



Entering the Era of Genomic Medicine

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



1

- I. First ~3 Decades of Genomics
- II. New Realities (& Opportunities)
- III. Strategic Planning: *Genomics2020*



2

- I. First ~3 Decades of Genomics
- II. New Realities (& Opportunities)
- III. Strategic Planning: *Genomics2020*



3

The Origin of “Genomics”: 1987

EDITORIAL

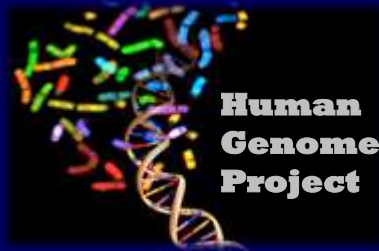
A New Discipline, A New Name, A New Journal

Genomics (1987)

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

4

Human Genome Project: 1990-2003



5

~3 Decades of Genomics

Human Genome Sequenced for First Time
by the Human Genome Project



6

Myriad Applications of Genomics



Health, Disease, & Medicine

7

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



8

The Journey to Genomic Medicine



Human Genome Project



Realization of Genomic Medicine

9



Nature



Nature



2003

Base Pairs to Bedside

2011 Health



10

~3 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



11



“...‘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.”

12

Human Genome Sequence

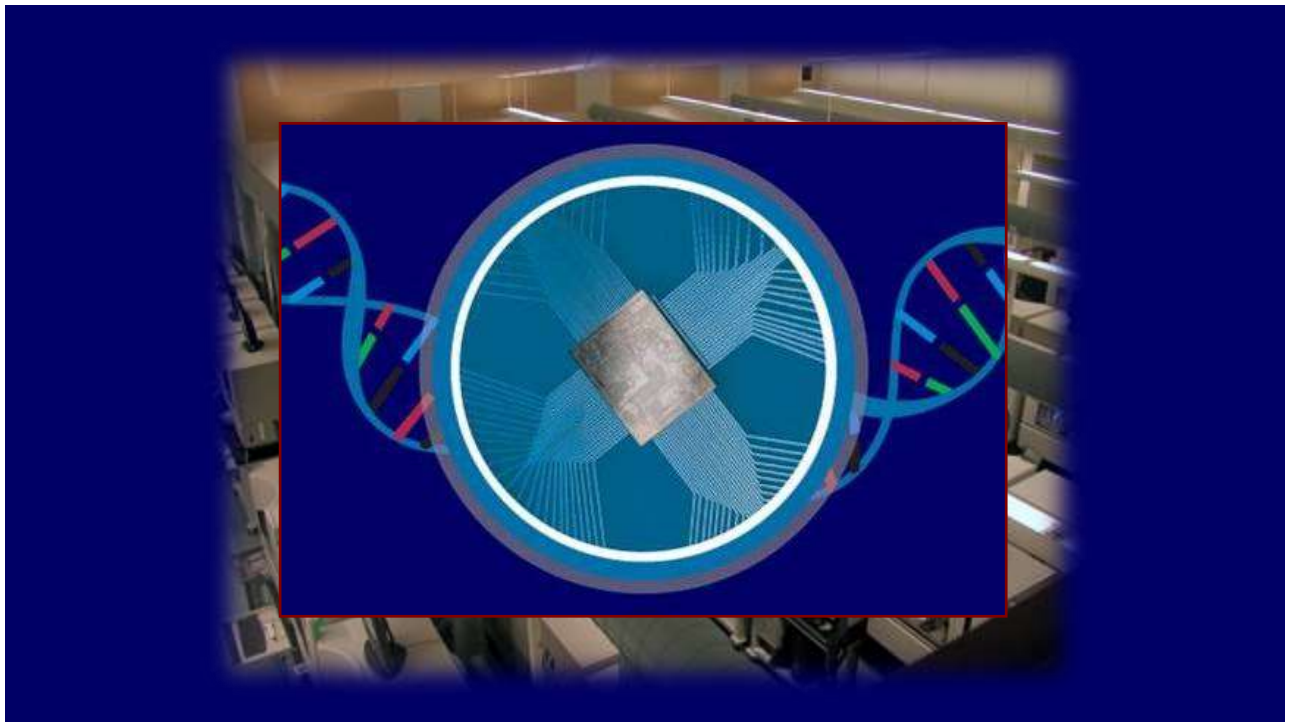
~\$1,000,000,000



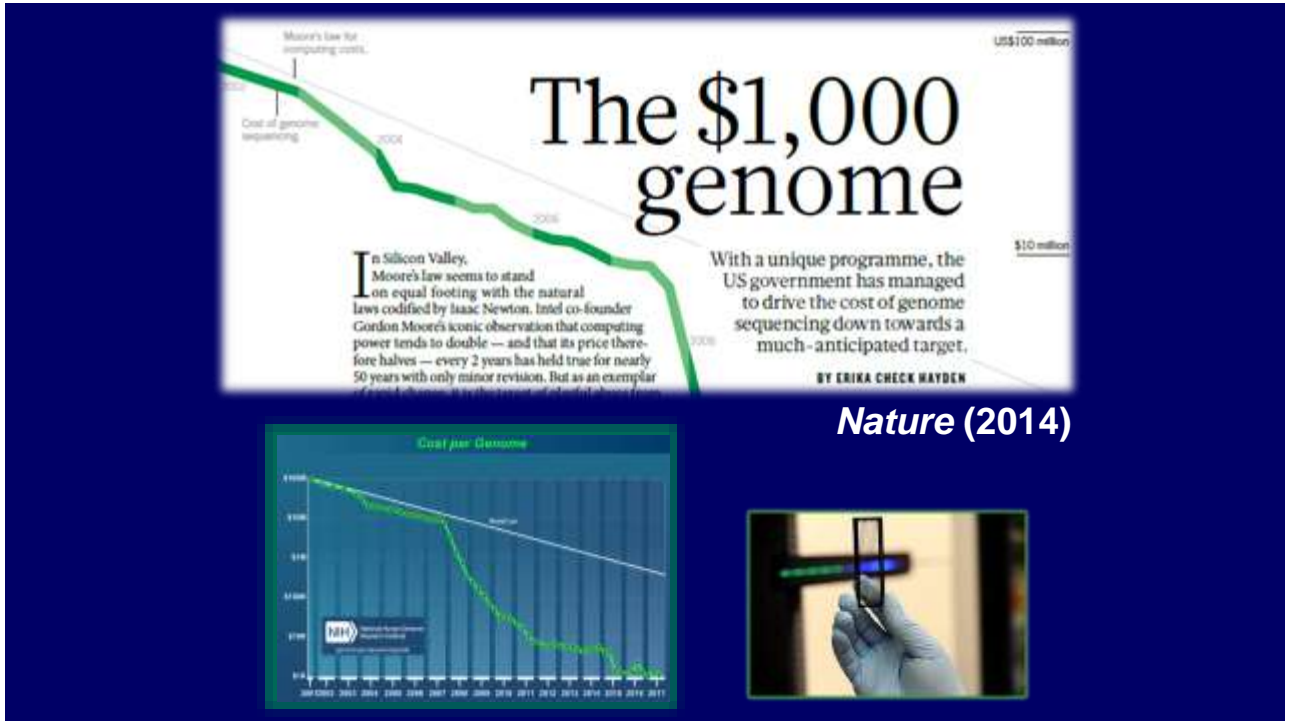
~\$1,000

"The \$1000 Genome"

13



14



15



16

~3 Decades of Genomics

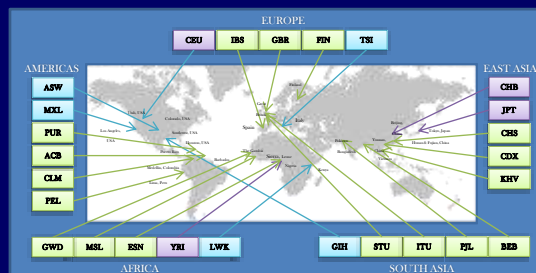
Human Genome Sequenced for First Time
by the Human Genome Project

