


From the Human Genome Project to Genomic Medicine

A Journey to Advance 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…

‘The Genome Institute’

Office for Human Genome Research

1988-1989

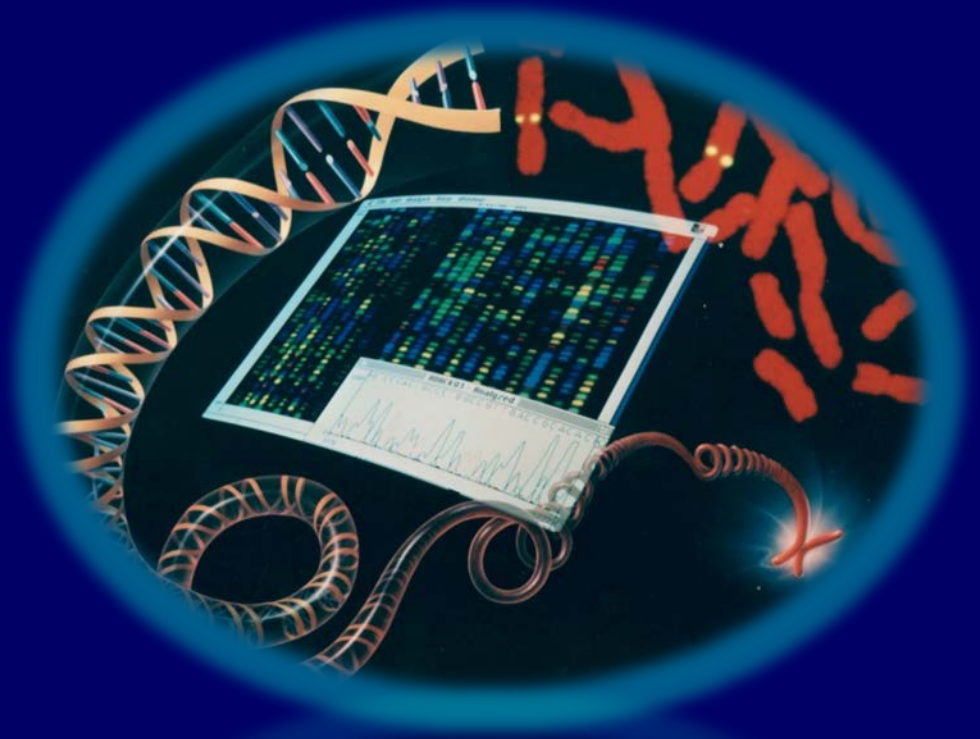
National Center for Human Genome Research

1989-1997

National Human Genome Research Institute

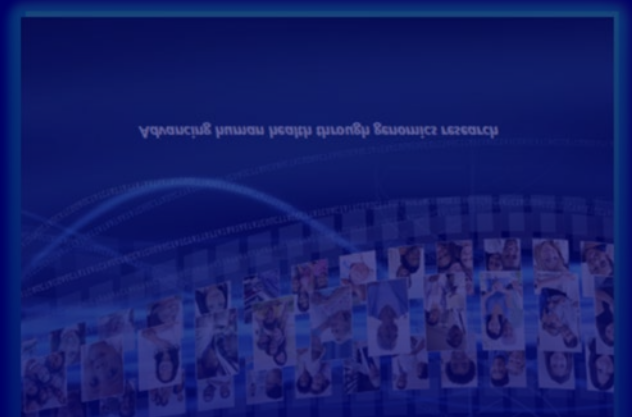
1997-present

NHGRI: *Circa 1990-2003*



Human Genome Project

NHGRI Today: Characteristic Features



- Relatively young (~28 years)
- Relatively small (~1.7% of NIH)
- Unusual historical origins (think ‘Human Genome Project’)
- Emphasis on ‘Team Science’ (think managed ‘consortia’)
- Rapidly disseminating footprint (think ‘genomics’)
- Novel societal/bioethics research component (think ‘ELSI’)
- Over-achievers for trans-NIH initiatives (think ‘Common Fund’)
- Vibrant (and large) Intramural Research Program

A Quarter Century of Genomics

Human Genome Sequenced for First Time by the Human Genome Project

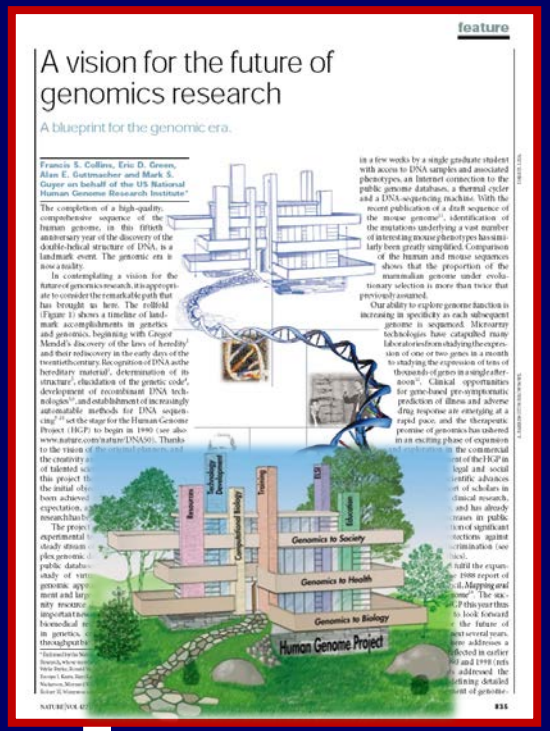
Genomic Medicine

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



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*

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.

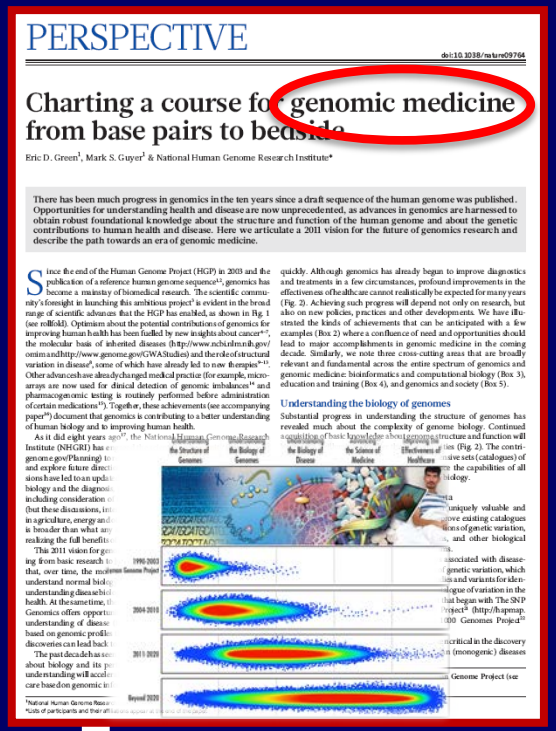
In contemplating a vision for the future of genomics research, it is appropriate to consider the remarkable path that has brought us here. The rollfold (Figure 1) shows a timeline of landmark accomplishments in genetics and genomics, beginning with Gregor Mendel's discovery of the laws of heredity[1] and their rediscovery in the early days of the twentieth century. Recognition of DNA as the hereditary material[2], determination of its structure[3], elucidation of the genetic code[4], development of recombinant DNA technologies[5,6] and establishment of increasingly automatable methods for DNA sequencing[7–10] set the stage for the Human Genome Project (HGP) to begin in 1990 (see also www.nature.com/naturedna50). Thanks to the vision of the original planners, and the creativity a… of talented sci… this project th… the initial obj… been achieved… expectation, a… research has b… The progra… experimental t… deadly diseas… gies genomic d… public databas… study of vari… genomic appr… ment and larg… nity resource… important bas… biomedical re… in genetics, … throughput te…

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 the mouse genome[11], identification of the mutations underlying a vast number 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 previously assumed.

