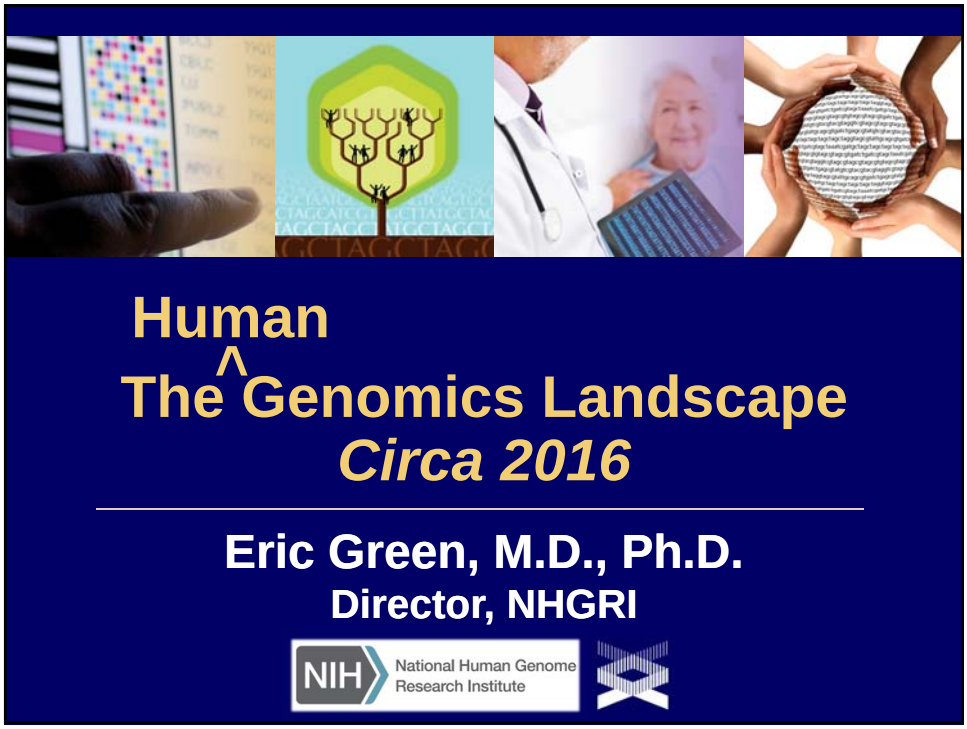
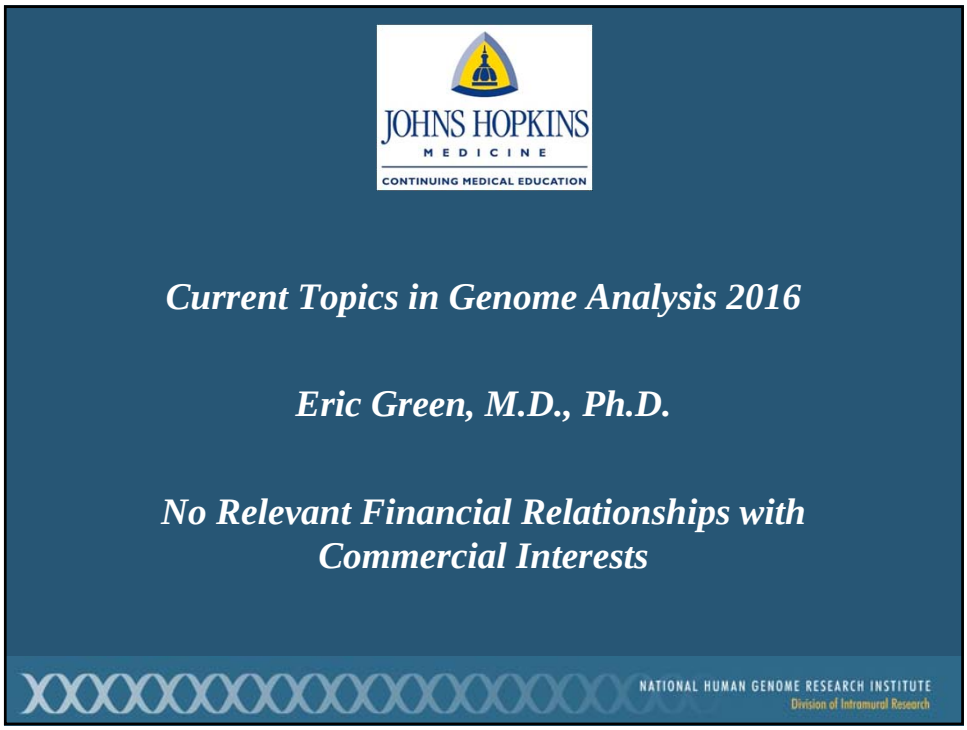
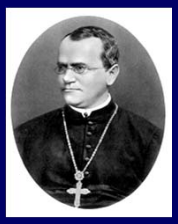

Human
The Genomics Landscape
Circa 2016
Eric Green, M.D., Ph.D.
Director, NHGRI
NIH
National Human Genome Research Institute


JOHNS HOPKINS
MEDICINE
CONTINUING MEDICAL EDUCATION
Current Topics in Genome Analysis 2016
Eric Green, M.D., Ph.D.
No Relevant Financial Relationships with Commercial Interests
NATIONAL HUMAN GENOME RESEARCH INSTITUTE
Division of Intramural Research

I. **Historical Context for Genomics**
II. **Major Achievements since the Human Genome Project**
III. **The Human Genomics Landscape: 2016 and Beyond**

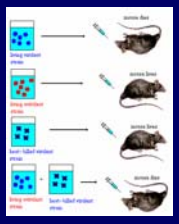
>> Goal: Place Other Speakers into a Broader Context <<

Foundational Milestones in Genetics & Genomics

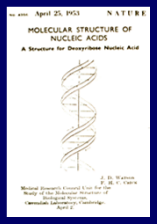


Mendel ***1865***

Miescher ***1871***

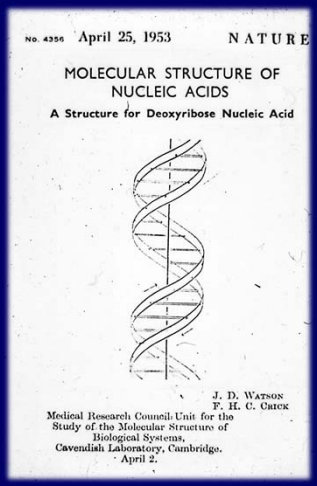


Avery ***1944***



Watson & Crick ***1953***

April, 1953



No. 4356 April 25, 1953 NATURE

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

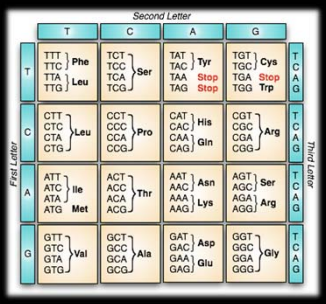
A Structure for Deoxyribose Nucleic Acid

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

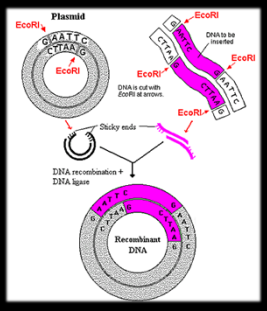


Second Letter

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

1980's



DNA Cloning

The Origin of "Genomics": 1987

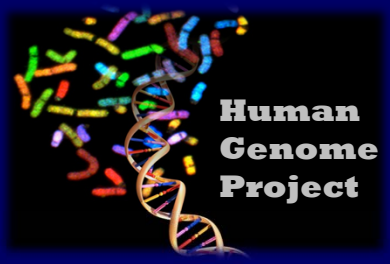
EDITORIAL

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



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)**

A Quarter Century of Genomics

Human Genome Sequenced for First Time by the Human Genome Project

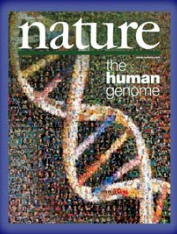
Myriad Applications of Genomics

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

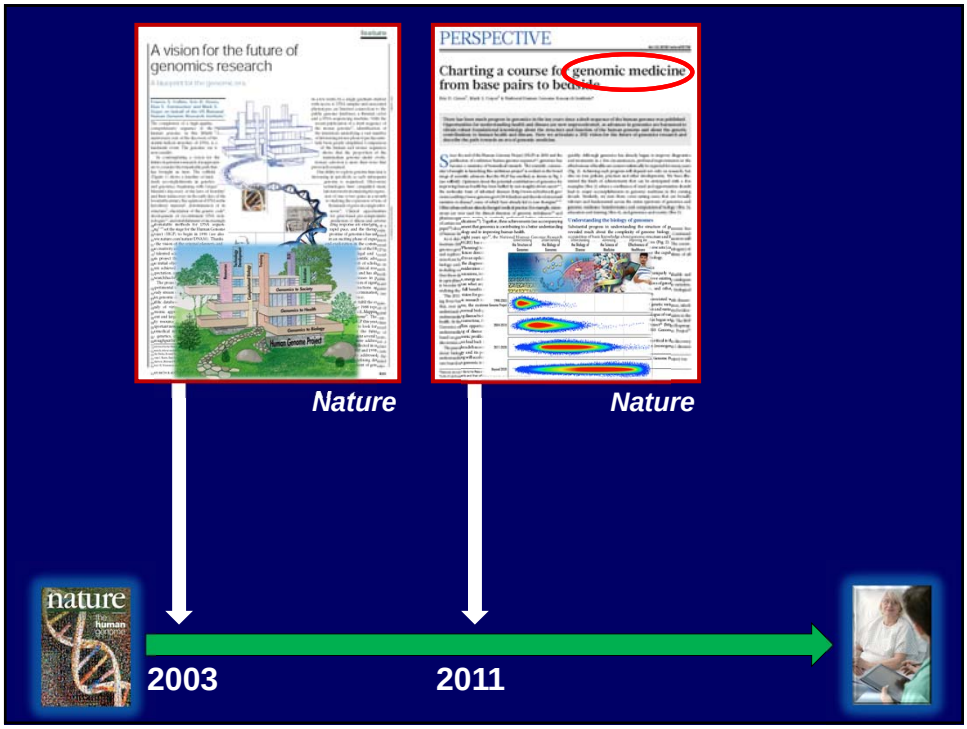
The Path to Genomic Medicine

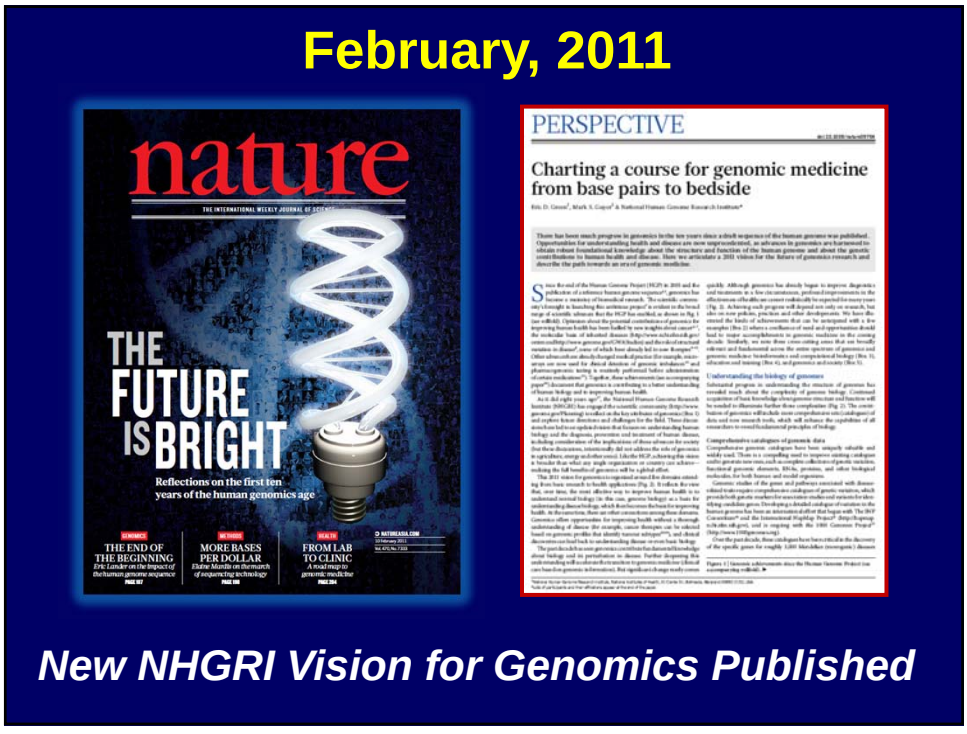


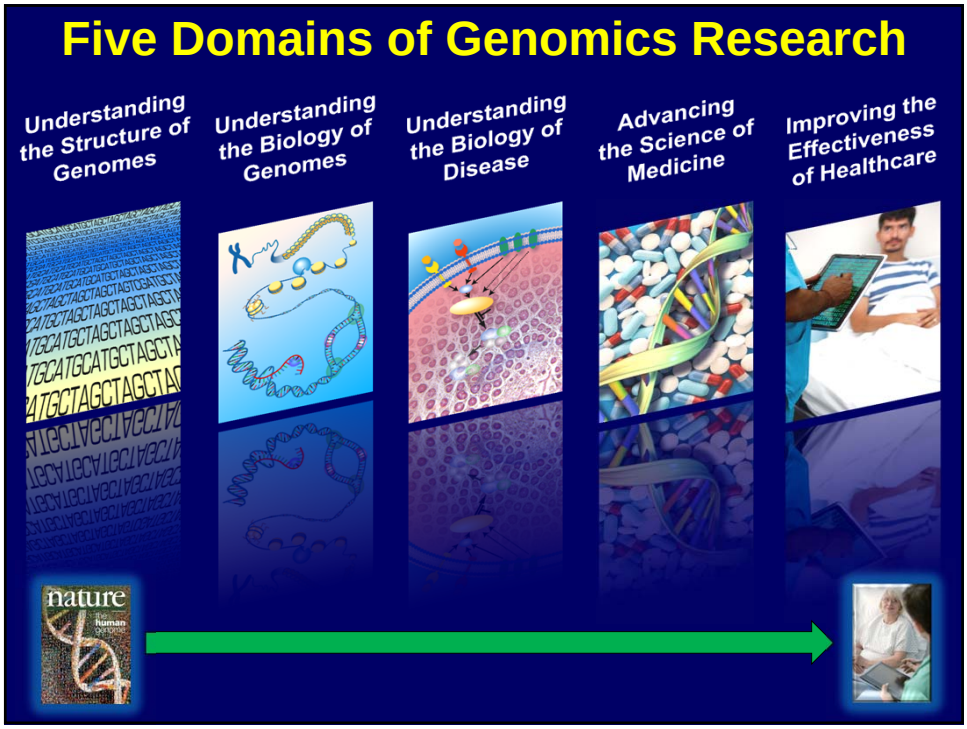
→ → ? → →

Human Genome Project

Realization of Genomic Medicine


A vision for the future of genomics research
PERSPECTIVE
Charting a course for genomic medicine from base pairs to bedside
Nature
Nature
nature
2003
2011


February, 2011
nature
THE FUTURE IS BRIGHT
Reflections on the first ten years of the human genomics age
THE END OF THE BEGINNING
MORE BASES PER DOLLAR
FROM LAB TO CLINIC
PERSPECTIVE
Charting a course for genomic medicine from base pairs to bedside
New NHGRI Vision for Genomics Published


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
nature


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.

