencing technology is the engine that powers the car that understanding disease biology, which then beckerned about the human genome itself over the past allows us to navigate the human genome roadmap. As that engine becomes ever more powerful, so will the questions we can ask and answer

Of course, a car with only an engine is unworkable; as such, DNA based on genomic profiles that identify tume for biomedical research. By providing a compreher sequencing technology provides an integral part of a larger system, one discoveries can lead back to understanding d human sequence has made it possible for scientists with multiple components that must be properly matched in order to The past decade has seen genomics contril fragmentary information into landscapes of biologi achieve high throughput and efficiency. It has essentially never been as about biology and its perturbation in dise function: maps of evolutionary conservation, gene tr 'easy' as simply buying sequencing instruments, plugging them in, and understanding will accelerate the transition t matinistructure, methylation patterns, genetic variation generating data. We need the raw materials, such as fuel (DNA), sparks to care based on genomic information). But sig distance, linkage disequilibrium, association to inherit ignite the fuel (reagents), mechanical parts to translate fuel and ignition alterations in cancer, selective sweeps during human into movement (robotics) and direction (bioinformatics), all working in a dimensional organization in the nucleus. By providin carefully engineered balance, and a driver (genome centre) to steer the cross-reference information across species, it has con automobile quickly and efficiently to the desired destination (biological of model systems to the physiology of the human. Fur understanding). By inference, as this 'engine' has achieved ever increasviding comprehensive catalogues of genomic informating horsepower, the supporting components have evolved to match its genes and proteins to be recognized based on unique 't output with corresponding levels of performance, and new or completely

> probes and proteins by detection of short peptide fri In 2001, the technology that sequenced the human genome was based spectrometer. In turn, these measurements have been on capillary electrophoresis of individual fluorescent-labelled Sanger cellular signatures' characteristic of specific cell types, st sequencing reaction products. Each instrument could detect 500and catalogues of the contents of organelles such as 600 bases from each of 96 reactions in around ten hours, with 24-hour unattended operation producing 115 kbp (thousand base pairs) per day. Broad Institute of MIT and Harvard, 7 Cambridge Canter, Cambridge, M Because of the increased scale required for the Human Genome Project, genome centres had developed a robust, highly automated and inexpensive preparatory process to feed their capillary sequencers. Once the data were produced, mature analysis software was applied to analyse the sequencing reads (each a ~500-bp sequence of A, C, G, T), then to assemble reads that shared sequence identity, reproducing that region of the genome. After assembly, each genomic region was further analysed to identify genes, repeat elements and other features. As the 'drivers' of these se quencing pipelines, genome centres could dial up capacity by increas-

processes, because sequence production, not sequence analysis, was rate

As I will describe, the ensuing 10 years has been marked by dramatic improvements in sequencing technology that have catapulted sequencing to the forefront of biological experimentation and have revolutionized the way that we approach genome-wide questions. One consequence of this revolution has been the coincident revitalization of bioinformatics, predominantly in development efforts aimed at data analysis and interpretation. Taken together, these un precedented sequencing and analysis capabilities have inspired new areas of enquiry, have solved major questions about the regulation, variability and diaspora of thehuman genome, and have introduced a genomic era in medical enquiry and (ultimately) practice that will bring about the originally envisioned impact of the Human Genome Project.