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 afternoon[12]. 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 … the commercial … nt of the HGP in … legal and social … ientific advances … rt of scholars in … linical research, … and has already … ases in public … t of significant … tractions against … crimination (see … ical).

…fulfil the expan… 1988 report of … il, Mapping and … nome'[13]. The suc… GP this year thus … to look forward … the future of … next several years. … ome addresses a … ddressed in earlier … 90 and 1998 (refs …) addressed the … defining detailed … ment of genome-

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.

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' 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[3–7], 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[9–12]. 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 e… genome.gov/Planning) to… and explore future direct… sions have led to an upda… biology and the diagnos… including consideration … (but these discussions, int… in agriculture, energy and … is broader than what any … realizing the full benefits …

This 2011 vision for ge… ing from basic research to… that, over time, the medicine… understand normal biolo… understanding disease biol… health. At the same time, t… Genomics offers opportu… understanding of disease … based on genomic profiles … discoveries can lead back …

The past decade has see… about biology and its po… understanding will accele… care based on genomic in…

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 … ies (Fig. 2). The contri… sive sets (catalogues) of … the capabilities of all … biology.

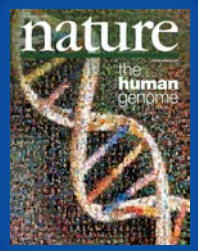
…uniquely valuable and …ove existing catalogues …ons of genetic variation, … and other biological …

…ssociated with disease- …genetic variation, which …ns and variants for iden- …logue of variation in the …hat began with The SNP …roject[8] (http://hapmap. …000 Genomes Project[18] …

