Genomica

Passato, presente e futuro della genomica applicata alla biomedicina

I. Historical Context for Genomics

II. Major Achievements since the Human Genome Project

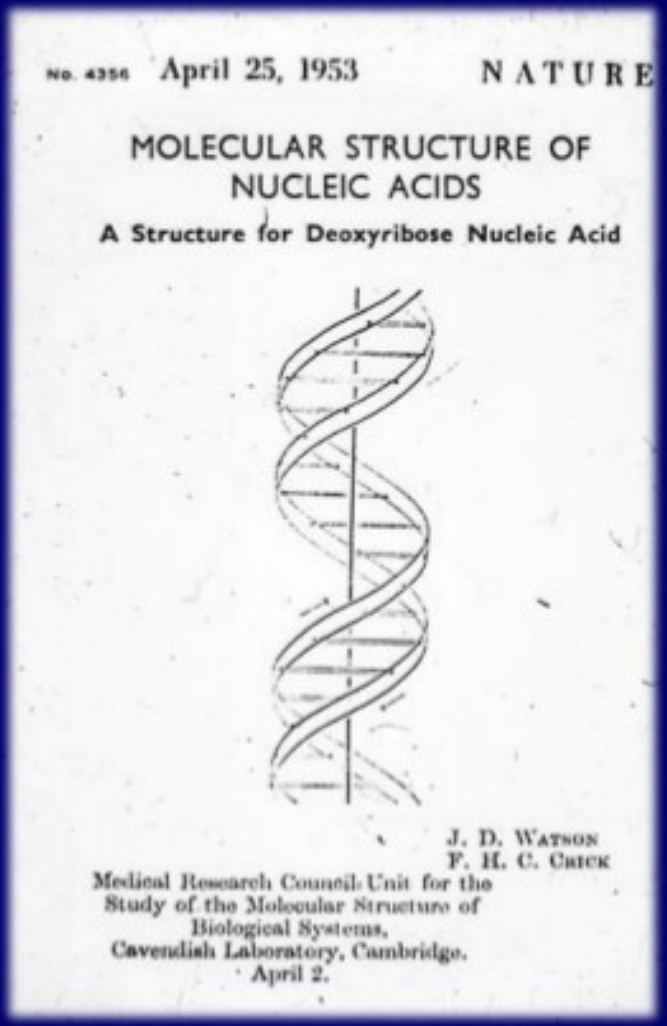
III. The Human Genomics Landscape: 2016 and Beyond

Foundational Milestones in Genetics & Genomics

Mendel

1865

April, 1953



No. 4356 April 25, 1953 NATURE

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

J. D. WATSON
F. H. C. CRICK

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems, Cavendish Laboratory, Cambridge.
April 2.

Discovery of Double-Helical Structure of DNA

1960's

First Letter	Second Letter: T	Second Letter: C	Second Letter: A	Second Letter: G	Third Letter
T	TTT, TTC: Phe; TTA, TTG: Leu	TCT, TCC, TCA, TCG: Ser	TAT, TAC: Tyr; TAA: Stop; TAG: Stop	TGT, TGC: Cys; TGA: Stop; TGG: Trp	T C A G
C	CTT, CTC, CTA, CTG: Leu	CCT, CCC, CCA, CCG: Pro	CAT, CAC: His; CAA, CAG: Gln	CGT, CGC, CGA, CGG: Arg	T C A G
A	ATT, ATC, ATA: Ile; ATG: Met	ACT, ACC, ACA, ACG: Thr	AAT, AAC: Asn; AAA, AAG: Lys	AGT, AGC: Ser; AGA, AGG: Arg	T C A G
G	GTT, GTC, GTA, GTG: Val	GCT, GCC, GCA, GCG: Ala	GAT, GAC: Asp; GAA, GAG: Glu	GGT, GGC, GGA, GGG: Gly	T C A G

The Genetic Code

The Origin of "Genomics": 1987

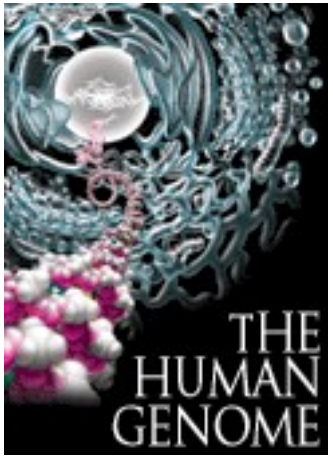
EDITORIAL

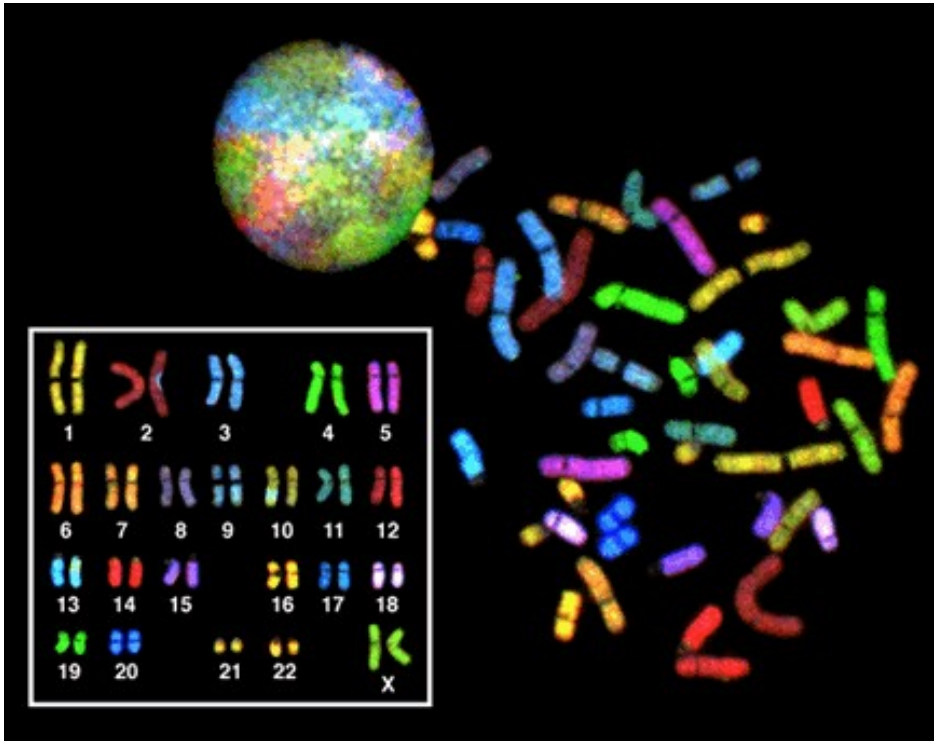
A New Discipline, A New Name, A New Journal

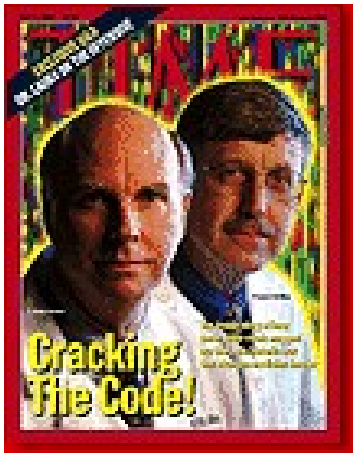
***Genomics* (1987)**

"For the newly developing discipline of [genome] mapping/sequencing (including the analysis of the information), we have adopted the term GENOMICS…

The Human Genome Project
1990-2003



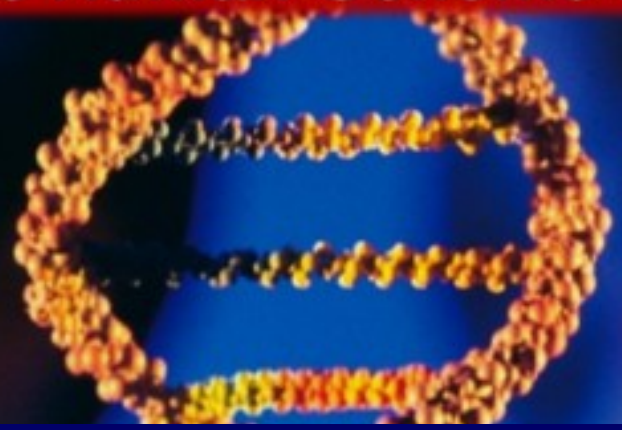




http://www.genome.gov/

A Quarter Century of Genomics

Human Genome Sequenced for First Time by the Human Genome Project



Twenty-five years of big biology

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

***Nature* (2015)**

Myriad Applications of Genomics

Agriculture

Ancestry

Livestock

Infectious Agents

Forensics

Bioenergy

Myriad Applications of Genomics

Health, Disease, & Medicine

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

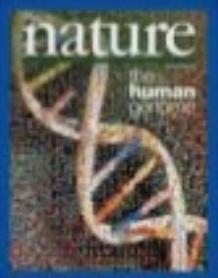
Human Genome Project

→ → ? → →

Realization of Genomic Medicine

Nature

Nature



2003

2011

February, 2011

PERSPECTIVE

Charting a course for genomic medicine from base pairs to bedside

Eric D. Green[1], Mark S. Guyer[2] & National Human Genome Research Institute[3]

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[1-3], genomics has become a mainstay of biomedical research. The scientific community's foresight in launching this ambitious project[4] is evident in the broad range of scientific advances that the HGP has enabled, as shown in Fig. 1 (see refs 5–62). Optimism about the potential contributions of genomics for improving human health has been fuelled by new insights about cancer[5–7], the molecular basis of inherited diseases (http://www.ncbi.nlm.nih.gov/sites/entrez?db=gene; www.genome.gov/GWAStudies) and the clinical significance of variation in disease[8], some of which have already led to new therapies[9–11]. Other advances are directly changing medical practice (for example, microarrays are now used for clinical detection of genomic imbalances[12] and pharmacogenomic testing is routinely performed before administration of certain medications[13]). Together, these achievements (see accompanying papers[14]) document that genomics is contributing to a better understanding of human biology and to improving human health.

As it did eight years ago[15], 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 led to an updated vision that focuses on understanding human biology and the dynamic properties and treatment of human disease, including consideration of the implications of these 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.

The 2011 vision for genomics is organized around five thematic areas ranging 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. As the years flow, 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[16–18]), and clinical discoveries can lead back to understanding disease on even basic biology.

The past decade has seen genomics contribute fundamental knowledge about biology and to particulars of disease. Further deepening this understanding will accelerate the transition to genomic medicine (clinical care based on genomic information). But significant challenges must be overcome quickly. Although genomics has already begun to improve diagnostics and treatments in a few circumstances, profound improvements in the effectiveness of the ability to connect molecularly to 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 issues 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 genomic biology. Continued acquisition of basic knowledge about genome structure and function will be needed to illuminate further these complexities (Fig. 2). The construction 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 humans and model organisms.

Genomic studies of the genes and pathways associated with human-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[19] and the International HapMap Project[20] (http://hapmap.ncbi.nlm.nih.gov), and is ongoing with the 1000 Genomes Project[21] (http://www.1000genomes.org).

Over the past decade, these catalogues have been critical for the discovery of the specific genes for roughly 1,000 Mendelian (monogenic) diseases

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

[1]National Human Genome Research Institute, National Institutes of Health, 31 Center Dr. MSC 2033, Bethesda, Maryland 20892-2033, USA. [2]NIH Distinguished Investigator and Past Director of the NHGRI.

New NHGRI Vision for Genomics Published

Long-Range Planning

Event: A Decade with the Human Genome Sequence: Charting a Course for Genomic Medicine

Past Long-Range Planning

White Papers: The 2008-2011 Planning Process

The Strategic Plan

Charting a course for genomic medicine from base pairs to bedside

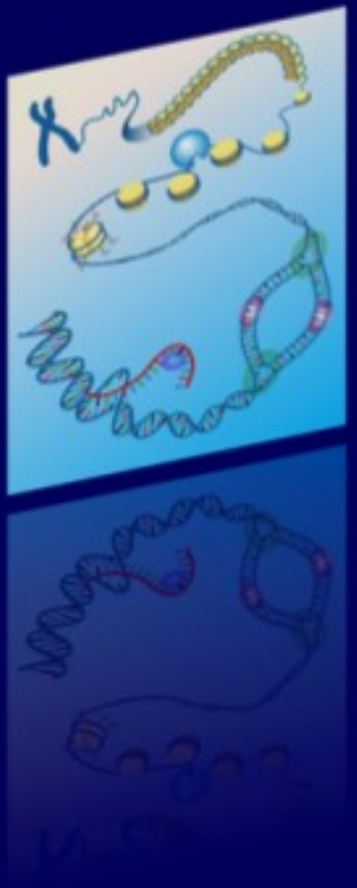
On February 10, 2011, *Nature* magazine published the National Human Genome Research Institute's (NHGRI) stra future of human genome research called *Charting a course for genomic medicine from base pairs to bedside*. This was developed in consultation with leading genome researchers over more than two years and is intended to inspir contribute to advancing genomic understanding, especially as other National Institutes of Health (NIH) institutes and genomic technologies on the diseases they study.

To celebrate the 10th anniversary of the first analysis of the draft human genome, and the launch of the new strate

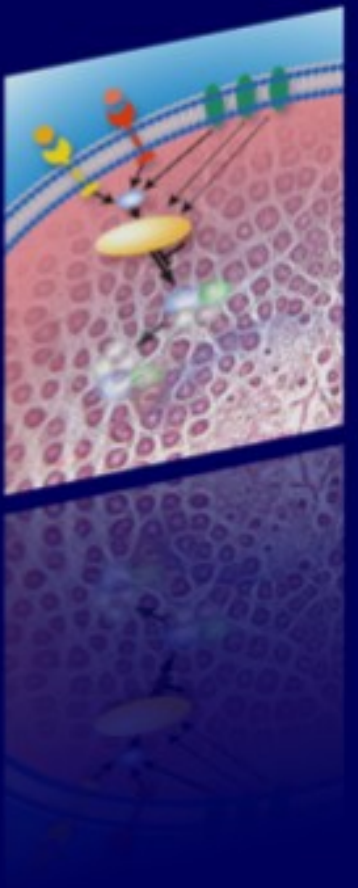
Five Domains of Genomics Research

Understanding the Structure of Genomes

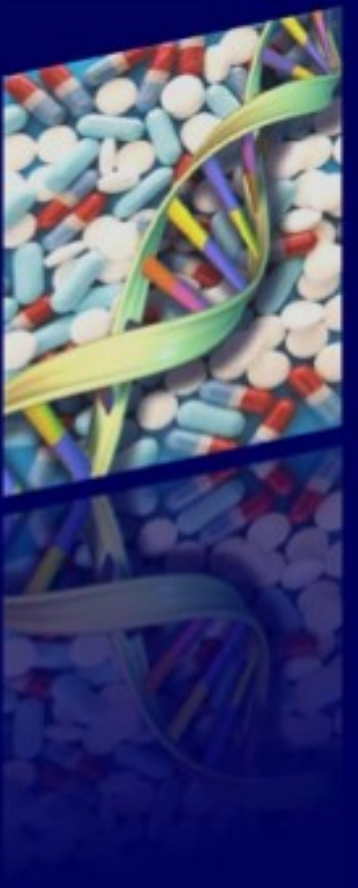
Understanding the Biology of Genomes



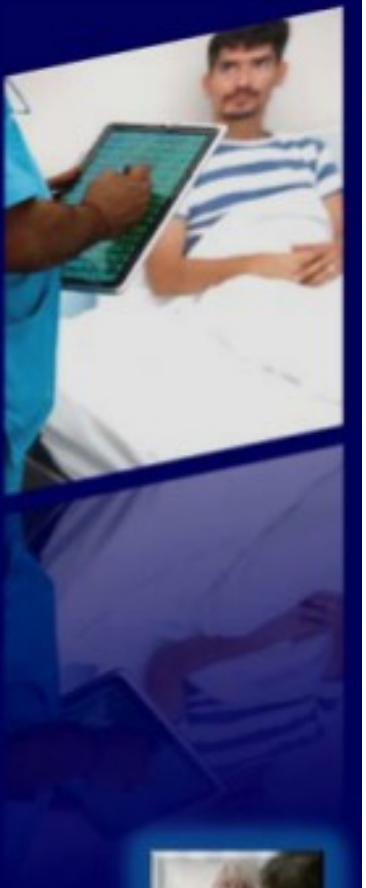
Understanding the Biology of Disease



Advancing the Science of Medicine



Improving the Effectiveness of Healthcare



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

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

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[2], 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 evolu-

"…'technological leaps' that seem so far off as to be almost fictional but which, if they could be achieved, would revolutionize biomedical research and clinical practice.

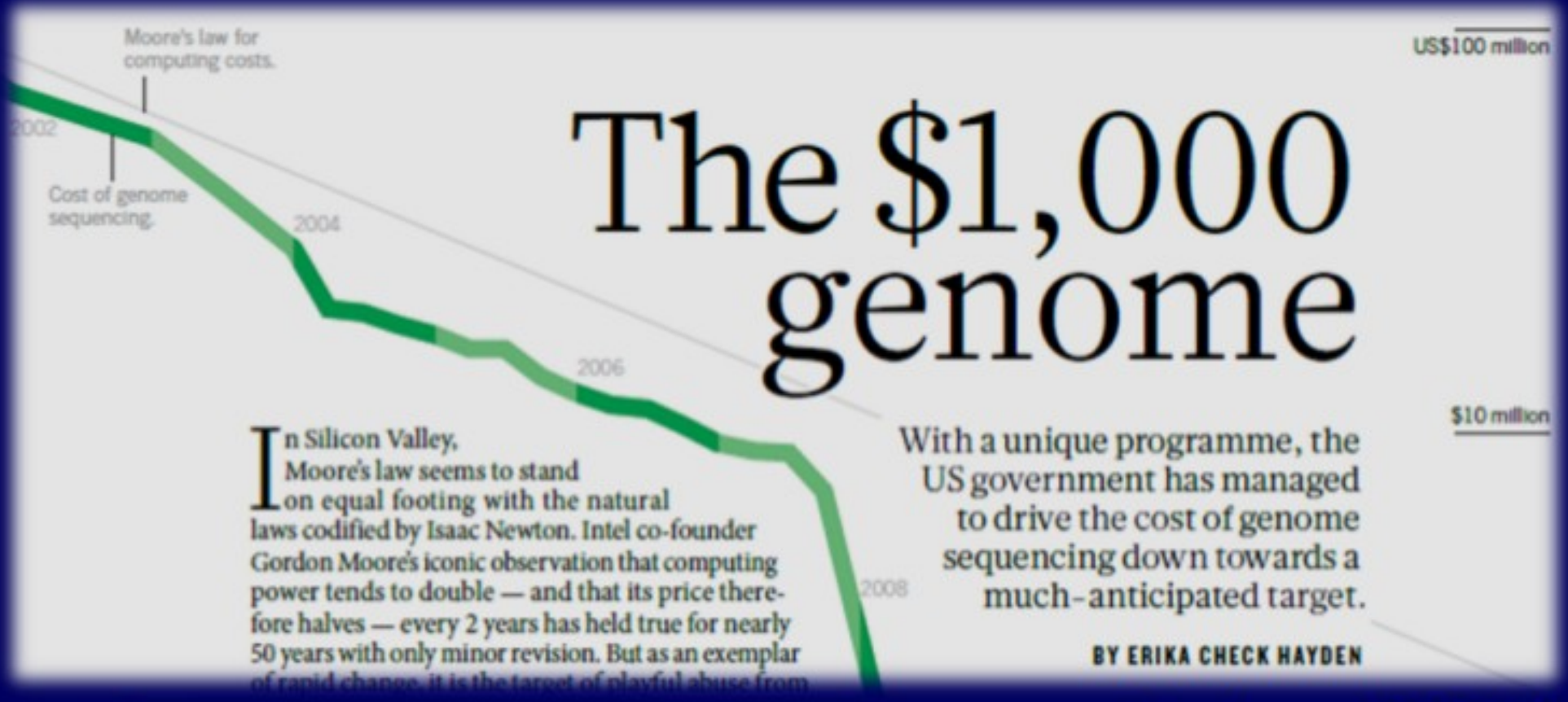
[For example,]…the ability to sequence DNA at costs that are lower by four to five orders of magnitude than the current cost, allowing a human genome to be sequenced for $1,000 or less."

