

Perspectives on the Human Genome Project

Francis S. Collins, M.D., Ph.D.
Director, NIH

NHGRI Science Writers Conference
June 7, 2010





nature



THE HUMAN GENOME AT TEN

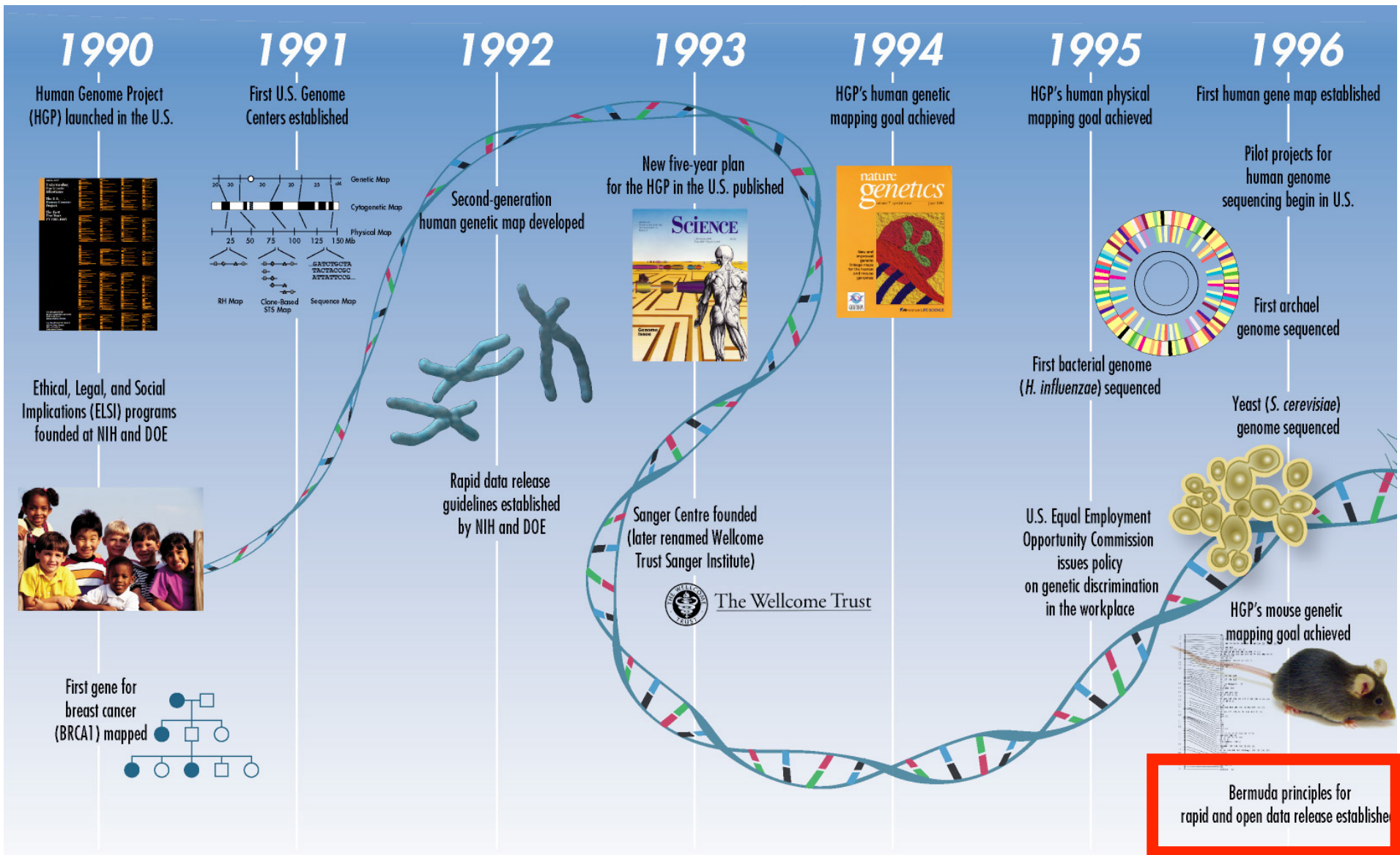
Growing pains of the
genomics age

THE FAINT YOUNG SUN
A climate paradox revisited

QUANTUM MECHANICS
Controlling objects you can see

SLEEPING SICKNESS
Drug target for a neglected disease

NATUREJOBS
Getting published



HUMAN GENOMIC SEQUENCE GENERATED BY LARGE SCALE CENTRES

RELEASE

- Automatic release of sequence assemblies >1kb (approximately daily)
- Immediate submission of finished annotated sequence