…critical in the discovery … (monogenic) diseases …

… Genome Project (see …

Nature



Base Pairs to Bedside

2003

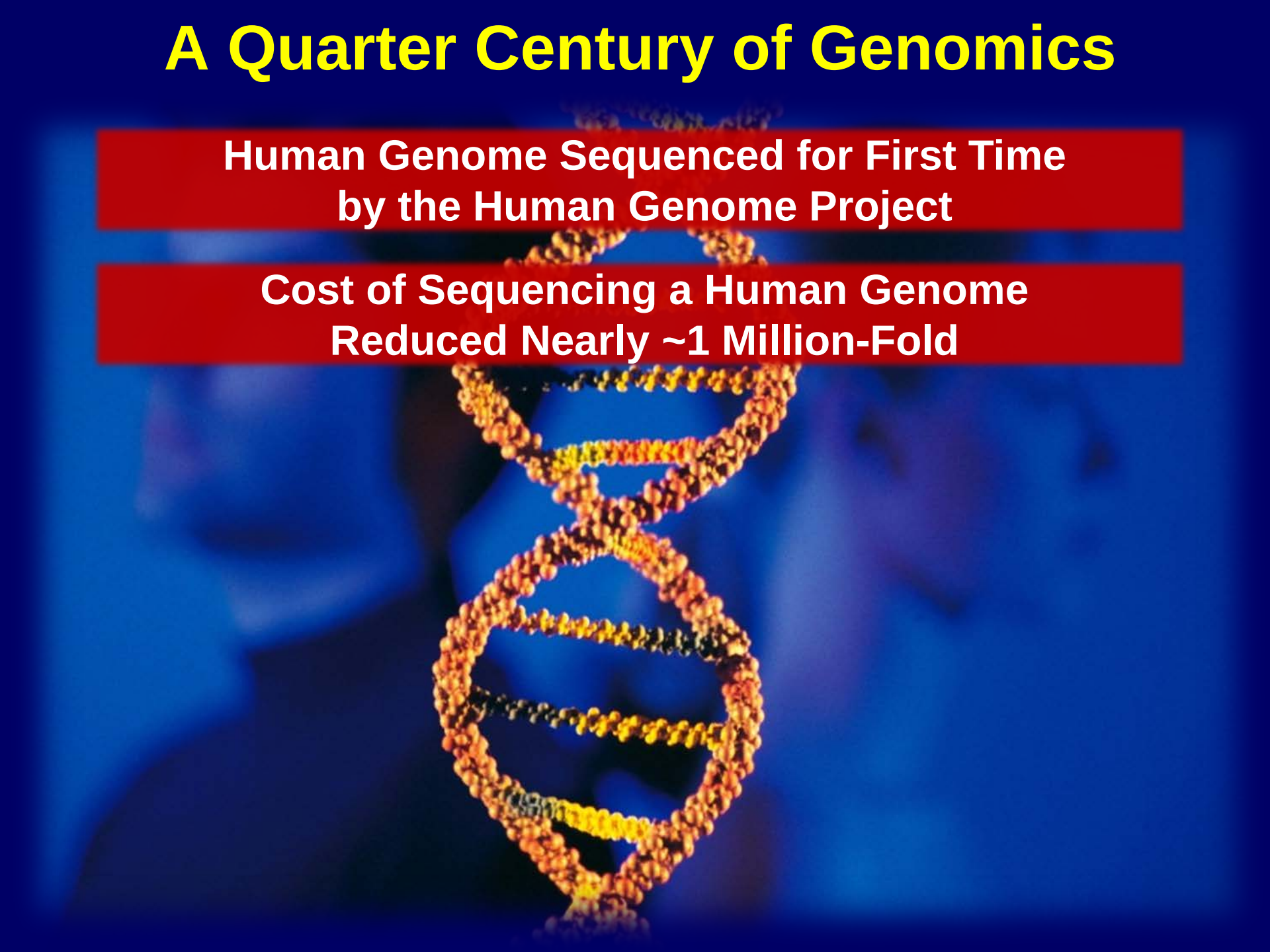
2011

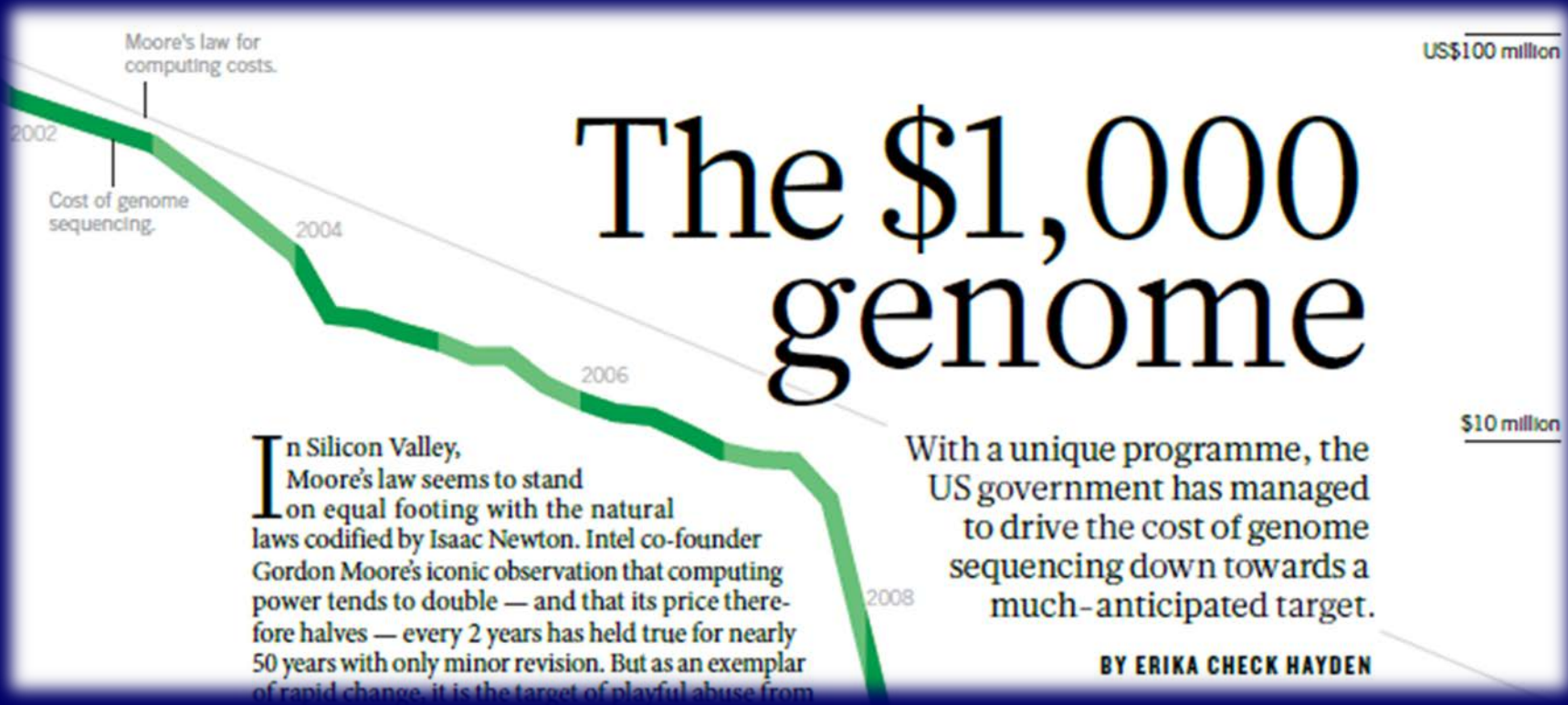
Health

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





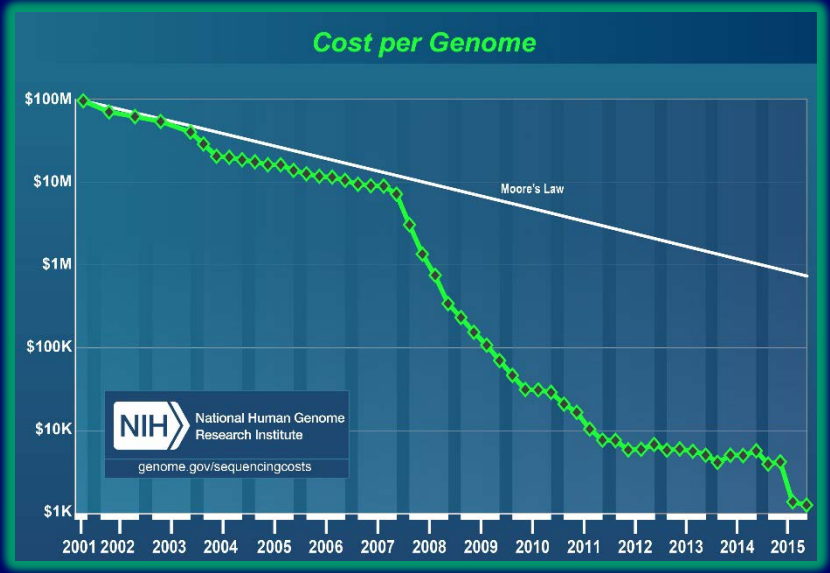
The $1,000 genome

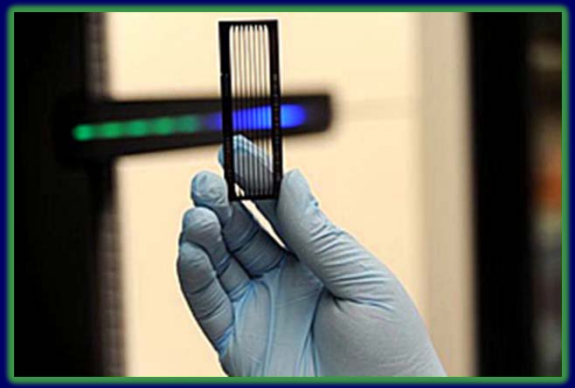
In Silicon Valley, Moore's law seems to stand on equal footing with the natural laws codified by Isaac Newton. Intel co-founder Gordon Moore's iconic observation that computing power tends to double — and that its price therefore halves — every 2 years has held true for nearly 50 years with only minor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

With a unique programme, the US government has managed to drive the cost of genome sequencing down towards a much-anticipated target.