Human Genome Sequence

~$1,000,000,000

~$1,000

"The $1000 Genome"



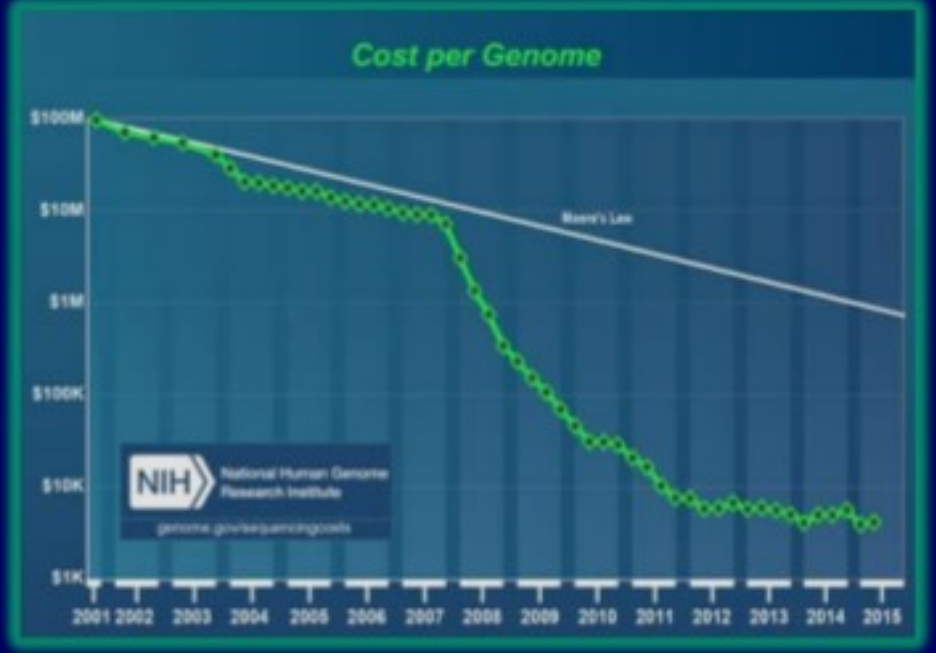
The $1,000 genome

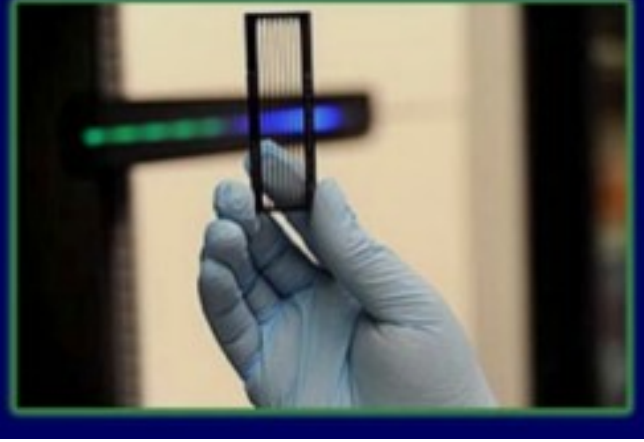
With a unique programme, the US government has managed to drive the cost of genome sequencing down towards a much-anticipated target.

BY ERIKA CHECK HAYDEN

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

***Nature* (2014)**





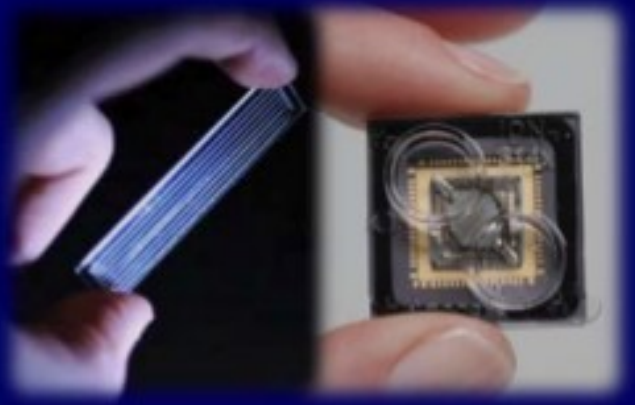
Sequencing a Human Genome

Human Genome Project (1st Sequence)

~$1B

~6-8 years

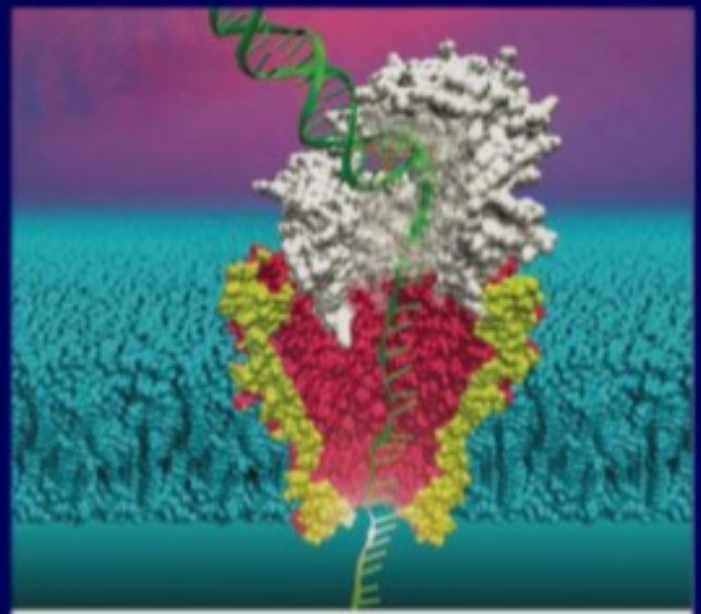
Today



~$2-3K

~1-3 days

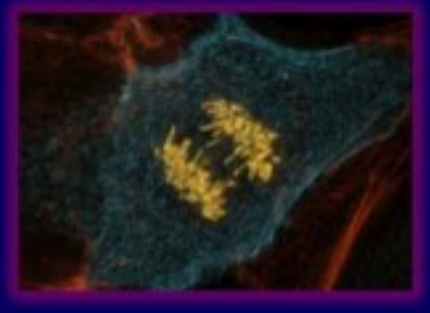
And Yet Newer Technologies…



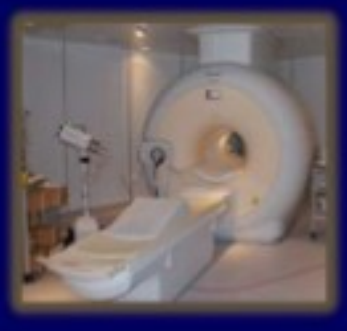
Search for Pore-fection

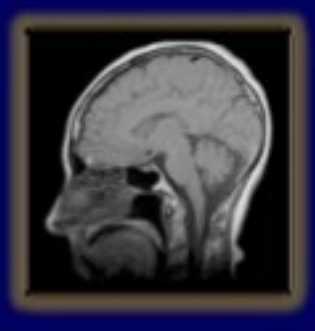
Technological Advances Drive Science

Astronomy



Cell Biology





Radiology

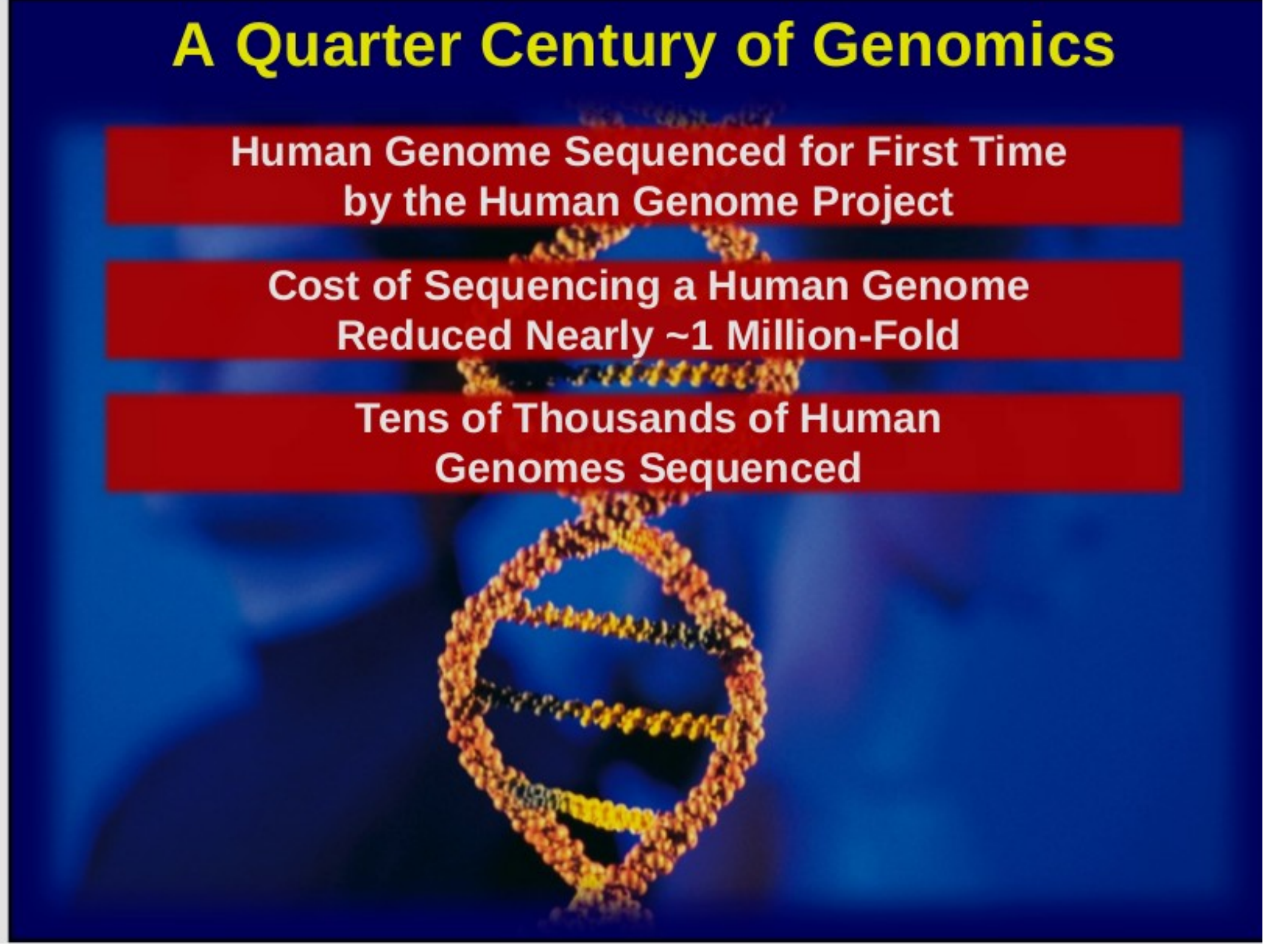
Genomics

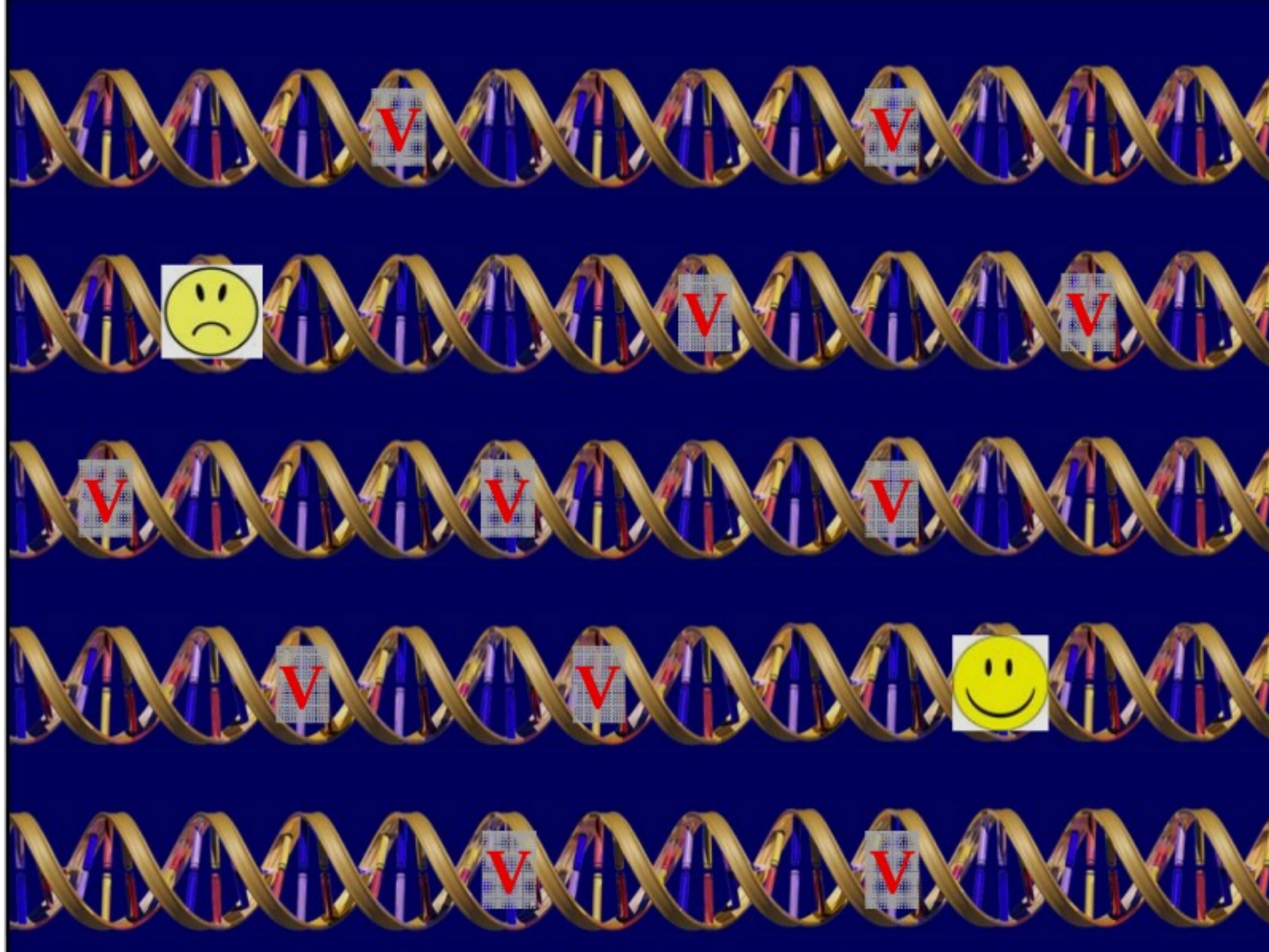
A Quarter Century of Genomics

Human Genome Sequenced for First Time
by the Human Genome Project

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

Tens of Thousands of Human
Genomes Sequenced

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A haplotype map of the human genome

The International HapMap Consortium*

Inherited genetic variation has a critical but as yet largely uncharacterized role in human disease. Here we report a public database of common variation in the human genome: more than one million single nucleotide polymorphisms (SNPs) for which accurate and complete genotypes have been obtained in 269 DNA samples from four populations, including ten 500-kilobase regions in which essentially all information about common DNA variation has been extracted. These data document the generality of recombination hotspots, a block-like structure of linkage disequilibrium and low haplotype diversity, leading to substantial correlations of SNPs with many of their neighbours. We show how the HapMap resource can guide the design and analysis of genetic association studies, shed light on structural variation and recombination, and identify loci that may have been subject to natural selection during human evolution.

2005

A second generation human haplotype map of over 3.1 million SNPs

The International HapMap Consortium*

We describe the Phase II HapMap, which characterizes over 3.1 million human single nucleotide polymorphisms (SNPs) genotyped in 270 individuals from four geographically diverse populations and includes 25–35% of common SNP variation in the populations surveyed. The map is estimated to capture untyped common variation with an average maximum r^2 of between 0.9 and 0.96 depending on population. We demonstrate that the current generation of commercial genome-wide genotyping products captures common Phase II SNPs with an average maximum r^2 of up to 0.8 in African and up to 0.95 in non-African populations, and that potential gains in power in association studies can be obtained through imputation. These data also reveal novel aspects of the structure of linkage disequilibrium. We show that 10–30% of pairs of individuals within a population share at least one region of extended genetic identity arising from recent ancestry and that up to 1% of all common variants are untaggable, primarily because they lie within recombination hotspots. We show that recombination rates vary systematically around genes and between genes of different function. Finally, we demonstrate increased differentiation at non-synonymous, compared to synonymous, SNPs, resulting from systematic differences in the strength or efficacy of natural selection between populations.

2007

Integrating common and rare genetic variation in diverse human populations

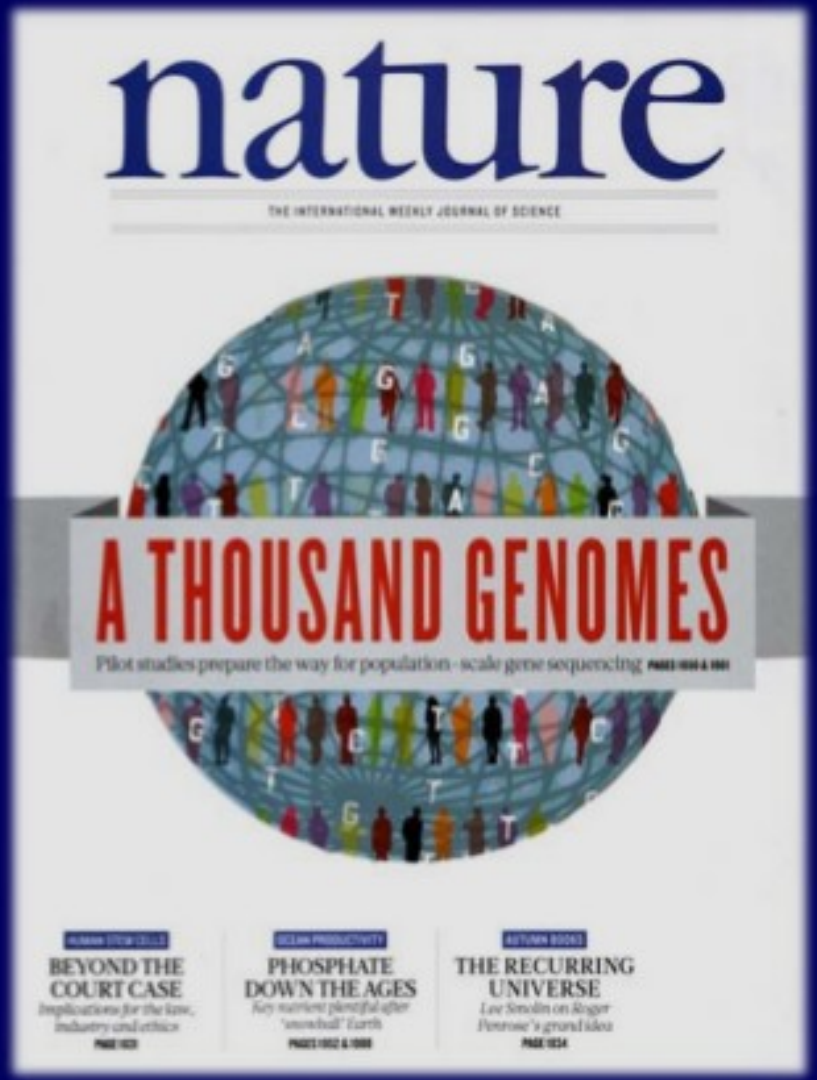
The International HapMap 3 Consortium*

Despite great progress in identifying genetic variants that influence human disease, most inherited risk remains unexplained. A more complete understanding requires genome-wide studies that fully examine less common alleles in populations with a wide range of ancestry. To inform the design and interpretation of such studies, we genotyped 1.6 million common single nucleotide polymorphisms (SNPs) in 1,184 reference individuals from 11 global populations, and sequenced ten 100-kilobase regions in 692 of these individuals. This integrated data set of common and rare alleles, called 'HapMap 3', includes both SNPs and copy number polymorphisms (CNPs). We characterized population-specific differences among low-frequency variants, measured the improvement in imputation accuracy afforded by the larger reference panel, especially in imputing SNPs with a minor allele frequency of ~5%, and demonstrated the feasibility of imputing newly discovered CNPs and SNPs. This expanded public resource of genome variants in global populations supports deeper interrogation of genomic variation and its role in human disease, and serves as a step towards a high-resolution map of the landscape of human genetic variation.

