

From the Human Genome Project to Precision Medicine

A Journey to Advance Human Health

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



National Human Genome
Research Institute

The **Forefront**
of Genomics[®]

- I. First Three Decades of Genomics
- II. New Realities (& Opportunities)



I. First Three Decades of Genomics

II. New Realities (& Opportunities)



The Origin of “Genomics”: 1987

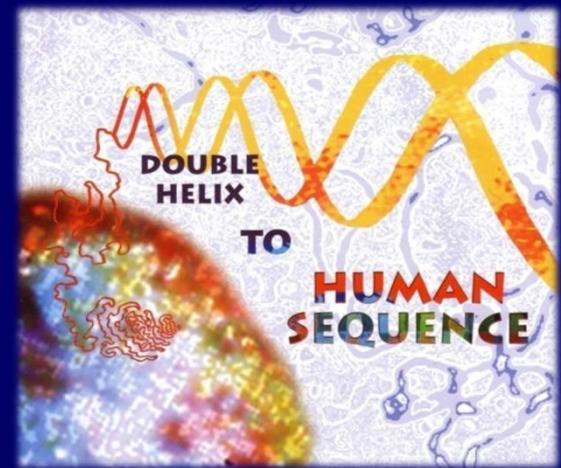
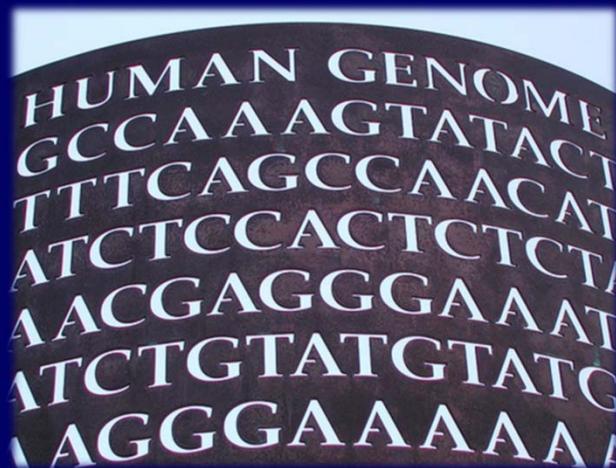
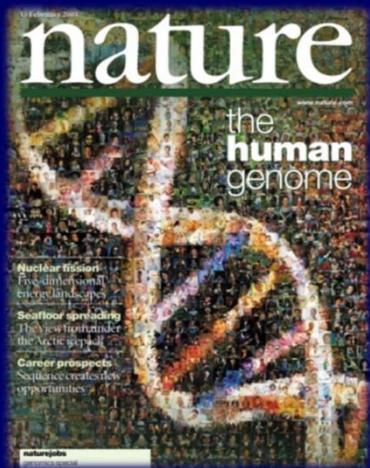
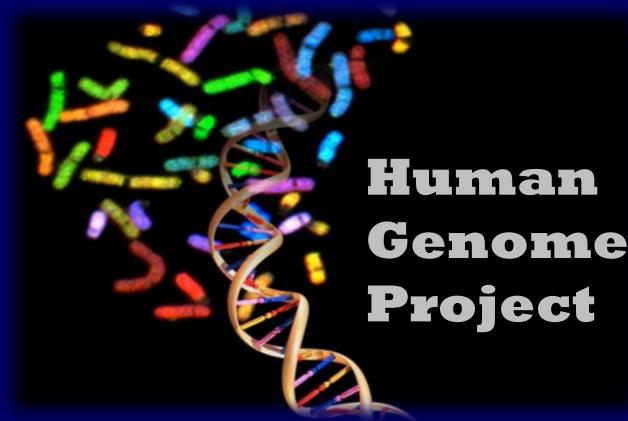
EDITORIAL

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...

Human Genome Project: 1990-2003



Three Decades of Genomics

**Human Genome Sequenced for First Time
by the Human Genome Project**



Myriad Applications of Genomics



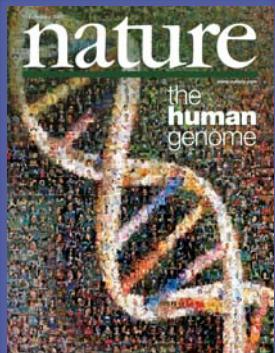
Health, Disease, & Medicine

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



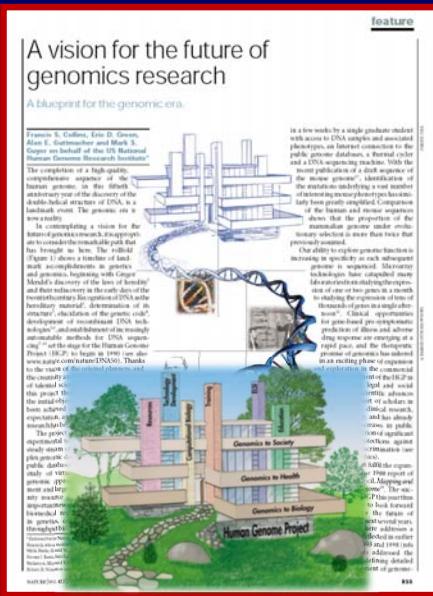
The Journey to Genomic Medicine



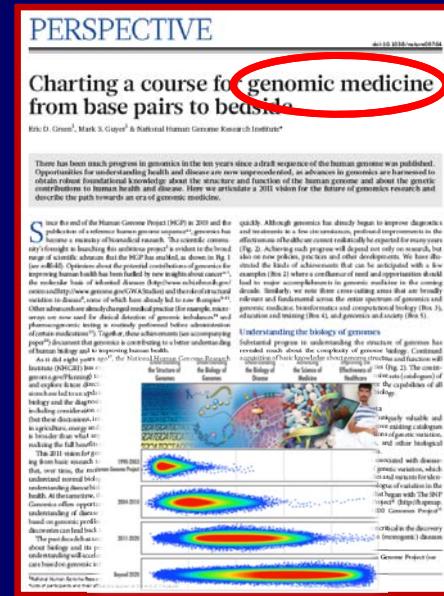
Human
Genome
Project



Realization of
Genomic
Medicine



Nature



Nature



2003

Base Pairs to Bedside



Three Decades of Genomics

**Human Genome Sequenced for First Time
by the Human Genome Project**

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



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 genome¹, 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 evolution

feature

“...‘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.”