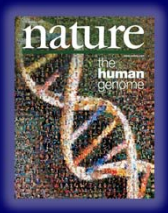
"…'technological leaps' that seem so far off as to be almost fictional but which, if they could be achieved, would revolutionize biomedical research and clinical practice.

[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."

Nature, April 2003

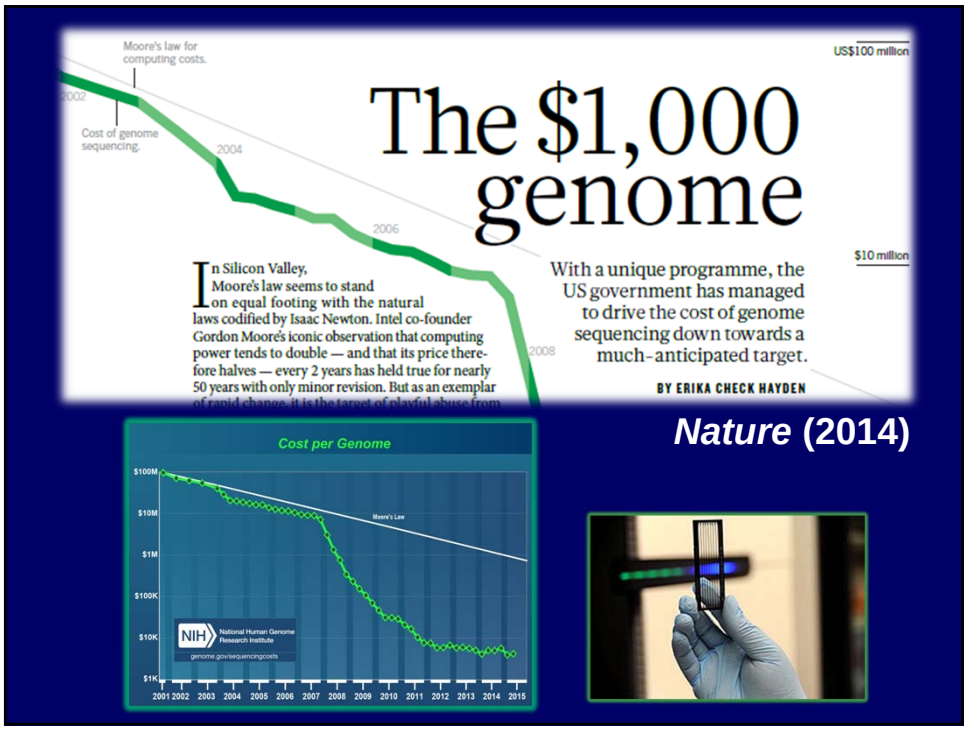
Human Genome Sequence

~$1,000,000,000



~$1,000

"The $1000 Genome"


Moore's law for computing costs.
Cost of genome sequencing.
2002
2004
2006
2008
US$100 million
$10 million
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)
Cost per Genome
$100M
$10M
$1M
$100K
$10K
$1K
Moore's Law
NIH
National Human Genome Research Institute
genome.gov/sequencingcosts
2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

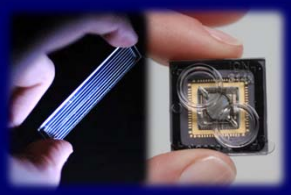
Sequencing a Human Genome

Human Genome Project (1st Sequence)

~$1B

~6-8 years

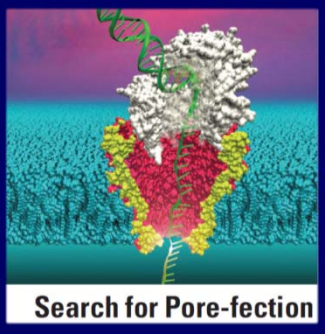
Today

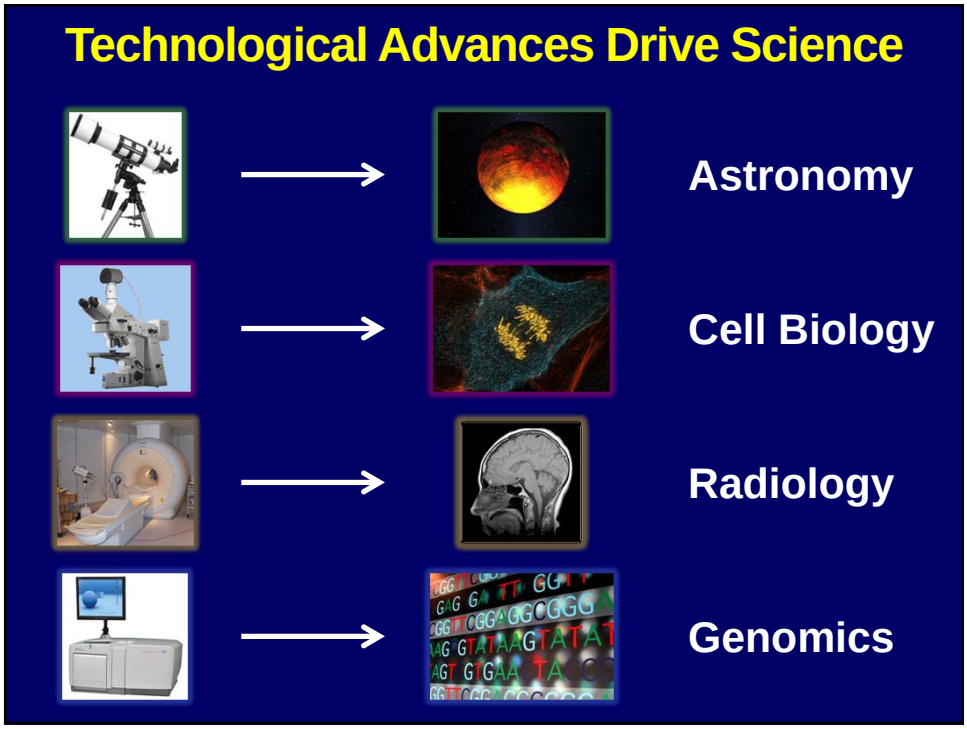


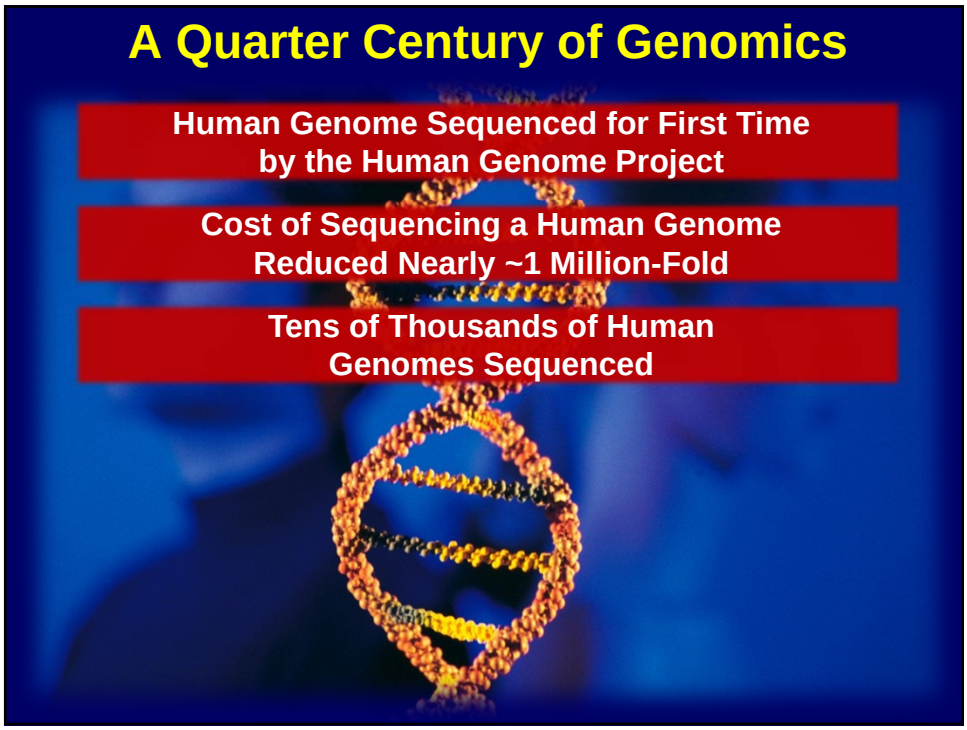
~$2-3K

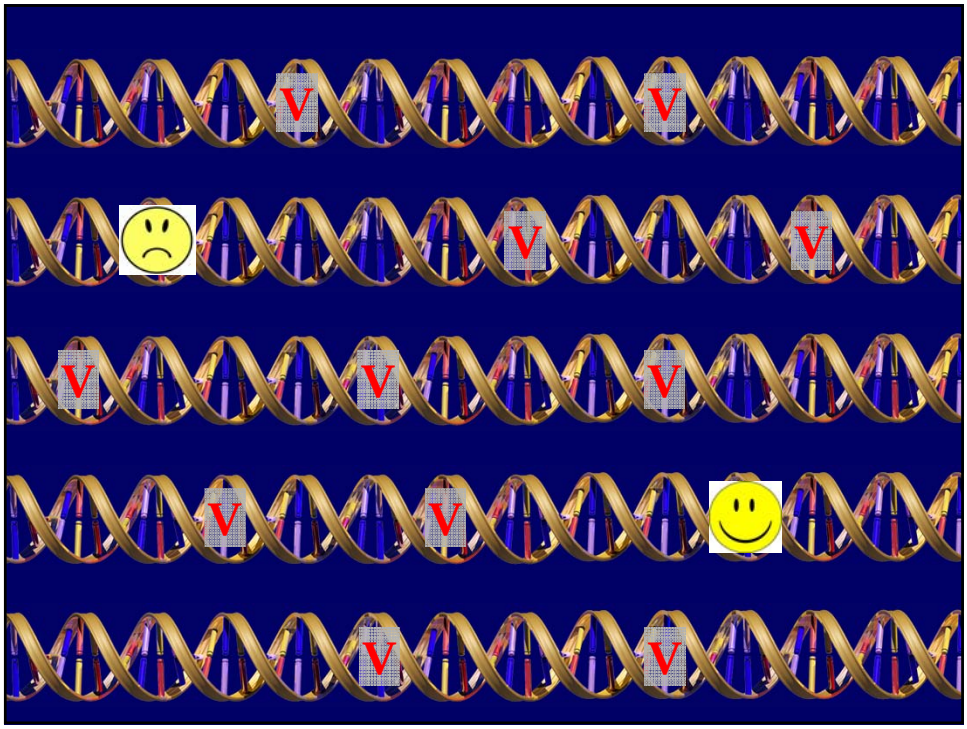
~1-3 days

And Yet Newer Technologies…



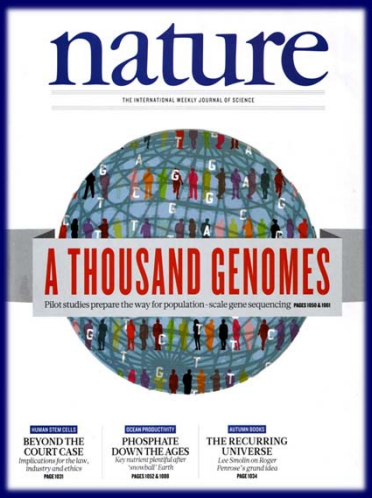

Technological Advances Drive Science
Astronomy
Cell Biology
Radiology
Genomics


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

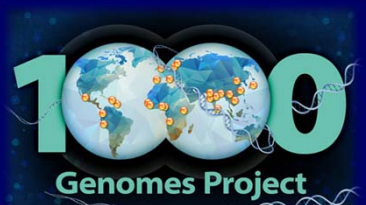

V
V
V
V
V
V
V
V
V
V
V
V

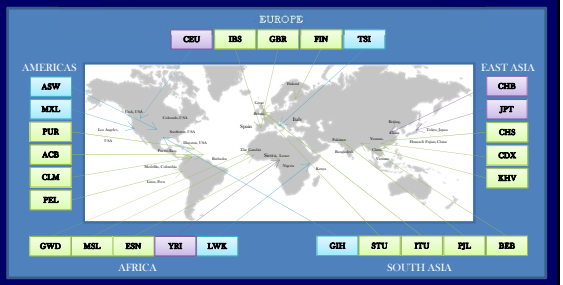

International HapMap Project
27 October 2005 | www.nature.com/nature | $10
THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE
nature
INSIDE
Why do we sleep?
nature insight
OPTOELECTRONICS
Germanium boost for silicon chips
LAW OF THE JUNGLE
Don't ask a chimpanzee for help
MEN OF LETTERS
If Darwin and Einstein had e-mail...
THE HAPMAP PROJECT
Chapter and verse on human genetic variation
NATUREJOBS
Biodefence boom
A haplotype map of the human genome
The International HapMap Consortium*
2005
A second generation human haplotype map of over 3.1 million SNPs
The International HapMap Consortium*
2007
Integrating common and rare genetic variation in diverse human populations
The International HapMap 3 Consortium*
2010