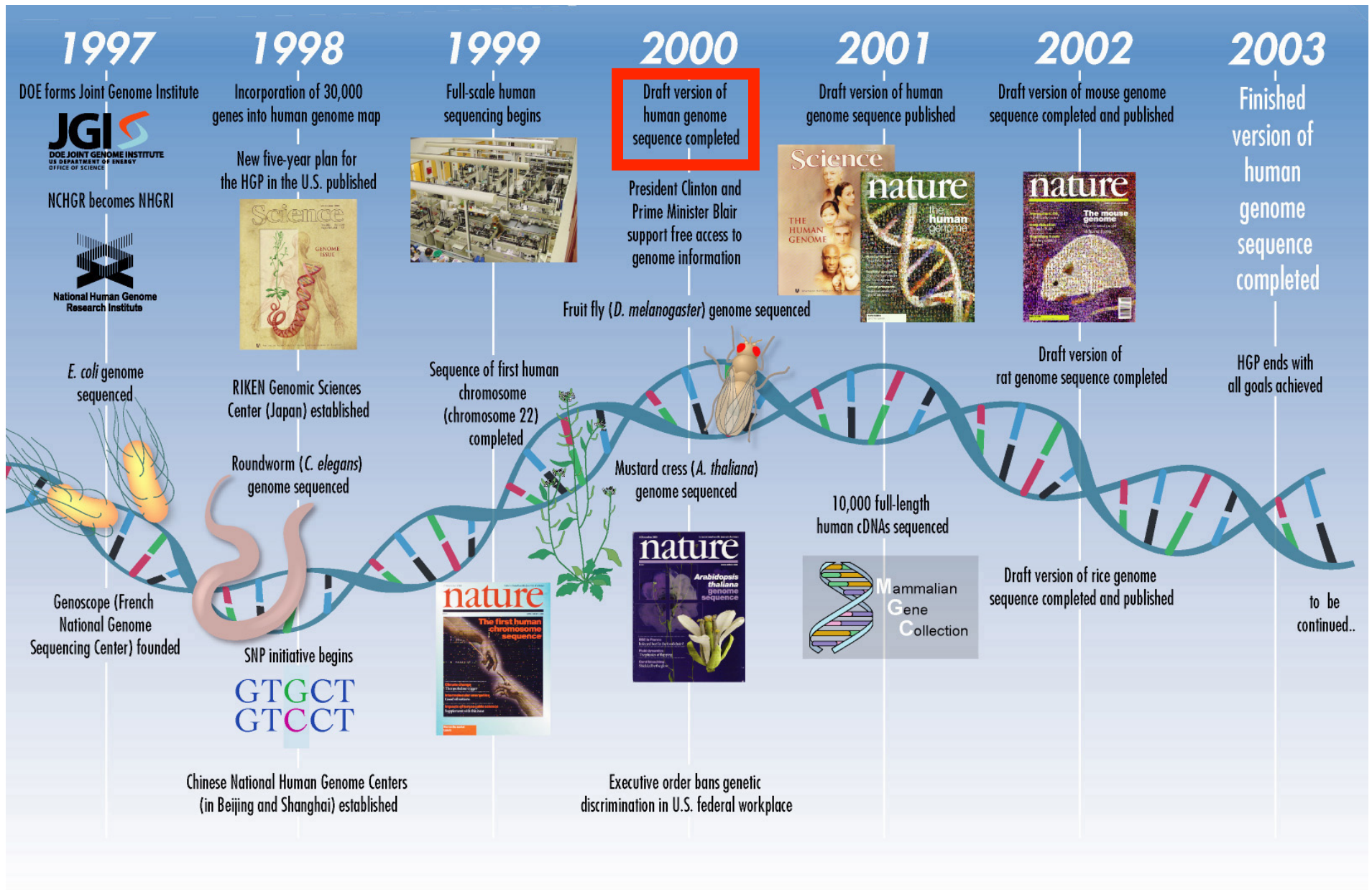


and in the public domain

- Aim to have all sequence freely available for both research and development, in order to maximise its benefit to society.