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

Hundreds of Thousands of Human
Genomes Sequenced

17

Human Genomic Variation



2535 Humans, 26 Populations

18

~3 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

Profound Advances in Understanding
How the Human Genome Functions

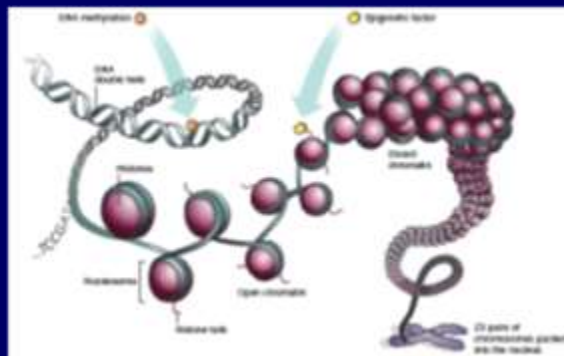


~3,000 bp (0.0001%) of Human Genome Sequence

TGCCGCGAACTTTI
GRACCCGACTAGGAI
CCGGAAGGAGGGTCTI
CCGGCACTGTCCGCC
AGAATCGGGAAAGGG
GAAAGCCGCTAGAGC
TGTCCGAGTAGGGC
GTCTTTGGCATTAGC
TGCTCCAAACTTTI
TGGGGTAAAGGAATF
AGAAGAGATGGAAGI
ATGCACTTGTTTTAI
ACACTTGATTGTCTI
TTGGGGTAGGTAGAF
AAAGCAATTTGTTC
CTGACATTTAATAAF
AATCTTAGGCAAGCI
ATGAATGAATAGTIF
TATAAATAGCTCATF
TCCGGTCTAAGGAC
TGAATTTATCCACCI
AAATATAGACTTTI
GTCTAARTACTTAAI
AATATAGGTTAAAAF
AAAAATTTTTCATAAG
TTACAACTTCCTTC
GTGGTAGCCTTTGGI
TGTGACTTGACCTTI
ATGGATTACCATATF
CTGGATATGCAATG
TTTCTATTGTATGTI

TECHNOLOGY FEATURE
**READING THE SECOND
GENOMIC CODE**

Nature (2012)

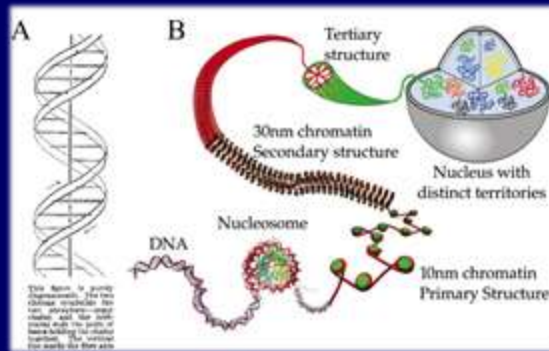


CTTGCAAACGTAACAG
GTCCTGGCCGACCTGA
TGGACCTAAGAGAGAG
AGGGAGGCTGGGAGTC
GTGCGTAGTGGGTGGA
CAAAAGGAGAGGGGTGG
GCACCCAGAGTAGTAG
TGGAAAAGGCCAGCGT
GTCTATGGGTGGGTT
AAACAGAAAGCATT
ACTCAAGTACGCTACT
CCCTTTCATGCGCTTGG
TCAGCCAACAAAAATT
GATTCTCAAAAAATTG
CCGAAGTTATATCCAA
TAGCATCTAAGTTCGG
TATATACTGGTGTGA
AAAAAGTCAAAATATGT
CAGTTAATCCTGGAAC
AATATCTTTTGTGT
AAATGTTAATTTGGCAT
GAATATTTTCATGGATA
ATCACCTGACACATTI
CTCATTTCTGTCTCC
CCTAAAAATACCAATGA
TTGCTTAGTTTTCAAA
CCTTAACATCTCTGTG
GTTAACGTCTATTATT
TTTTGTGACTCTCAAT
GGAACACGTCACATG
AAAAATATATGGTAT

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)