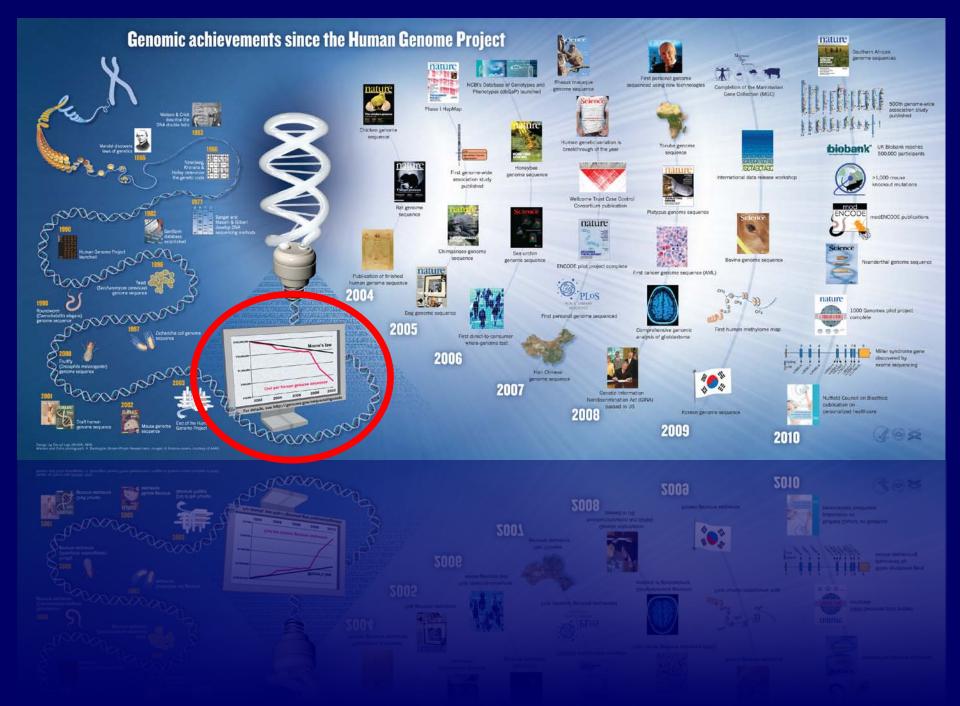
Massively parallel sequencing

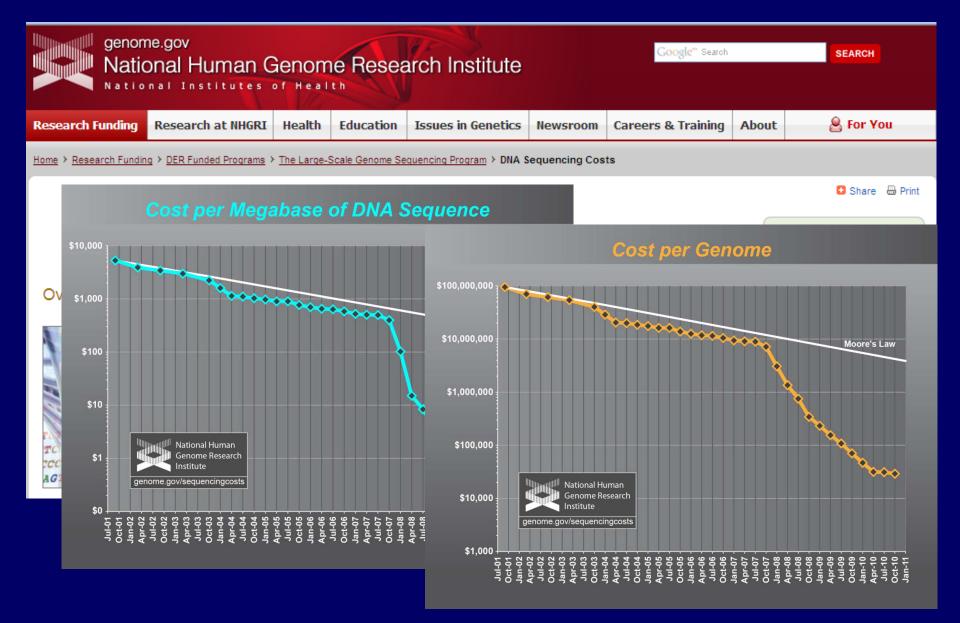
The first five years following the Human Genome Project provided further definition and annotation of the human genome sequence by comparative genomics; the sequencing of several model organism genomes-such as mouse2, rat3, chicken4, dog6, chimpanzee6, rhesus macaque7, duckbill platypus8 and cow9-provided information about highly conserved genomic elements that are likely to be functional owing to their conservation. These genomes were largely produced by conventional methods, including Sanger-based capillary sequencing. Starting in 2005, a variety of new 'engines' for DNA sequencing that were radically different from the capillary sequencers used to sequence the human and model organism genomes became available from several different manufacturers (Fig. 1). These new engines were 'turbo-charged' by several orders of magnitude compared to their predecessors, because the basic mechanisms for data generation had changed radically, producing far more sequence reads per instrument run and at a significantly lower expense. The availability of multiple commercially available instruments alone represented a paradigm shift from the previous decade, where a single capillary instrument produced by Applied Biosystems dominated the market. Many of these in novative approaches were initially developed with National Institutes of Health (NIH) funding through the "Technology development for the \$1,000 genome' program (http://www.genome.gov/ 11008124#al-4) introduced during Francis Collins' directorship at the National Human Genome Research Institute (NHGRI).