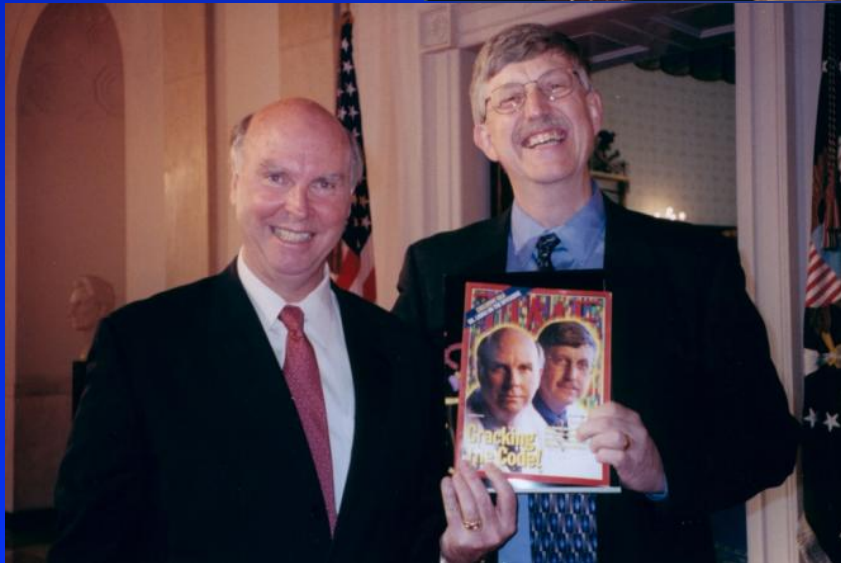
POLICY

- The funding agencies are urged to foster these policies



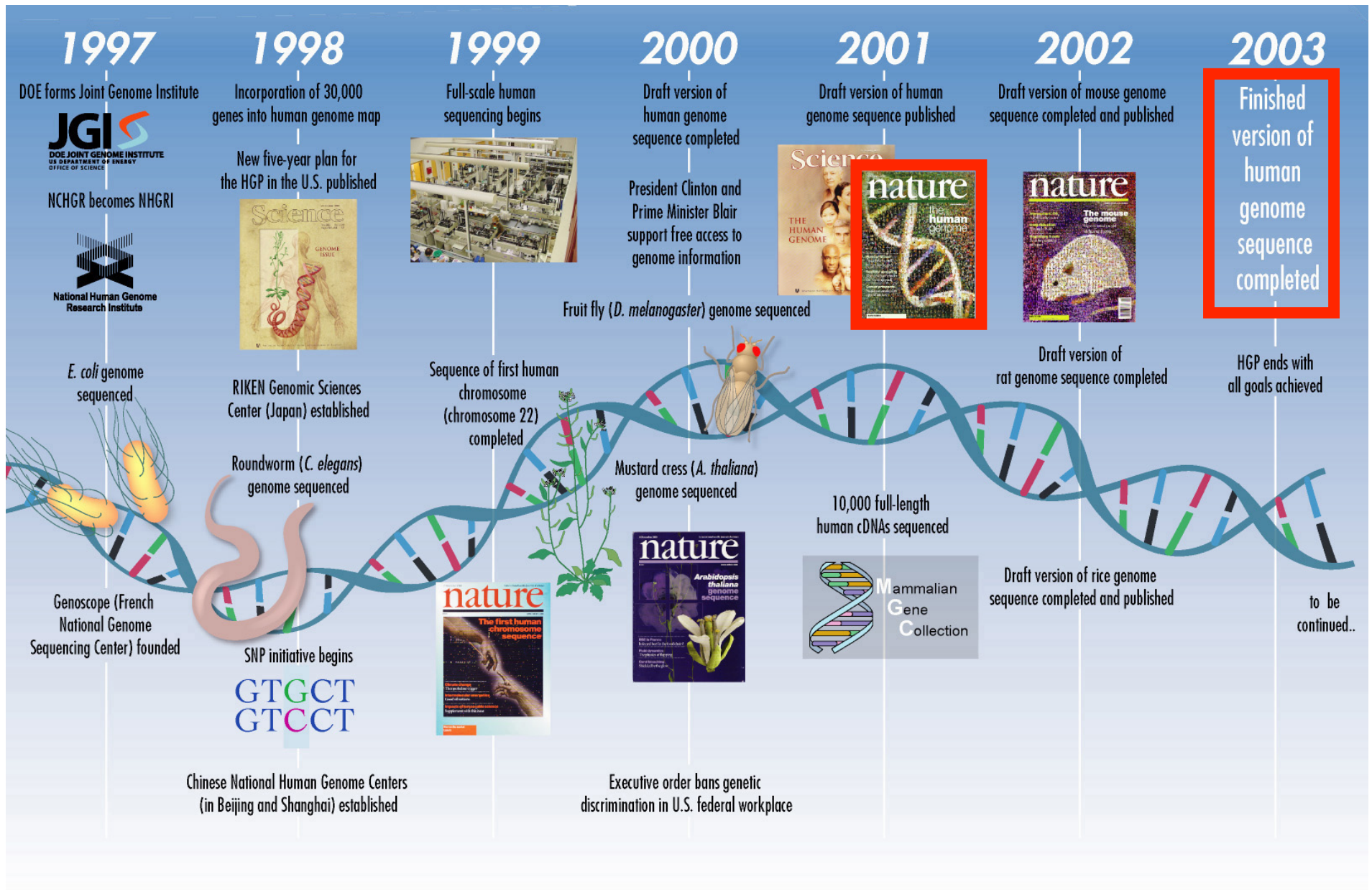
Collins et al., Nature 4/24/03

Science in the White House....



And later at the Hilton.