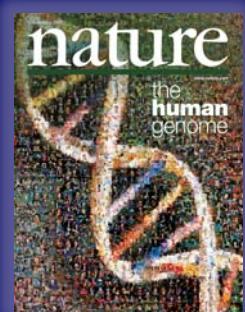
Human Genome Sequence

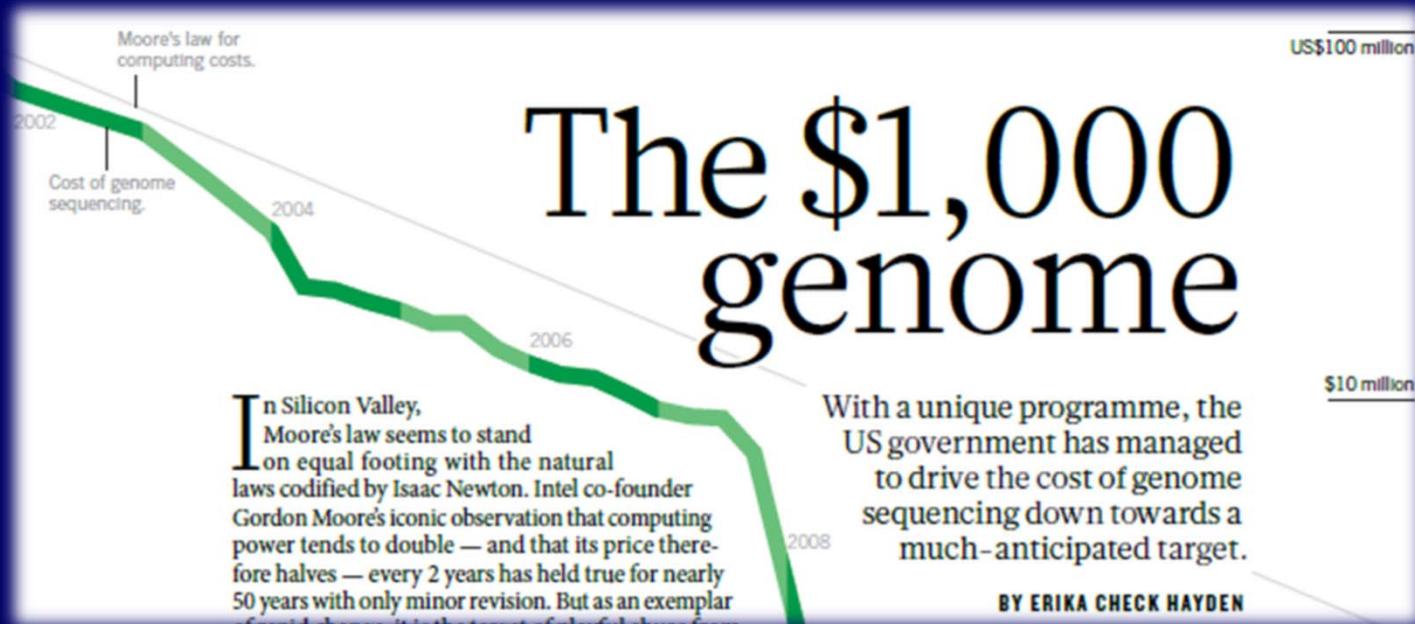
~\$1,000,000,000



~\$1,000

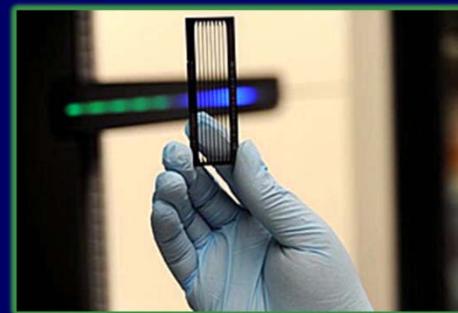
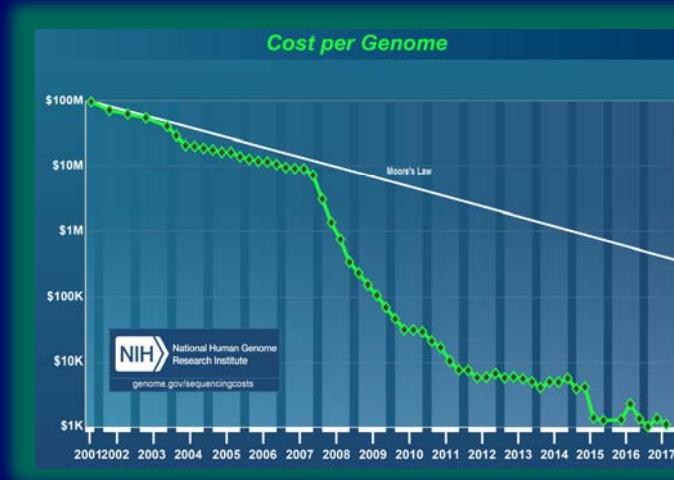
“The \$1000 Genome”





The \$1,000 genome

Nature (2014)