Since the introduction of these platforms, the past five years have been ing the amount of hardware used in the preparatory and sequencing marked by fierce competition between their manufacturers to greatly

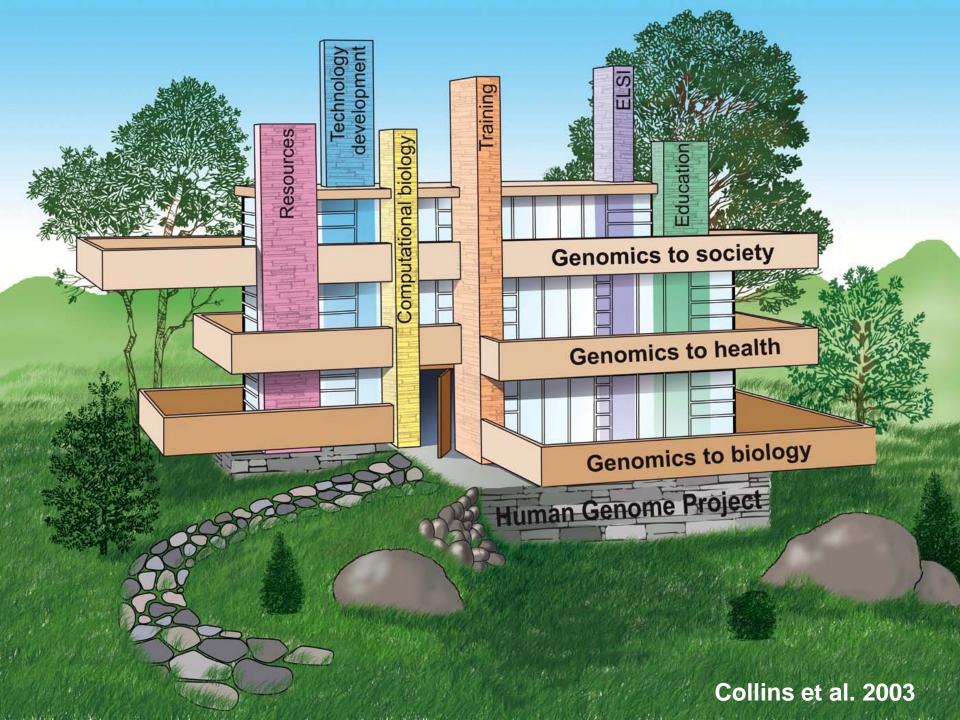
The Genome Center at Washington University School of Medicine, Department of Genetics, Washington University School of Medicine, St Louis, Missouri 63106, USA

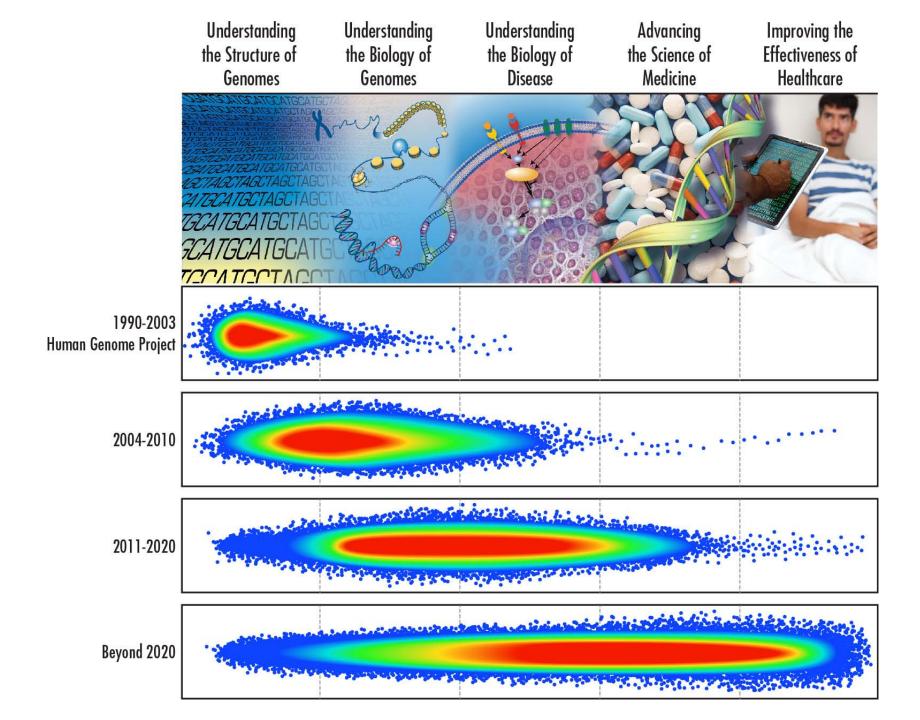






genome.gov/sequencingcosts





NHGRI Publishes 2011 Strategic Plan

PERSPECTIVE

Charting a course for genomic medicine from base pairs to bedside

Eric D. Green¹, Mark S. Guyer¹ & 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.