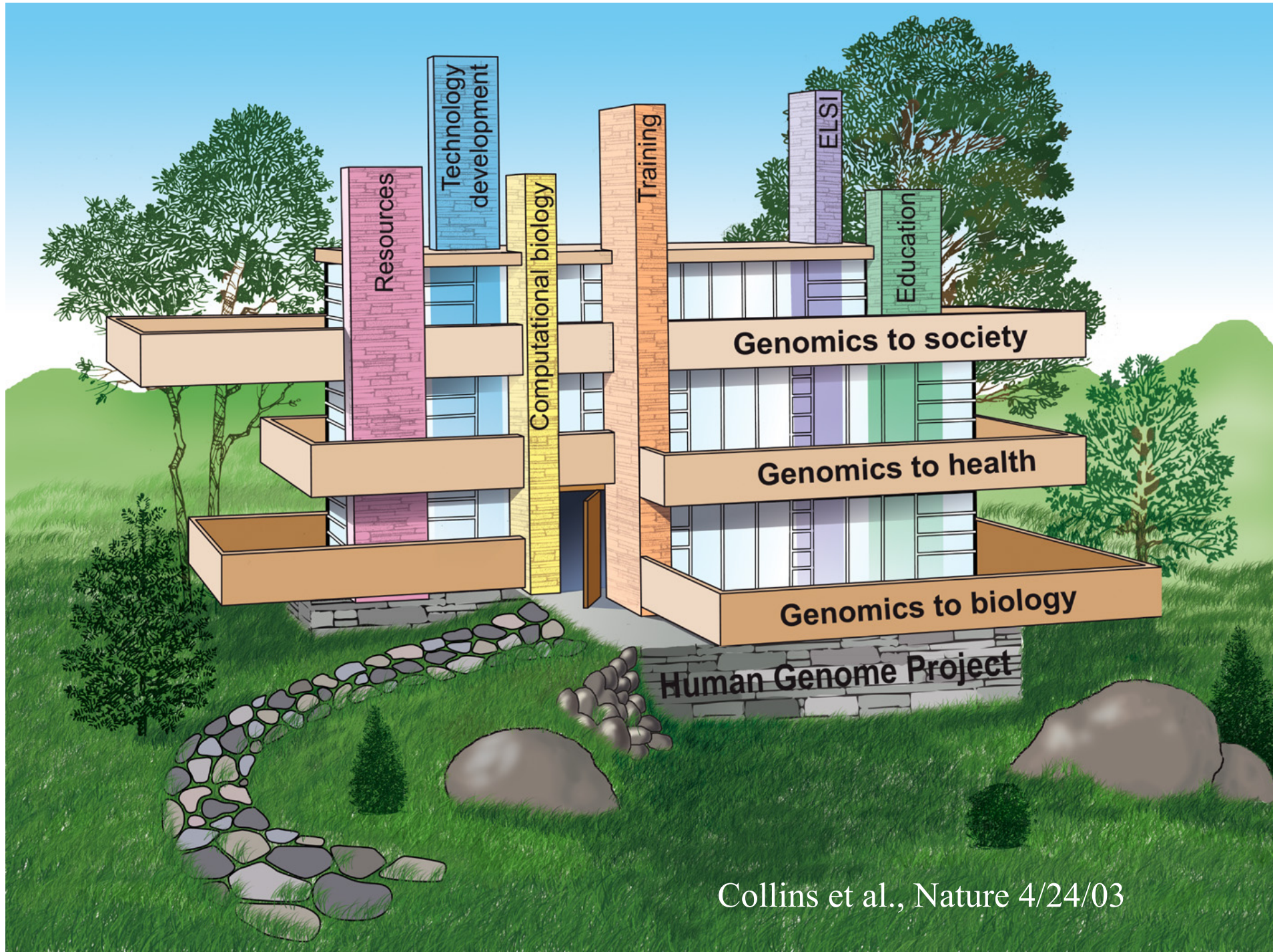


Collins et al., Nature 4/24/03



**I not only use all the brains I
have, but all I can borrow.**

Woodrow Wilson



Collins et al., Nature 4/24/03

5 December 2002

International weekly journal of science

nature

\$10.00

www.nature.com/nature

Atmospheric CO₂

A drop in the ocean

Drag reduction

Flexing in fluids

Regulatory T cells

Basis for persistent infection

The mouse genome

Experimental model for human biology

nature jobs
celebration of the mouse genome



1 April 2004

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The rat genome

Insights into mammalian evolution

Superconductivity

Diamond springs
a surprise

Office life

Make those
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Immunity induced
in mice

naturejobs bioinformatics

8 December 2005 | www.nature.com/nature | \$10