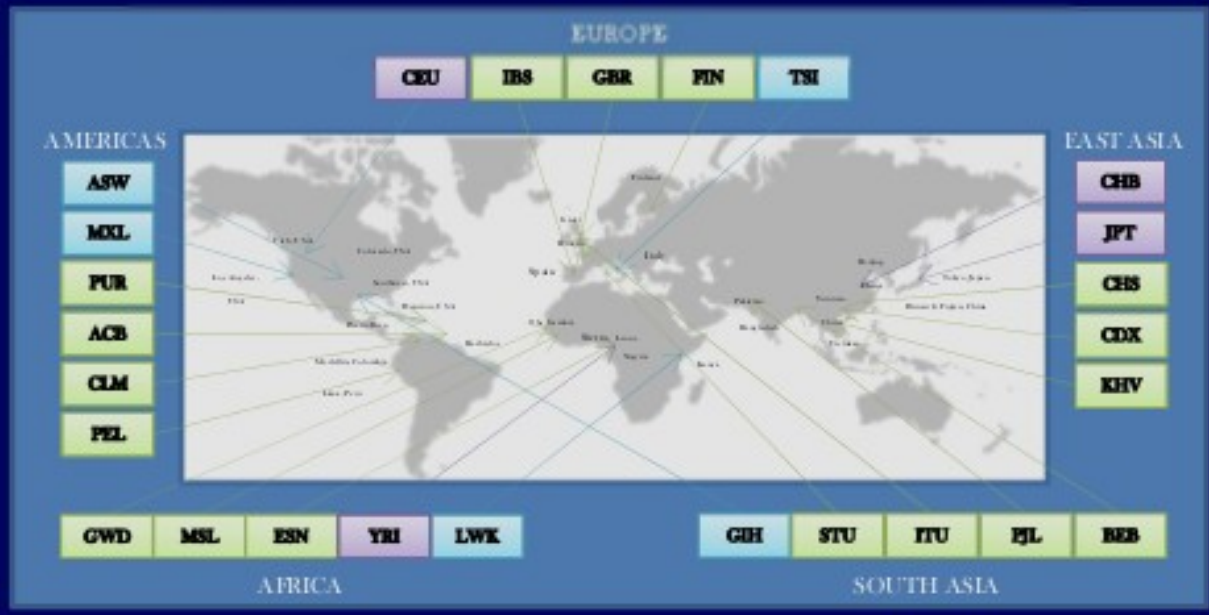
2010

1000 Genomes

A Deep Catalog of Human Genetic Variation



Nature (2010)

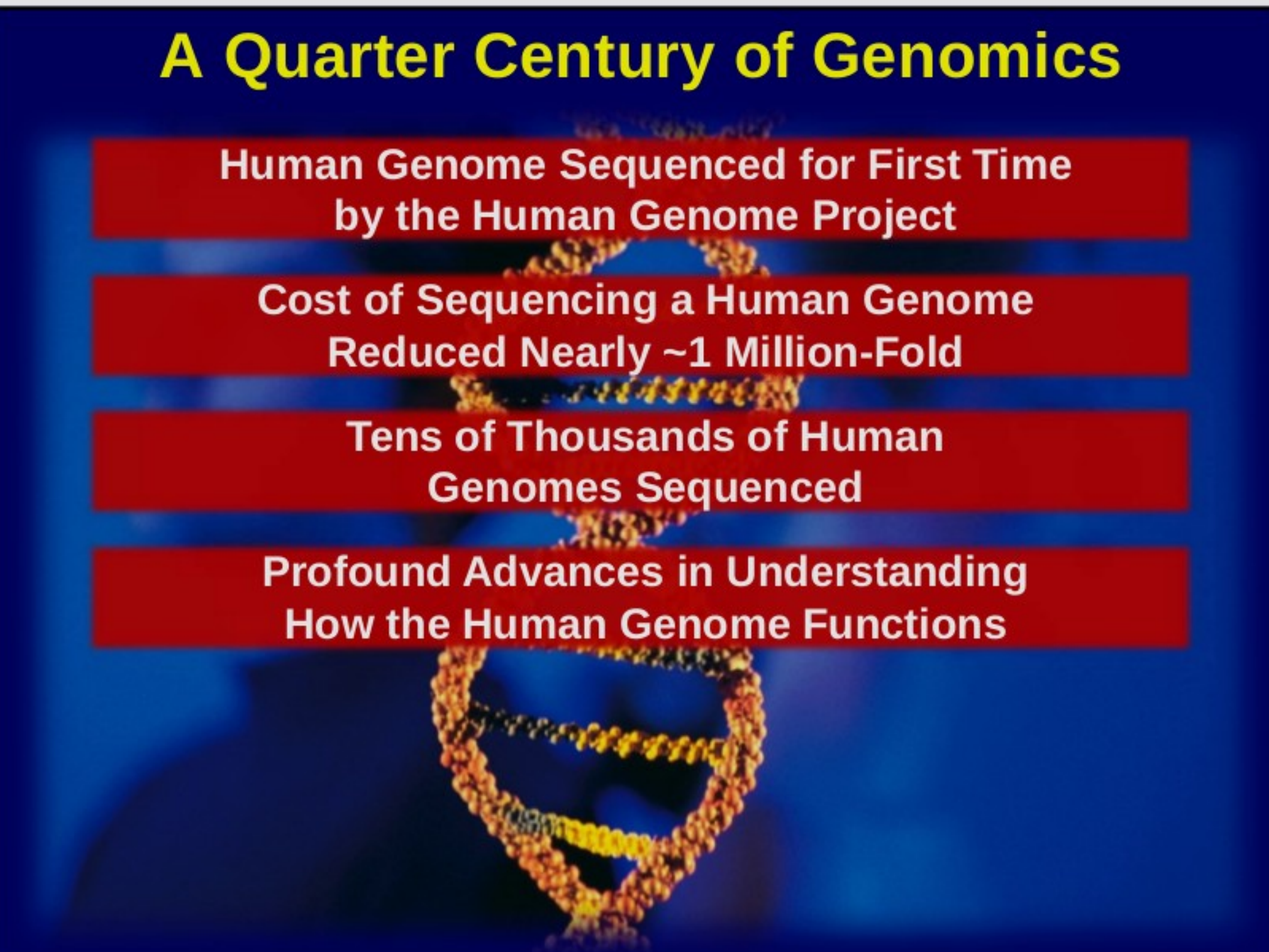


2535 Humans, 26 Populations

Your Genome: By the Numbers

- ~6B nucleotides
- ~3-5M single-nucleotide variants
  - ~150K not in databases
  - ~60 not in either parent

A Quarter Century of Genomics



Human Genome Sequenced for First Time
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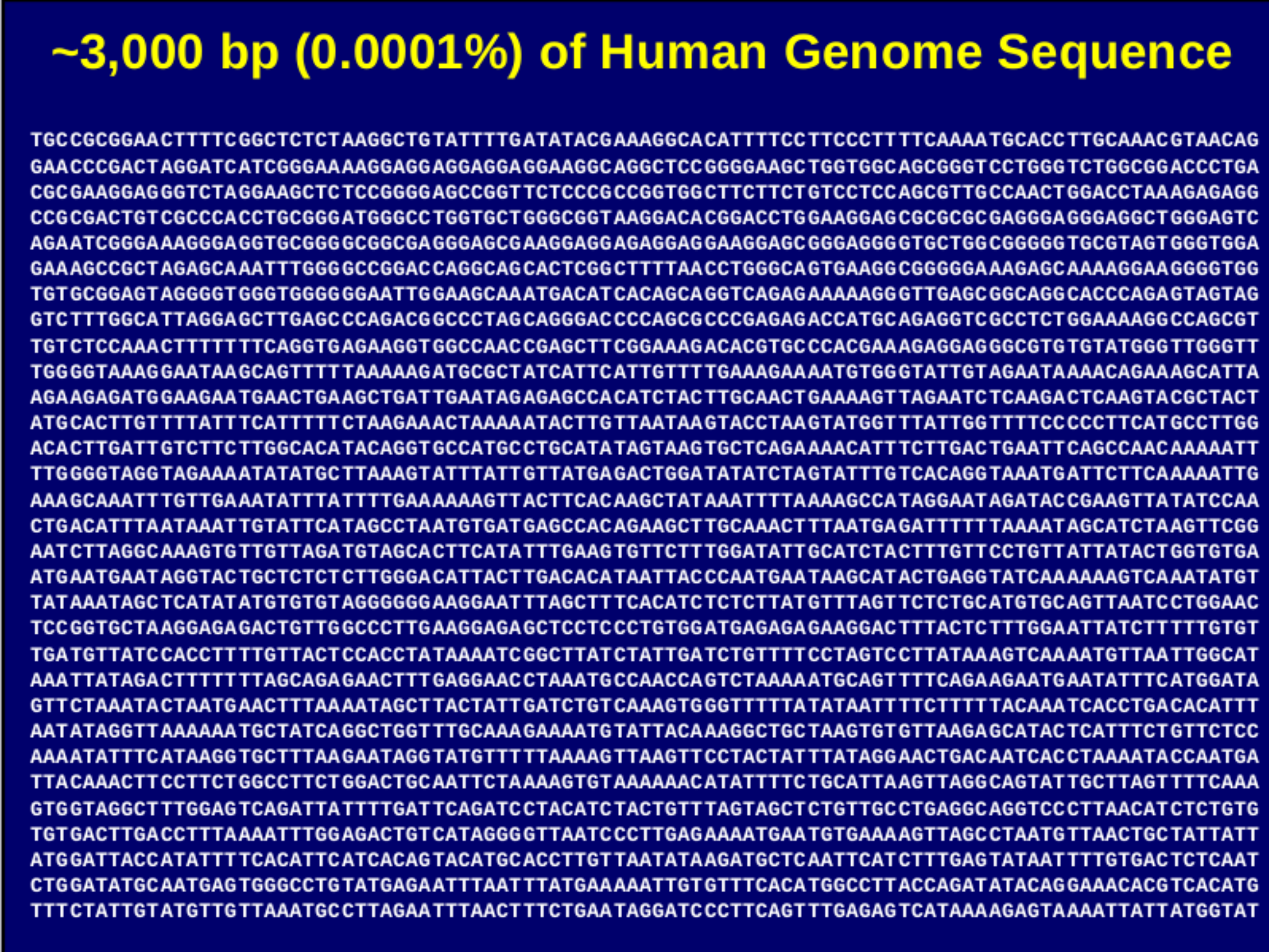
Cost of Sequencing a Human Genome
Reduced Nearly ~1 Million-Fold

Tens of Thousands of Human
Genomes Sequenced

Profound Advances in Understanding
How the Human Genome Functions

~3,000 bp (0.0001%) of Human Genome Sequence



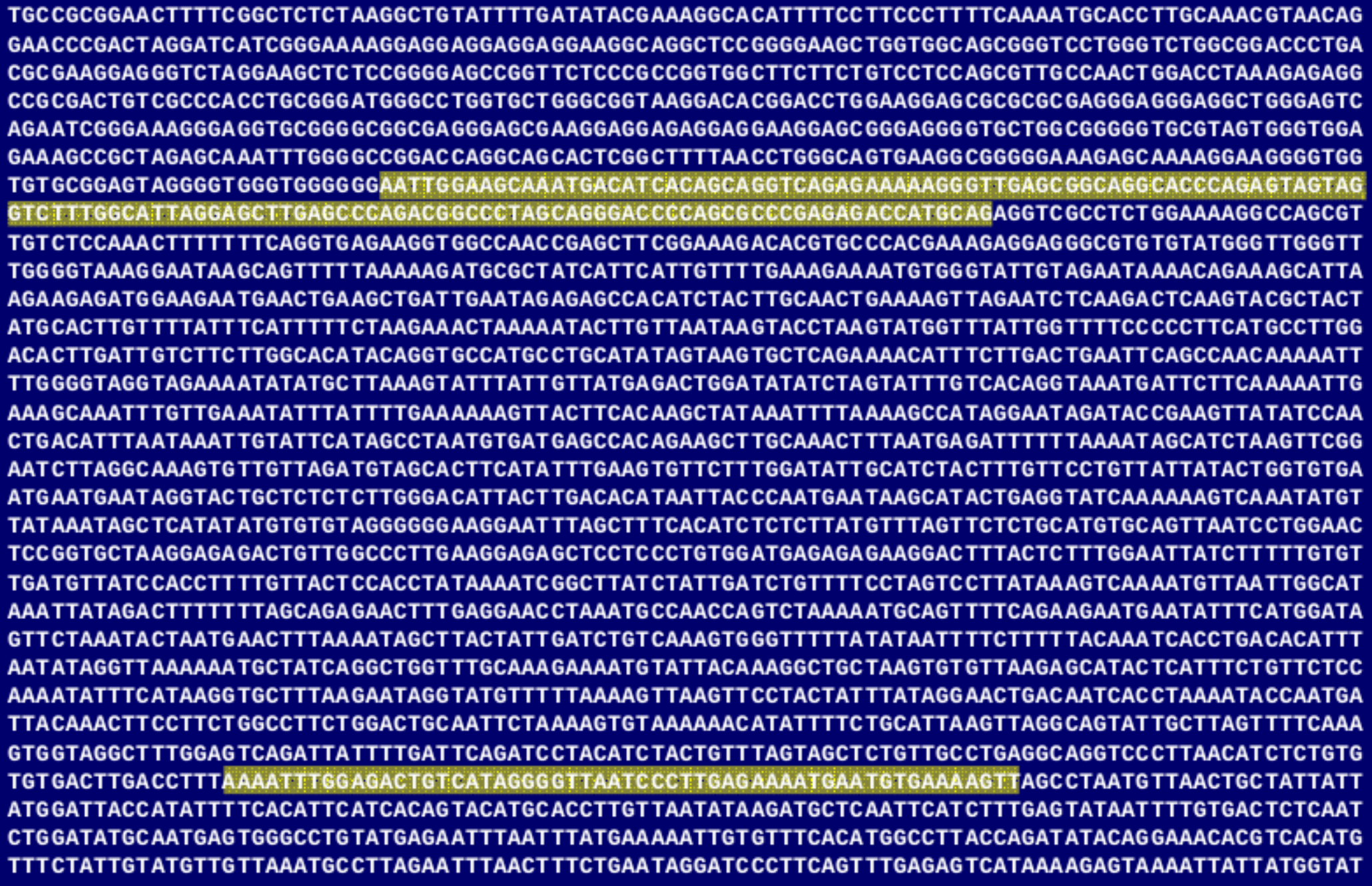
Coding Sequences (i.e., Genes)

Second Letter

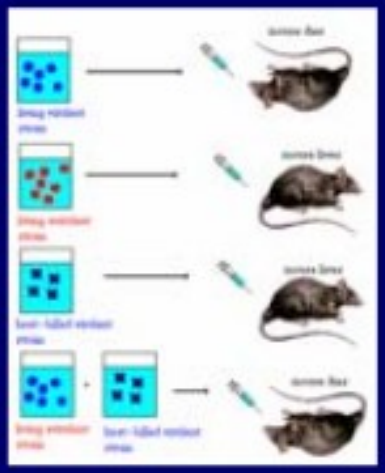
First Letter	T	C	A	G	Third Letter
T	TTT Phe TTC Phe TTA Leu TTG Leu	TCT Ser TCC Ser TCA Ser TCG Ser	TAT Tyr TAC Tyr TAA Stop TAG Stop	TGT Cys TGC Cys TGA Stop TGG Trp	T C A G
C	CTT Leu CTC Leu CTA Leu CTG Leu	CCT Pro CCC Pro CCA Pro CCG Pro	CAT His CAC His CAA Gln CAG Gln	CGT Arg CGC Arg CGA Arg CGG Arg	T C A G
A	ATT Ile ATC Ile ATA Ile ATG Met	ACT Thr ACC Thr ACA Thr ACG Thr	AAT Asn AAC Asn AAA Lys AAG Lys	AGT Ser AGC Ser AGA Arg AGG Arg	T C A G
G	GTT Val GTC Val GTA Val GTG Val	GCT Ala GCC Ala GCA Ala GCG Ala	GAT Asp GAC Asp GAA Glu GAG Glu	GGT Gly GGC Gly GGA Gly GGG Gly	T C A G

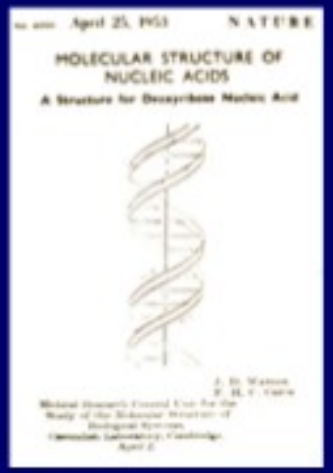
The Genetic Code

~3,000 bp (0.0001%) of Human Genome Sequence



Foundational Milestones in Genetics & Genomics





Darwin *1859*

Mendel *1865*

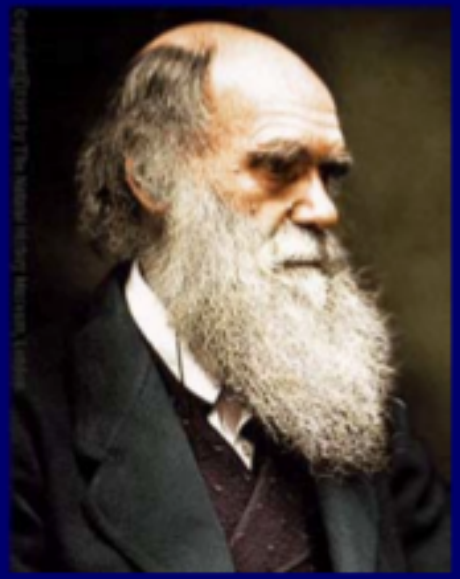
Miescher *1871*

Avery *1944*

Watson & Crick *1953*

"It is not the strongest of the species that survives, nor the most intelligent that survives. It is the one that is the most adaptable to change."

(Attributed to Darwin)



Charles Darwin (1809-1882)

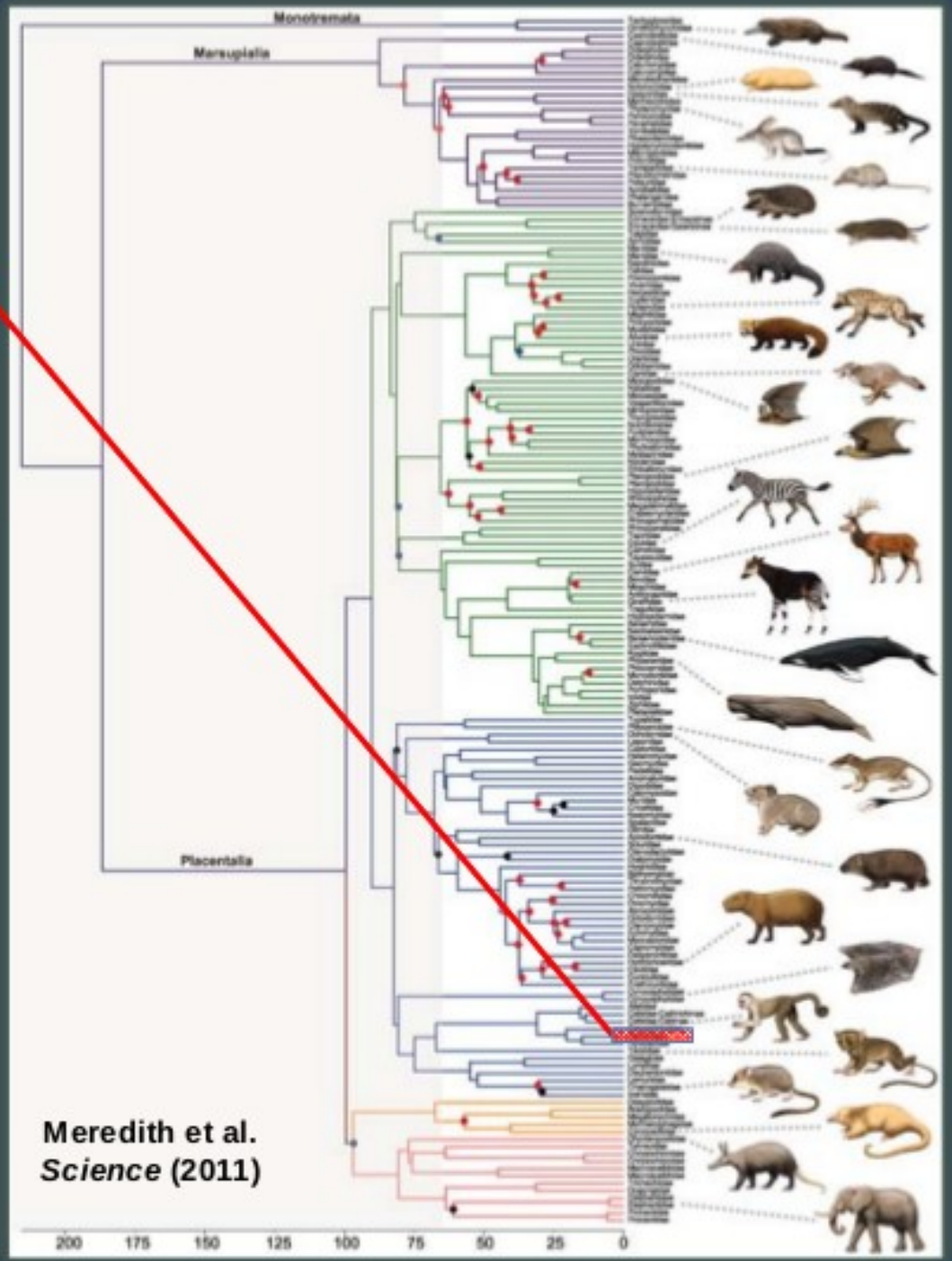
"For the last three and a half billion years, evolution has been taking notes."