BY ERIKA CHECK HAYDEN

***Nature* (2014)**





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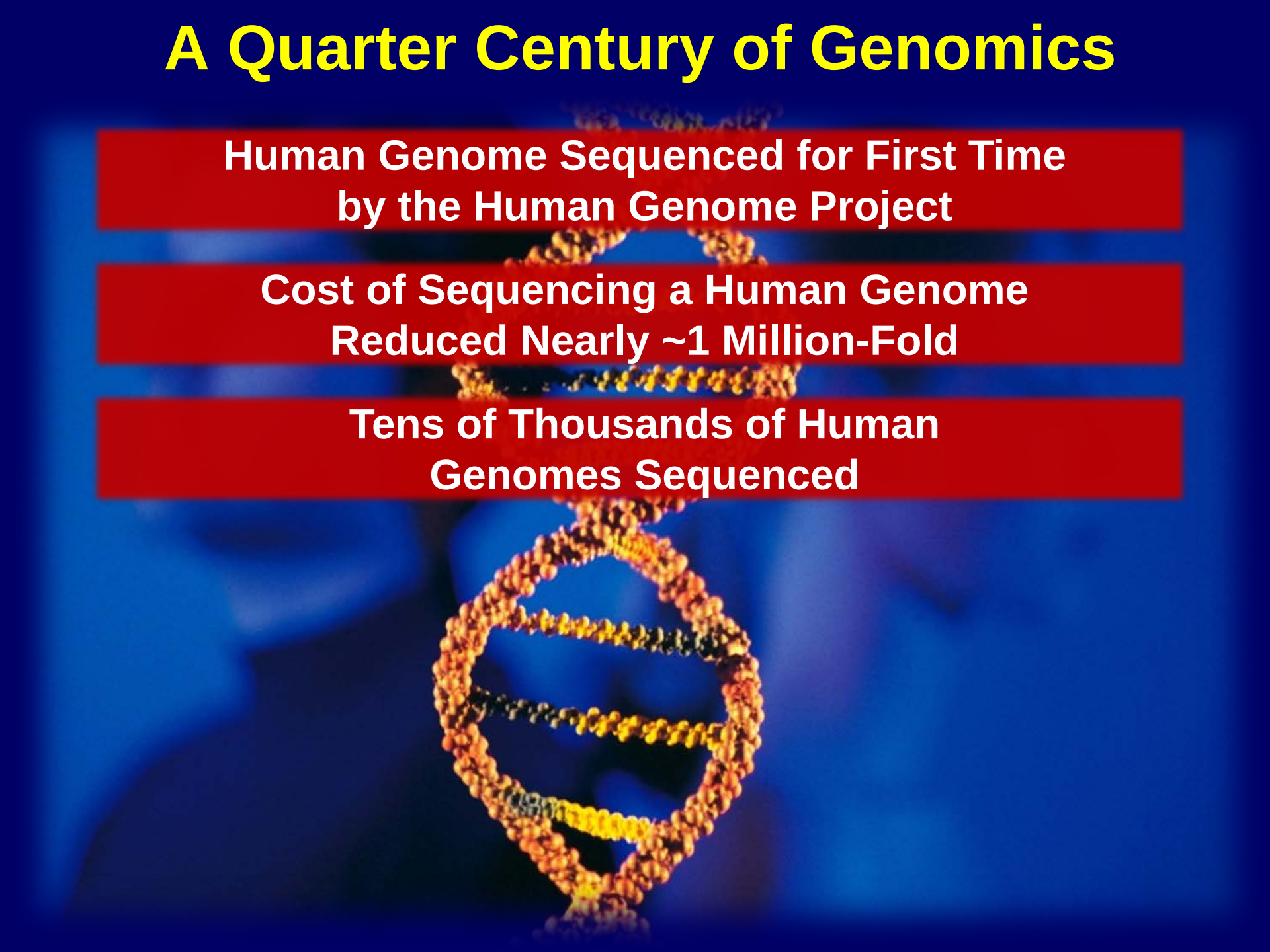
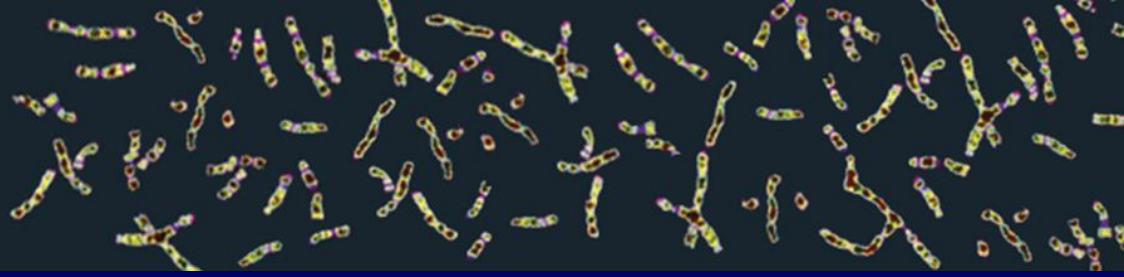
Tens of Thousands of Human Genomes Sequenced