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As it did eight years ago17, 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 achieverealizing 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.

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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

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Comprehensive catalogues of genomic data

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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 Consortium20 and the International HapMap Project2 (http://hapmap. nchi.nlm.nih.gov), and is ongoing with the 1000 Genomes Project2 (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 pape



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A Decade with the **Human Genome Sequence**

Charting a Course for Genomic Medicine

Anticipating the Next Decade of the Genome Frencis Collins, M.D., Ph.D

The Human Genome at 10: An Overview

Reading Genomes Bit by Bit

nes, Genomes, and the Future of Medicine Richard Lifton, M.D., Ph.D.

Fevers, Genes, and Targeted Therapies: Adventures in the Genomics of Inflammation

Exploring Your Genetic Blueprint:

A Panel Discussion
Moderated by Sharon Terry, M.A.
Genotic Alliance
Featuring Jones Watson, Ph.D.
Cold Spring Harbor Laboratory

Systematic Surveys of Human Epigenomes

Ethical, Legal, and Social Issues in Genomics: Reflecting Back, Planning Ahead

The Public Place in Personal Genomics

The Path Ahead

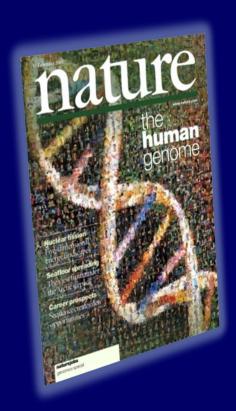
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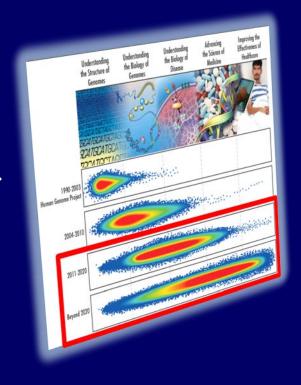
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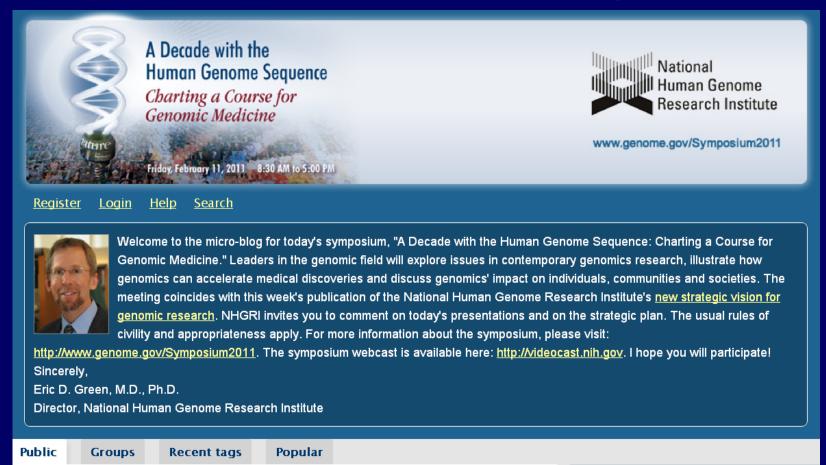
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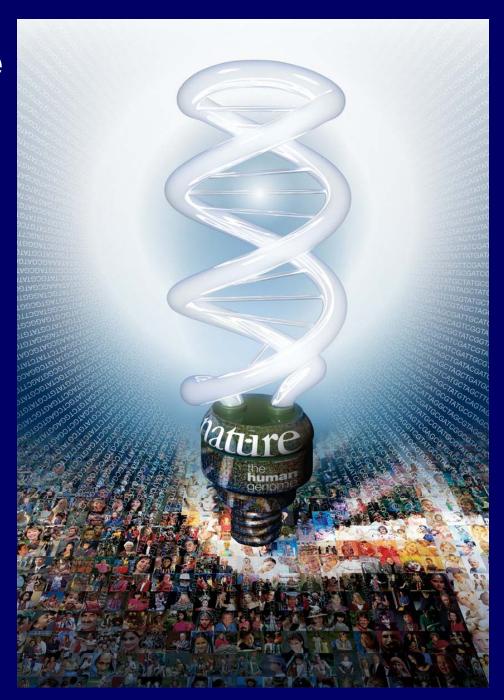




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