1000 Genomes
A Deep Catalog of Human Genetic Variation



Nature (2010)

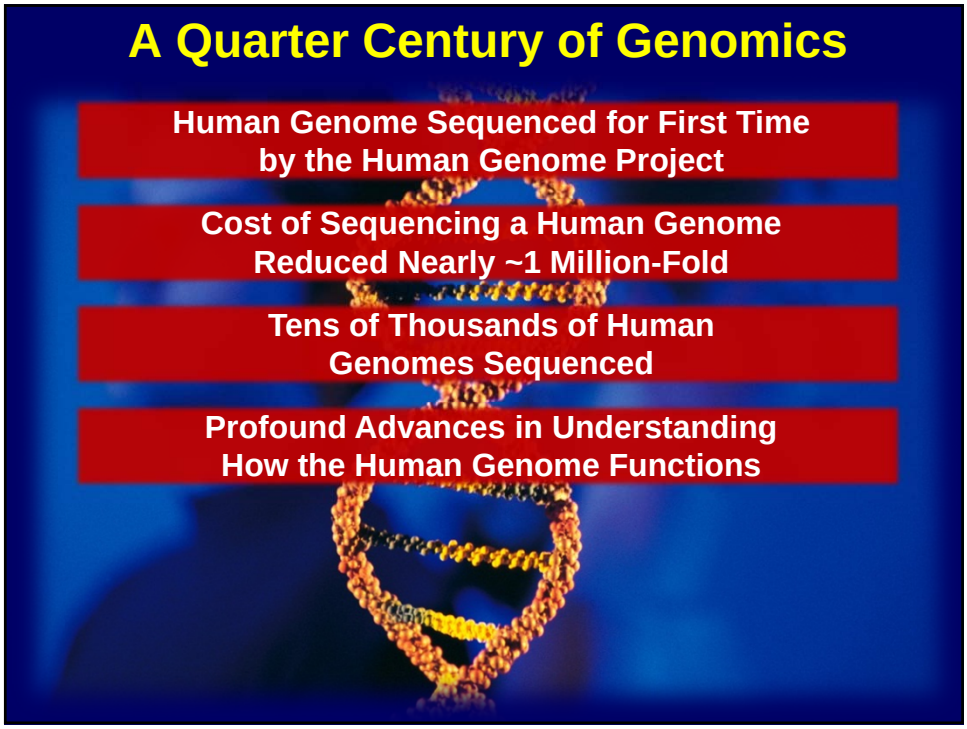


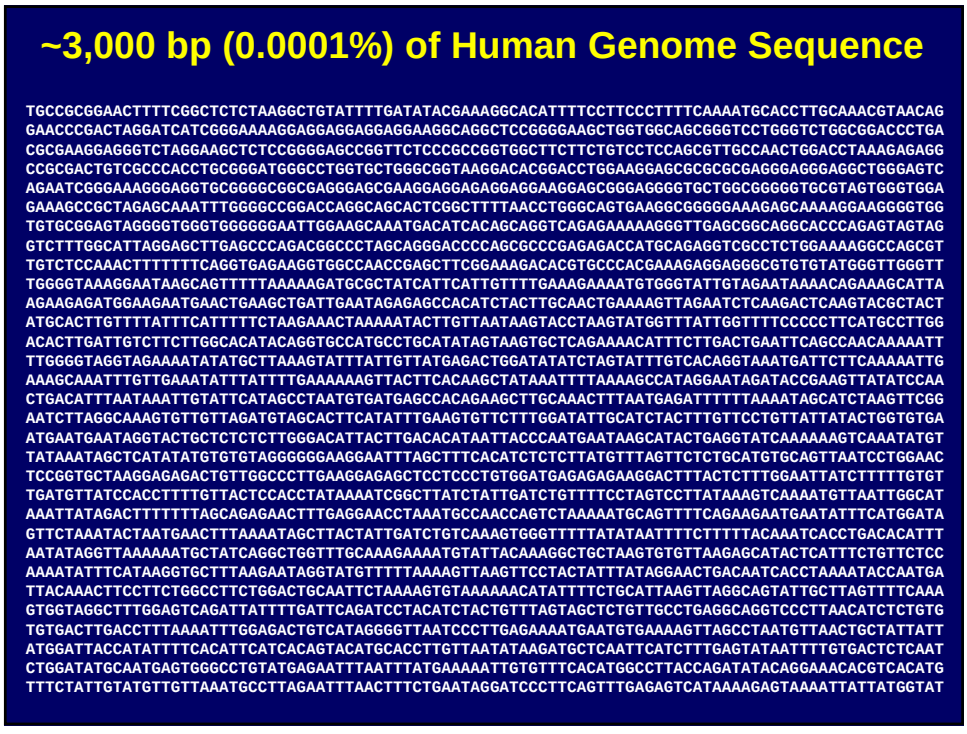


2535 Humans, 26 Populations

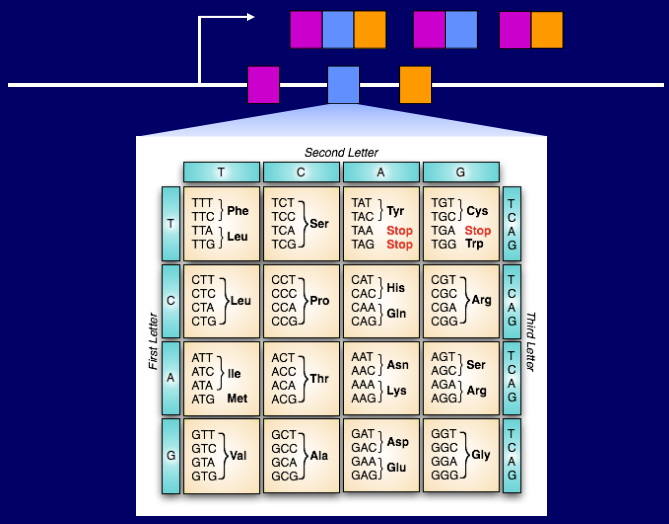
Your Genome: By the Numbers

- ~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 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


~3,000 bp (0.0001%) of Human Genome Sequence
TGCCGCGGAACTTTTCGGCTCTCTAAGGCTGTATTTTGATATACGAAAGGCACATTTTCCTTCCCTTTTCAAAATGCACCTTGCAAACGTAACAG
GAACCCGACTAGGATCATCGGGAAAAGGAGGAGGAGGAGGAAGGCAGGCTCCGGGGAAGCTGGTGGCAGCGGGTCCTGGGTCTGGCGGACCCTGA
CGCGAAGGAGGGTCTAGGAAGCTCTCCGGGGAGCCGGTTCTCCCGCCGGTGGCTTCTTCTGTCCTCCAGCGTTGCCAACTGGACCTAAAGAGAGG
CCGCGACTGTCGCCCACCTGCGGGATGGGCCTGGTGCTGGGCGGTAAGGACACGGACCTGGAAGGAGCGCGCGCGAGGGAGGGAGGCTGGGAGTC
AGAATCGGGAAAGGGAGGTGCGGGGCGGCGAGGGAGCGAAGGAGGAGAGGAGGAAGGAGCGGGAGGGGTGCTGGCGGGGGTGCGTAGTGGGTGGA
GAAAGCCGCTAGAGCAAATTTGGGGCCGGACCAGGCAGCACTCGGCTTTTAACCTGGGCAGTGAAGGCGGGGGAAAGAGCAAAAGGAAGGGGTGG
TGTGCGGAGTAGGGGTGGGTGGGGGGAATTGGAAGCAAATGACATCACAGCAGGTCAGAGAAAAAGGGTTGAGCGGCAGGCACCCAGAGTAGTAG
GTCTTTGGCATTAGGAGCTTGAGCCCAGACGGCCCTAGCAGGGACCCCAGCGCCCGAGAGACCATGCAGAGGTCGCCTCTGGAAAAGGCCAGCGT
TGTCTCCAAACTTTTTTTCAGGTGAGAAGGTGGCCAACCGAGCTTCGGAAAGACACGTGCCCACGAAAGAGGAGGGCGTGTGTATGGGTTGGGTT
TGGGGTAAAGGAATAAGCAGTTTTTAAAAAGATGCGCTATCATTCATTGTTTTGAAAGAAAATGTGGGTATTGTAGAATAAAACAGAAAGCATTA
AGAAGAGATGGAAGAATGAACTGAAGCTGATTGAATAGAGAGCCACATCTACTTGCAACTGAAAAGTTAGAATCTCAAGACTCAAGTACGCTACT
ATGCACTTGTTTTATTTCATTTTTCTAAGAAACTAAAAATACTTGTTAATAAGTACCTAAGTATGGTTTATTGGTTTTCCCCCTTCATGCCTTGG
ACACTTGATTGTCTTCTTGGCACATACAGGTGCCATGCCTGCATATAGTAAGTGCTCAGAAAACATTTCTTGACTGAATTCAGCCAACAAAAATT
TTGGGGTAGGTAGAAAATATATGCTTAAAGTATTTATTGTTATGAGACTGGATATATCTAGTATTTGTCACAGGTAAATGATTCTTCAAAAATTG
AAAGCAAATTTGTTGAAATATTTATTTTGAAAAAAGTTACTTCACAAGCTATAAATTTTAAAAGCCATAGGAATAGATACCGAAGTTATATCCAA
CTGACATTTAATAAATTGTATTCATAGCCTAATGTGATGAGCCACAGAAGCTTGCAAACTTTAATGAGATTTTTTAAAATAGCATCTAAGTTCGG
AATCTTAGGCAAAGTGTTGTTAGATGTAGCACTTCATATTTGAAGTGTTCTTTGGATATTGCATCTACTTTGTTCCTGTTATTATACTGGTGTGA
ATGAATGAATAGGTACTGCTCTCTCTTGGGACATTACTTGACACATAATTACCCAATGAATAAGCATACTGAGGTATCAAAAAAGTCAAATATGT
TATAAATAGCTCATATATGTGTGTAGGGGGGAAGGAATTTAGCTTTCACATCTCTCTTATGTTTAGTTCTCTGCATGTGCAGTTAATCCTGGAAC
TCCGGTGCTAAGGAGAGACTGTTGGCCCTTGAAGGAGAGCTCCTCCCTGTGGATGAGAGAGAAGGACTTTACTCTTTGGAATTATCTTTTTGTGT
TGATGTTATCCACCTTTTGTTACTCCACCTATAAAATCGGCTTATCTATTGATCTGTTTTCCTAGTCCTTATAAAGTCAAAATGTTAATTGGCAT
AAATTATAGACTTTTTTTAGCAGAGAACTTTGAGGAACCTAAATGCCAACCAGTCTAAAAATGCAGTTTTCAGAAGAATGAATATTTCATGGATA
GTTCTAAATACTAATGAACTTTAAAATAGCTTACTATTGATCTGTCAAAGTGGGTTTTTATATAATTTTCTTTTTACAAATCACCTGACACATTT
AATATAGGTTAAAAAATGCTATCAGGCTGGTTTGCAAAGAAAATGTATTACAAAGGCTGCTAAGTGTGTTAAGAGCATACTCATTTCTGTTCTCC
AAAATATTTCATAAGGTGCTTTAAGAATAGGTATGTTTTTAAAAGTTAAGTTCCTACTATTTATAGGAACTGACAATCACCTAAAATACCAATGA
TTACAAACTTCCTTCTGGCCTTCTGGACTGCAATTCTAAAAGTGTAAAAAACATATTTTCTGCATTAAGTTAGGCAGTATTGCTTAGTTTTCAAA
GTGGTAGGCTTTGGAGTCAGATTATTTTGATTCAGATCCTACATCTACTGTTTAGTAGCTCTGTTGCCTGAGGCAGGTCCCTTAACATCTCTGTG
TGTGACTTGACCTTTAAAATTTGGAGACTGTCATAGGGGTTAATCCCTTGAGAAAATGAATGTGAAAAGTTAGCCTAATGTTAACTGCTATTATT
ATGGATTACCATATTTTCACATTCATCACAGTACATGCACCTTGTTAATATAAGATGCTCAATTCATCTTTGAGTATAATTTTGTGACTCTCAAT
CTGGATATGCAATGAGTGGGCCTGTATGAGAATTTAATTTATGAAAAATTGTGTTTCACATGGCCTTACCAGATATACAGGAAACACGTCACATG
TTTCTATTGTATGTTGTTAAATGCCTTAGAATTTAACTTTCTGAATAGGATCCCTTCAGTTTGAGAGTCATAAAAGAGTAAAATTATTATGGTAT