Three Decades of Genomics

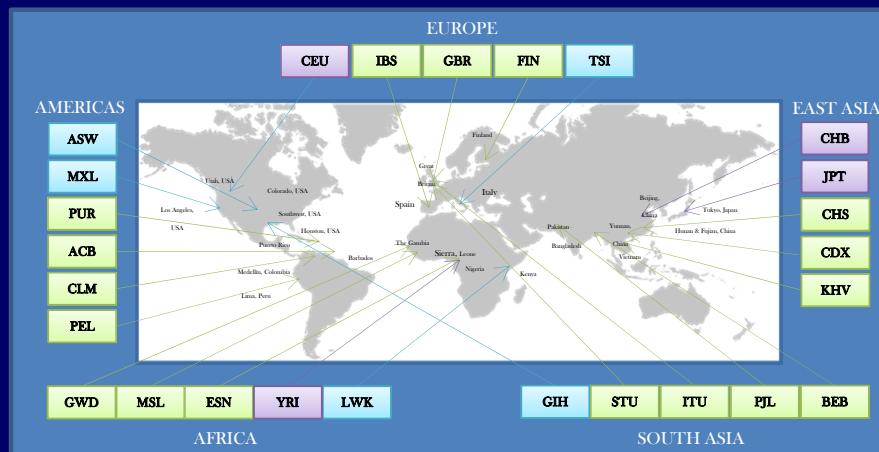
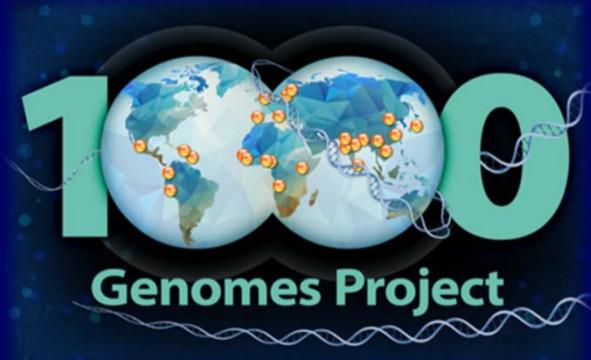
**Human Genome Sequenced for First Time
by the Human Genome Project**

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

**Hundreds of Thousands of Human
Genomes Sequenced**



Human Genomic Variation



2535 Humans, 26 Populations

Three Decades of Genomics

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**Profound Advances in Understanding
How the Human Genome Functions**



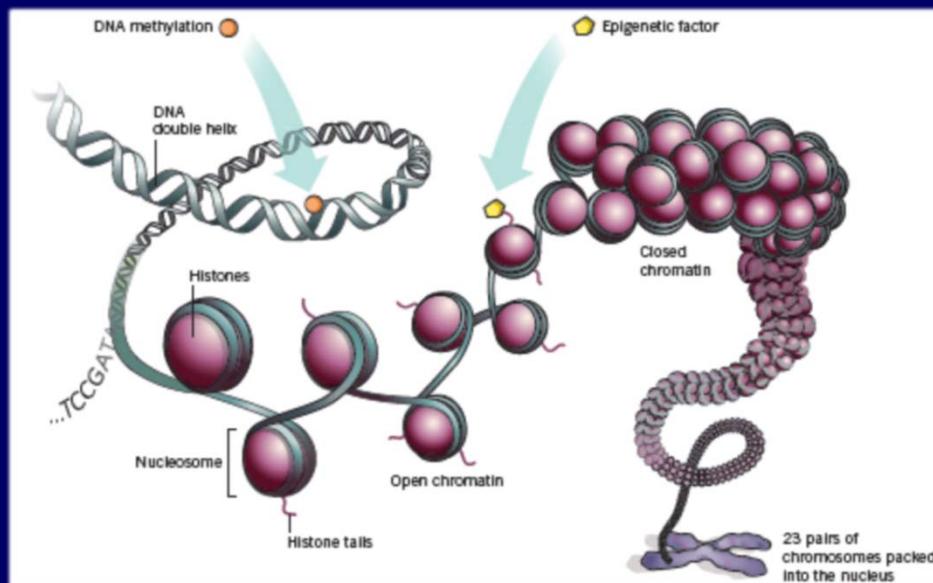
~3,000 bp (0.0001%) of Human Genome Sequence

TGCCGCGGAACCTTT
GAACCCGACTAGGAAT
CGCGAAGGAGGGTCT
CCGCGACTGTGCCCC
AGAACGGAAAGGC
GAAAGCCCTAGAGC
TGTGCGGAGTAGGGC
GTCTTGGCATTAGC
TGTCTCAAACCTTT
TGGGGTAAAGGAAT
AGAAGAGATGGAAGA
ATGCACTTGTTTTA
ACACTTGATTGTCT
TTGGGGTAGGTAGA
AAAGCAAATTGTTG
CTGACATTTAATAAF
AATCTTAGGCAAAG
ATGAATGAATAGGT
TATAATAGCTCAT
TCCGGTGTAAAGGAC
TGATGTTATCCACCT
AAATTATAGACTTT
GTTCTAAATACTAA
AATATAGGTAAAAA
AAAATATTCATAAC
TTACAAACTCCCTC
GTGGTAGGCTTGGA
TGTGACTTGACCTT
ATGGATTACCATAT
CTGGATATGCAATG
TTTCTATTGTATGT

TECHNOLOGY FEATURE

READING THE SECOND GENOMIC CODE

Nature (2012)