1000 Genomes

A Deep Catalog of Human Genetic Variation



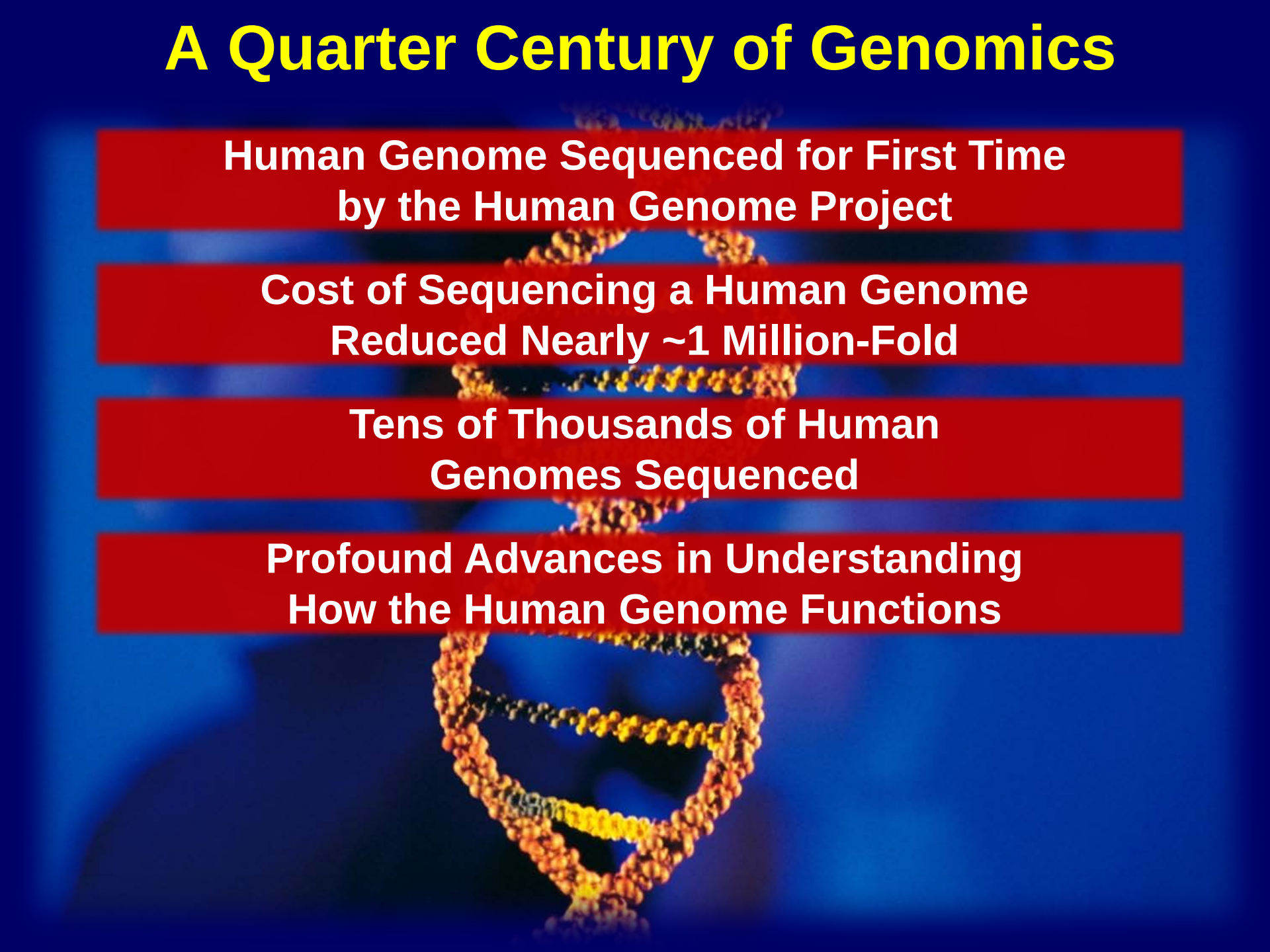
ARTICLE

A global reference for human genetic variation

The 1000 Genomes Project Consortium*

***Nature* (2015)**

A Quarter Century of Genomics



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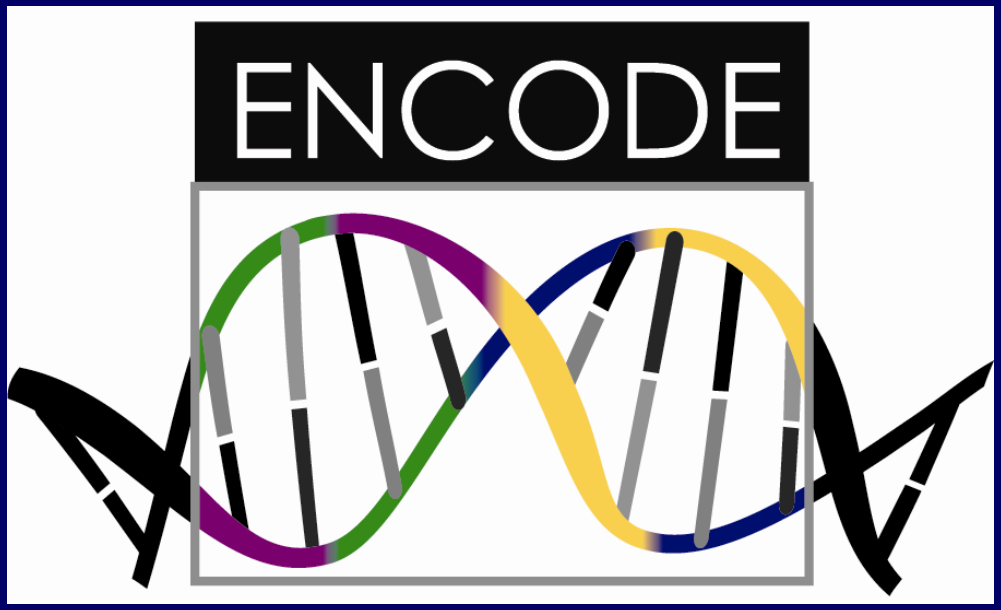
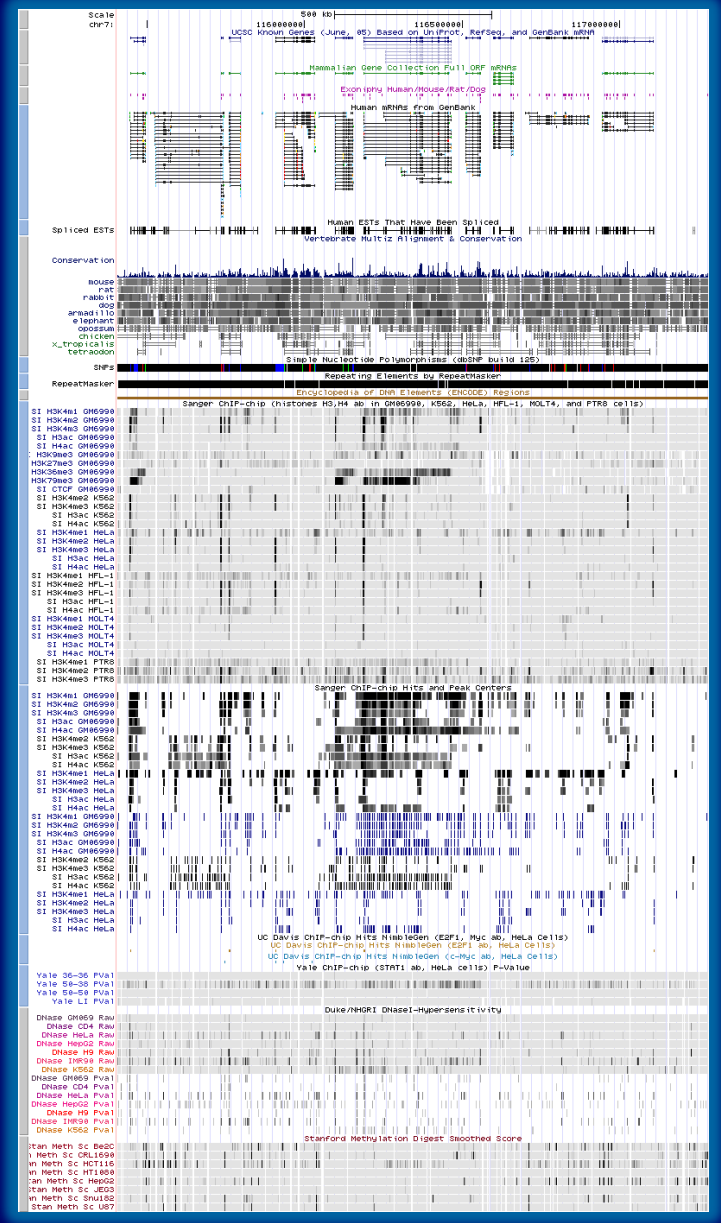
Tens of Thousands of Human Genomes Sequenced

Profound Advances in Understanding How the Human Genome Functions

ENCODE: Giving ‘GPS’ Views of Genomes





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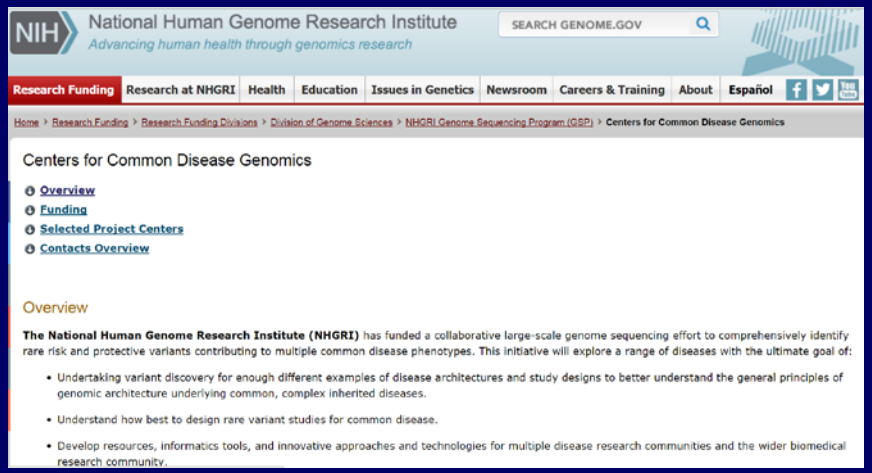
Significant Advances in Unraveling the Genomic Bases of Human Disease

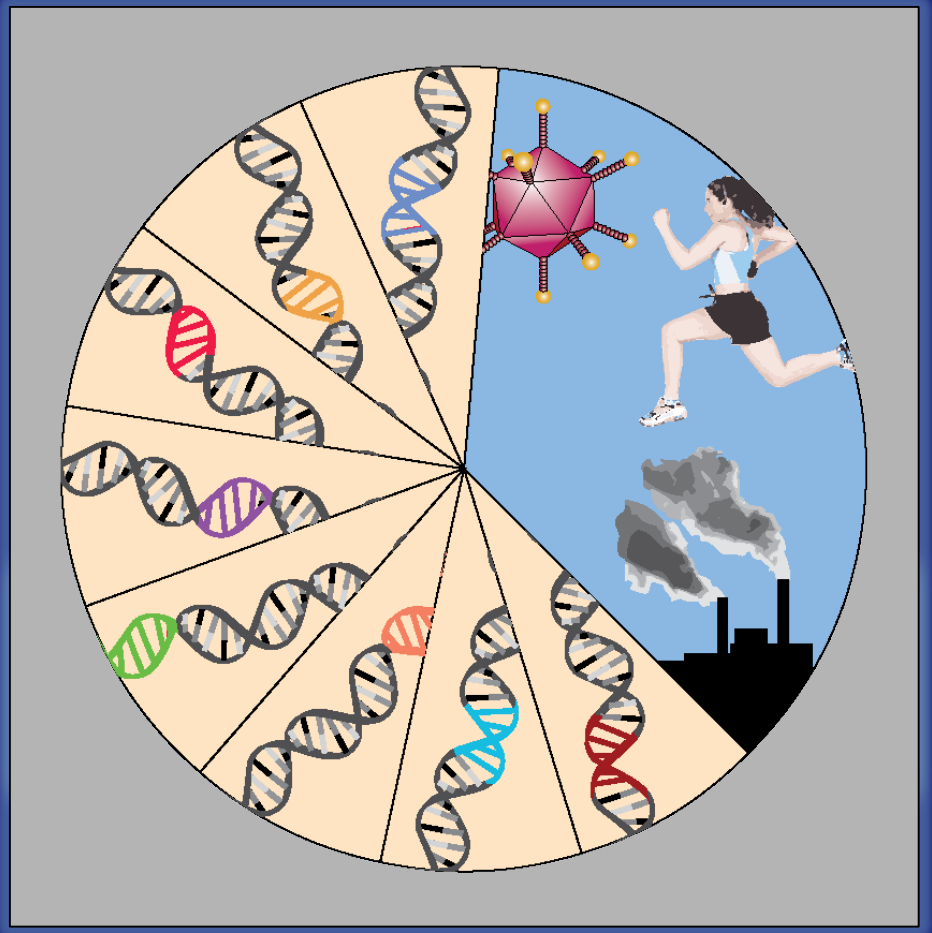
Genomic Architecture of Genetic Diseases