21

Some Genomic Variants



**Traits
(i.e., Phenotypes)**

22

~3 Decades of Genomics

Human Genome Sequenced for First Time
by the Human Genome Project

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

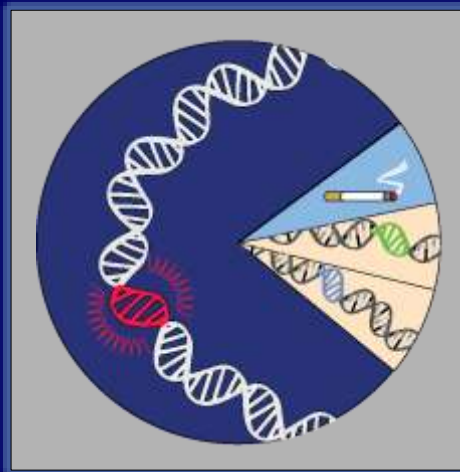
Hundreds of Thousands of Human
Genomes Sequenced

Profound Advances in Understanding
How the Human Genome Functions

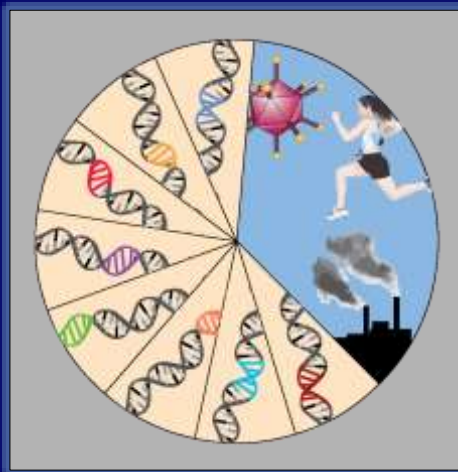
Significant Advances in Unraveling the
Genomic Bases of Human Disease

23

Genomic Architecture of Genetic Diseases



Rare, Simple, Monogenic,
Mendelian...



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

Manolio et al., J Clin Invest (2008)

24

~3 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

Profound Advances in Understanding
How the Human Genome Functions

Significant Advances in Unraveling the
Genomic Bases of Human Disease

Vivid Examples of Genomic Medicine
Now Emerging

25

Bringing Genomic Medicine Into Focus



26

'Hot Areas' in Genomic Medicine



Cancer Genomics



Pharmacogenomics



Rare Genetic Disease
Diagnostics



Prenatal Genomic Testing



27

- I. First ~3 Decades of Genomics
- II. New Realities (& Opportunities)
- III. Strategic Planning: *Genomics2020*



28

New Reality (& Opportunity) #1



29

Generating a Human Genome Sequence is (Almost) Trivial

ATCCCTCCGCTCCGTCGAGGAAACTTGAACACCAATTGGGTCGAGGAAACTTGAAC
ACGATGCTCCGTCGAGGAAACTTGAACACCAATTGGGTCGAGGAAACTTGAACACC
CGAGGAAACTTGAACACCAATTGGCACGATGCTCCGTCGAGGAAACTTGAACACC
TGAACACCAATTGGCACGATGCTCCGTCGAGGAAACTTGAACACCAATTGGGTCGAG
GCACGATGCTCCGTCGAGGAAACTTGAACACCAATTGGGTCGAGGAAACTTGAAC
ACGATGCTCCGTCGAGGAAACTTGAACACCAATTGGGTCGAGGAAACTTGAACACC
CGAGGAAACTTGAACACCAATTGGCACGATGCTCCGTCGAGGAAACTTGAACACC
TGAACACCAATTGGCACGATGCTCCGTCGAGGAAACTTGAACACCAATTGGGTCGAG
GCACGATGCTCCGTCGAGGAAACTTGAACACCAATTGGGTCGAGGAAACTTGAAC
ACGATGCTCCGTCGAGGAAACTTGAACACCAATTGGGTCGAGGAAACTTGAACACC
CGAGGAAACTTGAACACCAATTGGCACGATGCTCCGTCGAGGAAACTTGAACACC
TGAACACCAATTGGCACGATGCTCCGTCGAGGAAACTTGAACACCAATTGGGTCGAG
GCACGATGCTCCGTCGAGGAAACTTGAACACCAATTGGGTCGAGGAAACTTGAAC

30

Generating a Human Genome Sequence is (Almost) Trivial



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

31

New Reality (& Opportunity) #2



32

The Relevance of Genomics Has Changed



Biomedical Researchers



Healthcare Professionals



Patients (and Friends & Relatives of Patients)