Coding Sequences (i.e., Genes)



The Genetic Code

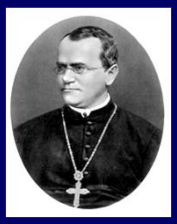
~3,000 bp (0.0001%) of Human Genome Sequence

TGCCGCGGAACTTTTCGGCTCTCTAAGGCTGTATTTTGATATACGAAAGGCACATTTTCCTTCCCTTTTCAAAATGCACCTTGCAAACGTAACAG
GAACCCGACTAGGATCATCGGGAAAAGGAGGAGGAGGAGGAAGGCAGGCTCCGGGGAAGCTGGTGGCAGCGGGTCCTGGGTCTGGCGGACCCTGA
CGCGAAGGAGGGTCTAGGAAGCTCTCCGGGGAGCCGGTTCTCCCGCCGGTGGCTTCTTCTGTCCTCCAGCGTTGCCAACTGGACCTAAAGAGAGG
CCGCGACTGTCGCCCACCTGCGGGATGGGCCTGGTGCTGGGCGGTAAGGACACGGACCTGGAAGGAGCGCGCGCGAGGGAGGGAGGCTGGGAGTC
AGAATCGGGAAAGGGAGGTGCGGGGCGGCGAGGGAGCGAAGGAGGAGAGGAGGAAGGAGCGGGAGGGGTGCTGGCGGGGGTGCGTAGTGGGTGGA
GAAAGCCGCTAGAGCAAATTTGGGGCCGGACCAGGCAGCACTCGGCTTTTAACCTGGGCAGTGAAGGCGGGGGAAAGAGCAAAAGGAAGGGGTGG
TGTGCGGAGTAGGGGTGGGTGGGGGGAATTGGAAGCAAATGACATCACAGCAGGTCAGAGAGAAAAAGGGTTGAGCGGCAGGCACCCAGAGTAGTAG
GTCTTTGGCATTAGGAGCTTGAGCCCAGACGGCCCTAGCAGGGACCCCAGCGCCCGAGAGACCATGCAGAGGTCGCCTCTGGAAAAGGCCAGCGT
TGTCTCCAAACTTTTTTTCAGGTGAGAAGGTGGCCAACCGAGCTTCGGAAAGACACGTGCCCACGAAAGAGGAGGGCGTGTGTATGGGTTGGGTT
TGGGGTAAAGGAATAAGCAGTTTTTAAAAAGATGCGCTATCATTCATTGTTTTGAAAGAAAATGTGGGTATTGTAGAATAAAACAGAAAGCATTA
AGAAGAGATGGAAGAATGAACTGAAGCTGATTGAATAGAGAGCCACATCTACTTGCAACTGAAAAGTTAGAATCTCAAGACTCAAGTACGCTACT
ATGCACTTGTTTTATTTCATTTTTCTAAGAAACTAAAAATACTTGTTAATAAGTACCTAAGTATGGTTTATTGGTTTTCCCCCTTCATGCCTTGG
ACACTTGATTGTCTTCTTGGCACATACAGGTGCCATGCCTGCATATAGTAAGTGCTCAGAAAACATTTCTTGACTGAATTCAGCCAACAAAAATT
TTGGGGTAGGTAGAAAATATATGCTTAAAGTATTTATTGTTATGAGACTGGATATATCTAGTATTTGTCACAGGTAAATGATTCTTCAAAAATTG
AAAGCAAATTTGTTGAAATATTTATTTTGAAAAAAGTTACTTCACAAGCTATAAATTTTAAAAGCCATAGGAATAGATACCGAAGTTATATCCAA
CTGACATTTAATAAATTGTATTCATAGCCTAATGTGATGAGCCACAGAAGCTTGCAAACTTTAATGAGATTTTTTAAAATAGCATCTAAGTTCGG
AATCTTAGGCAAAGTGTTGTTAGATGTAGCACTTCATATTTGAAGTGTTCTTTGGATATTGCATCTACTTTGTTCCTGTTATTATACTGGTGTGA
ATGAATGAATAGGTACTGCTCTCTCTTGGGACATTACTTGACACATAATTACCCAATGAATAAGCATACTGAGGTATCAAAAAAGTCAAATATGT
TATAAATAGCTCATATATGTGTGTAGGGGGGAAGGAATTTAGCTTTCACATCTCTCTTATGTTTAGTTCTCTGCATGTGCAGTTAATCCTGGAAC
TCCGGTGCTAAGGAGAGACTGTTGGCCCTTGAAGGAGAGCTCCTCCCTGTGGATGAGAGAGAAGGACTTTACTCTTTGGAATTATCTTTTTGTGT
TGATGTTATCCACCTTTTGTTACTCCACCTATAAAATCGGCTTATCTATTGATCTGTTTTCCTAGTCCTTATAAAGTCAAAATGTTAATTGGCAT
AAATTATAGACTTTTTTTAGCAGAGAACTTTGAGGAACCTAAATGCCAACCAGTCTAAAAATGCAGTTTTCAGAAGAATGAATATTTCATGGATA
GTTCTAAATACTAATGAACTTTAAAATAGCTTACTATTGATCTGTCAAAGTGGGTTTTTATATAATTTTCTTTTTACAAATCACCTGACACATTT
AATATAGGTTAAAAAATGCTATCAGGCTGGTTTGCAAAGAAAATGTATTACAAAGGCTGCTAAGTGTGTTAAGAGCATACTCATTTCTGTTCTCC
AAAATATTTCATAAGGTGCTTTAAGAATAGGTATGTTTTTAAAAGTTAAGTTCCTACTATTTATAGGAACTGACAATCACCTAAAATACCAATGA
TTACAAACTTCCTTCTGGCCTTCTGGACTGCAATTCTAAAAGTGTAAAAAACATATTTTCTGCATTAAGTTAGGCAGTATTGCTTAGTTTTCAAA
GTGGTAGGCTTTGGAGTCAGATTATTTTGATTCAGATCCTACATCTACTGTTTAGTAGCTCTGTTGCCTGAGGCAGGTCCCTTAACATCTCTGTG
TGTGACTTGACCTTTAAAATTTGGAGACTGTCATAGGGGTTAATCCCTTGAGAAAATGAATGTGAAAAGTTAGCCTAATGTTAACTGCTATTATT
ATGGATTACCATATTTTCACATTCATCACAGTACATGCACCTTGTTAATATAAGATGCTCAATTCATCTTTGAGTATAATTTTGTGACTCTCAAT
CTGGATATGCAATGAGTGGGCCTGTATGAGAATTTAATTTATGAAAAATTGTGTTTCACATGGCCTTACCAGATATACAGGAAACACGTCACATG
TTTCTATTGTATGTTGTTAAATGCCTTAGAATTTAACTTTCTGAATAGGATCCCTTCAGTTTGAGAGTCATAAAAGAGTAAAATTATTATGGTAT

Foundational Milestones in Genetics & Genomics

Darwin

1859

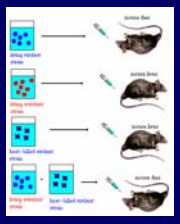


Mendel

1865

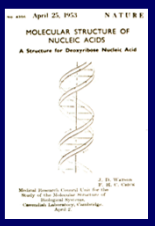
Miescher

1871



Avery

1944

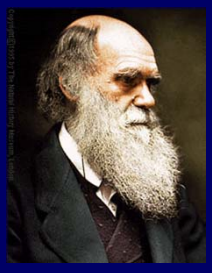


Watson & Crick

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)

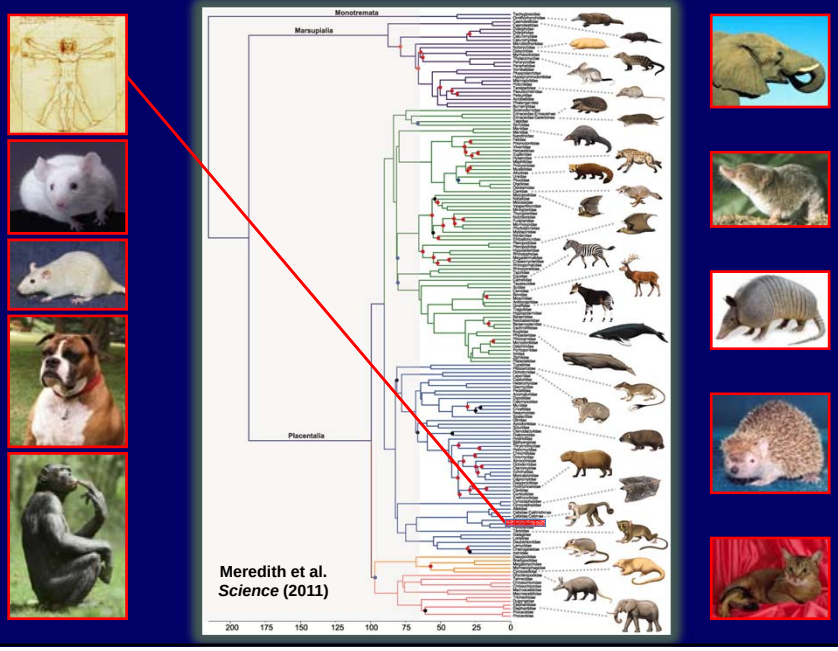


Charles Darwin (1809-1882)

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

— **Eric Lander**

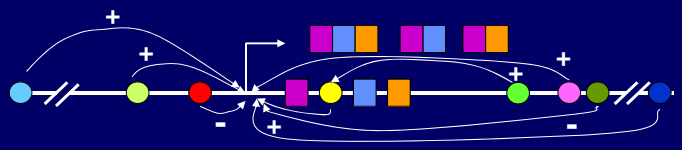
Comparative Genome Sequencing



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

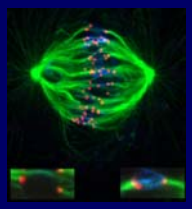
TGCCGCGGAACTTTTCGGCTCTCTAAGGCTGTATTTTGATATACGAAAGGCACATTTTCCTTCCCTTTTCAAAATGCACCTTGCAAACGTAACAG
GAACCCGACTAGGATCATCGGGAAAAGGAGGAGGAGGAGGAAGGCAGGCTCCGGGGAAGCTGGTGGCAGCGGGTCCTGGGTCTGGCGGACCCTGA
CGCGAAGGAGGGTCTAGGAAGCTCTCCGGGGAGCCGGTTCTCCCGCCGGTGGCTTCTTCTGTCCTCCAGCGTTGCCAACTGGACCTAAAGAGAGG
CCGCGACTGTCGCCCACCTGCGGGATGGGCCTGGTGCTGGGCGGTAAGGACACGGACCTGGAAGGAGCGCGCGCGAGGGAGGGAGGCTGGGAGTC
AGAATCGGGAAAGGGAGGTGCGGGGCGGCGAGGGAGCGAAGGAGGAGAGGAGGAAGGAGCGGGAGGGGTGCTGGCGGGGGTGCGTAGTGGGTGGA
GAAAGCCGCTAGAGCAAATTTGGGGCCGGACCAGGCAGCACTCGGCTTTTAACCTGGGCAGTGAAGGCGGGGGAAAGAGCAAAAGGAAGGGGTGG
TGTGCGGAGTAGGGGTGGGTGGGGGGAATTGGAAGCAAATGACATCACAGCAGGTCAGAGAAAAAGGGTTGAGCGGCAGGCACCCAGAGTAGTAG
GTCTTTGGCATTAGGAGCTTGAGCCCAGACGGCCCTAGCAGGGACCCCAGCGCCCGAGAGACCATGCAGAGGTCGCCTCTGGAAAAGGCCAGCGT
TGTCTCCAAACTTTTTTTCAGGTGAGAAGGTGGCCAACCGAGCTTCGGAAAGACACGTGCCCACGAAAGAGGAGGGCGTGTGTATGGGTTGGGTT
TGGGGTAAAGGAATAAGCAGTTTTTAAAAAGATGCGCTATCATTCATTGTTTTGAAAGAAAATGTGGGTATTGTAGAATAAAACAGAAAGCATTA
AGAAGAGATGGAAGAATGAACTGAAGCTGATTGAATAGAGAGCCACATCTACTTGCAACTGAAAAGTTAGAATCTCAAGACTCAAGTACGCTACT
ATGCACTTGTTTTATTTCATTTTTCTAAGAAACTAAAAATACTTGTTAATAAGTACCTAAGTATGGTTTATTGGTTTTCCCCCTTCATGCCTTGG
ACACTTGATTGTCTTCTTGGCACATACAGGTGCCATGCCTGCATATAGTAAGTGCTCAGAAAACATTTCTTGACTGAATTCAGCCAACAAAAATT
TTGGGGTAGGTAGAAAATATATGCTTAAAGTATTTATTGTTATGAGACTGGATATATCTAGTATTTGTCACAGGTAAATGATTCTTCAAAAATTG
AAAGCAAATTTGTTGAAATATTTATTTTGAAAAAAGTTACTTCACAAGCTATAAATTTTAAAAGCCATAGGAATAGATACCGAAGTTATATCCAA
CTGACATTTAATAAATTGTATTCATAGCCTAATGTGATGAGCCACAGAAGCTTGCAAACTTTAATGAGATTTTTTAAAATAGCATCTAAGTTCGG
AATCTTAGGCAAAGTGTTGTTAGATGTAGCACTTCATATTTGAAGTGTTCTTTGGATATTGCATCTACTTTGTTCCTGTTATTATACTGGTGTGA
ATGAATGAATAGGTACTGCTCTCTCTTGGGACATTACTTGACACATAATTACCCAATGAATAAGCATACTGAGGTATCAAAAAAGTCAAATATGT
TATAAATAGCTCATATATGTGTGTAGGGGGGAAGGAATTTAGCTTTCACATCTCTCTTATGTTTAGTTCTCTGCATGTGCAGTTAATCCTGGAAC
TCCGGTGCTAAGGAGAGACTGTTGGCCCTTGAAGGAGAGCTCCTCCCTGTGGATGAGAGAGAAGGACTTTACTCTTTGGAATTATCTTTTTGTGT
TGATGTTATCCACCTTTTGTTACTCCACCTATAAAATCGGCTTATCTATTGATCTGTTTTCCTAGTCCTTATAAAGTCAAAATGTTAATTGGCAT
AAATTATAGACTTTTTTTAGCAGAGAACTTTGAGGAACCTAAATGCCAACCAGTCTAAAAATGCAGTTTTCAGAAGAATGAATATTTCATGGATA
GTTCTAAATACTAATGAACTTTAAAATAGCTTACTATTGATCTGTCAAAGTGGGTTTTTATATAATTTTCTTTTTACAAATCACCTGACACATTT
AATATAGGTTAAAAAATGCTATCAGGCTGGTTTGCAAAGAAAATGTATTACAAAGGCTGCTAAGTGTGTTAAGAGCATACTCATTTCTGTTCTCC
AAAATATTTCATAAGGTGCTTTAAGAATAGGTATGTTTTTAAAAGTTAAGTTCCTACTATTTATAGGAACTGACAATCACCTAAAATACCAATGA
TTACAAACTTCCTTCTGGCCTTCTGGACTGCAATTCTAAAAGTGTAAAAAACATATTTTCTGCATTAAGTTAGGCAGTATTGCTTAGTTTTCAAA
GTGGTAGGCTTTGGAGTCAGATTATTTTGATTCAGATCCTACATCTACTGTTTAGTAGCTCTGTTGCCTGAGGCAGGTCCCTTAACATCTCTGTG
TGTGACTTGACCTTTAAAATTTGGAGACTGTCATAGGGGTTAATCCCTTGAGAAAATGAATGTGAAAAGTTAGCCTAATGTTAACTGCTATTATT
ATGGATTACCATATTTTCACATTCATCACAGTACATGCACCTTGTTAATATAAGATGCTCAATTCATCTTTGAGTATAATTTTGTGACTCTCAAT
CTGGATATGCAATGAGTGGGCCTGTATGAGAATTTAATTTATGAAAAATTGTGTTTCACATGGCCTTACCAGATATACAGGAAACACGTCACATG
TTTCTATTGTATGTTGTTAAATGCCTTAGAATTTAACTTTCTGAATAGGATCCCTTCAGTTTGAGAGTCATAAAAGAGTAAAATTATTATGGTAT