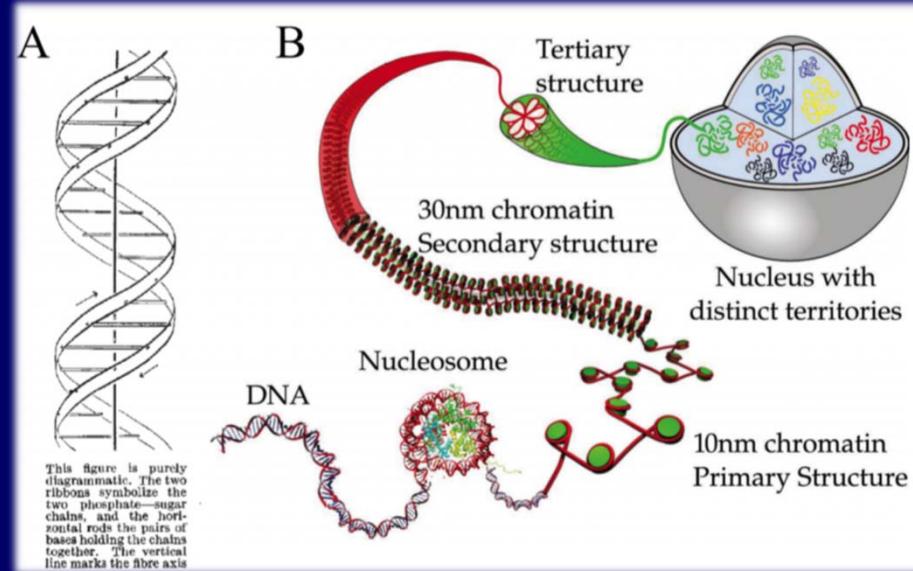
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TGGAAAAGGCCAGCGT
GTGTATGGGTTGGGTT
AAAACAGAAAGCATT
ACTCAAGTACGCTACT
CCCCTTCATGCCTTG
TCAGCCAACAAAAATT
GATTCTTCAAAATTG
CCGAAGTTATATCCAA
TAGCATCTAAGTTCGG
TATTATACTGGTGTGA
AAAAAGTCAAATATGT
CAGTTAACCTGGAAC
AATTATCTTTGTGT
AAATGTTAATTGGCAT
GAATATTCATGGATA
ATCACCTGACACATT
CTCATTTCCTGTTCTCC
CCTAAATACCAATGA
TTGCTTAGTTTCAAA
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AAAATTATTATGGTAT

TECHNOLOGY FEATURE

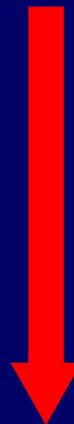
GENOMES IN THREE DIMENSIONS

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

Nature (2011)



Some Genomic Variants



Traits
(i.e., Phenotypes)

Three Decades of Genomics

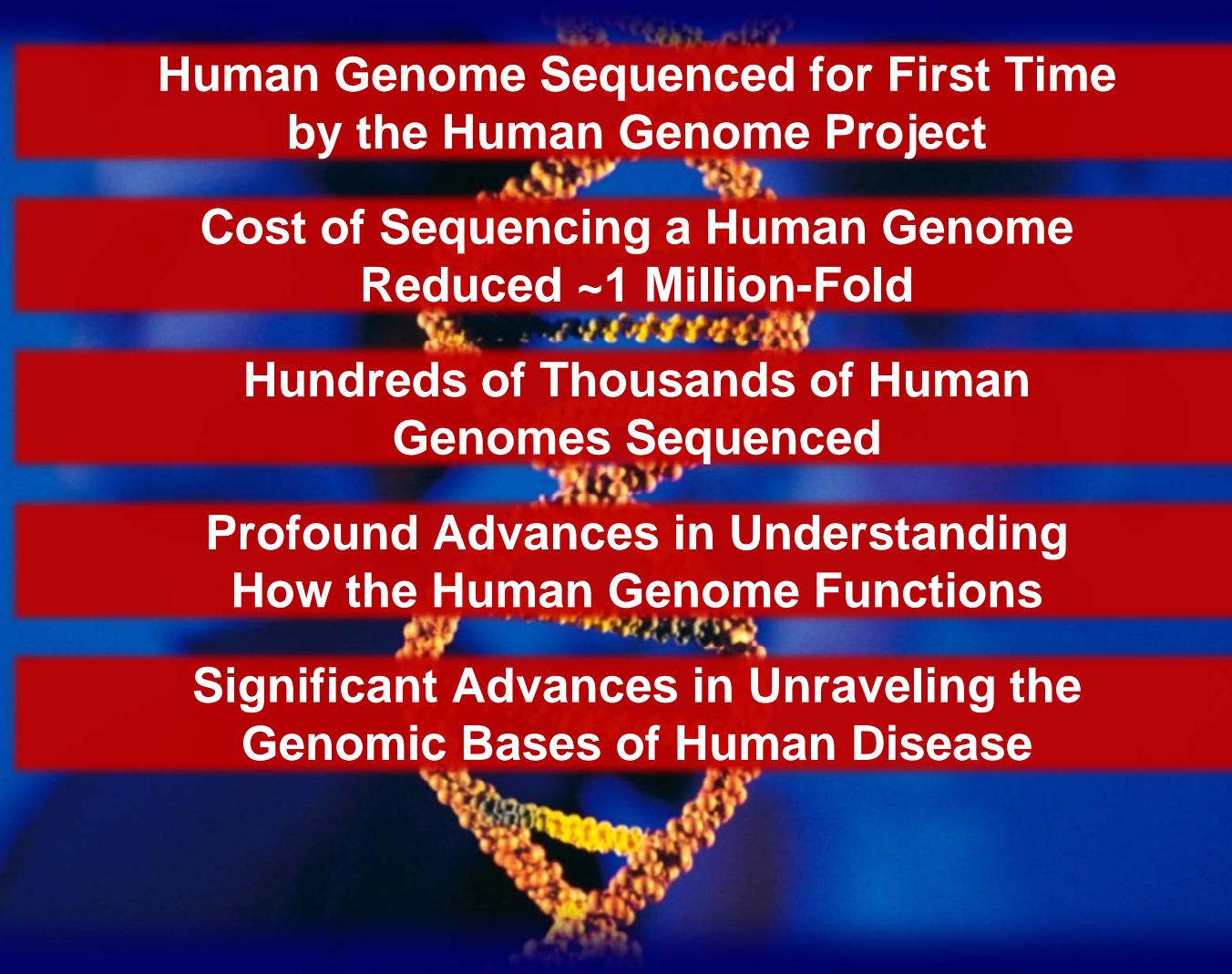
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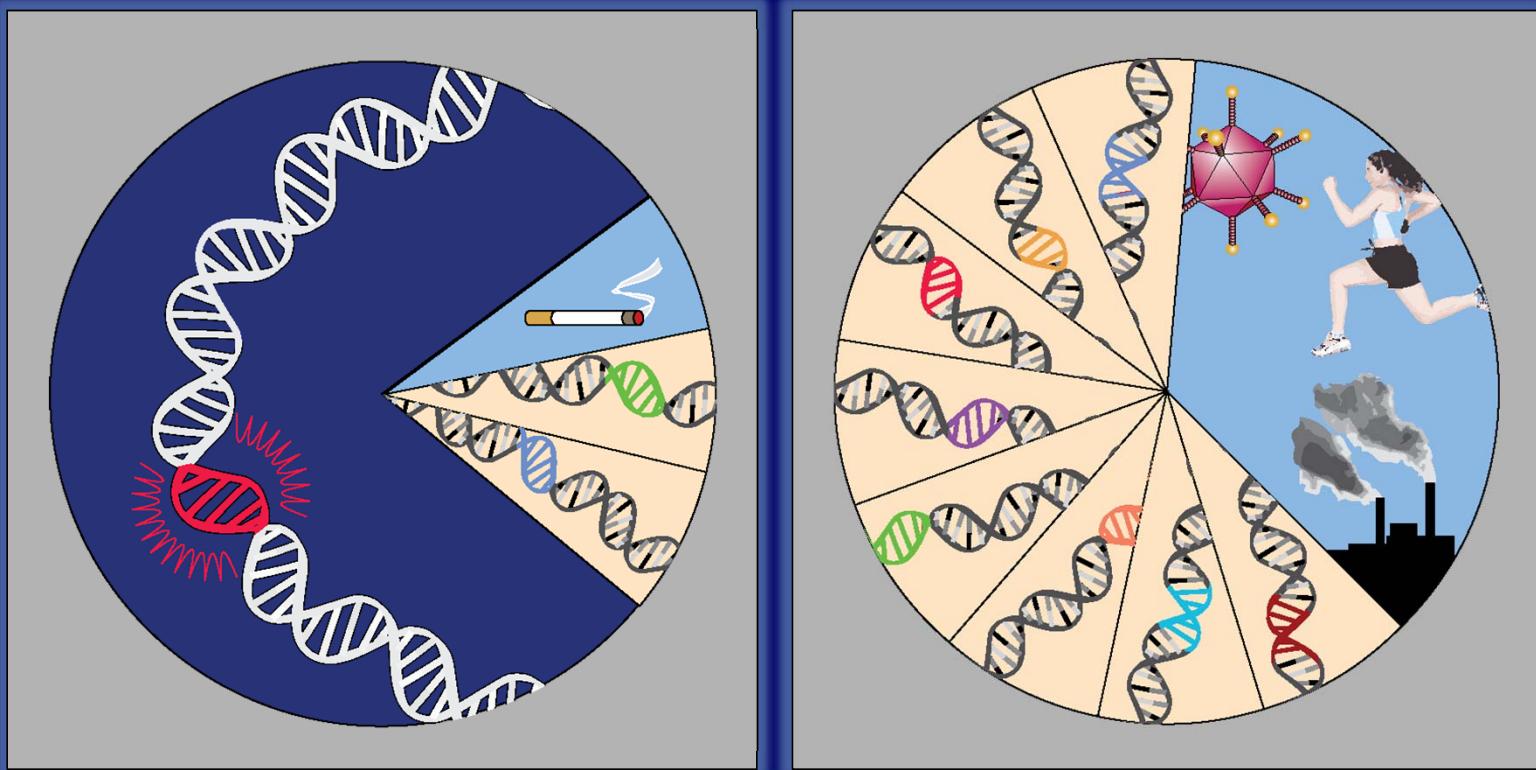
**Hundreds of Thousands of Human
Genomes Sequenced**