NHGRI Centers for Common Disease Genomics



genome.gov/27563570

Cardiovascular Disease
Hemorrhagic Stroke
Autism
Epilepsy
Asthma



Common, Complex, Multigenic, Non-Mendelian…

Manolio et al., J Clin Invest (2008)

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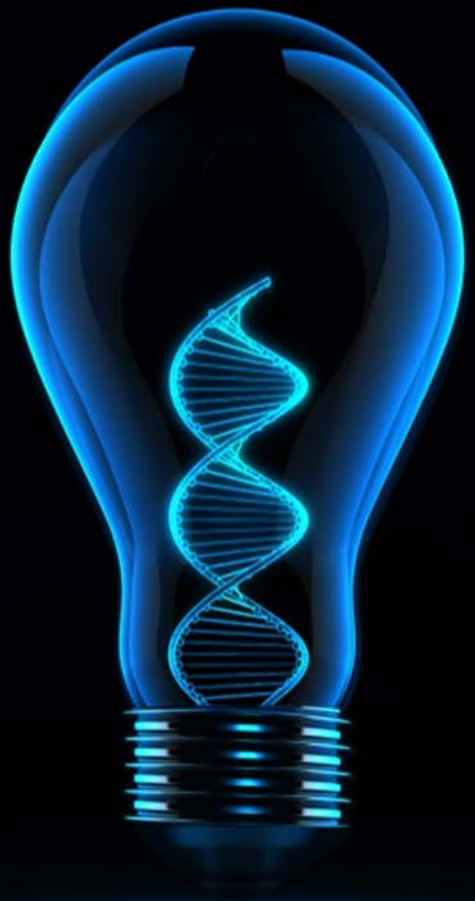
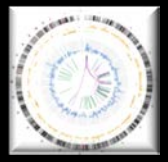
Vivid Examples of Genomic Medicine in Action Now Emerging