Non-Coding Functional Sequences

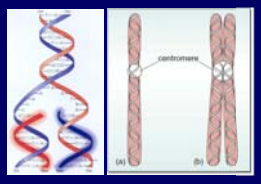


Gene Regulation

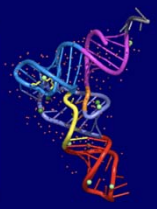
Chromosome Packaging



Chromosome Segregation



Chromosome Replication



Non-Coding RNAs

?

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

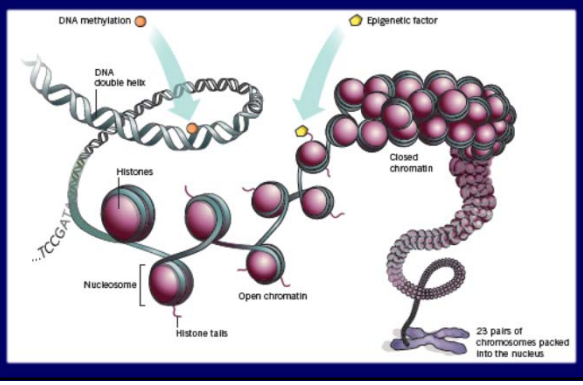
TGCCGCGGAACTTTTCGGCTCTCTAAGGCTGTATTTTGATATACGAAAGGCACATTTTCCTTCCCTTTTCAAAATGCACCTTGCAAACGTAACAG
GAACCCGACTAGGATCATCGGGAAAAGGAGGAGGAGGAGGAAGGCAGGCTCCGGGGAAGCTGGTGGCAGCGGGTCCTGGGTCTGGCGGACCCTGA
CGCGAAGGAGGGTCTAGGAAGCTCTCCGGGGAGCCGGTTCTCCCGCCGGTGGCTTCTTCTGTCCTCCAGCGTTGCCAACTGGACCTAAAGAGAGG
CCGCGACTGTCGCCCACCTGCGGGATGGGCCTGGTGCTGGGCGGTAAGGACACGGACCTGGAAGGAGCGCGCGCGAGGGAGGGAGGCTGGGAGTC
AGAATCGGGAAAGGGAGGTGCGGGGCGGCGAGGGAGCGAAGGAGGAGAGGAGGAAGGAGCGGGAGGGGTGCTGGCGGGGGTGCGTAGTGGGTGGA
GAAAGCCGCTAGAGCAAATTTGGGGCCGGACCAGGCAGCACTCGGCTTTTAACCTGGGCAGTGAAGGCGGGGGAAAGAGCAAAAGGAAGGGGTGG
TGTGCGGAGTAGGGGTGGGTGGGGGGAATTGGAAGCAAATGACATCACAGCAGGTCAGAGAAAAAGGGTTGAGCGGCAGGCACCCAGAGTAGTAG
GTCTTTGGCATTAGGAGCTTGAGCCCAGACGGCCCTAGCAGGGACCCCAGCGCCCGAGAGACCATGCAGAGGTCGCCTCTGGAAAAGGCCAGCGT
TGTCTCCAAACTTTTTTTCAGGTGAGAAGGTGGCCAACCGAGCTTCGGAAAGACACGTGCCCACGAAAGAGGAGGGCGTGTGTATGGGTTGGGTT
TGGGGTAAAGGAATAAGCAGTTTTTAAAAAGATGCGCTATCATTCATTGTTTTGAAAGAAAATGTGGGTATTGTAGAATAAAACAGAAAGCATTA
AGAAGAGATGGAAGAATGAACTGAAGCTGATTGAATAGAGAGCCACATCTACTTGCAACTGAAAAGTTAGAATCTCAAGACTCAAGTACGCTACT
ATGCACTTGTTTTATTTCATTTTTCTAAGAAACTAAAAATACTTGTTAATAAGTACCTAAGTATGGTTTATTGGTTTTCCCCCTTCATGCCTTGG
ACACTTGATTGTCTTCTTGGCACATACAGGTGCCATGCCTGCATATAGTAAGTGCTCAGAAAACATTTCTTGACTGAATTCAGCCAACAAAAATT
TTGGGGTAGGTAGAAAATATATGCTTAAAGTATTTATTGTTATGAGACCTGGATATATCTAGTATTTGTCACAGGTAAATGATTCTTCAAAAATTG
AAAGCAAATTTGTTGAAATATTTATTTTGAAAAAAGTTACTTCACAAGCTATAAATTTTAAAAGCCATAGGAATAGATACCGAAGTTATATCCAA
CTGACATTTAATAAATTGTATTCATAGCCTAATGTGATGAGCCACAGAAGCTTGCAAACTTTAATGAGATTTTTTAAAATAGCATCTAAGTTCGG
AATCTTAGGCAAAGTGTTGTTAGATGTAGCACTTCATATTTGAAGTGTTCTTTGGATATTGCATCTACTTTGTTCCTGTTATTATACTGGTGTGA
ATGAATGAATAGGTACTGCTCTCTCTTGGGACATTACTTGACACATAATTACCCAATGAATAAGCATACTGAGGTATCAAAAAAGTCAAATATGT
TATAAATAGCTCATATATGTGTGTAGGGGGGAAGGAATTTAGCTTTCACATCTCTCTTATGTTTAGTTCTCTGCATGTGCAGTTAATCCTGGAAC
TCCGGTGCTAAGGAGAGACTGTTGGCCCTTGAAGGAGAGCTCCTCCCTGTGGATGAGAGAGAAGGACTTTACTCTTTGGAATTATCTTTTTGTGT
TGATGTTATCCACCTTTTGTTACTCCACCTATAAAATCGGCTTATCTATTGATCTGTTTTCCTAGTCCTTATAAAGTCAAAATGTTAATTGGCAT
AAATTATAGACTTTTTTTAGCAGAGAACTTTGAGGAACCTAAATGCCAACCAGTCTAAAAATGCAGTTTTCAGAAGAATGAATATTTCATGGATA
GTTCTAAATACTAATGAACTTTAAAATAGCTTACTATTGATCTGTCAAAGTGGGTTTTTATATAATTTTCTTTTTACAAATCACCTGACACATTT
AATATAGGTTAAAAAATGCTATCAGGCTGGTTTGCAAAGAAAATGTATTACAAAGGCTGCTAAGTGTGTTAAGAGCATACTCATTTCTGTTCTCC
AAAATATTTCATAAGGTGCTTTAAGAATAGGTATGTTTTTAAAAGTTAAGTTCCTACTATTTATAGGAACTGACAATCACCTAAAATACCAATGA
TTACAAACTTCCTTCTGGCCTTCTGGACTGCAATTCTAAAAGTGTAAAAAACATATTTTCTGCATTAAGTTAGGCAGTATTGCTTAGTTTTCAAA
GTGGTAGGCTTTGGAGTCAGATTATTTTGATTCAGATCCTACATCTACTGTTTAGTAGCTCTGTTGCCTGAGGCAGGTCCCTTAACATCTCTGTG
TGTGACTTGACCTTTAAAATTTGGAGACTGTCATAGGGGTTAATCCCTTGAGAAAATGAATGTGAAAAGTTAGCCTAATGTTAACTGCTATTATT
ATGGATTACCATATTTTCACATTCATCACAGTACATGCACCTTGTTAATATAAGATGCTCAATTCATCTTTGAGTATAATTTTGTGACTCTCAAT
CTGGATATGCAATGAGTGGGCCTGTATGAGAATTTAATTTATGAAAAATTGTGTTTCACATGGCCTTACCAGATATACAGGAAACACGTCACATG
TTTCTATTGTATGTTGTTAAATGCCTTAGAATTTAACTTTCTGAATAGGATCCCTTCAGTTTGAGAGTCATAAAAGAGTAAAATTATTATGGTAT

The Epigenomics Landscape

TECHNOLOGY FEATURE

READING THE SECOND GENOMIC CODE

***Nature* (2012)**

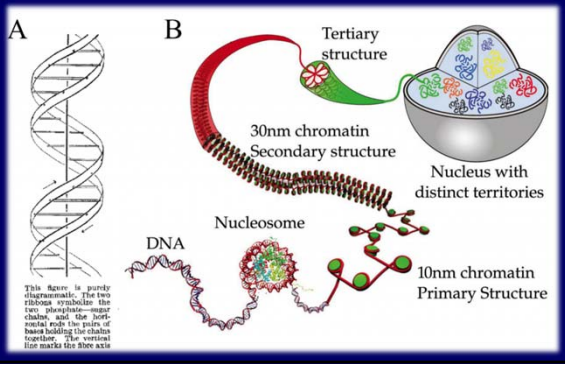


TECHNOLOGY FEATURE

GENOMES IN THREE DIMENSIONS

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

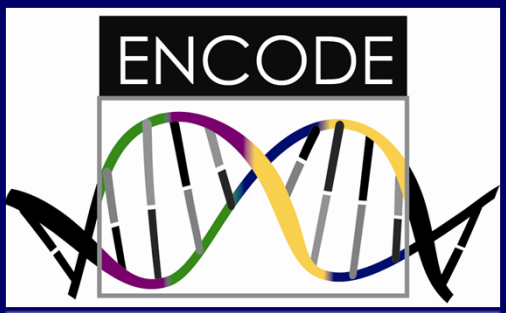
***Nature* (2011)**

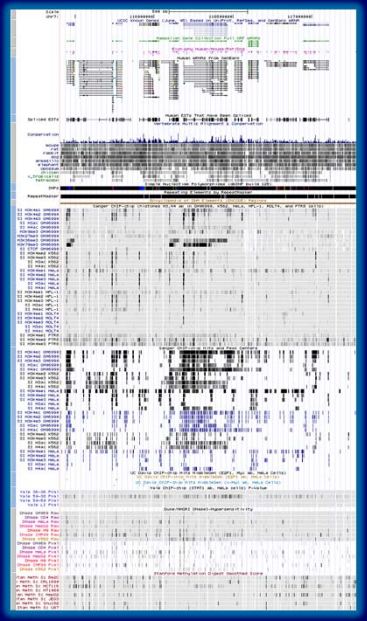


Elucidating Genome Function

'Team Science'