— Eric Lander

Comparative Genome Sequencing





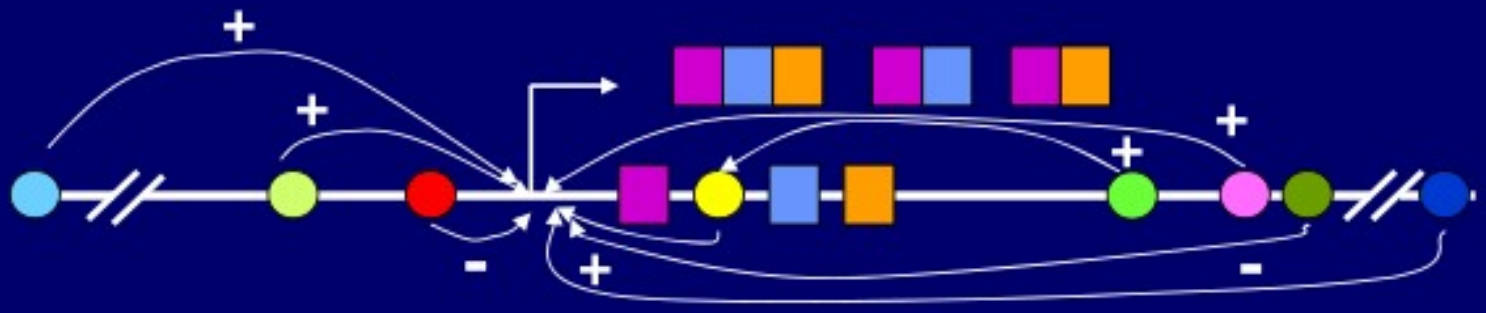






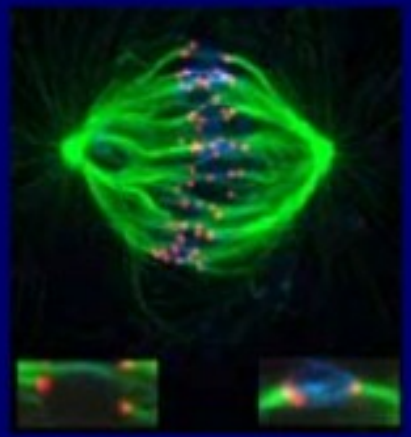
~3,000 bp (0.0001%) of Human Genome Sequence

Non-Coding Functional Sequences

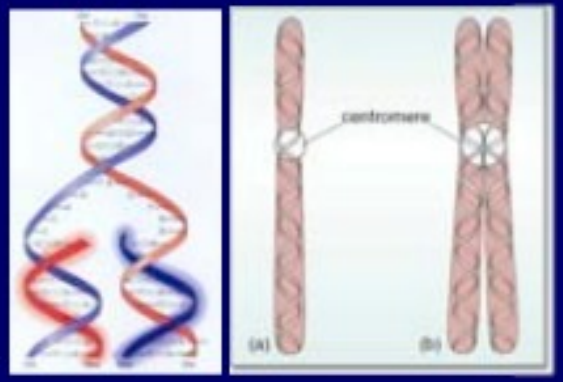


Gene Regulation

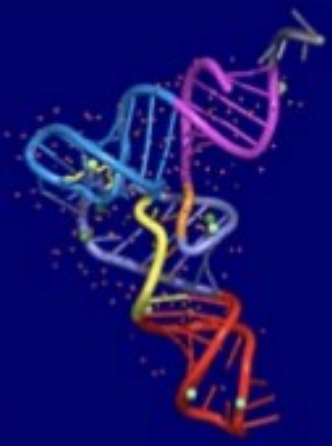
Chromosome Packaging



Chromosome Segregation



Chromosome Replication

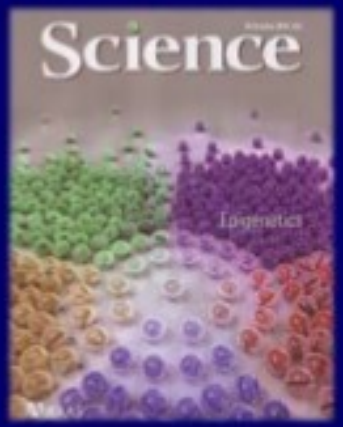


Non-Coding RNAs

?

~3,000 bp (0.0001%) of Human Genome Sequence

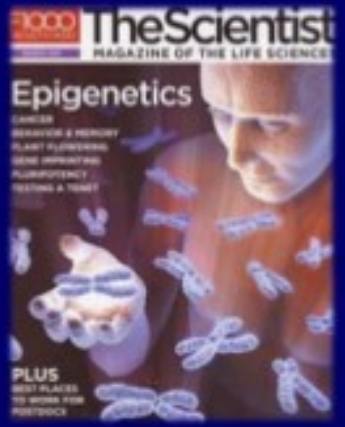
The Epigenomics Landscape

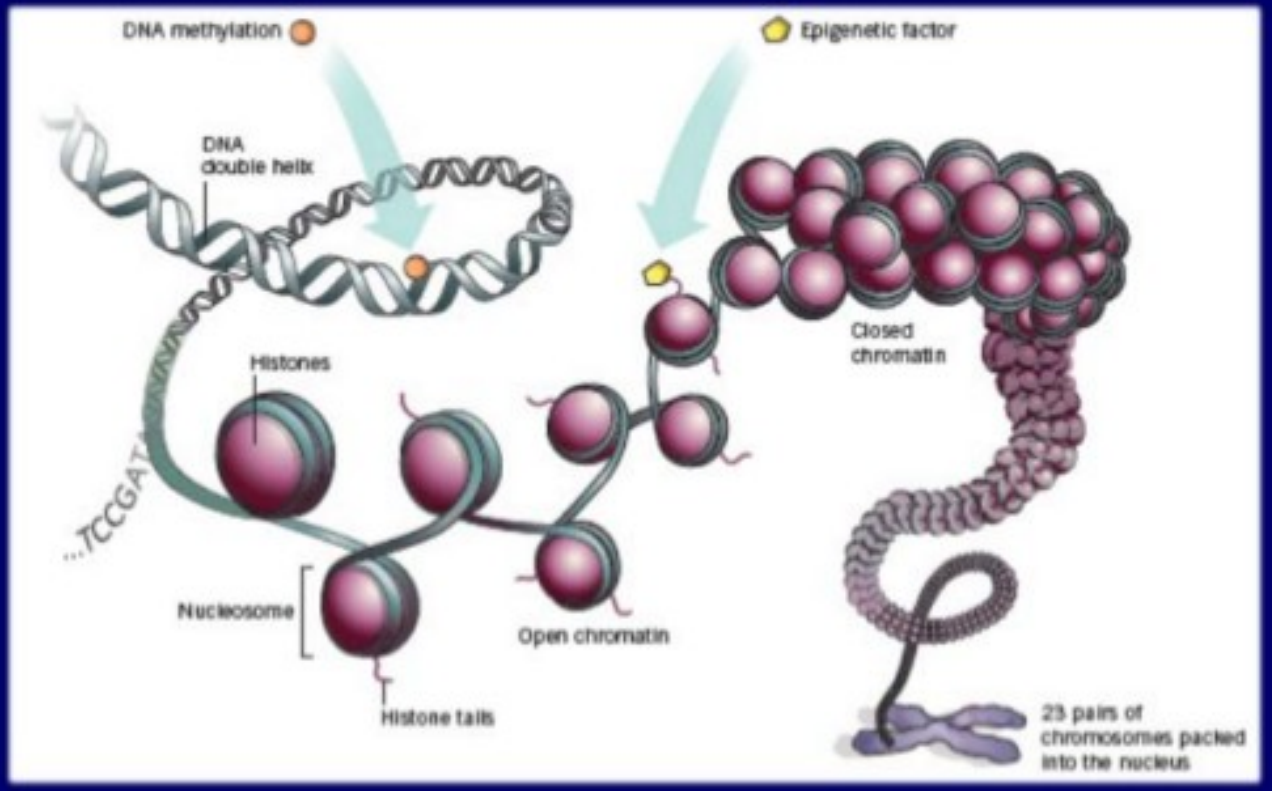


TECHNOLOGY FEATURE

READING THE SECOND GENOMIC CODE

Nature (2012)



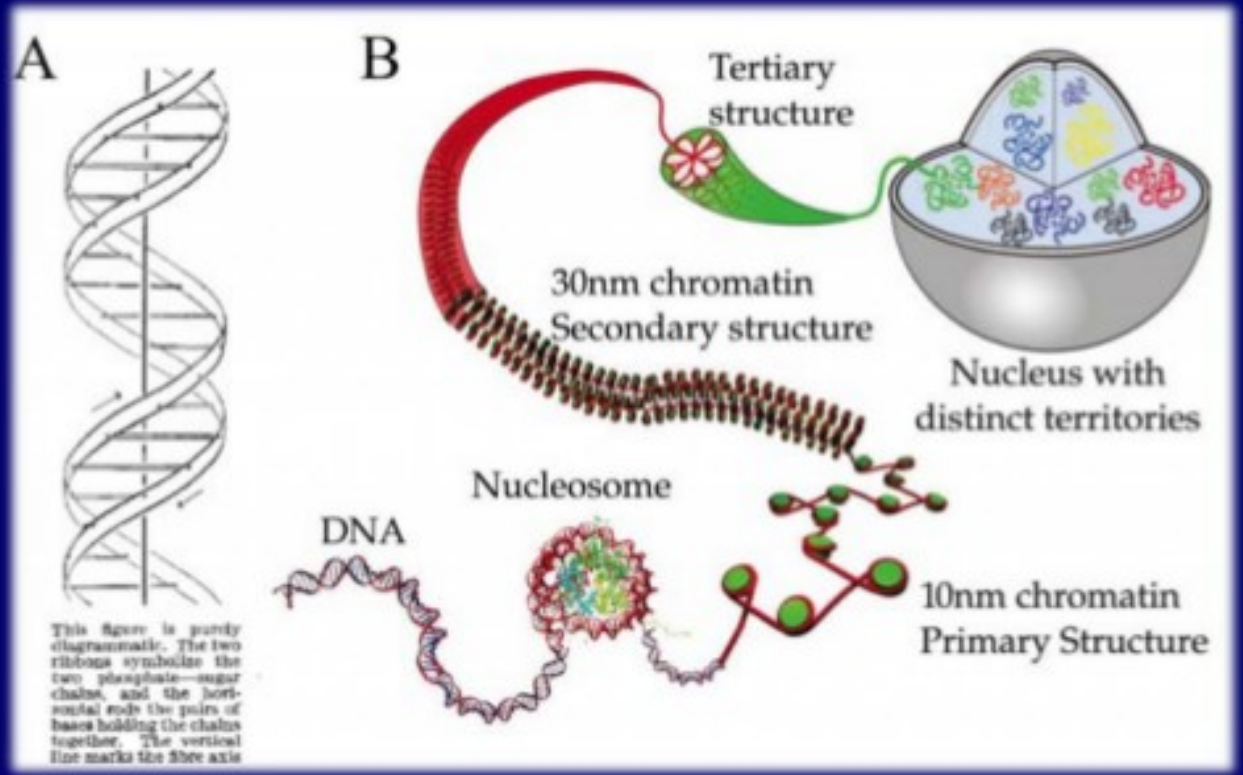


TECHNOLOGY FEATURE

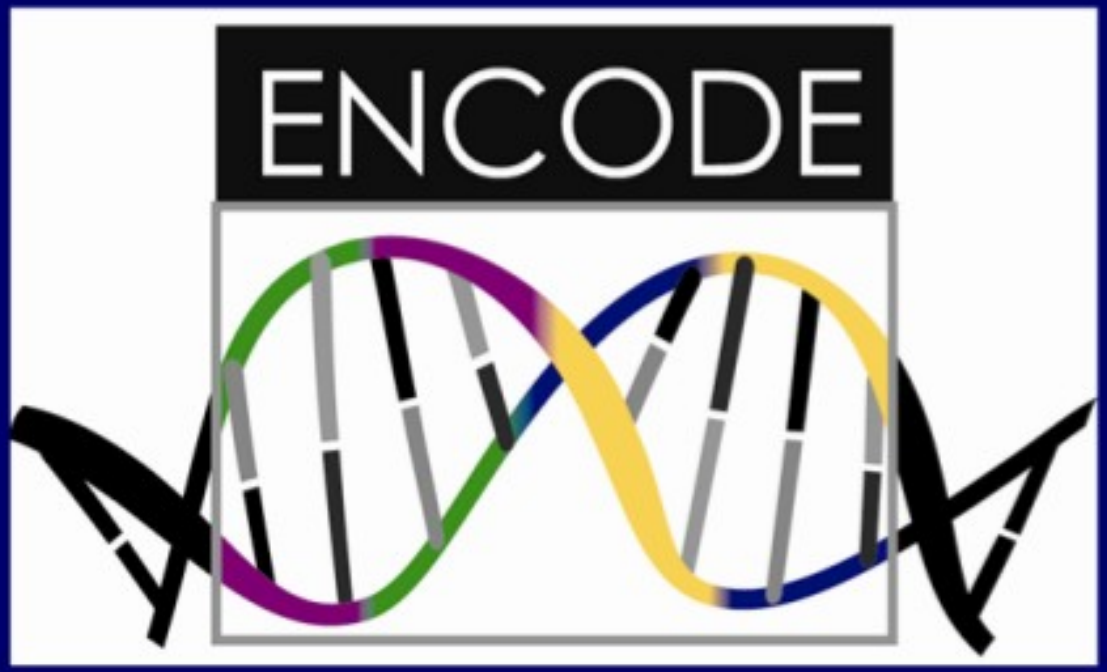
GENOMES IN THREE DIMENSIONS

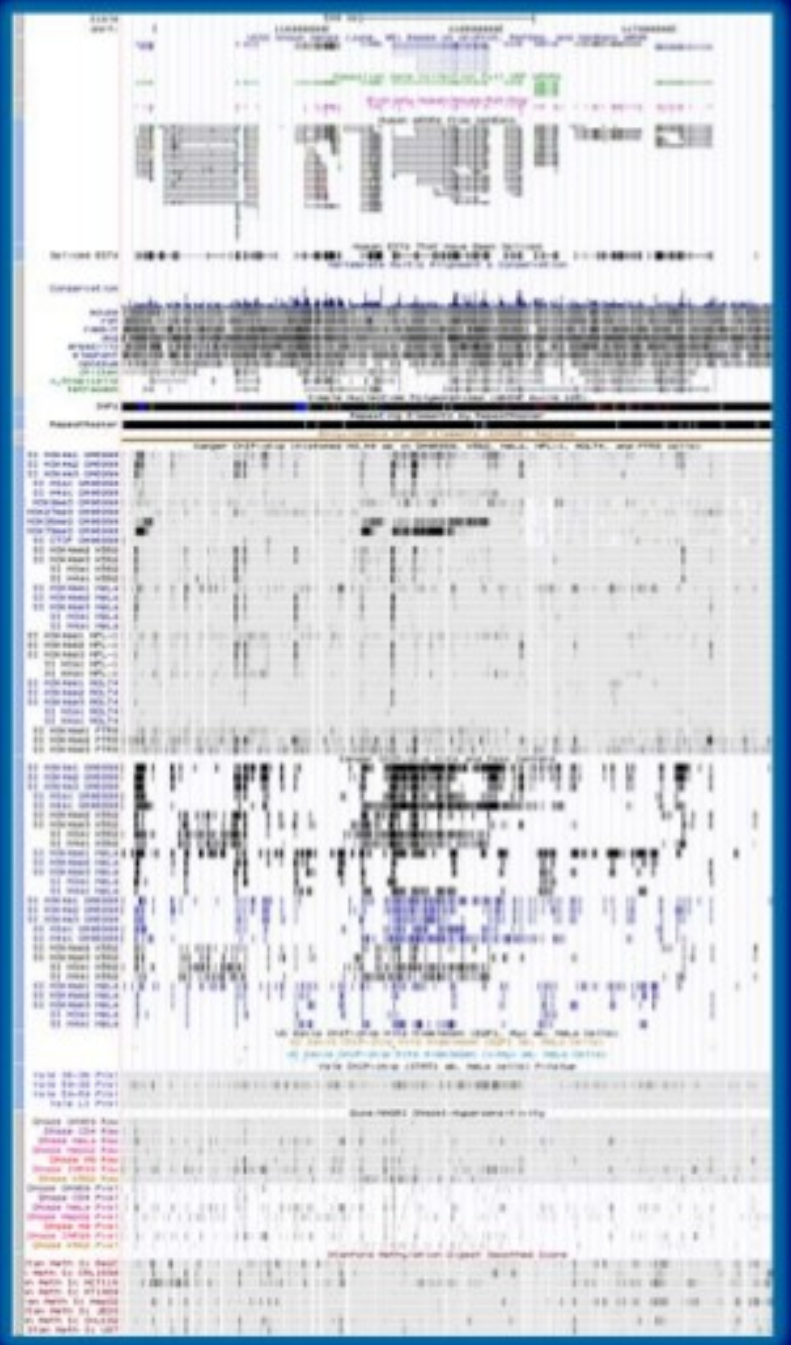
A DNA sequence isn't enough; to understand the workings of the genome, we must study chromosome structure.

***Nature* (2011)**



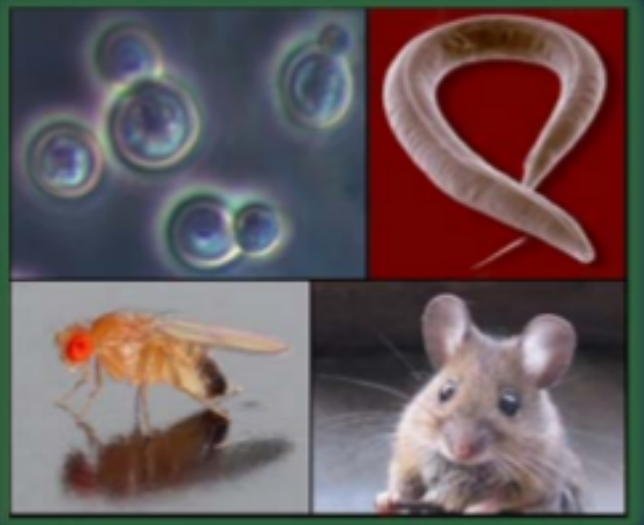
ENCODE: Giving ‘GPS’ Views of Genomes





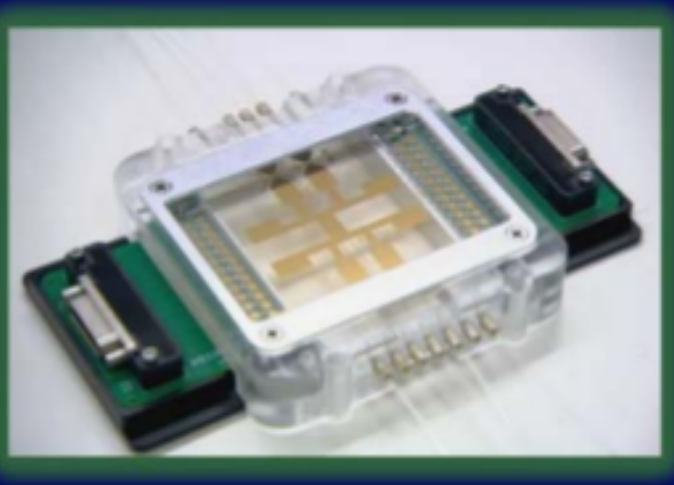
Elucidating Genome Function

'Team Science'



Model Organisms

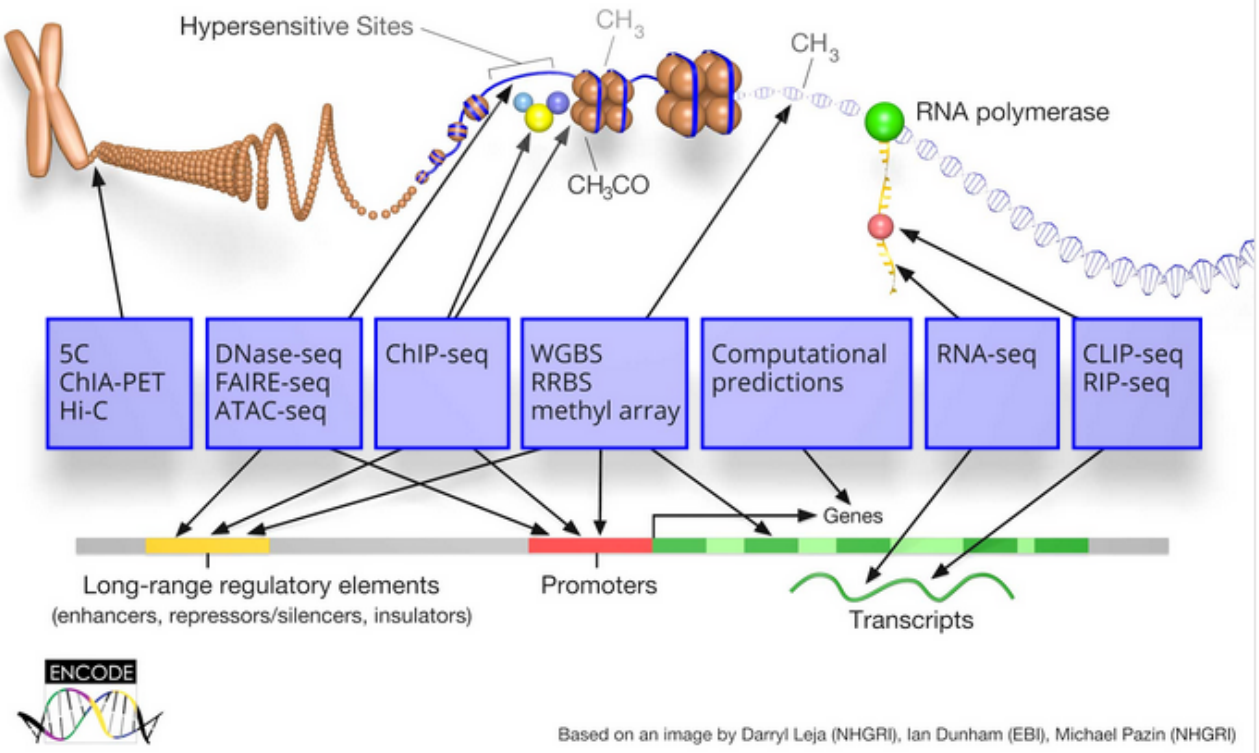
Computational Modeling



Technology Development

ENCODE Data Encyclopedia Materials & Methods Help Search...