**Profound Advances in Understanding
How the Human Genome Functions**

**Significant Advances in Unraveling the
Genomic Bases of Human Disease**



Genomic Architecture of Genetic Diseases



Rare, Simple, Monogenic,
Mendelian...

Common, Complex, Multigenic,
Non-Mendelian...

Manolio et al., J Clin Invest (2008)

Three Decades of Genomics

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**Vivid Examples of Genomic Medicine
Now Emerging**

Bringing Genomic Medicine Into Focus



'Hot Areas' in Genomic Medicine

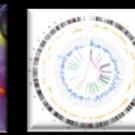


Cancer Genomics

Pharmacogenomics

Rare Genetic Disease
Diagnostics

Prenatal Genomic Testing



I. First Three Decades of Genomics

II. New Realities (& Opportunities)



New Reality (& Opportunity) #1



Generating a Human Genome Sequence is (Almost) Trivial

GGCACGATGCTCCGTCGAGGAAACTTGAACACCATTGGGTGAGGAAACTTGAACAC
CACGATGCTCCGTCGAGGAAACTTGAACACCATTGGGTGAGGAAACTTGAACAC
TCGAGGAAACTTGAACACCATTGGCACGATGCTCCGTCGAGGAAACTTGAACAC
TGAACACCATTGGCACGATGCTCCGTCGAGGAAACTTGAACACCATTGGGTGAG
GGCACGATGCTCCGTCGAGGAAACTTGAACACCATTGGGTGAGGAAACTTGAAC
CACGATGCTCCGTCGAGGAAACTTGAACACCATTGGGTGAGGAAACTTGAACAC
TCGAGGAAACTTGAACACCATTGGCACGATGCTCCGTCGAGGAAACTTGAACAC
TGAACACCATTGGCACGATGCTCCGTCGAGGAAACTTGAACACCATTGGGTGAG
GGCACGATGCTCCGTCGAGGAAACTTGAACACCATTGGGTGAGGAAACTTGAAC
CACGATGCTCCGTCGAGGAAACTTGAACACCATTGGGTGAGGAAACTTGAACAC
TCGAGGAAACTTGAACACCATTGGCACGATGCTCCGTCGAGGAAACTTGAACAC
TGAACACCATTGGCACGATGCTCCGTCGAGGAAACTTGAACACCATTGGGTGAG
GGCACGATGCTCCGTCGAGGAAACTTGAACACCATTGGGTGAGGAAACTTGAAC