ENCODE: Giving 'GPS' Views of Genomes





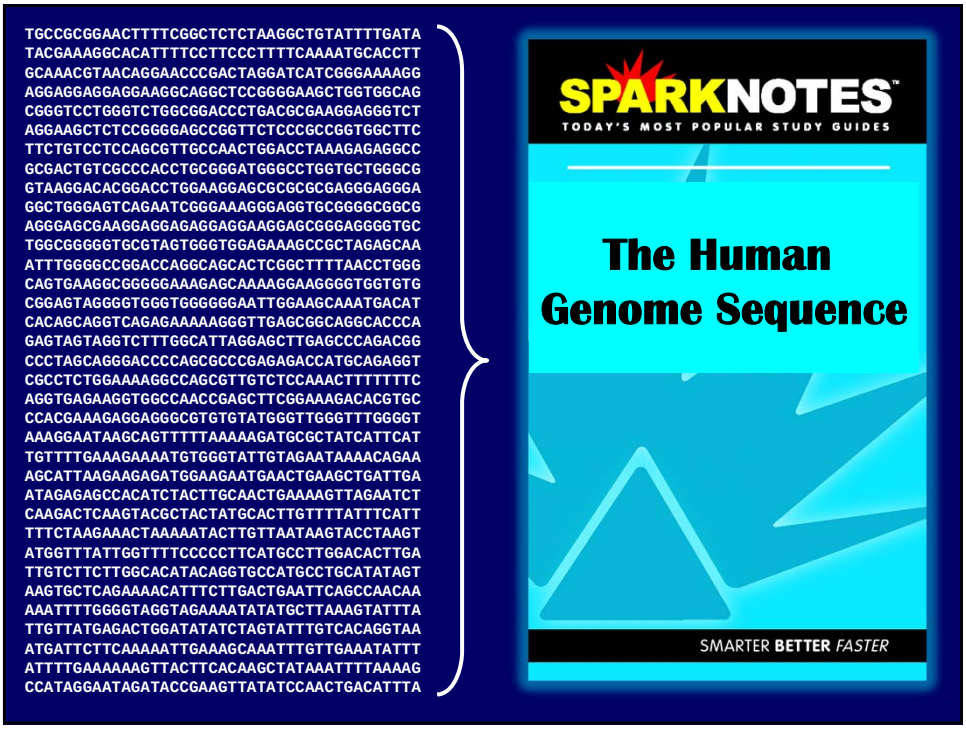
Elucidating Genome Function

'Team Science'

Model Organisms

Computational Modeling

Technology Development

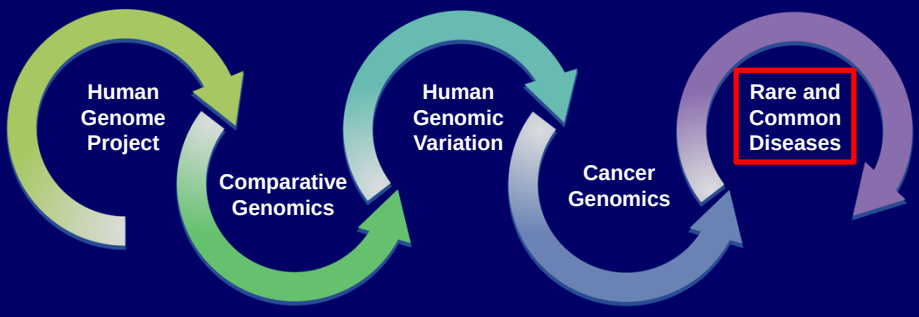


A Quarter Century of Genomics

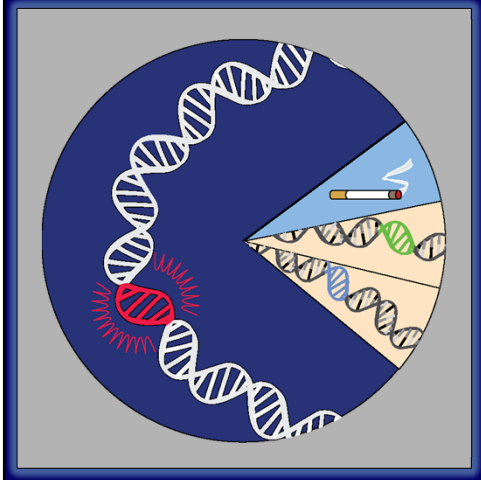
- Human Genome Sequenced for First Time by the Human Genome Project
- Cost of Sequencing a Human Genome Reduced Nearly ~1 Million-Fold
- Tens of Thousands of Human Genomes Sequenced
- Profound Advances in Understanding How the Human Genome Functions
- Significant Advances in Unraveling the Genomic Bases of Human Disease

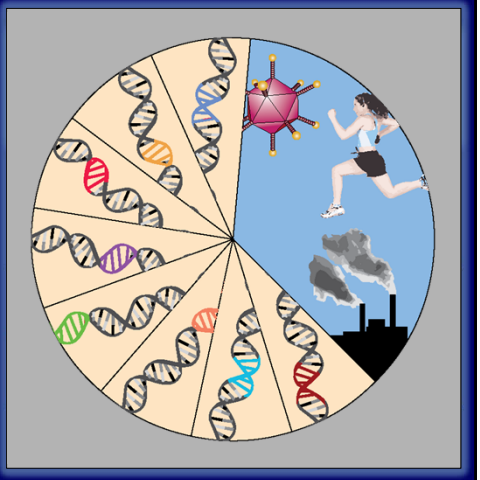
NHGRI Genome Sequencing Program

At the cutting edge of genome analysis



Genomic Architecture of Genetic Diseases



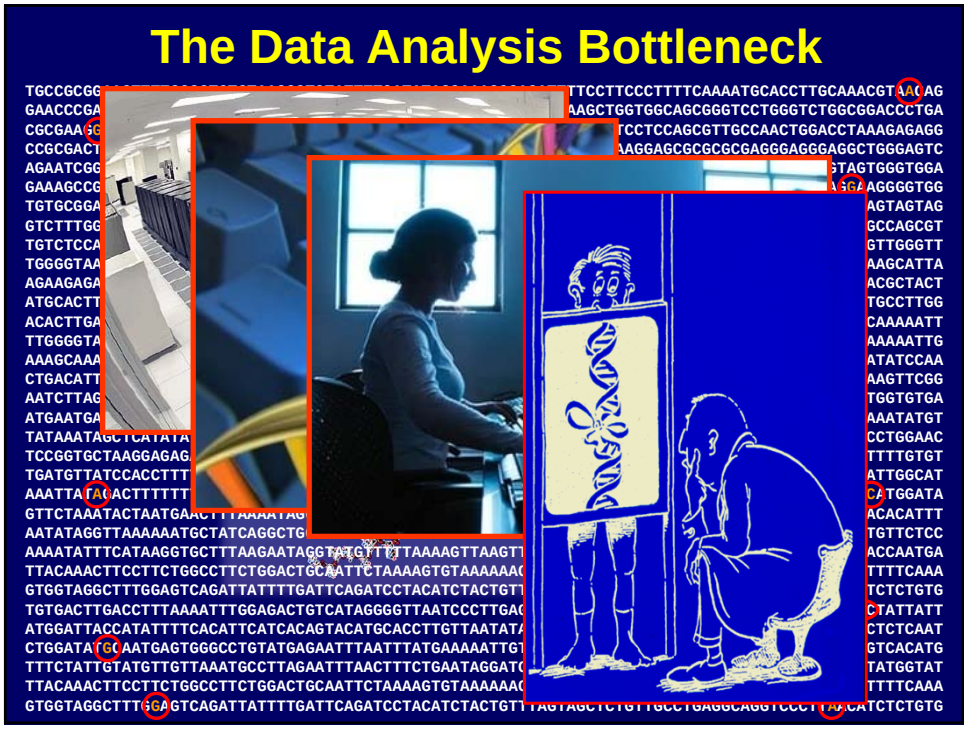


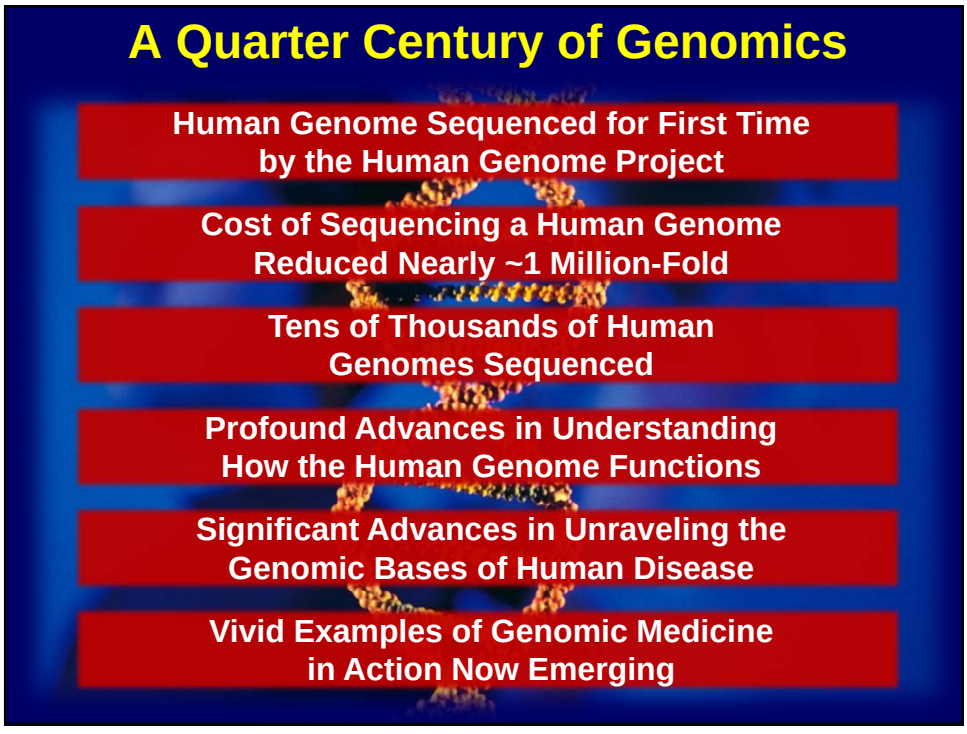
Rare, Simple, Monogenic, Mendelian…

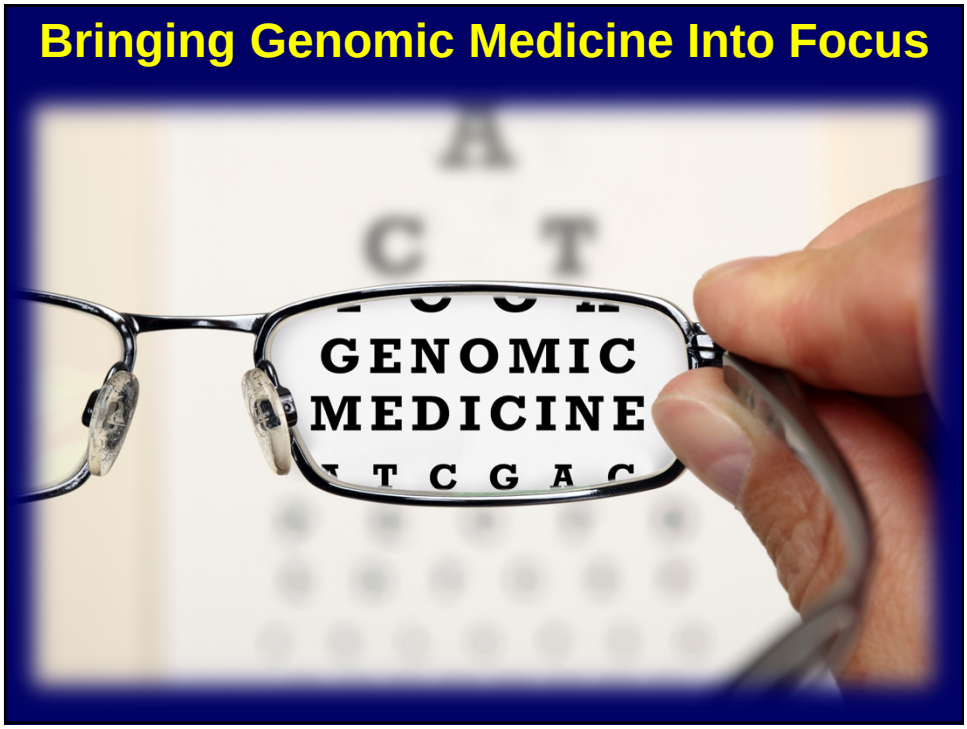
Common, Complex, Multigenic, Non-Mendelian…

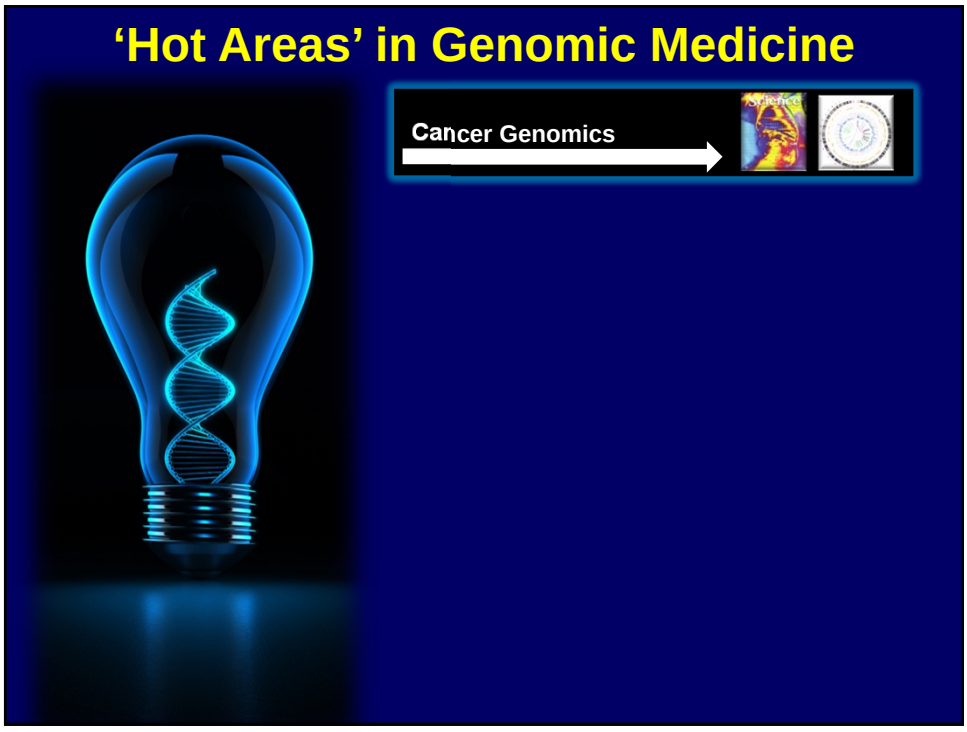
Manolio et al., J Clin Invest (2008)