ENCODE: Encyclopedia of DNA Elements

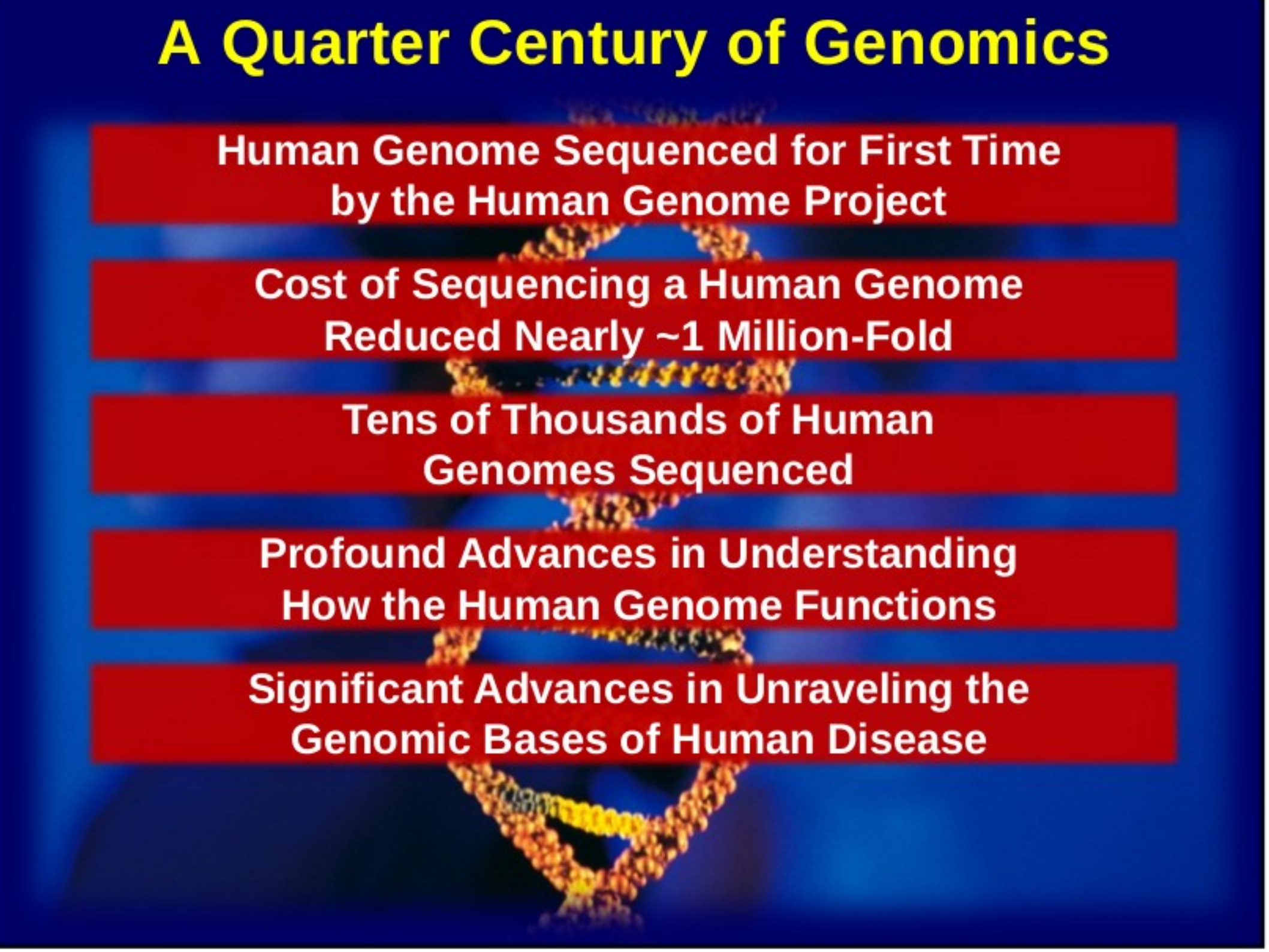


The ENCODE (Encyclopedia of DNA Elements) Consortium is an international collaboration of research groups funded by the National Human Genome Research Institute (NHGRI). The goal of ENCODE is to build a comprehensive parts list of functional elements in the human genome, including elements that act at the protein and RNA levels, and regulatory elements that control cells and circumstances in which a gene is active.

Get Started

https://www.encodeproject.org

A Quarter Century of Genomics



Human Genome Sequenced for First Time by the Human Genome Project

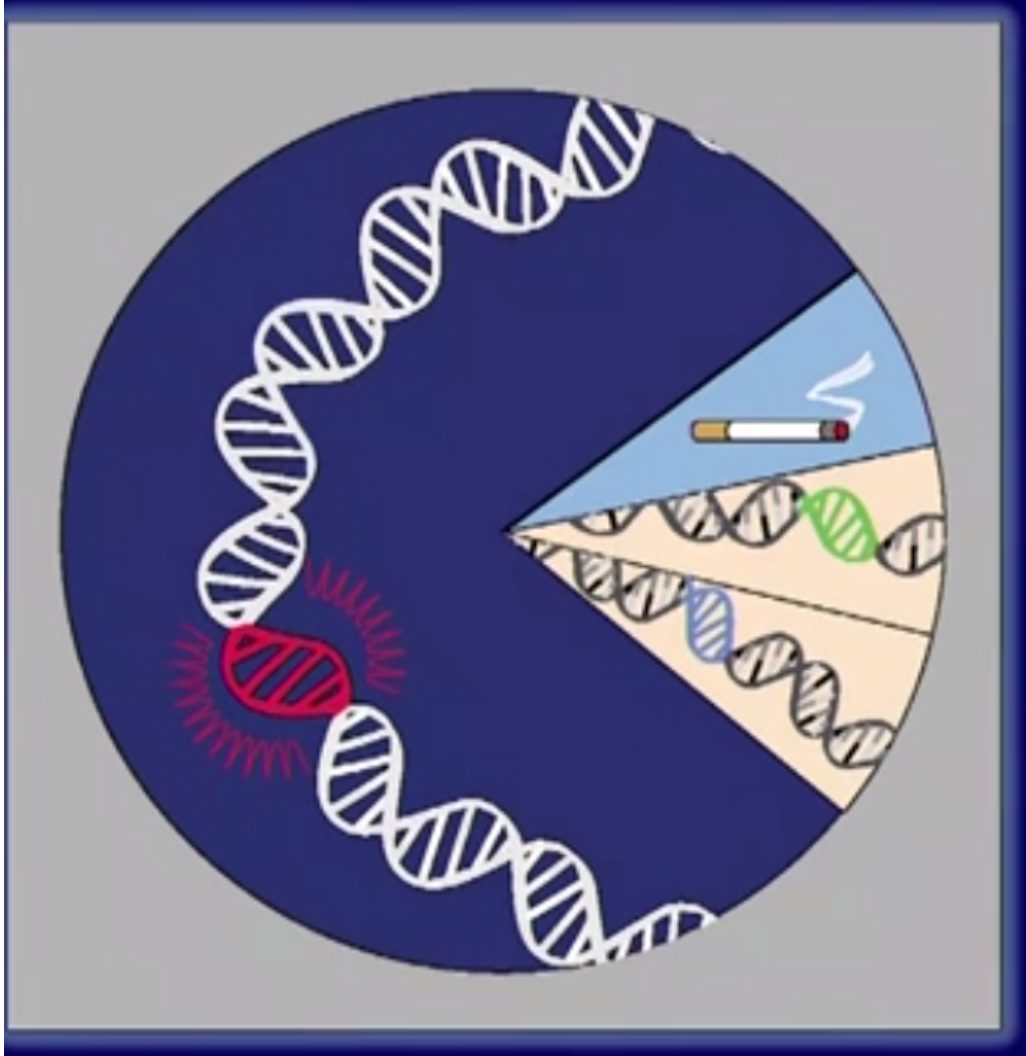
Cost of Sequencing a Human Genome Reduced Nearly ~1 Million-Fold

Tens of Thousands of Human Genomes Sequenced

Profound Advances in Understanding How the Human Genome Functions

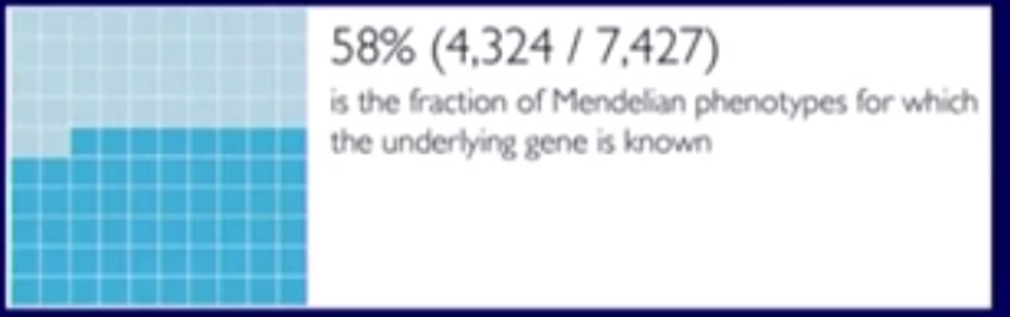
Significant Advances in Unraveling the Genomic Bases of Human Disease

Genomic Architecture of Genetic Diseases



AGTC
Centers for Mendelian Genomics

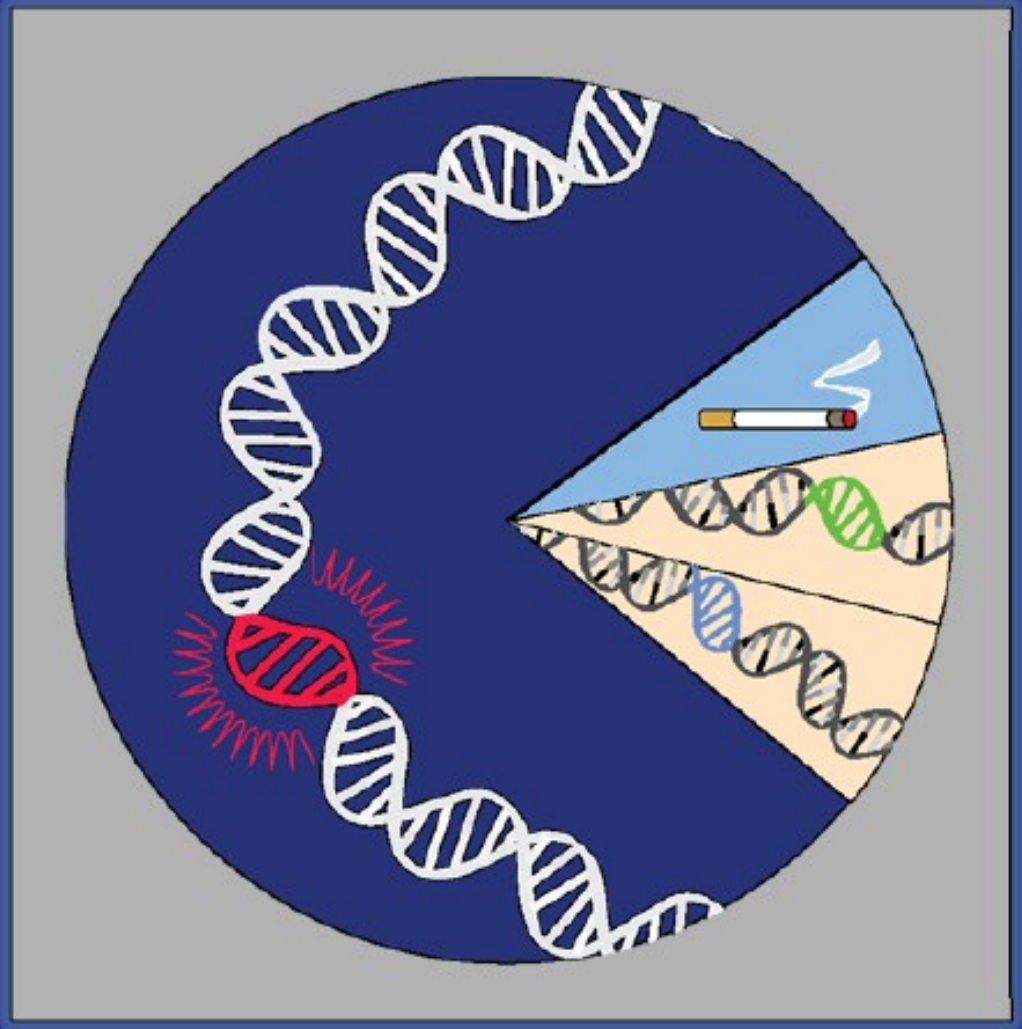
www.mendelian.org



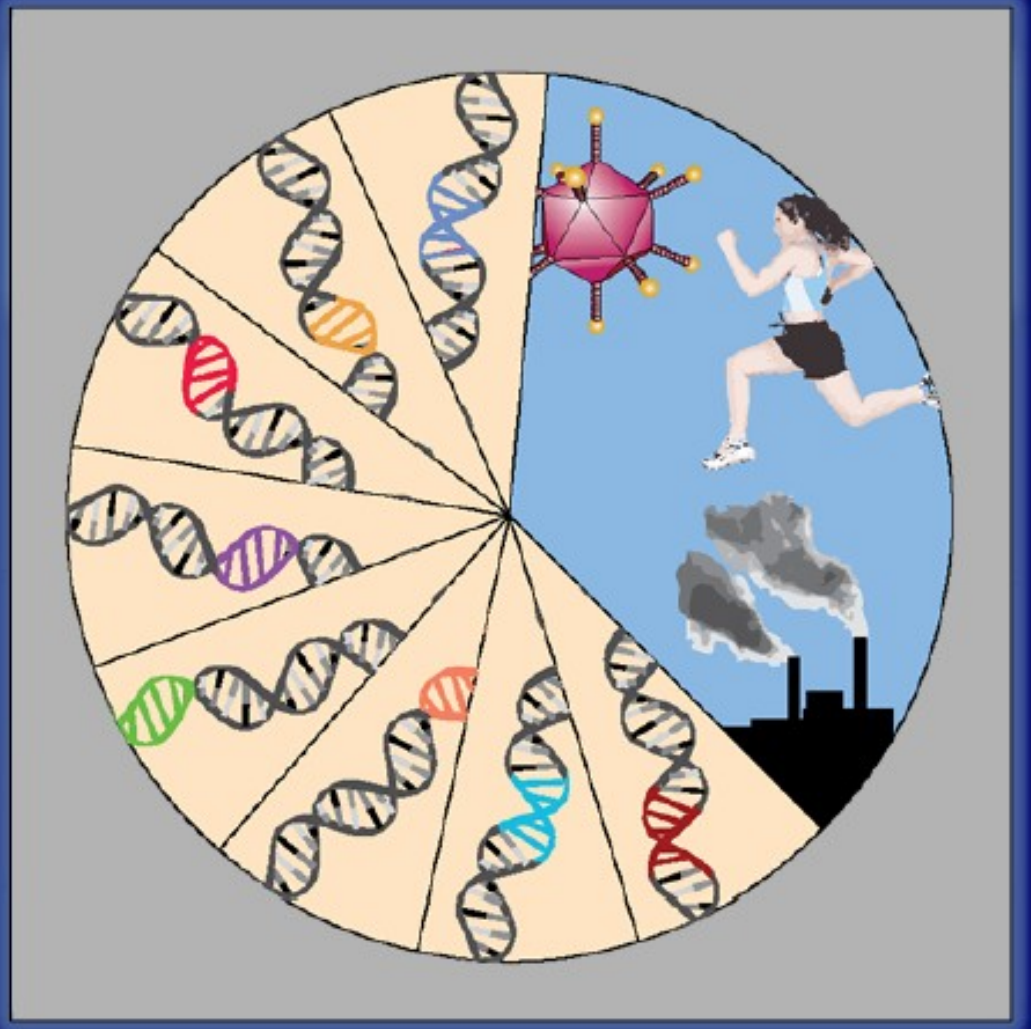
Rare, Simple, Monogenic, Mendelian…

Manolio et al., J Clin Invest (2008)

Genomic Architecture of Genetic Diseases



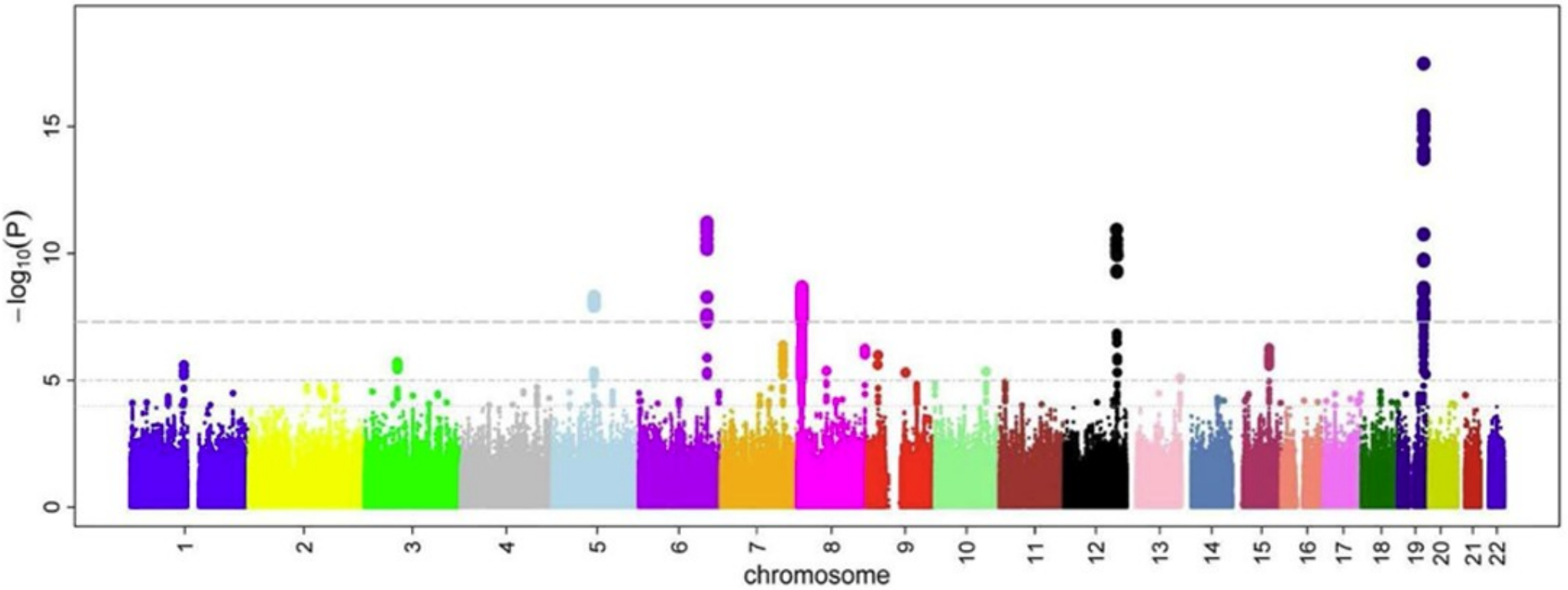
Rare, Simple, Monogenic, Mendelian…



Common, Complex, Multigenic, Non-Mendelian…

Manolio et al., J Clin Invest (2008)

WGA/GWAS/GWA



https://www.ebi.ac.uk/gwas/

NHGRI Genome Sequencing Program (GSP)

Centers for Common Disease Genomics

Overview

The National Human Genome Research Institute (NHGRI) has funded a collaborative large-scale genome sequencing effort to comprehensively identify rare risk and protective variants contributing to multiple common disease phenotypes. This initiative will explore a range of diseases with the ultimate goal of:

- Undertaking variant discovery for enough different examples of disease architectures and study designs to better understand the general principles of genomic architecture underlying common, complex inherited diseases.
- Understand how best to design rare variant studies for common disease.
- Develop resources, informatics tools, and innovative approaches and technologies for multiple disease research communities and the wider biomedical research community.