Generating a Human Genome Sequence is (Almost) Trivial



But Clinically Understanding a Patient's Genome Sequence is NOT Trivial

New Reality (& Opportunity) #2



The Relevance of Genomics Has Changed



Biomedical Researchers

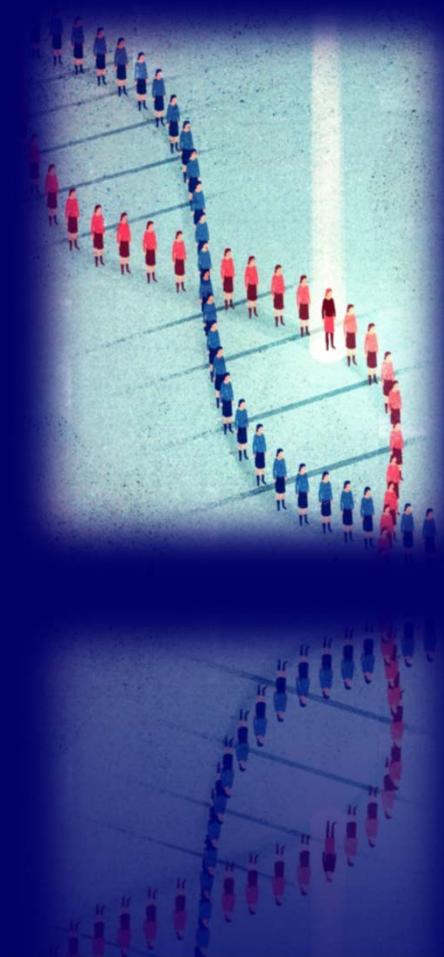


Healthcare Professionals



Patients (and Friends & Relatives of Patients)

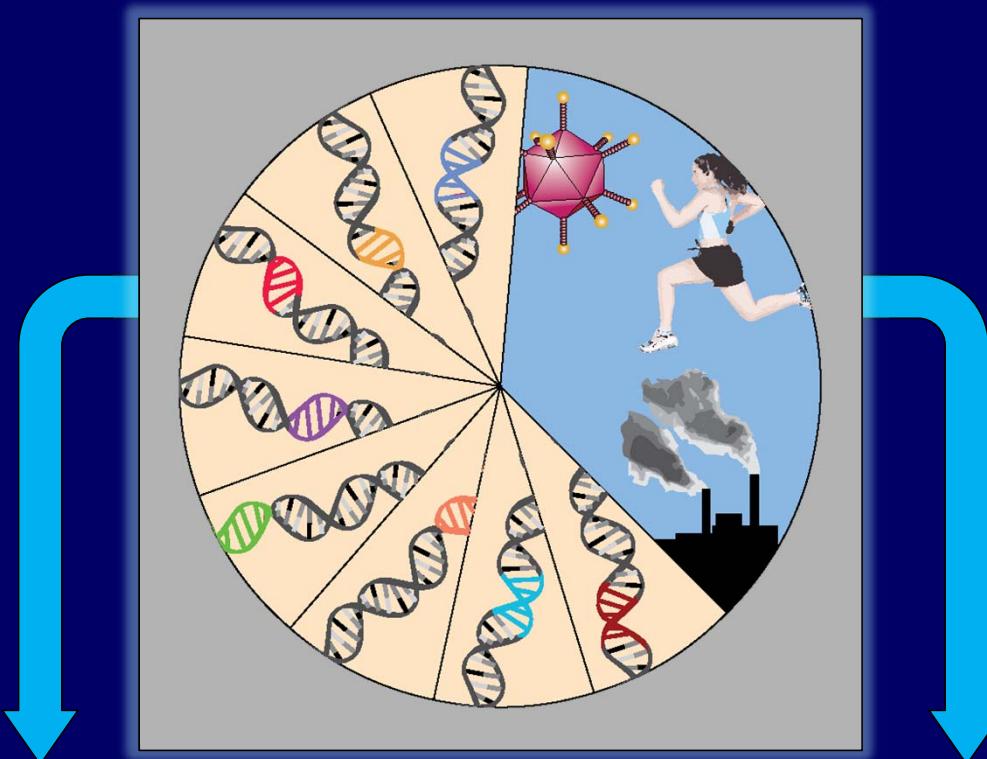
Genomics and Society



New Reality (& Opportunity) #3



Both Genomics and Other Factors Play a Role in Human Disease



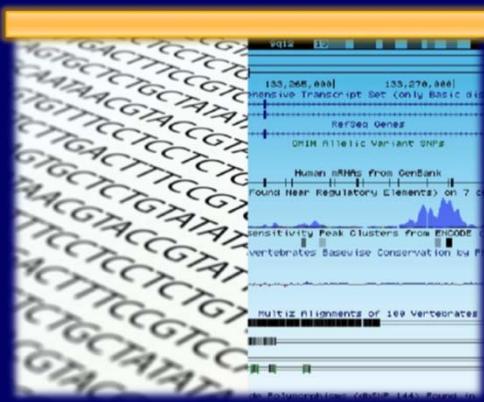
**Genome Analysis
Technologies**

**Health and Environmental
Monitoring Technologies**

Precision Medicine

More Precise Accounting for Individual Variability

Genomics

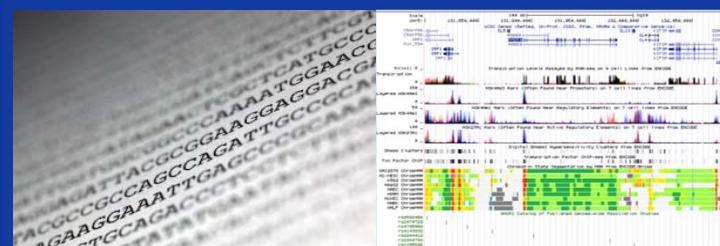


Physiology



Lifestyle ← → Environment





Genomics



EHRs



Technologies

All of Us Research Program



- >1 million U.S. volunteers
- Participants to share genomic data, lifestyle information, biological samples – all linked to their EHRs
- Open, responsible data sharing with strong privacy protections