The Largest Current Bottleneck in Genomics…

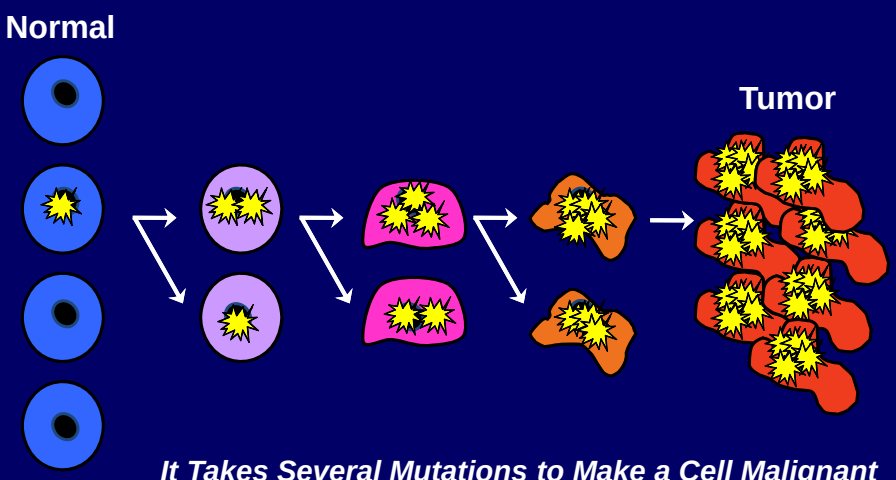

The Data Analysis Bottleneck


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
Vivid Examples of Genomic Medicine in Action Now Emerging


Bringing Genomic Medicine Into Focus
GENOMIC
MEDICINE


'Hot Areas' in Genomic Medicine
Cancer Genomics

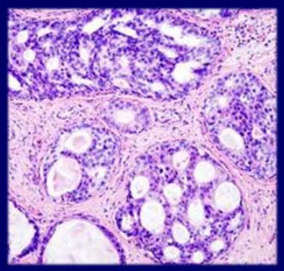
Cancer is a Disease of the Genome



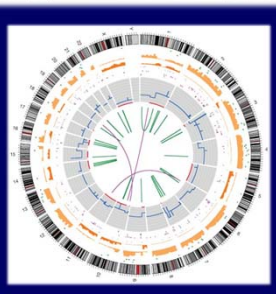
It Takes Several Mutations to Make a Cell Malignant

Routine Cancer Diagnostic Tools

Cancer Histopathology

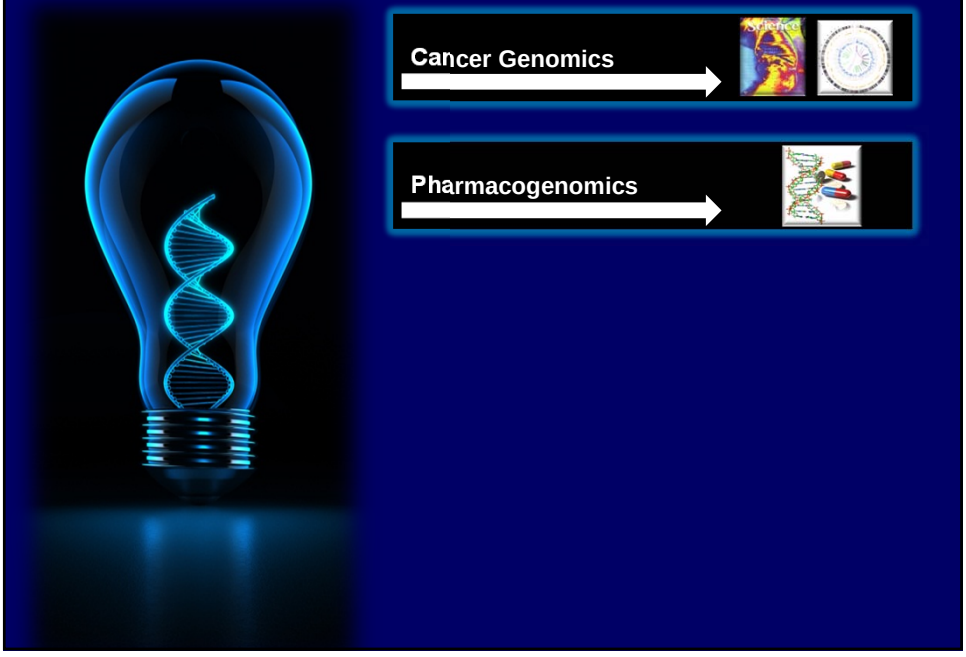


Cancer Genome Sequencing



Genomics and Cancer: Here and Now

'Hot Areas' in Genomic Medicine

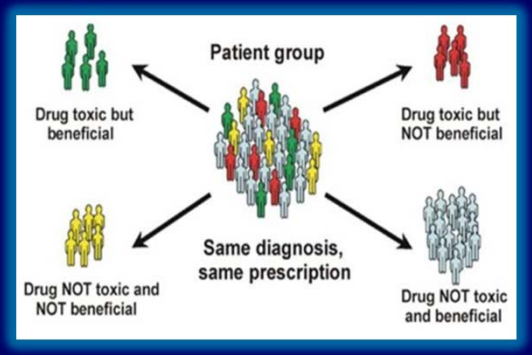



Because Everyone Responds Differently.


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.

***Nature* (2015)**

Pharmacogenomics



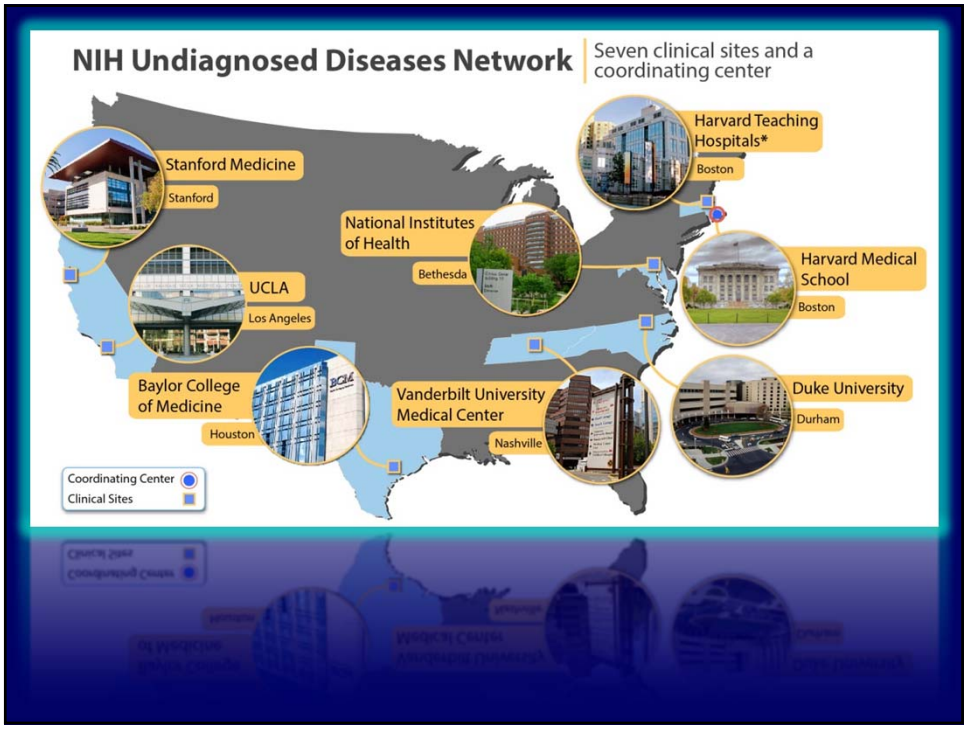
'Hot Areas' in Genomic Medicine

- Cancer Genomics
- Pharmacogenomics
- Rare Genetic Disease Diagnostics

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

***Nature* (2014)**

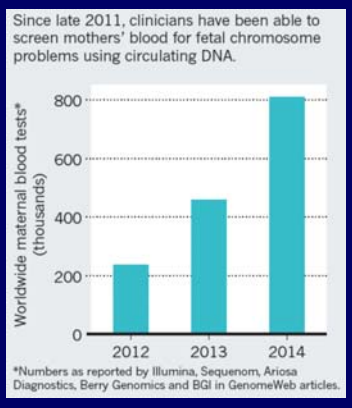

Undiagnosed Diseases


NIH Undiagnosed Diseases Network
Seven clinical sites and a coordinating center
Stanford Medicine
Stanford
UCLA
Los Angeles
Baylor College of Medicine
Houston
National Institutes of Health
Bethesda
Harvard Teaching Hospitals*
Boston
Harvard Medical School
Boston
Vanderbilt University Medical Center
Nashville
Duke University
Durham
Coordinating Center
Clinical Sites

'Hot Areas' in Genomic Medicine

- Cancer Genomics
- Pharmacogenomics
- Rare Genetic Disease Diagnostics
- Genomics of Pregnancy

Noninvasive Prenatal Genome Sequencing



DW Bianchi, *Nature* (2015)

Newborn Genome Sequencing


HEALTH RESEARCH

In 2025, Everyone Will Get DNA Mapped At Birth

Alice Park @aliceparkny June 30, 2014

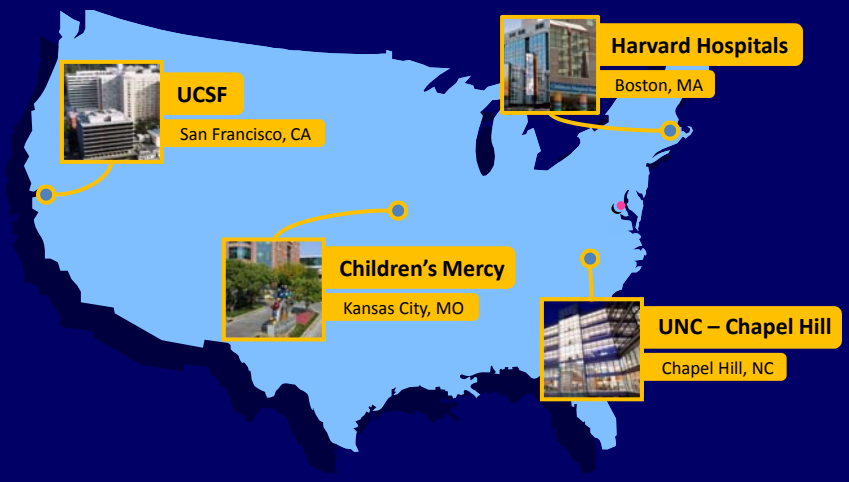
Scientists have scoured trends in research grants, patents and more to come up with these 10 innovations that will be reality in 10 years (or so they think)

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)



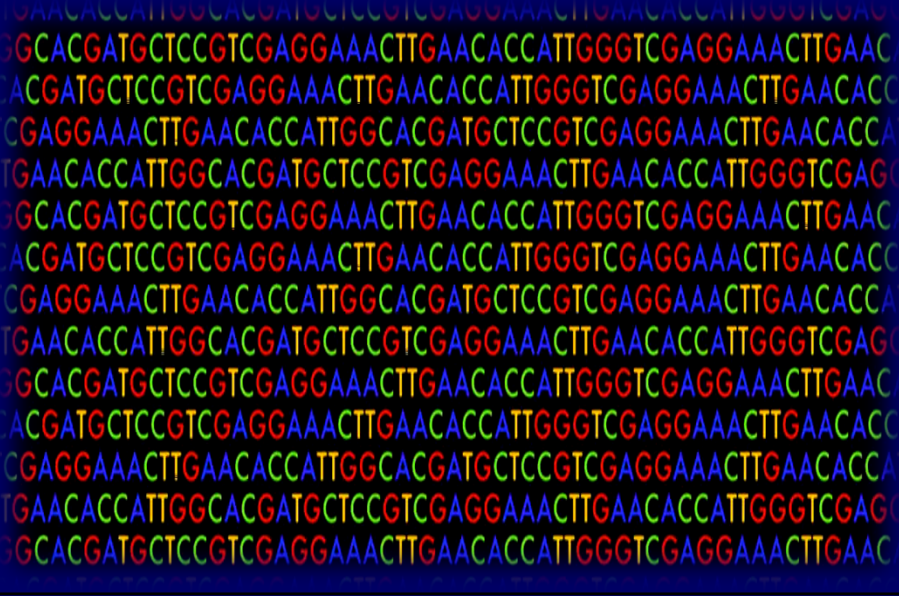
Genome Sequencing of Acutely Sick Newborns