33

Genomics and Society



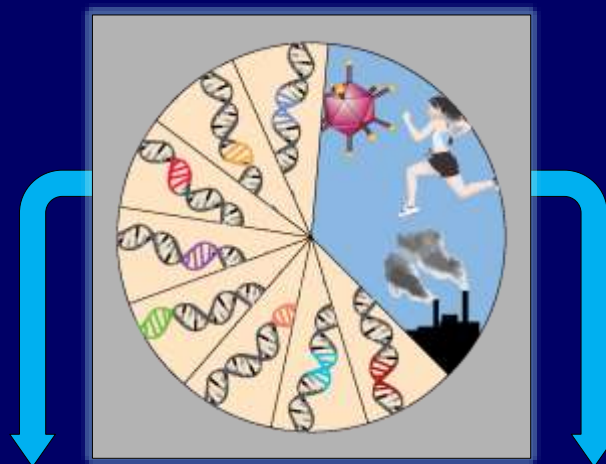
34

New Reality (& Opportunity) #3



35

Both Genomics and Other Factors Play a Role in Human Disease



**Genome Analysis
Technologies**

**Health and Environmental
Monitoring Technologies**

36

Precision Medicine

More Precise Accounting for Individual Variability

Genomics



Physiology



Lifestyle ← → **Environment**



37



Genomics



EHRs



Technologies

38

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**

39

A screenshot of the NIH All of Us Research Program website. The header includes the NIH logo, navigation links for 'ABOUT', 'FUNDING', and 'NEWS, EVENTS, & MEDIA', a 'JoinAllOfUs.org' button, and a search bar. The main content area features a diverse group of people standing together, with the headline 'The future of health begins with you'. Below the headline is a paragraph describing the program's goal to gather data from one million or more people to accelerate research and improve health. A 'WATCH VIDEO' button is located at the bottom right of the main content area.

allofus.nih.gov

40

New Reality (& Opportunity) #4



43

The World of Human Genome Sequencing is Changing



2012

~1%

2018

~20%

2022

>80%

% of generated human genome sequences funded by healthcare systems

ga4gh.org

44

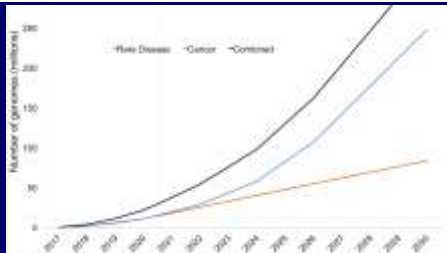
Human Genome Sequences: Looking Ahead



Global Alliance
for Genomics & Health
Collaborate. Innovate. Accelerate.

Genomics in healthcare: GA4GH looks to 2022

Ewan Birney¹, Jessica Vamathevan¹ and Peter Goodhand²



bioRxiv (2017)

By 2022:

- **>80%** from healthcare (as opposed to research)
- **~40-50M** human genome sequences generated

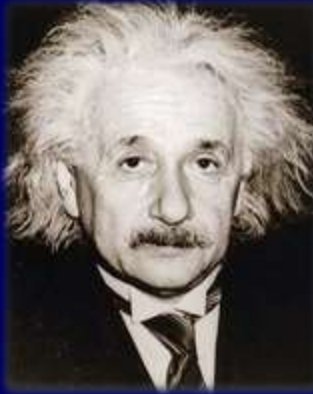
45

Research
^
It's A Journey



46

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



47

- I. First ~3 Decades of Genomics
- II. New Realities (& Opportunities)
- III. Strategic Planning: *Genomics2020*



48

Genomics2020



En Route to a “2020 Vision for Genomics”