U.S. Department of Health & Human Services

National Institutes of Health



National Institutes of Health
All of Us Research Program

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[JoinAllofUs.org](#) ▾

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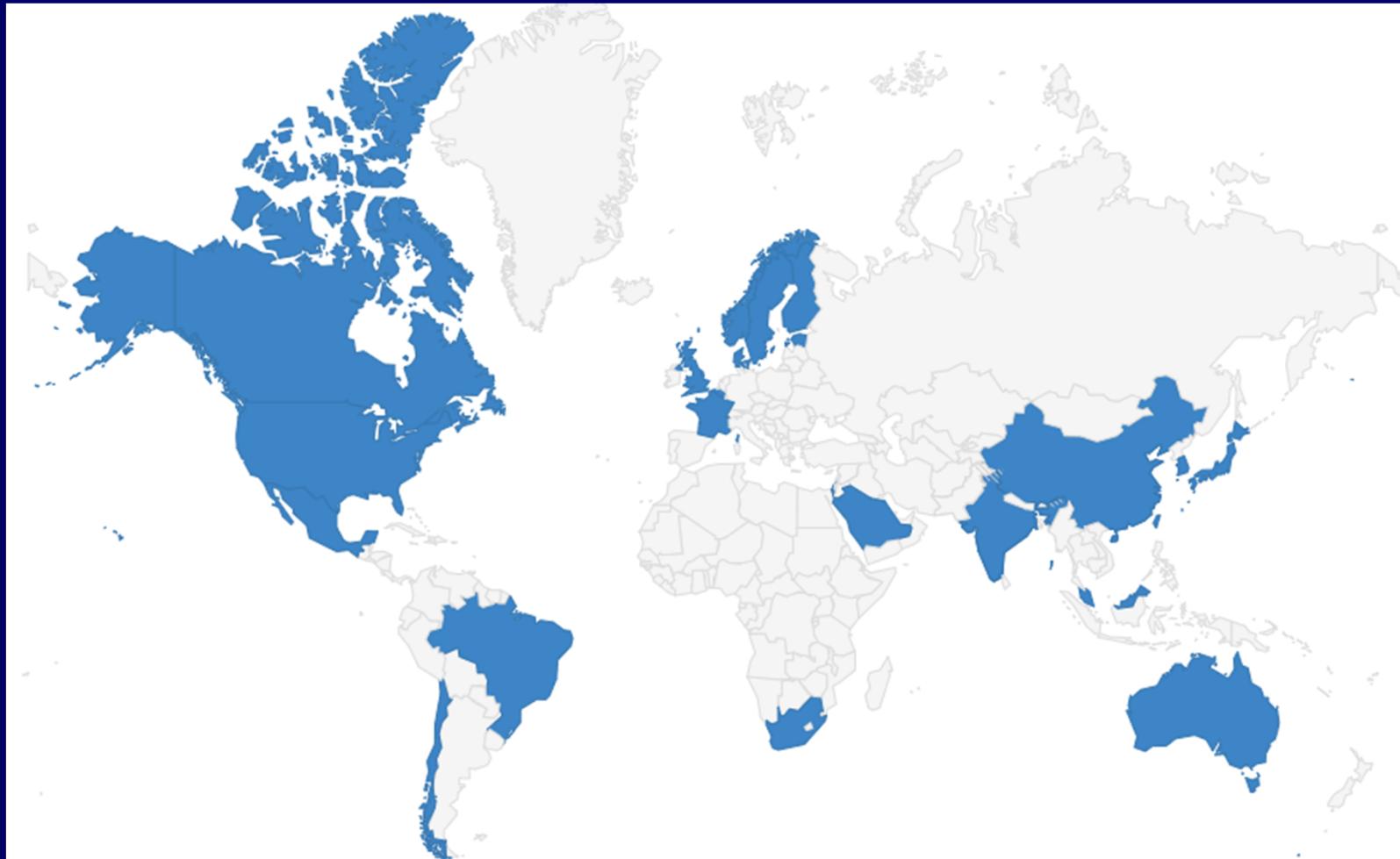
The future of health begins with you

The *All of Us* Research Program is a historic effort to gather data from one million or more people living in the United States to accelerate research and improve health. By taking into account individual differences in lifestyle, environment, and biology, researchers will uncover paths toward delivering precision medicine.