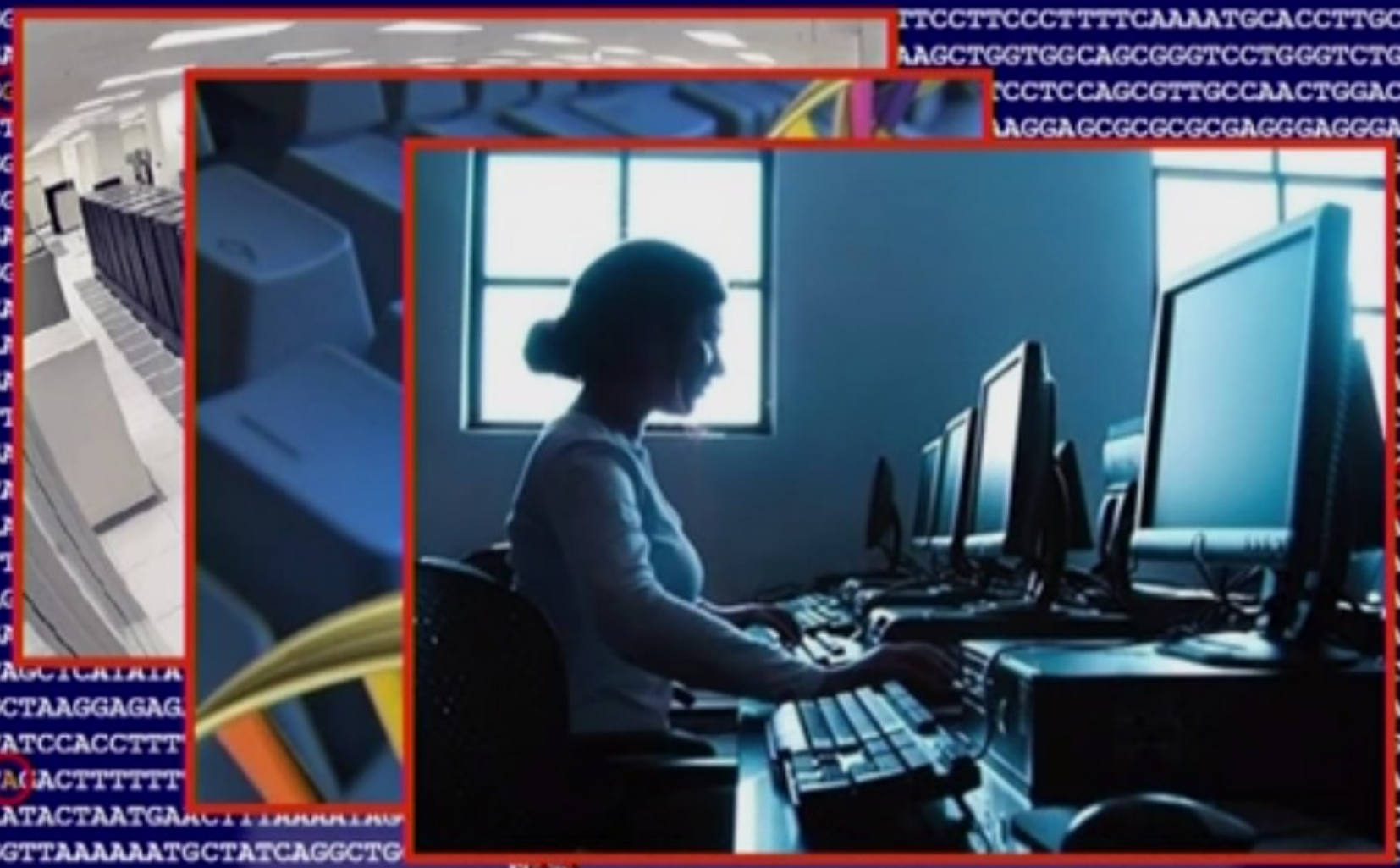
The initial focus of the CCDGs will be in cardiovascular disease (early onset heart disease, hemorrhagic stroke), and neuropsychiatric disease (autism). The program is designed to consider additional example diseases over time. Currently, the program is considering additional studies in autoimmune/inflammatory diseases (such as asthma, Type 1 diabetes, and inflammatory bowel disease), and bone disorders (osteoporosis). The choice of these, and any additional diseases, will be made based on criteria derived from those stated in the original RFA. These include the ability to undertake a comprehensive, well-powered study, the potential of the new example disease to broaden the range of different disease architectures being studied, or to explore new study designs. At a future date, the CCDG program will develop procedures to identify new studies with the involvement of the scientific community, either through direct interactions or through collaborations with other NIH institutes and centers.

Because the program will undertake multiple disease studies it was designed to encourage collaborations, continuing the productive collaborations enjoyed by the previous iteration of the GSP on large projects in type 2 diabetes, cancer, and Alzheimer's disease. The CCDG program will be co-funded by the National Heart Lung and Blood Institute (NHLBI) which will be providing co-funding for studies of direct interest to the NHLBI community.

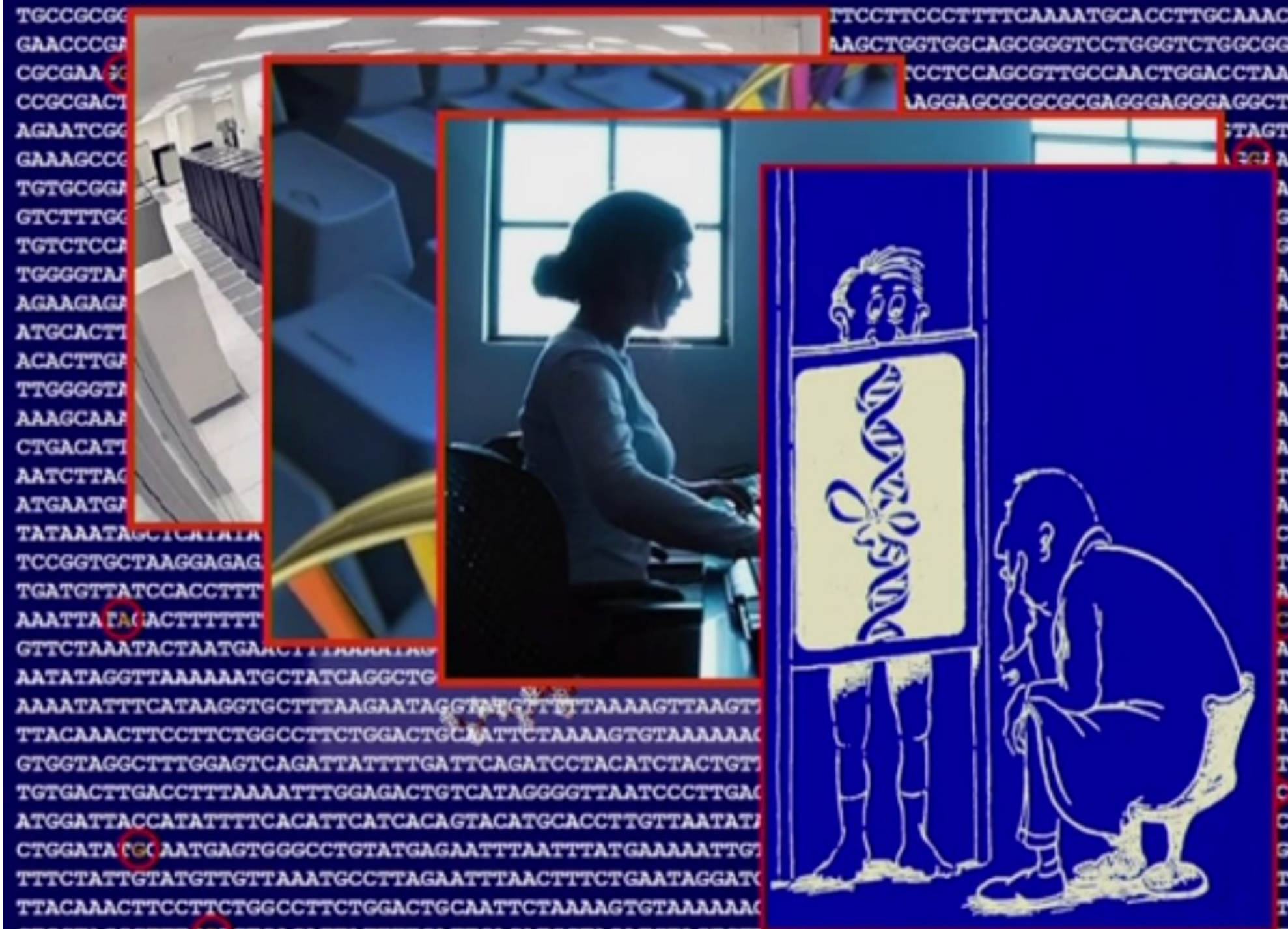
We currently estimate that the CCDG program will sequence 150K-200K whole genomes during the life of the program.

The Data Analysis Bottleneck

The Data Analysis Bottleneck



The Data Analysis Bottleneck



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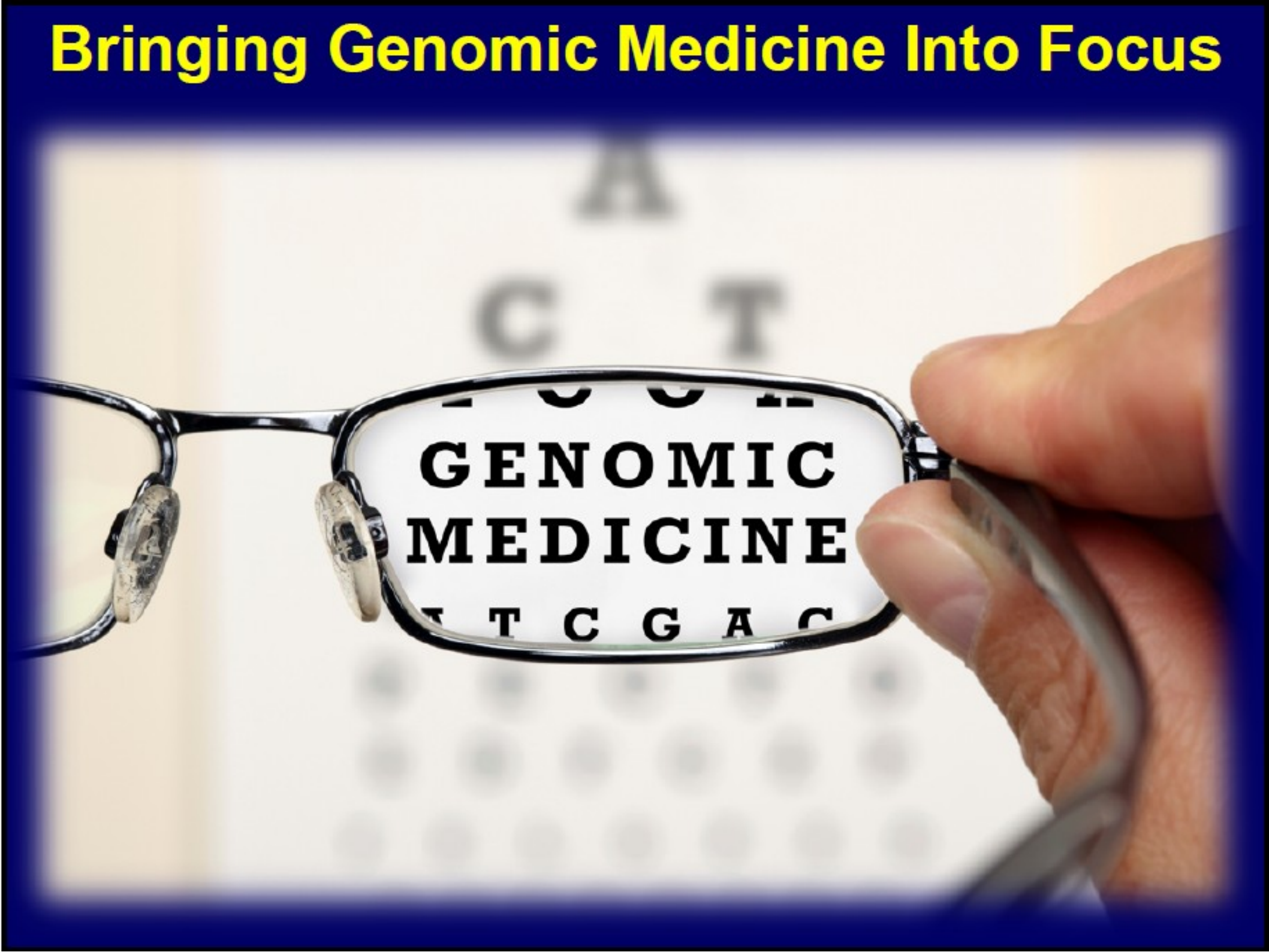
Vivid Examples of Genomic Medicine in Action Now Emerging

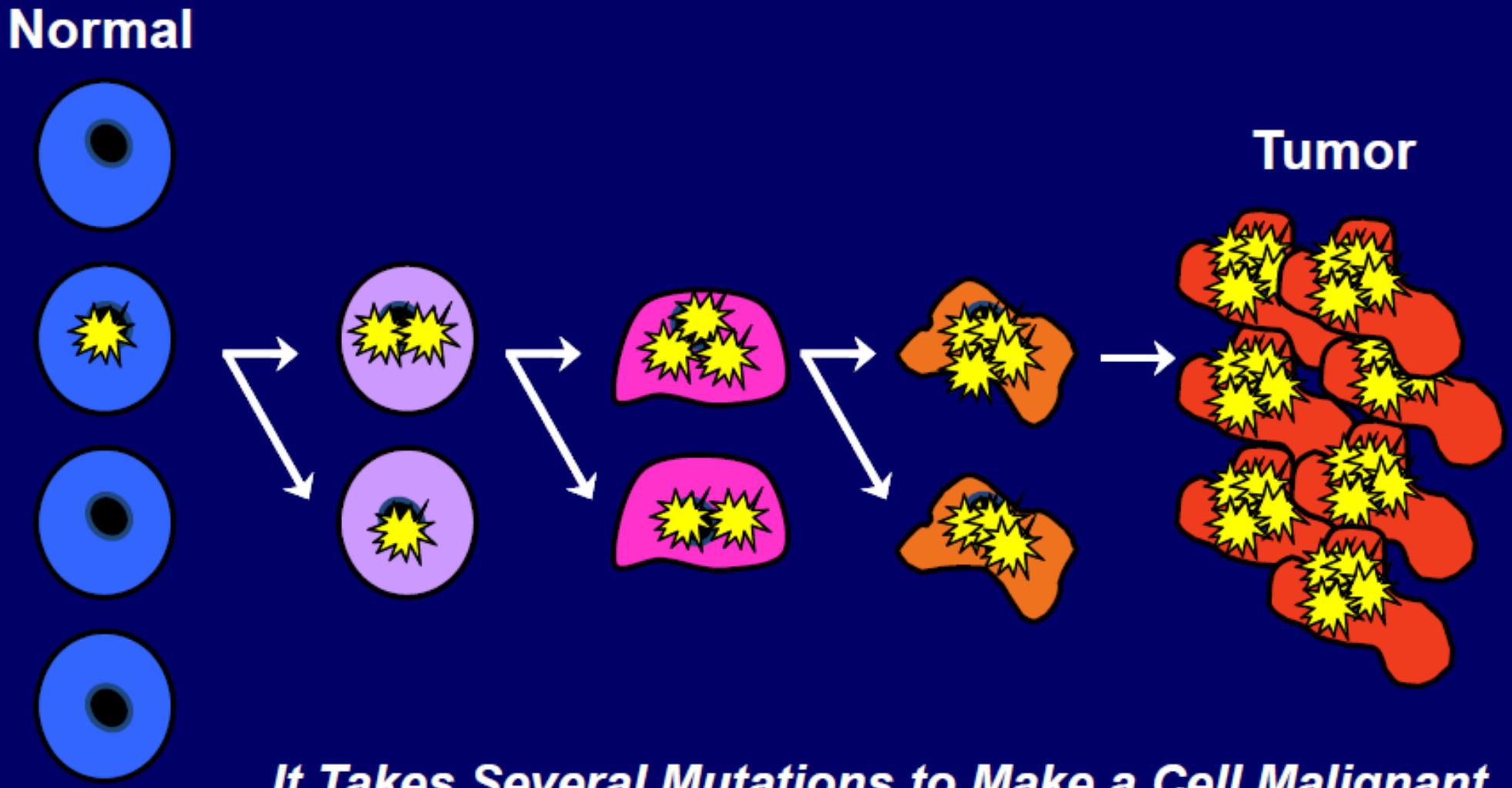
Bringing Genomic Medicine Into Focus



‘Hot Areas’ in Genomic Medicine

Cancer Genomics

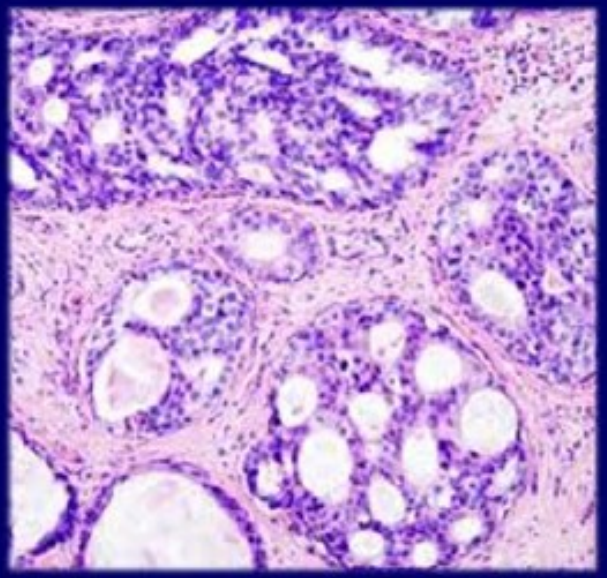
Cancer is a Disease of the Genome



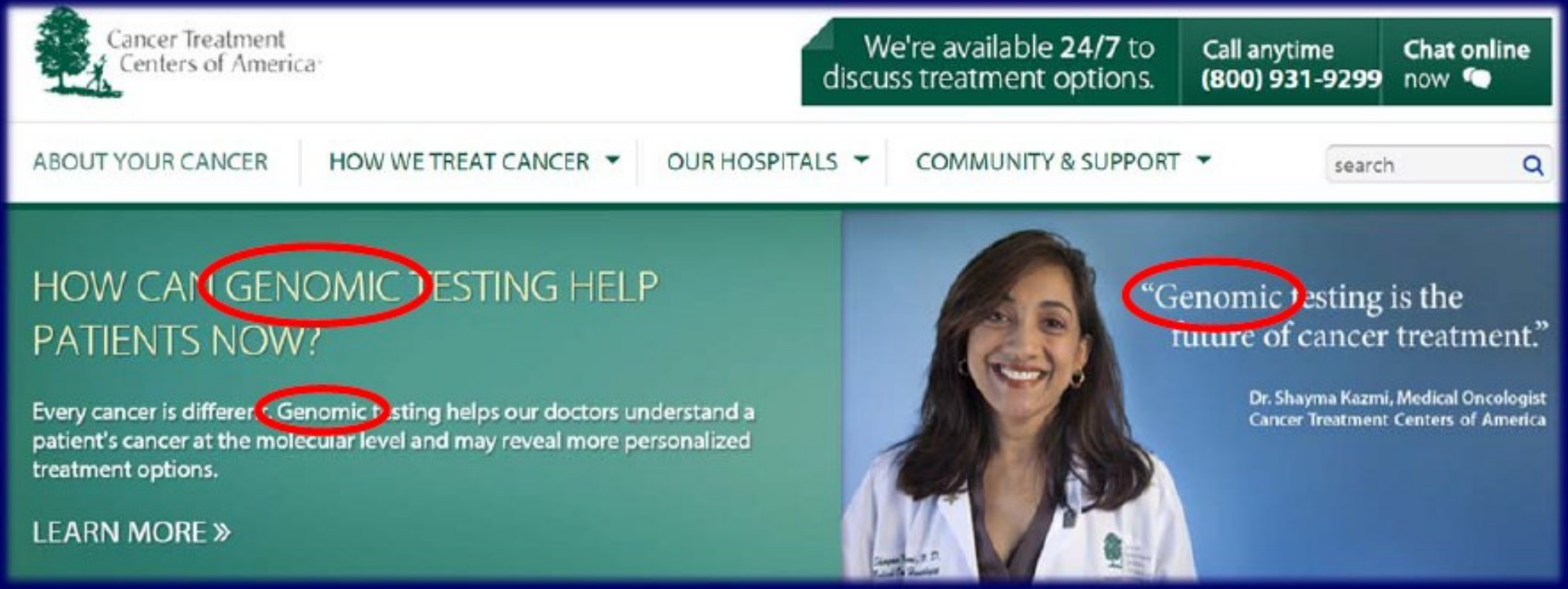
It Takes Several Mutations to Make a Cell Malignant

Routine Cancer Diagnostic Tools

Cancer Histopathology



Genomics and Cancer: Here and Now



‘Hot Areas’ in Genomic Medicine

Cancer Genomics

Pharmacogenomics

Because Everyone Responds Differently.

All of these work.

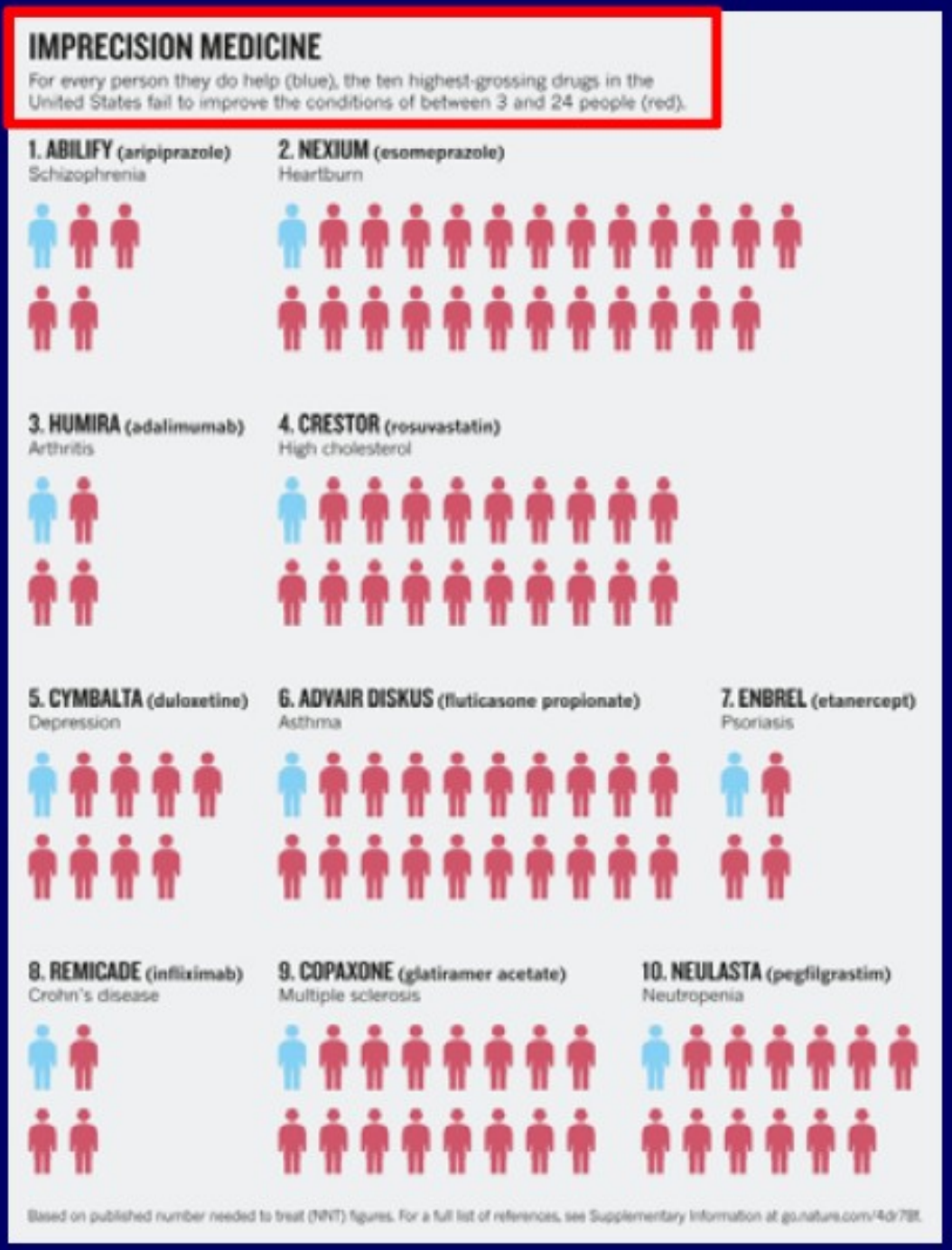
Just not for everyone.