***Nature* (2014)**

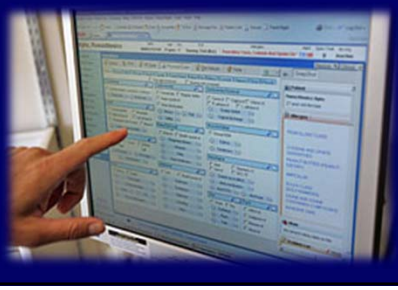
'Hot Areas' in Genomic Medicine

- Cancer Genomics
- Pharmacogenomics
- Rare Genetic Disease Diagnostics
- Genomics of Pregnancy
- Clinical Genomics Information Systems

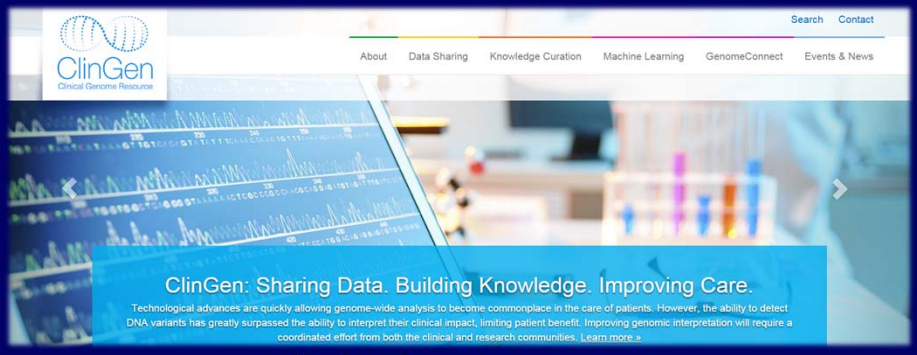
Generating a Human Genome Sequence is (Almost) Trivial



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

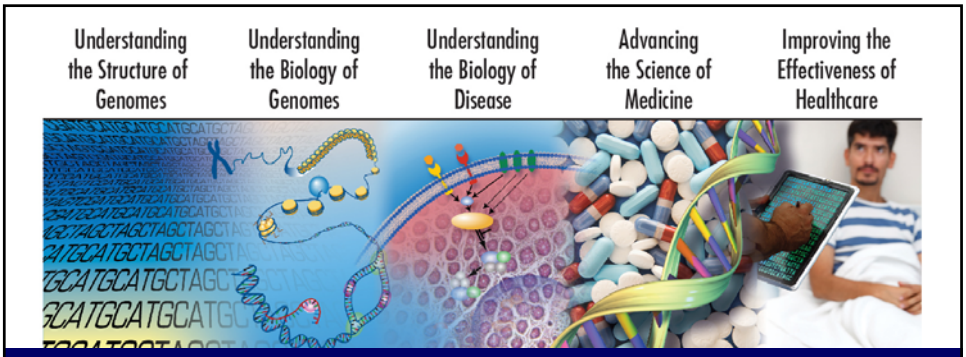
Healthcare Delivery

The Genomic Medicine Ecosystem

Education & Genomic Literacy

The Genomic Medicine Ecosystem

Regulatory Oversight



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

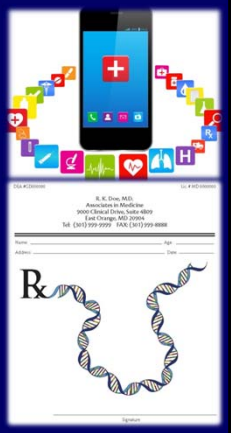
Patients (and Friends & Relatives of Patients)

Genomics, Society, and Public Health

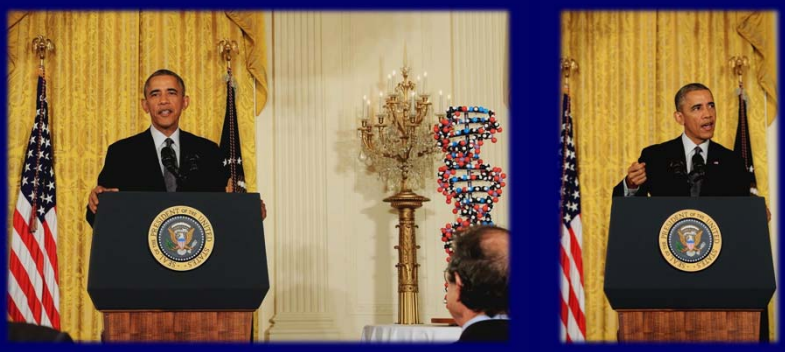

Precision Medicine
A broader context for 'individualizing' medical care to advance human health

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)

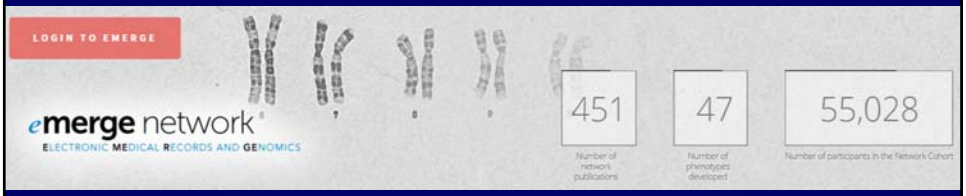
Information from the Human Genome Project will be vital for defining the genetic and environmental factors that contribute to health and disease. Well-designed case–control studies of people with and without a particular disease are essential for this, but rigorous and unbiased conclusions about the 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.

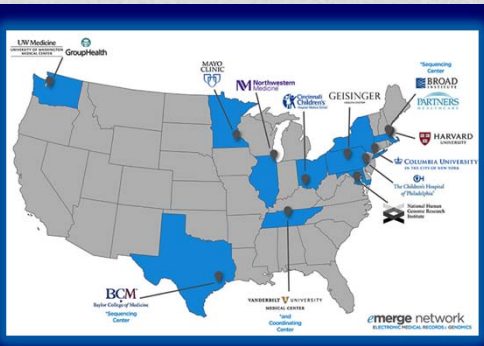
***Nature* (2004)**

Genomics

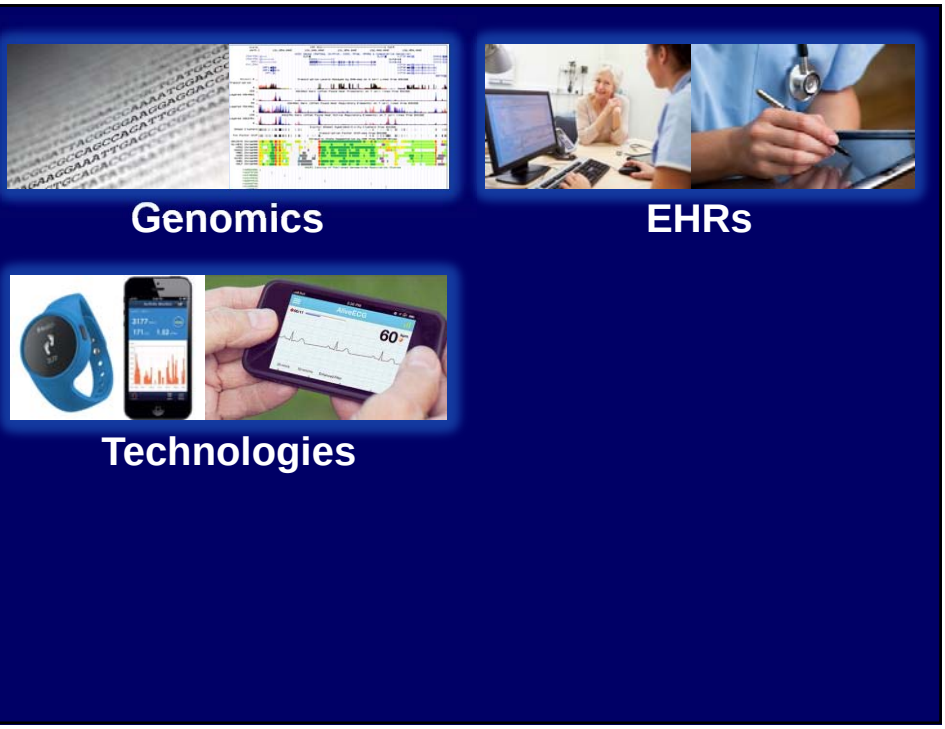
EHRs

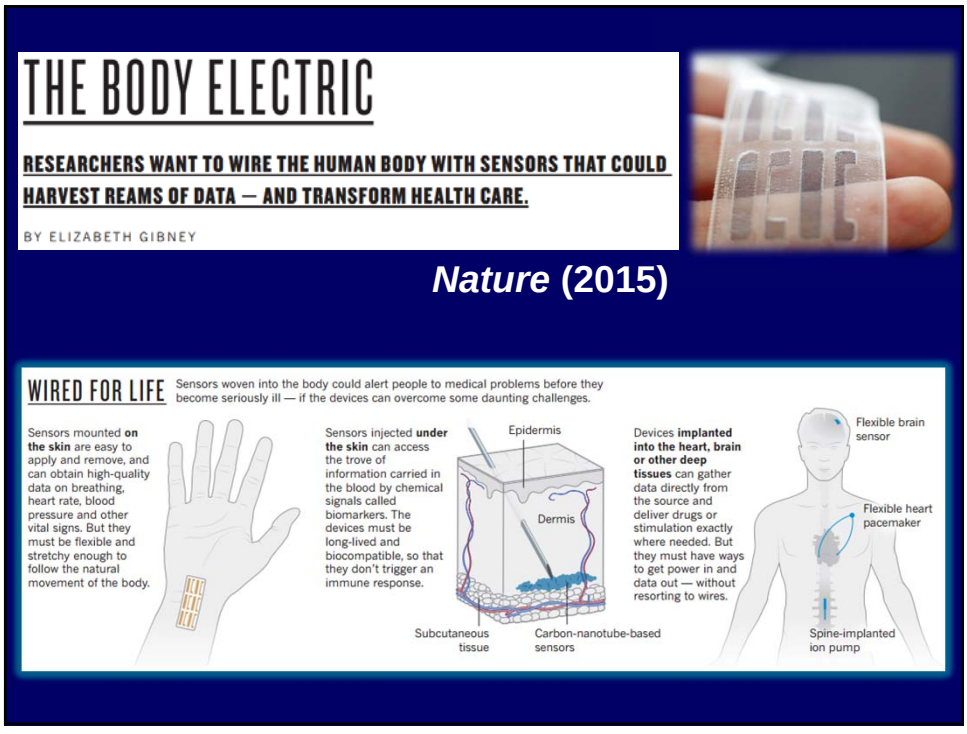
Electronic Medical Records and Genomics (eMERGE) Network





emerge.mc.vanderbilt.edu

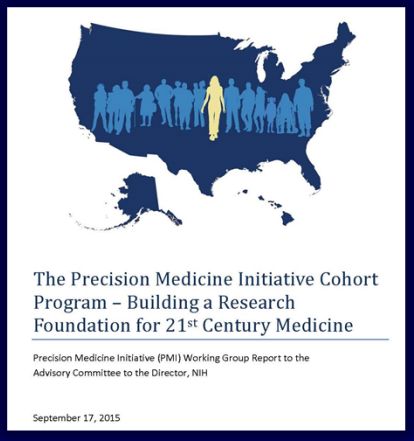

Genomics
EHRs
Technologies


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.
Epidermis
Dermis
Subcutaneous tissue
Carbon-nanotube-based sensors
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.
Flexible brain sensor
Flexible heart pacemaker
Spine-implanted ion pump

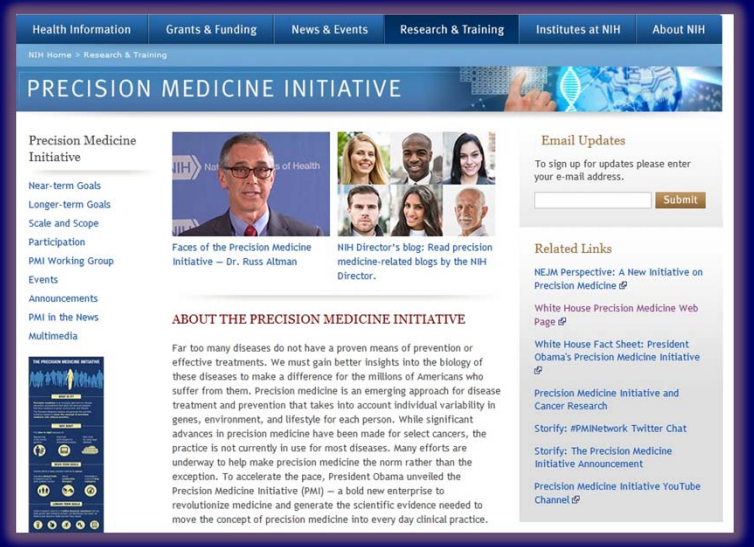

Genomics
EHRs
Technologies
Data Science


nature
THE BITER BIT
Viral infections for viruses
TROPICAL CYCLONES
The strong get stronger
BLACK HOLE PHYSICS
A new window on the Galactic Centre
BIG DATA
SCIENCE IN THE PETABYTE ERA
Science
data
information
climate
research
analysis
visualization
AAAS

Report on Precision Medicine Initiative Cohort Program



Precision Medicine Initiative



www.nih.gov/precisionmedicine

Déjà Vu, All Over Again?

Human Genome Project

Circa Winter 1990

Precision Medicine Initiative

Circa Winter 2015


The Genomics Landscape
A monthly newsletter from the NHGRI Director
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