49

1991-1995
Understanding the Genetic Inheritance of the Human Genome Project

1993-1998
A New Five-Year Plan for the U.S. Human Genome Project

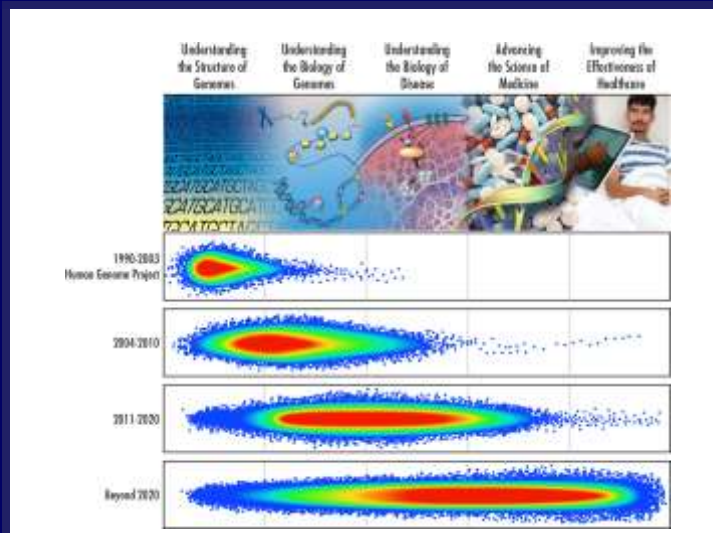
1998-2003
A vision for the future of genomics research

2003-2010
PERSPECTIVE
Charting a course for genomic medicine from base pairs to bedside

2011-Present

50

2011-Present *En Route to Genomic Medicine*

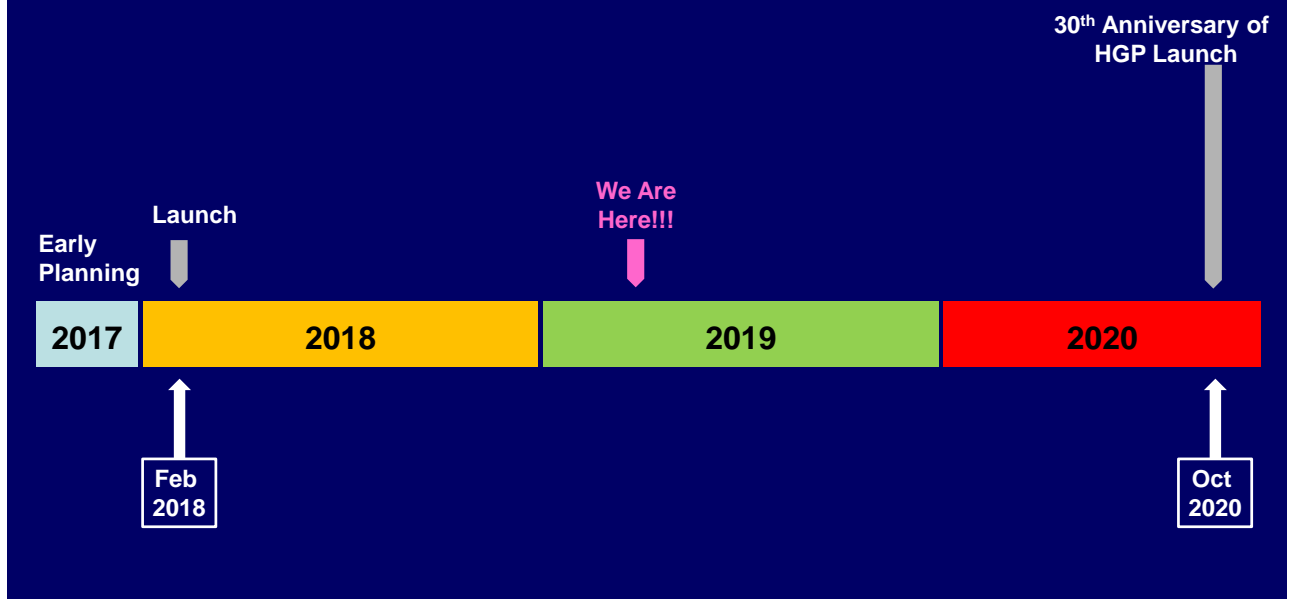


51

It is hard to claim (or believe) that a **2011** strategic plan represents a suitable blueprint for genomics or NHGRI in **2020 (and beyond)**

52

'Genomics2020' Strategic Planning Timeline



53

—
The **Forefront**
of **Genomics**[®]
—

54

Seeking Your Ideas



Website: genome.gov/genomics2020

Email: genomics2020@mail.nih.gov

Hashtag: [#genomics2020](https://twitter.com/genomics2020)

55

Inter-Society Coordinating Committee for Practitioner Education in Genomics



56



To subscribe, go to:
genome.gov/email

57



58