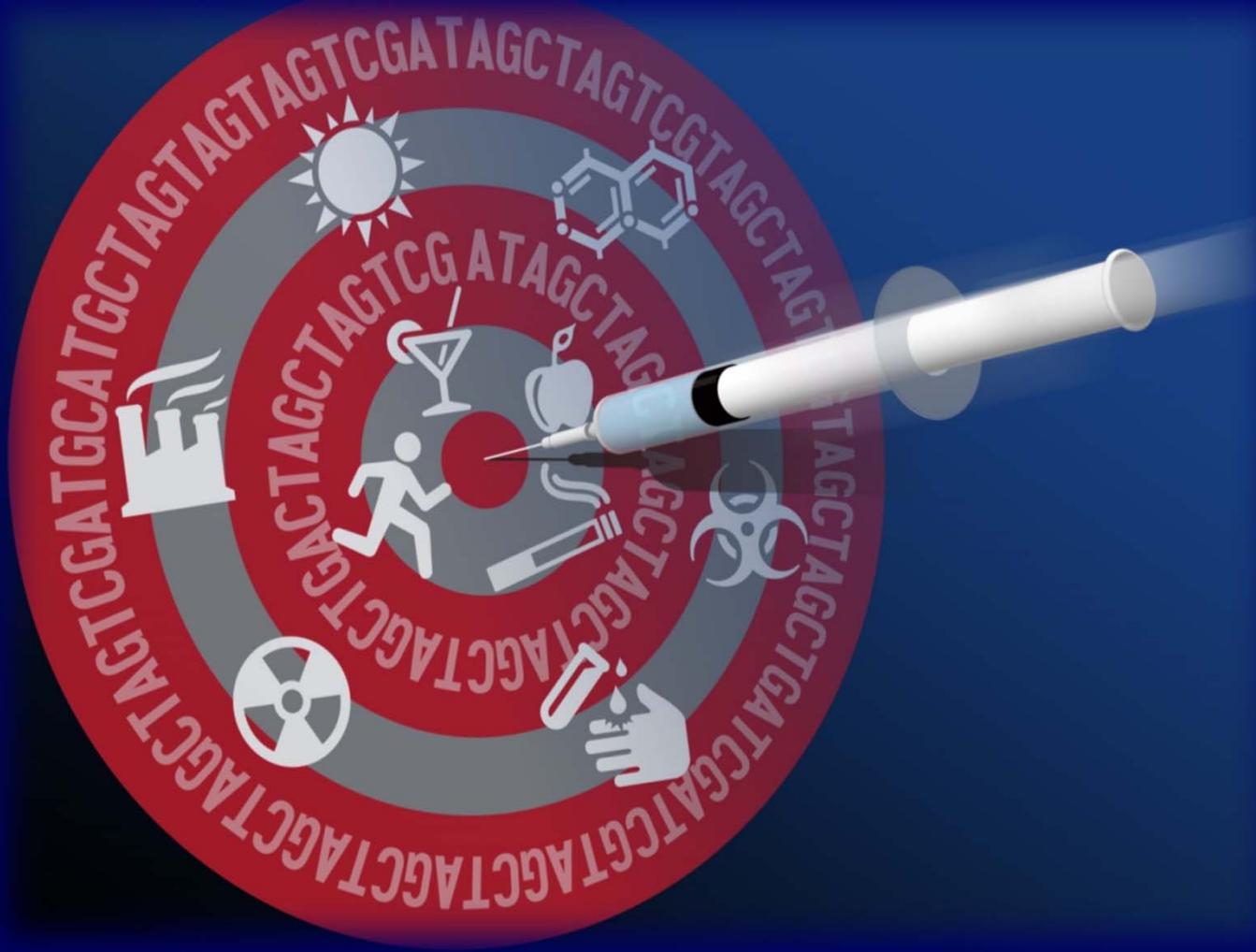
[WATCH VIDEO](#) ▶

allofus.nih.gov

Major Cohort Studies Worldwide



Opportunities for Precision Medicine Research

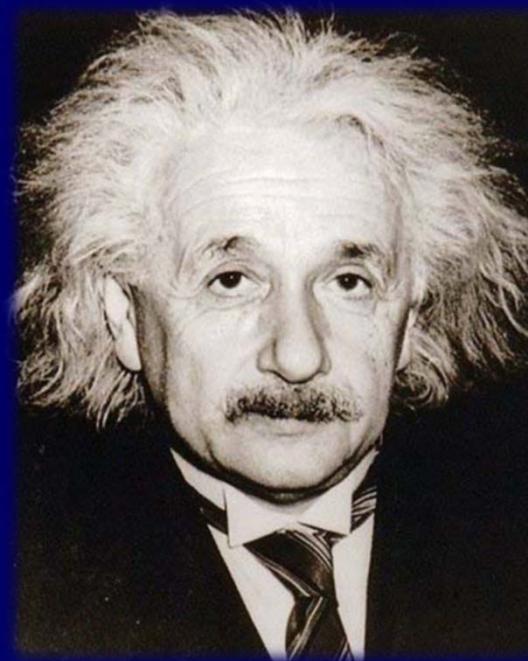


Research
It's A Journey ^

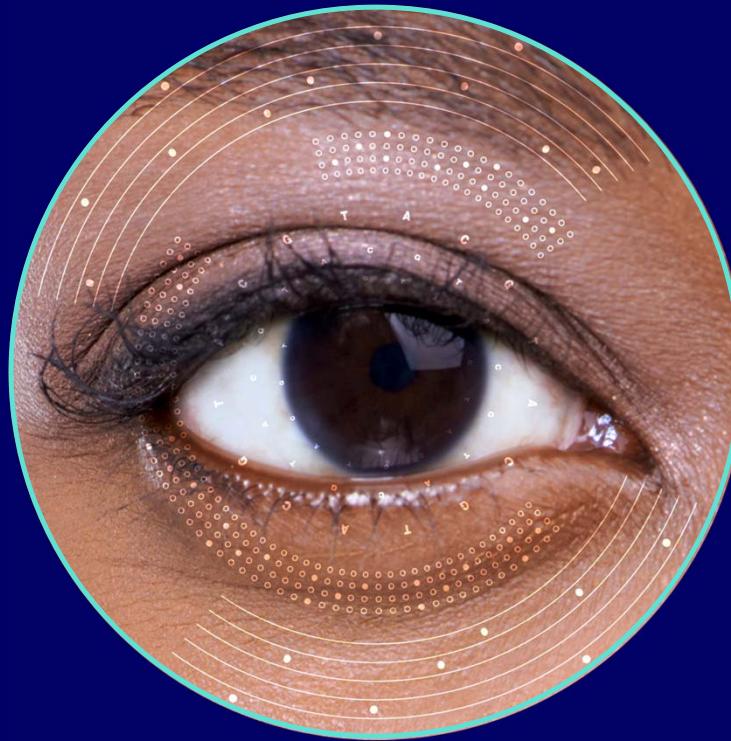


If we knew what we were doing, it wouldn't be called Research.

-A. Einstein



Genomics2020



En Route to a “2020 Vision for Genomics”



September 6, 2018



The Genomics Landscape

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genome.gov/email



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of **Genomics**®