Bringing Genomic Medicine Into Focus

‘Hot Areas’ in Genomic Medicine

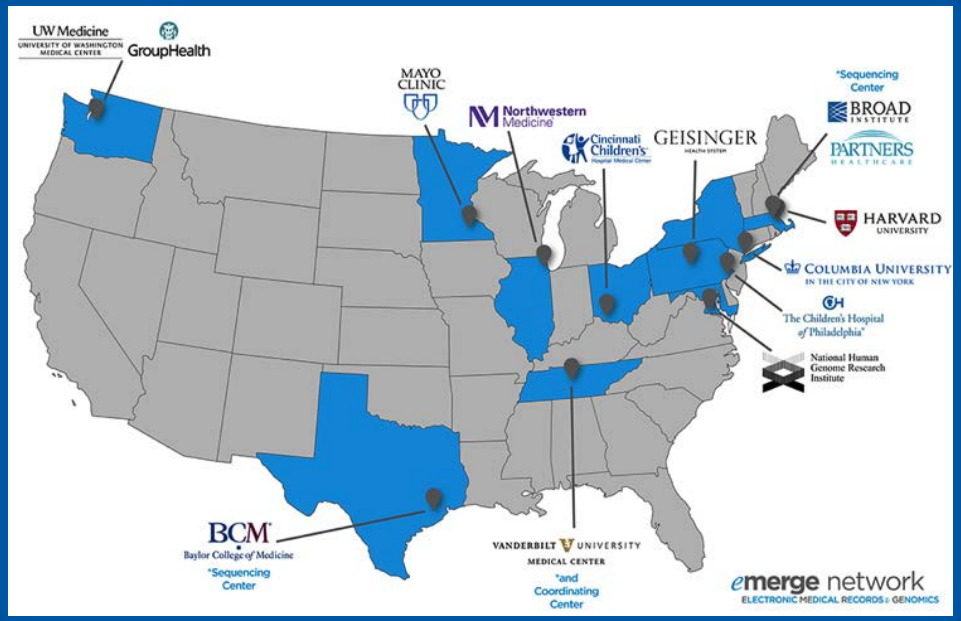


Cancer Genomics



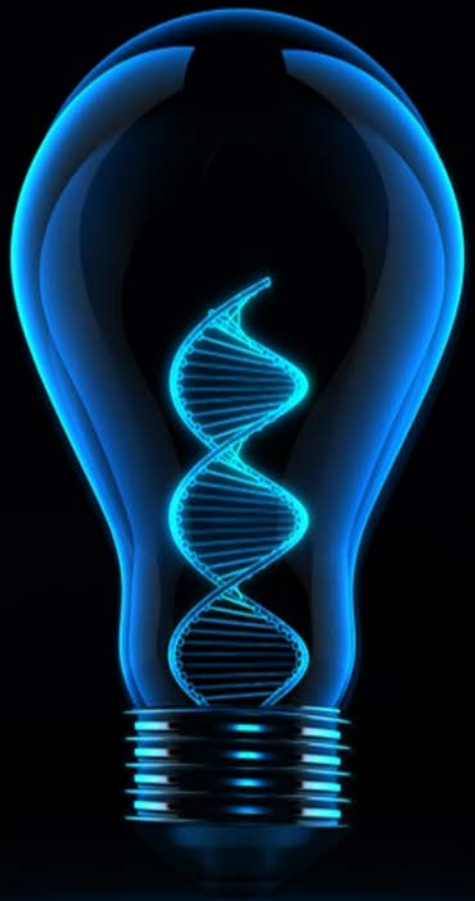
Pharmacogenomics

Electronic Medical Records and Genomics (eMERGE) Network

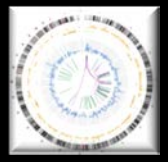


emerge.mc.vanderbilt.edu

‘Hot Areas’ in Genomic Medicine



Cancer Genomics



Pharmacogenomics

Rare Genetic Disease Diagnostics

TECHNOLOGY FEATURE

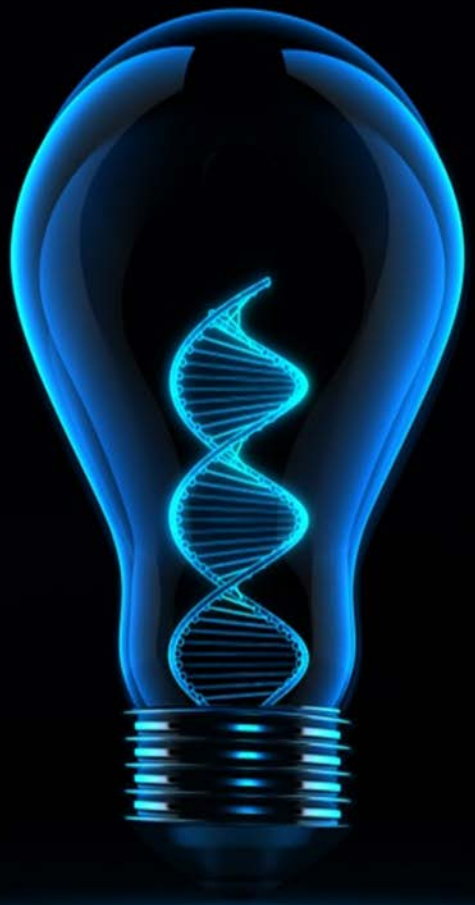
WHEN DISEASE STRIKES FROM NOWHERE

When healthy parents have a child with a genetic disorder, the cause is sometimes a new mutation. Tools are emerging to meet the challenge of finding such changes.

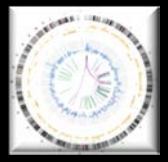
“ …disorders not readily explained by standard tests can sometimes be diagnosed through genome sequencing and analysis.”

***Nature* (2014)**

‘Hot Areas’ in Genomic Medicine



Cancer Genomics



Pharmacogenomics

Rare Genetic Disease Diagnostics

Newborn Genome Sequencing

Newborn Genome Sequencing

HEALTH RESEARCH

In 2025, Everyone Will Get DNA Mapped At Birth

Alice Park @aliceparkny | June 30, 2014

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)

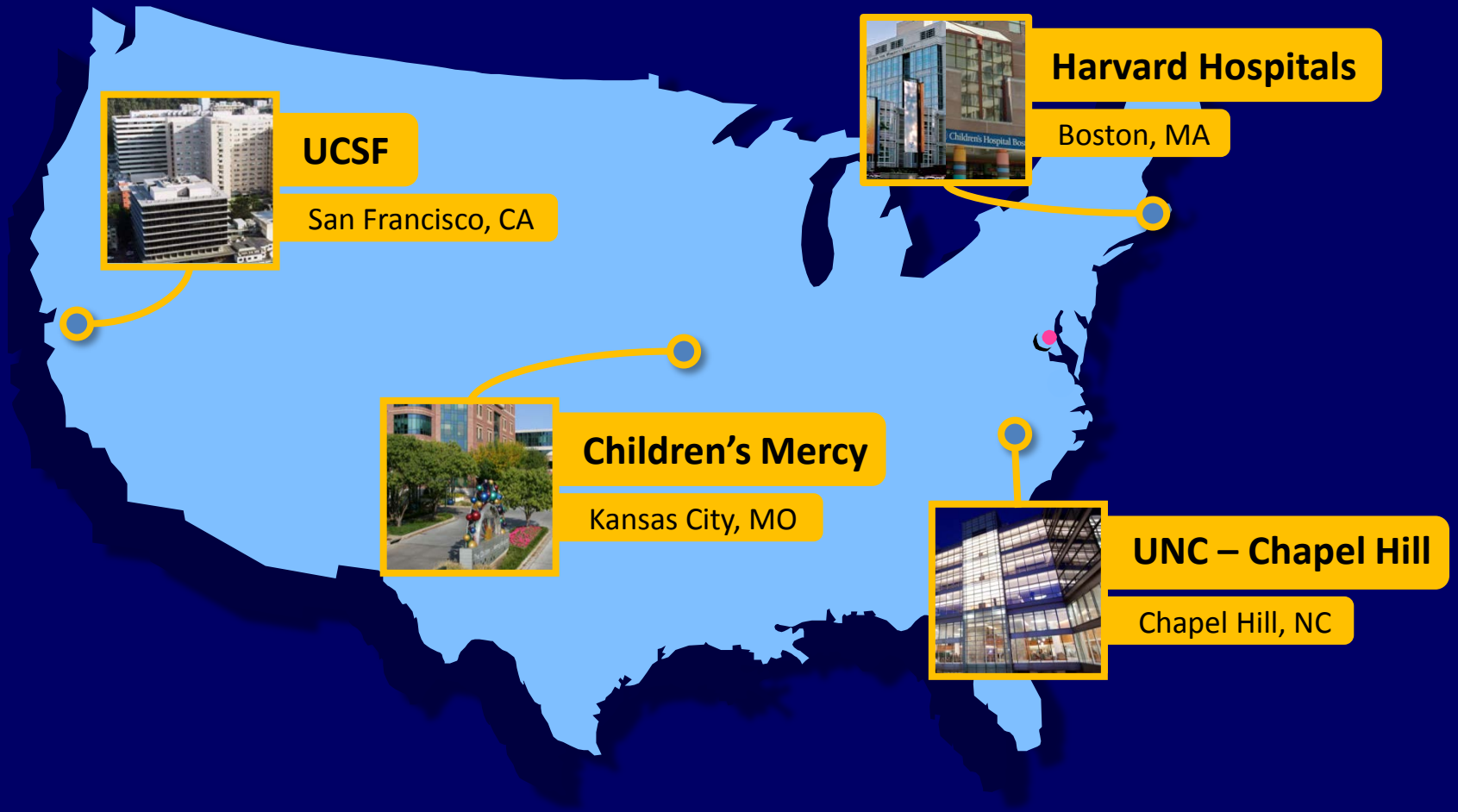
Everybody likes to blue-sky it when it comes to technology. Driverless cars! Fat-burning pills! Telepathic butlers! But the folks at Thomson Reuters Intellectual Property & Science do it for a living—and they do it with data.

What will the future hold?

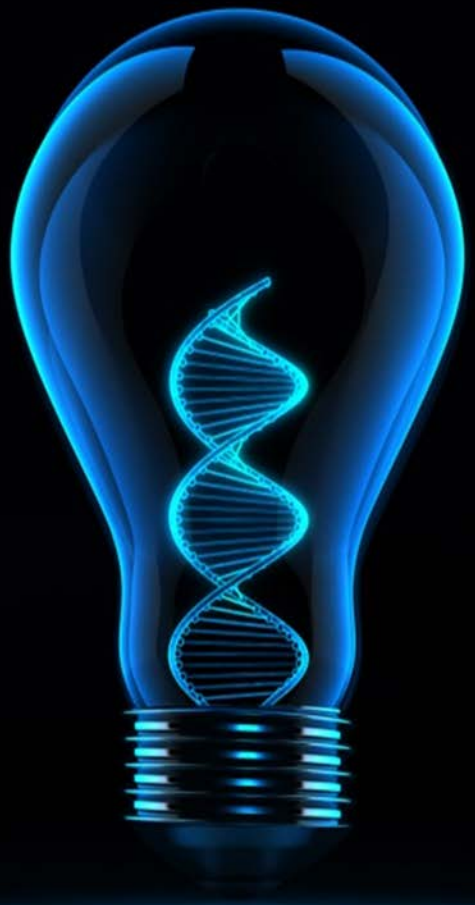
REB Images—Getty Images/Blend Images

Time (2014)