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

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

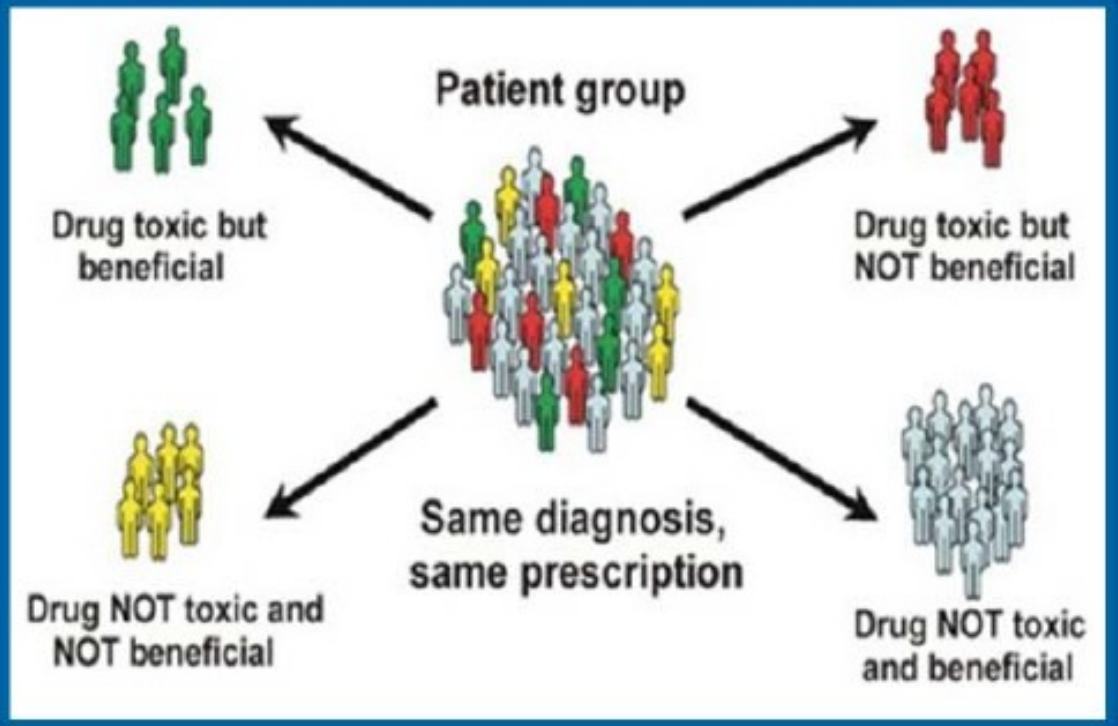
Perlegen's exceptional coverage of the genome and experienced team of analysts could help you get clinically relevant answers, not just data, in a matter of months.

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


IMPRECISION MEDICINE
For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).
1. ABILIFY (aripiprazole)
Schizophrenia
2. NEXIUM (esomeprazole)
Heartburn
3. HUMIRA (adalimumab)
Arthritis
4. CRESTOR (rosuvastatin)
High cholesterol
5. CYMBALTA (duloxetine)
Depression
6. ADVAIR DISKUS (fluticasone propionate)
Asthma
7. ENBREL (etanercept)
Psoriasis
8. REMICADE (infliximab)
Crohn's disease
9. COPAXONE (glatiramer acetate)
Multiple sclerosis
10. NEULASTA (pegfilgrastim)
Neutropenia
Based on published number needed to treat (NNT) figures. For a full list of references, see Supplementary Information at go.nature.com/4dr7tt.

***Nature* (2015)**

Pharmacogenomics



‘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)**

Undiagnosed Diseases

NIH Undiagnosed Diseases Network

Seven clinical sites and a coordinating center

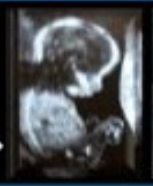
‘Hot Areas’ in Genomic Medicine

Cancer Genomics

Pharmacogenomics

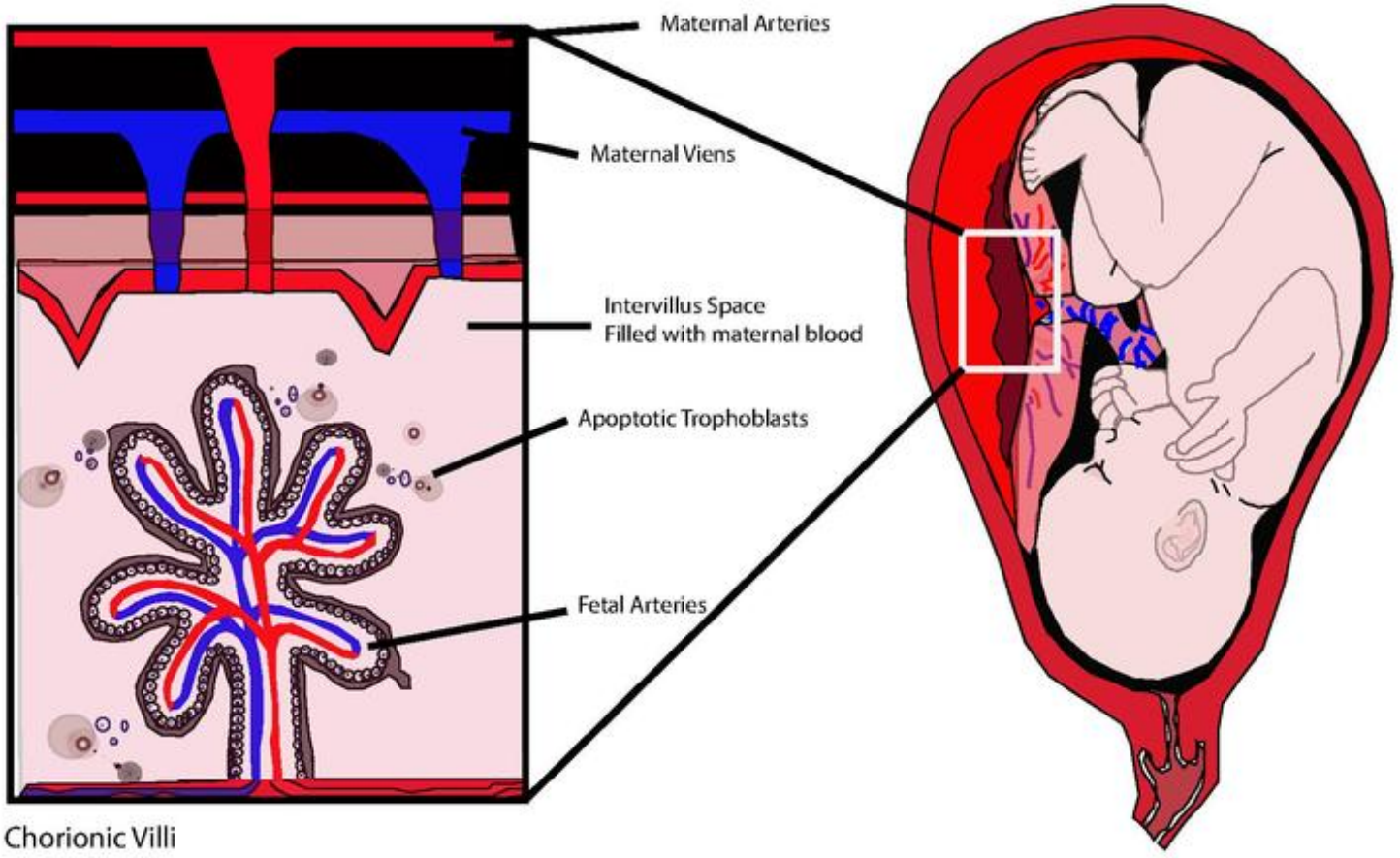
Rare Genetic Disease Diagnostics

Genomics of Pregnancy



Noninvasive Prenatal Genome Sequencing



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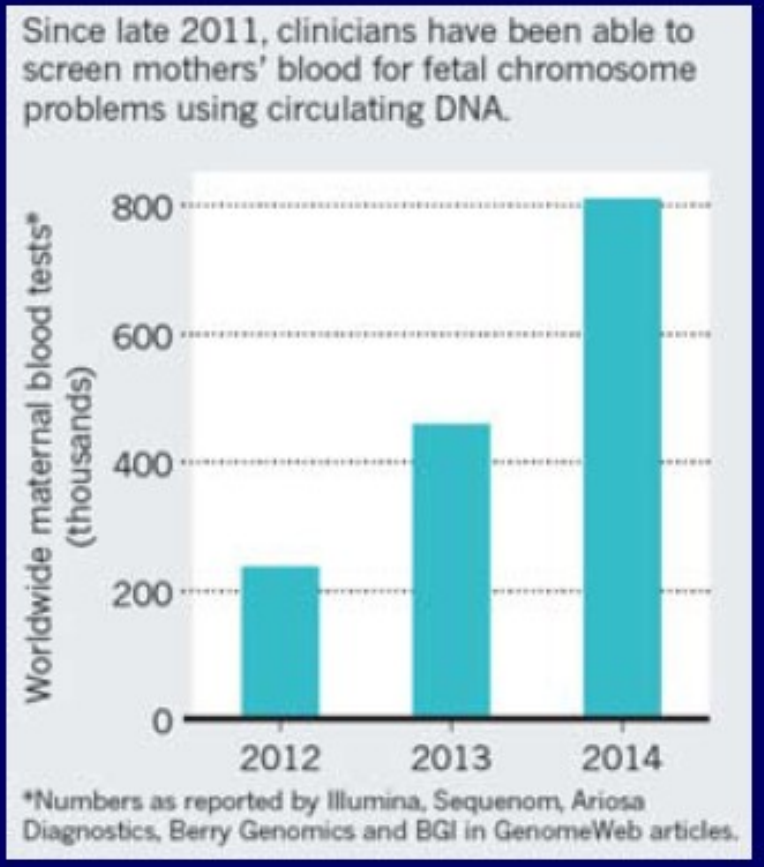


DW Bianchi, *Nature* (2015)

Newborn Genome Sequencing

HEALTH RESEARCH

In 2025, Everyone Will Get DNA Mapped At Birth

Alice Park @aliceparkny June 30, 2014

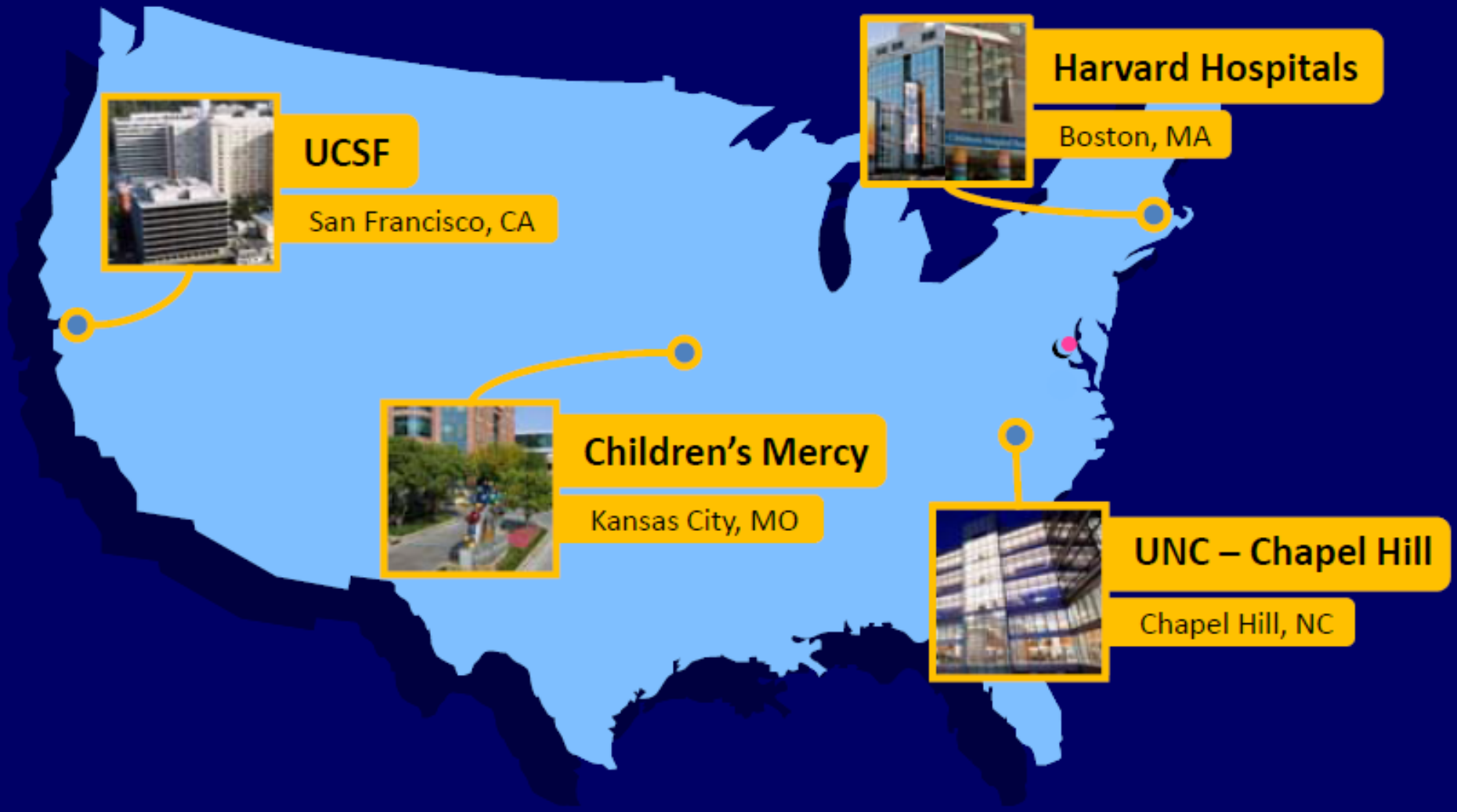
Scientists have scoured trends in research grants, patents and more to come up with these 10 innovations that will be reality in 10 years (or so they think)

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?

Time (2014)

Newborn Sequencing In Genomic medicine and public HealTh (NSIGHT)



https://www.aphl.org/conferences/proceedings/Documents/2016%20Newborn%20Screening%20and%20Genetic%20Testing%20Symposium/11Powell.pdf

Genome Sequencing of Acutely Sick Newborns

The genomes of ill newborns can be sequenced in less than 24 hours to give clinicians a rapid diagnosis.

GENOMICS

Fast sequencing saves newborns

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

***Nature* (2014)**

‘Hot Areas’ in Genomic Medicine

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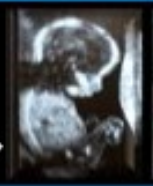
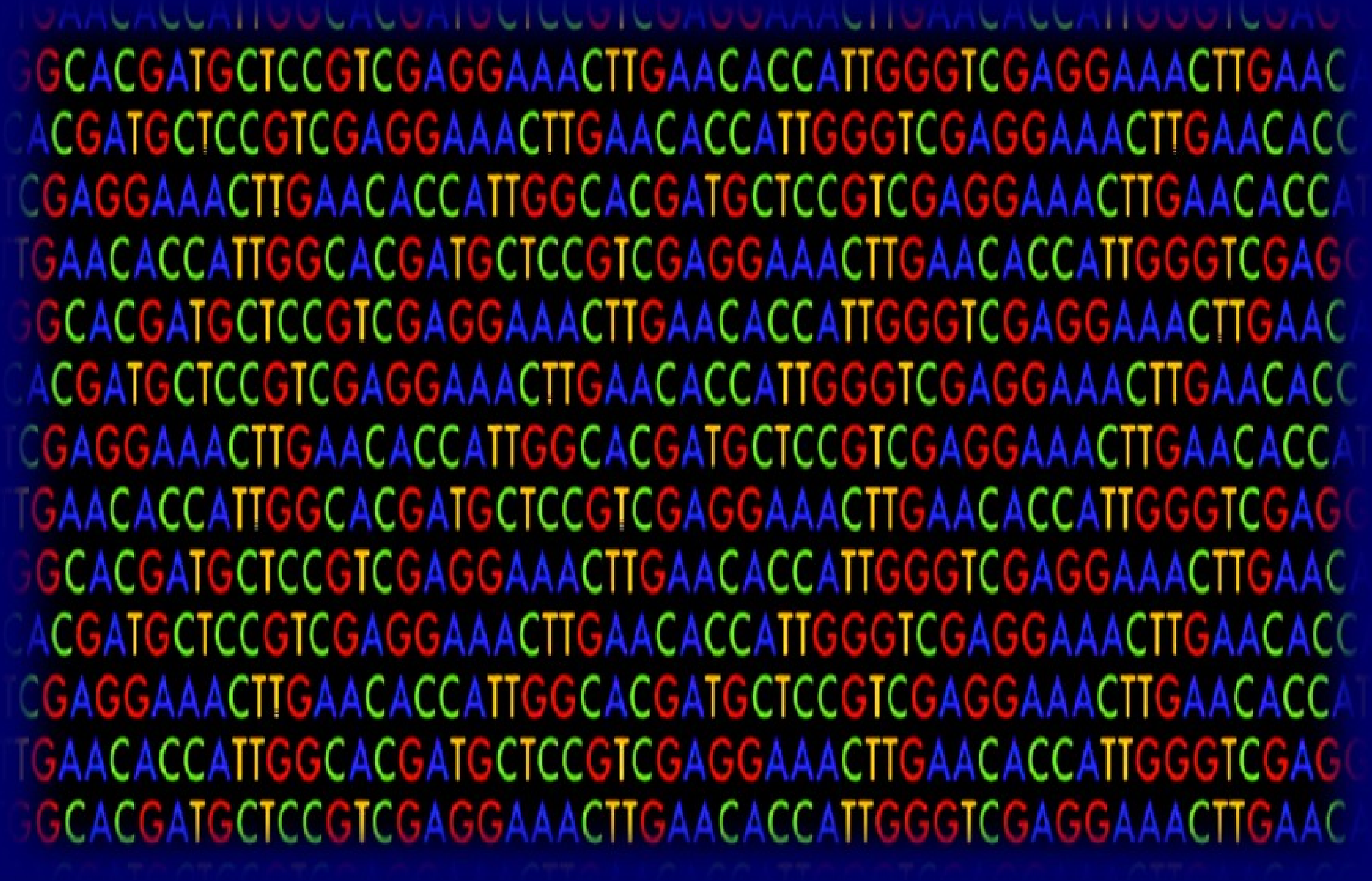
Genomics of Pregnancy



Clinical Genomics Information Systems

Generating a Human Genome Sequence is (Almost) Trivial




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

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)**

The Genomic Medicine Ecosystem

Healthcare Delivery

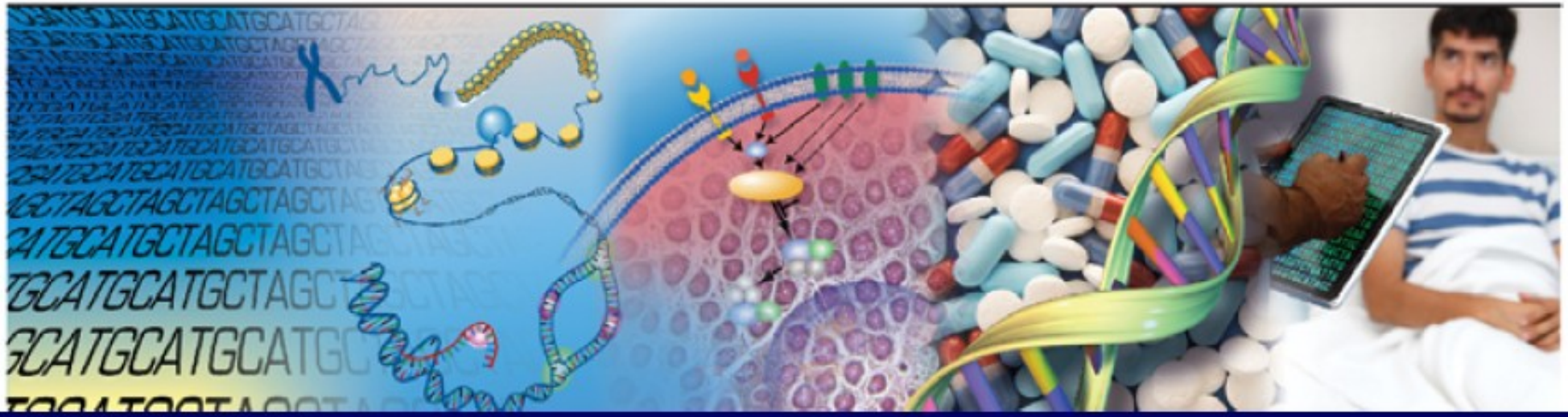
The Genomic Medicine Ecosystem

Education & Genomic Literacy

The Genomic Medicine Ecosystem

Regulatory Oversight

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



A pessimist sees the difficulty in every opportunity.
An optimist sees the opportunity in every difficulty.

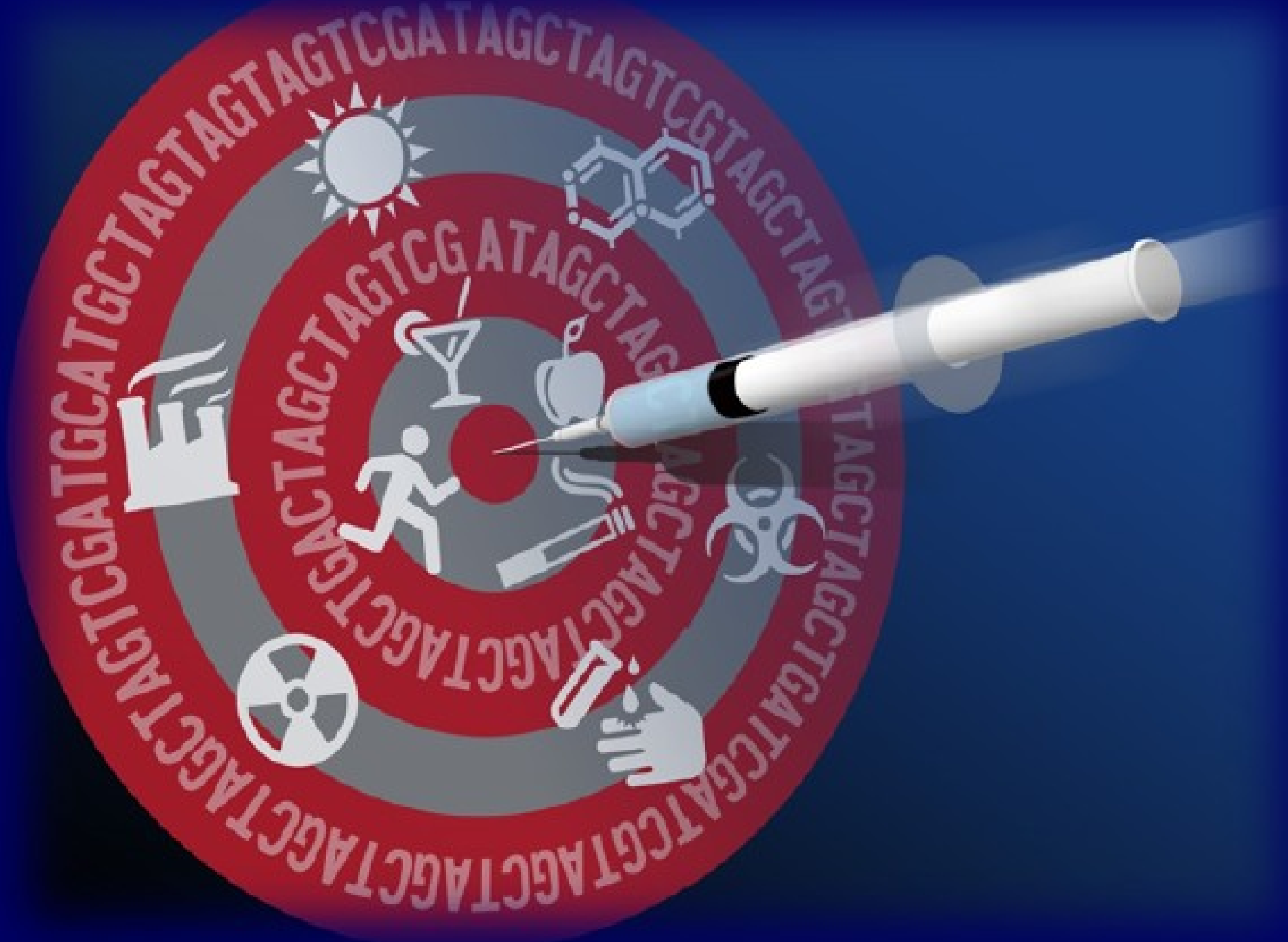
--Winston Churchill

The Relevance of Genomics

Biomedical Researchers

Healthcare Professionals

Patients (and Friends & Relatives of Patients)



Precision Medicine

A broader context for 'individualizing' medical care to advance human health

Precision Medicine

- **Today:** most medical care based on expected response of the average patient

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

How do we get from today to tomorrow?

"…[the] new Precision Medicine Initiative [will bring] America closer to curing diseases like cancer and diabetes, and gives all of us access, potentially, to the personalized information that we need to keep ourselves and our families healthier."

President Barack Obama

January 30, 2015

The NEW ENGLAND JOURNAL of MEDICINE

January 30, 2015

Perspective

A New Initiative on Precision Medicine

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

> "Tonight, I'm launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes — and to give all of us access to the personalized information we need to keep ourselves and our families healthier."
>
> — President Barack Obama, State of the Union Address, January 20, 2015

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

U.S. National Research Cohort

- >1 million U.S. volunteers
- Participants to share genomic data, lifestyle information, biological samples – all linked to their EHRs
- Forge new model for 'doing science' that emphasizes:
  - Engaged participants
  - Open, responsible data sharing
  - Strong privacy protections

Everything Old is New Again

insight commentary

The case for a US prospective cohort study of genes and environment

Francis S. Collins

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

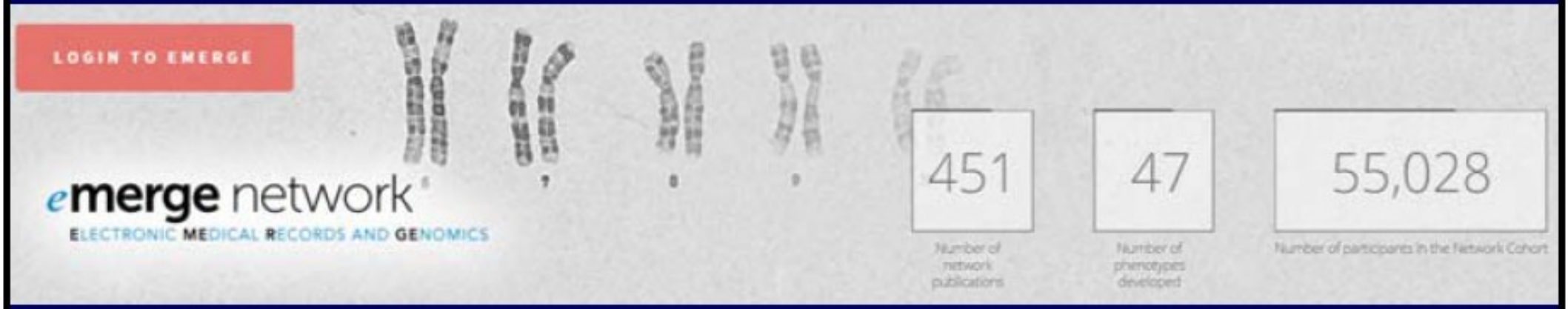
Information from the Human Genome Project will be vital for defining the genetic and environmental factors that contribute to health and disease. Well-designed case–control studies of people with and without a particular disease are essential for this, but rigorous and unbiased conclusions about the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

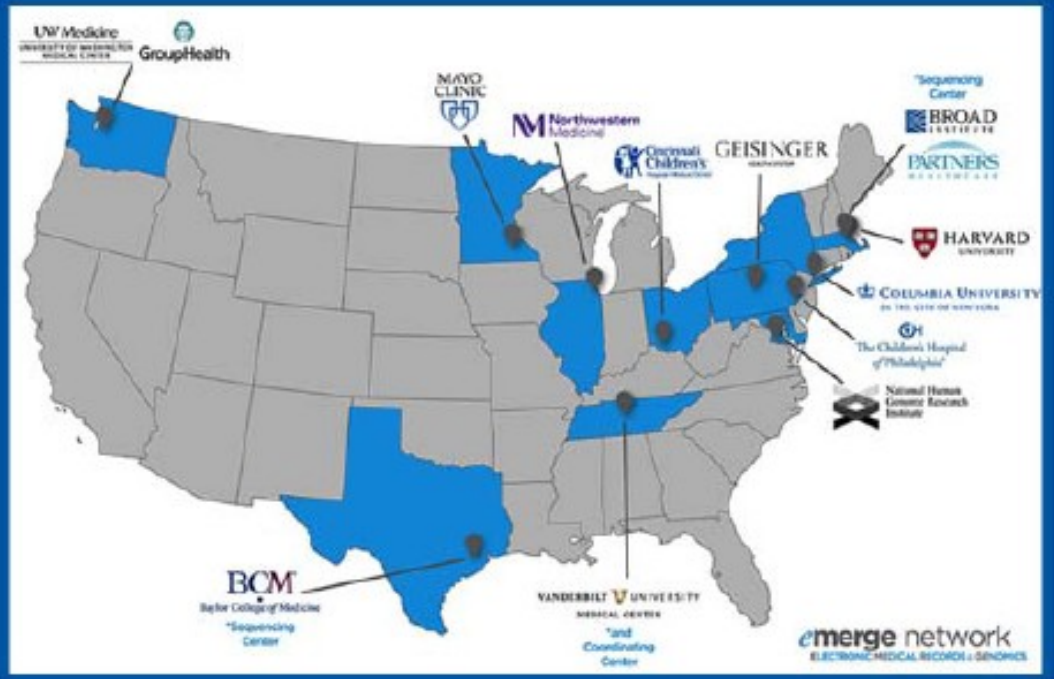
***Nature* (2004)**

Genomics

EHRs

Electronic Medical Records and Genomics (eMERGE) Network





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THE BODY ELECTRIC

RESEARCHERS WANT TO WIRE THE HUMAN BODY WITH SENSORS THAT COULD HARVEST REAMS OF DATA — AND TRANSFORM HEALTH CARE.

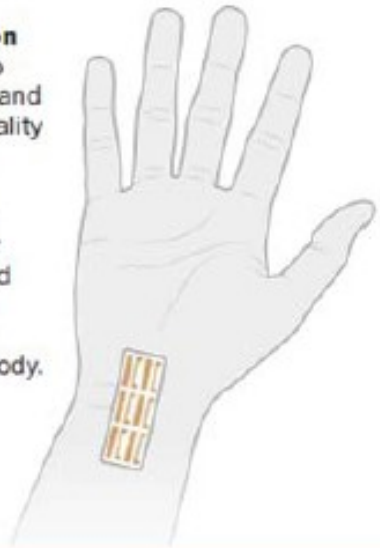
BY ELIZABETH GIBNEY

***Nature* (2015)**

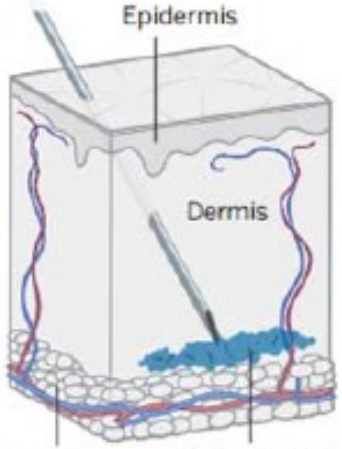
WIRED FOR LIFE

Sensors woven into the body could alert people to medical problems before they become seriously ill — if the devices can overcome some daunting challenges.

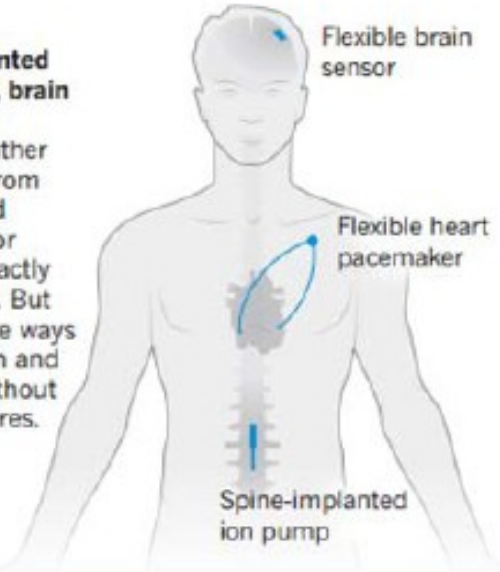
Sensors mounted **on the skin** are easy to apply and remove, and can obtain high-quality data on breathing, heart rate, blood pressure and other vital signs. But they must be flexible and stretchy enough to follow the natural movement of the body.



Sensors injected **under the skin** can access the trove of information carried in the blood by chemical signals called biomarkers. The devices must be long-lived and biocompatible, so that they don't trigger an immune response.



Devices **implanted into the heart, brain or other deep tissues** can gather data directly from the source and deliver drugs or stimulation exactly where needed. But they must have ways to get power in and data out — without resorting to wires.



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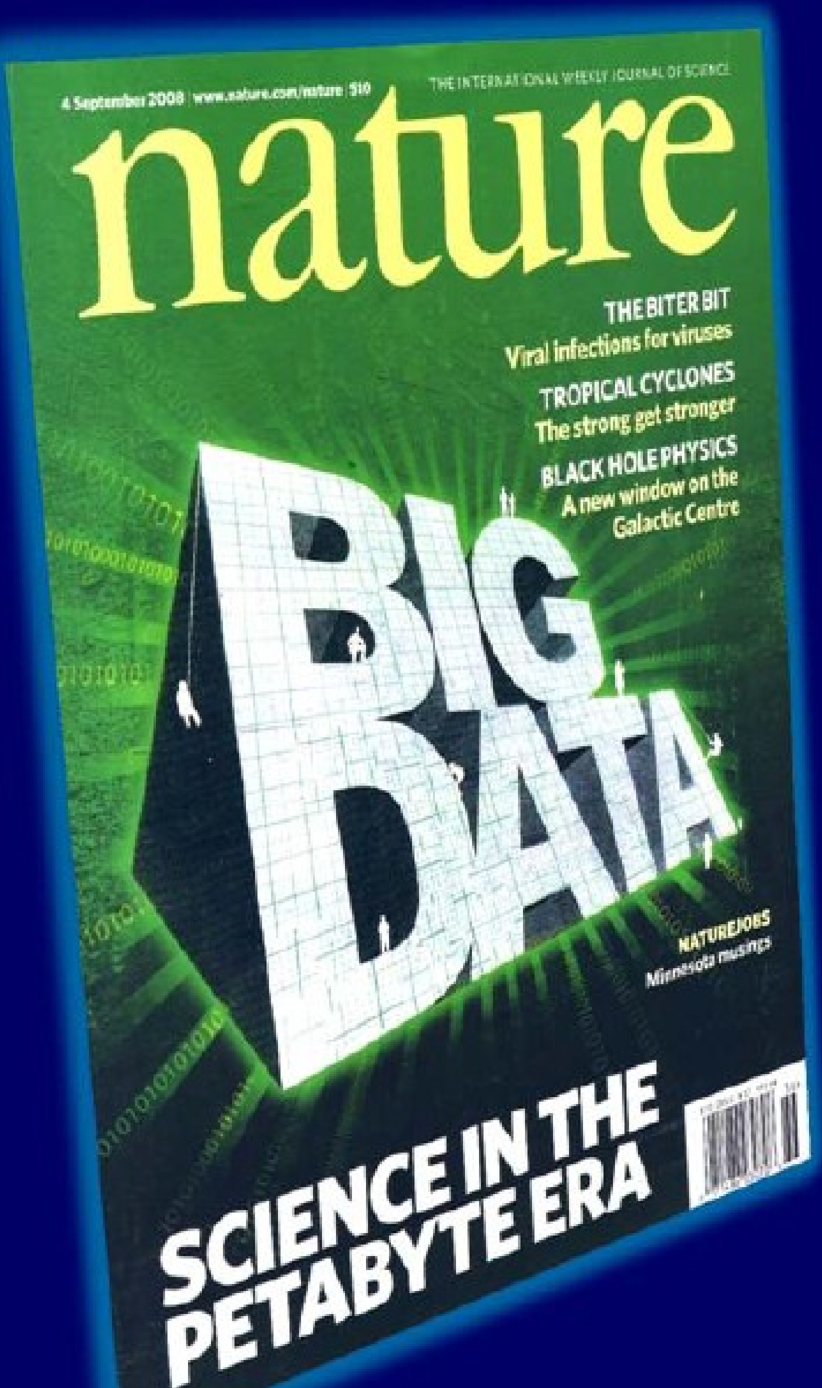

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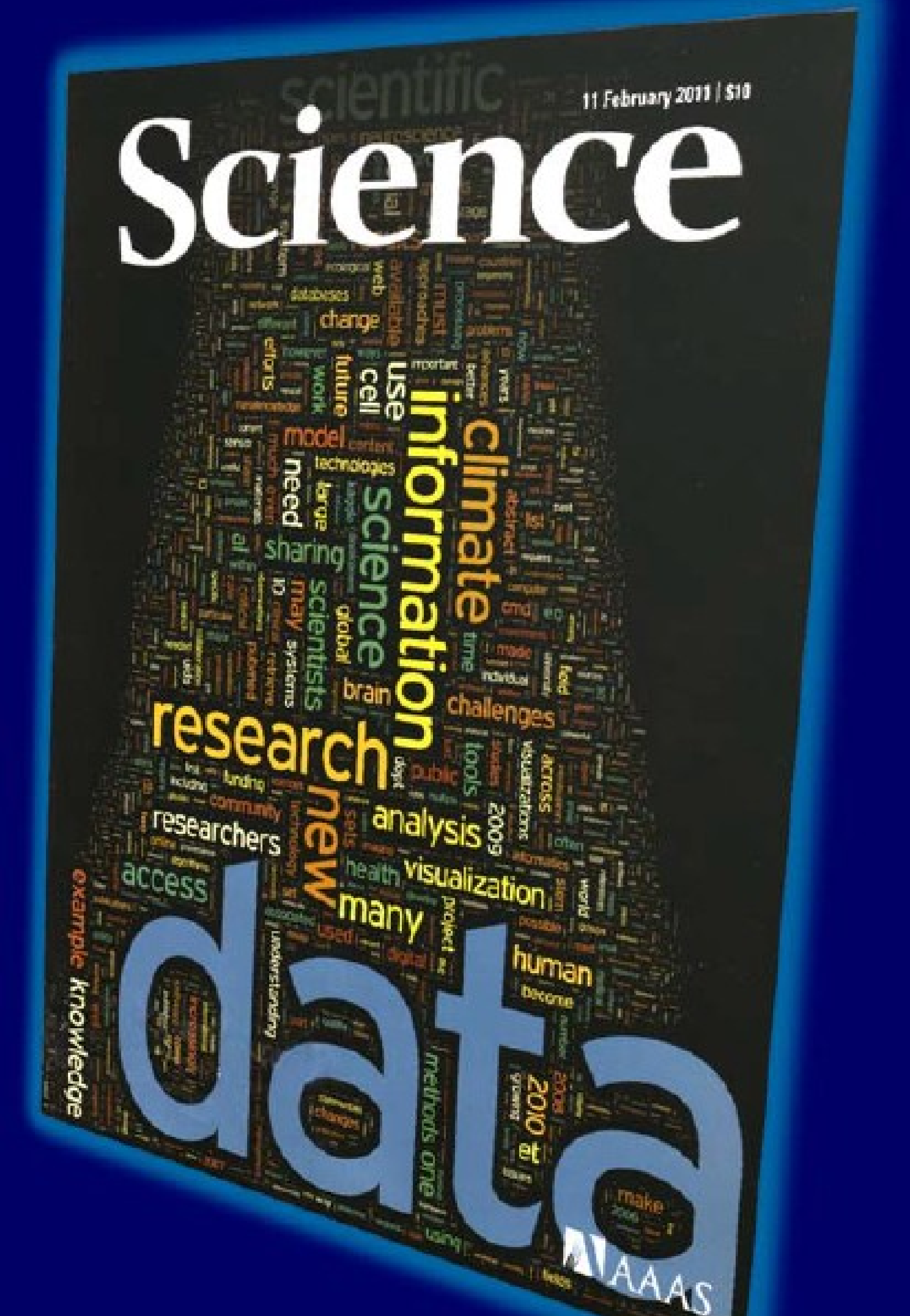

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PRECISION MEDICINE INITIATIVE

Precision Medicine Initiative

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Faces of the Precision Medicine Initiative – Dr. Russ Altman

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ABOUT THE PRECISION MEDICINE INITIATIVE

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

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Déjà Vu, All Over Again?

Human Genome Project

Circa Winter 1990

Precision Medicine Initiative

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