Newborn Sequencing In Genomic medicine and public HealTh (NSIGHT)



‘Hot Areas’ in Genomic Medicine



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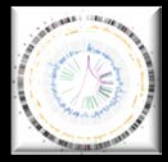


Pharmacogenomics

Rare Genetic Disease Diagnostics

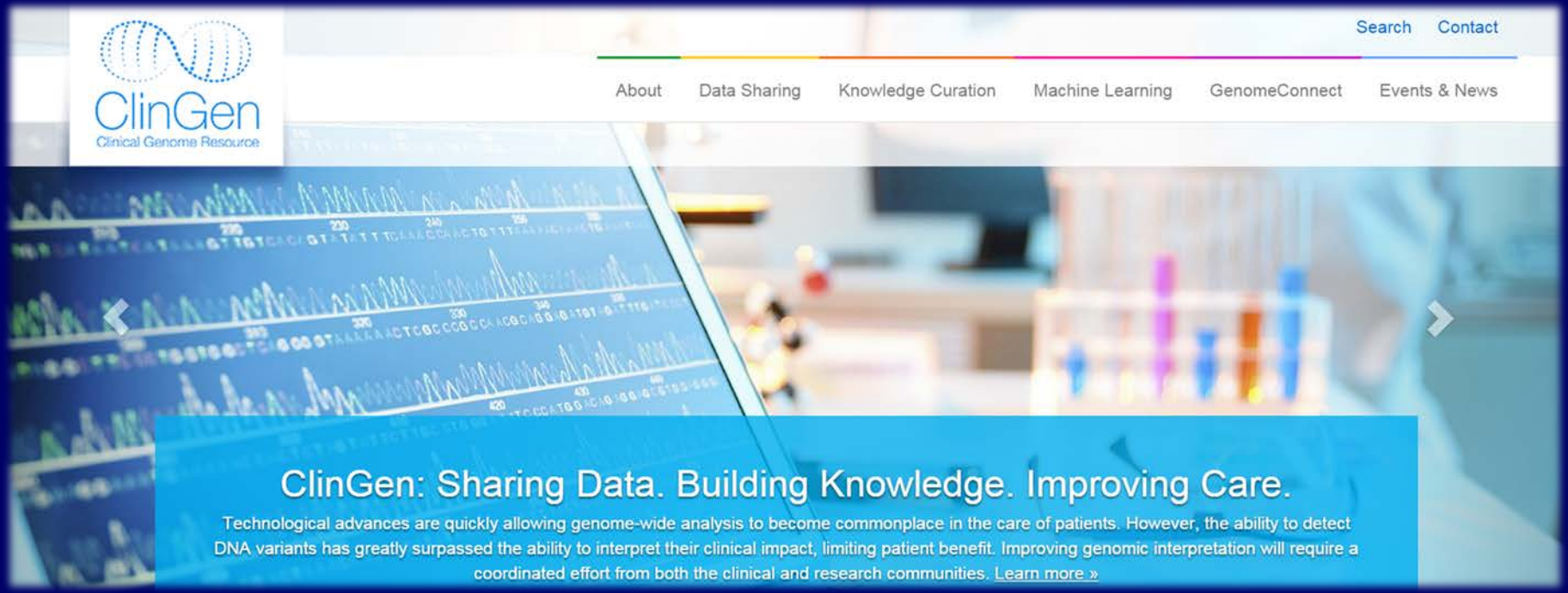
Newborn Genome Sequencing

Clinical Genomics Information Systems


GTACT
CAAGT
CTA
TAC
CCGA
TAGG
ATCC
TGG
ATCC
S. Myers

Clinical Genomics Information Systems

Clinical Genome Resource (ClinGen)



clinicalgenome.org

ClinGen — The Clinical Genome Resource

Heidi L. Rehm, Ph.D., Jonathan S. Berg, M.D., Ph.D., Lisa D. Brooks, Ph.D., Carlos D. Bustamante, Ph.D., James P. Evans, M.D., Ph.D., Melissa J. Landrum, Ph.D., David H. Ledbetter, Ph.D., Donna R. Maglott, Ph.D., Christa Lese Martin, Ph.D., Robert L. Nussbaum, M.D., Sharon E. Plon, M.D., Ph.D., Erin M. Ramos, Ph.D., Stephen T. Sherry, Ph.D., and Michael S. Watson, Ph.D., for ClinGen

***NEJM* (2015)**

Genomics and Society

NHGRI Extramural Research Program: *Circa 2016*

$1000 Genome
Technology Development Program

TCGA
The Cancer Genome Atlas

PAGE
Population Architecture using Genomics and Epidemiology

ENCODE
Encyclopedia of DNA Elements Project

GGR
Genomics of Gene Regulation

eMERGE
Electronic Medical Records and Genomics

PhenX
Consensus Measures for Phenotypes and eXposures

NoVa
Non-Coding Variants Program

CEGS
Centers of Excellence in Genomic Science

CSER
Clinical Sequencing Exploratory Research

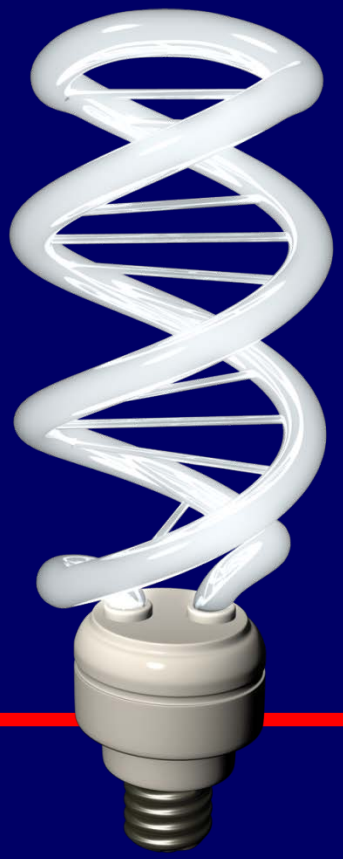
IGNITE
Implementing Genomics in Practice Network

CCDG
Centers for Common Disease Genomics

CMG
Centers for Mendelian Genomics

NSIGHT
Newborn Sequencing In Genomic medicine and public HealTh

ClinGen
Clinical Genome Resource



ELSI
Ethical, Legal, and Social Implications Program

CEERs
Centers for Excellence in ELSI Research

BD2K
Big Data to Knowledge Initiative

PMI
Precision Medicine Initiative

KOMP2
KOMP Phenotyping

HMP
Human Microbiome Project

GTEx
Genotype-Tissue Expression

UDN
Undiagnosed Diseases Network

Protein Capture Reagents

LINCS
Library of Integrated Network-based Cellular Signatures

H3Africa
Human Heredity and Health in Africa

Kids First
Gabriella Miller Pediatric Research Program

October 6, 2015

This month brought a historic 'odometer moment' for the field of genomics – October 1, 2015, marked the 25th anniversary of the launch of the Human Genome Project. I, for one, cannot believe a quarter-century has now passed since many of us started working on the Project. At the same time, it is truly incredible to think about how far genomics has progressed since that time. I thought the significance of this anniversary warranted making this topic the lead story in this month's *The Genomics Landscape*; in addition, I reflect on this important anniversary in a recent video interview now available on the NHGRI web site.

To subscribe, follow link from:

genome.gov/Director


NATIONAL HUMAN GENOME
RESEARCH INSTITUTE
Advancing human health
through genomics research