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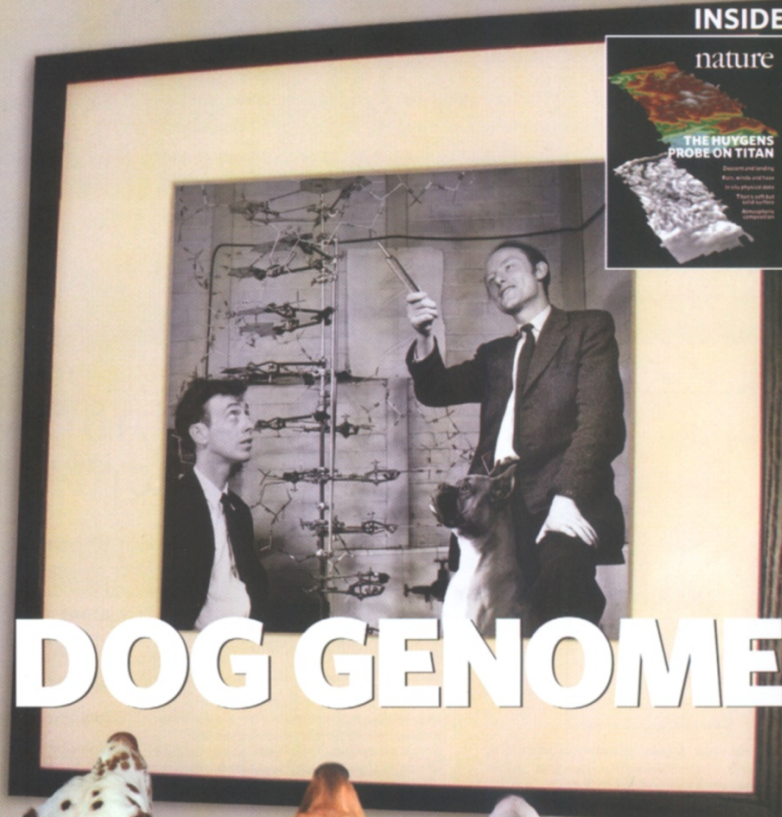
**QUANTUM
MEMORY**
Controlling
single photons

**THE GENETICS
OF NONSENSE**
A cellular
balancing act

**IN PURSUIT
OF PLEASURE**
Dopamine's
role revisited

INSIDE

nature



THE DOG GENOME



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STAR FORMATION

A massive protostar unveiled

CANCER IMMUNOLOGY

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AIR POLLUTION

China's NO₂ build-up
seen from space

NATUREJOBS

Membrane proteomics

THE CHIMPANZEE GENOME





13 April 2007 | \$10

Science

The
Macaque
Genome

AAAS

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nature



NUCLEAR FORENSICS
Attribution as a defence
against terrorism

AUTUMN BOOKS
On mind wars, morals,
Goodall and Crick

RHEUMATOID ARTHRITIS
DNA build-up induces
polyarthritis in animal model

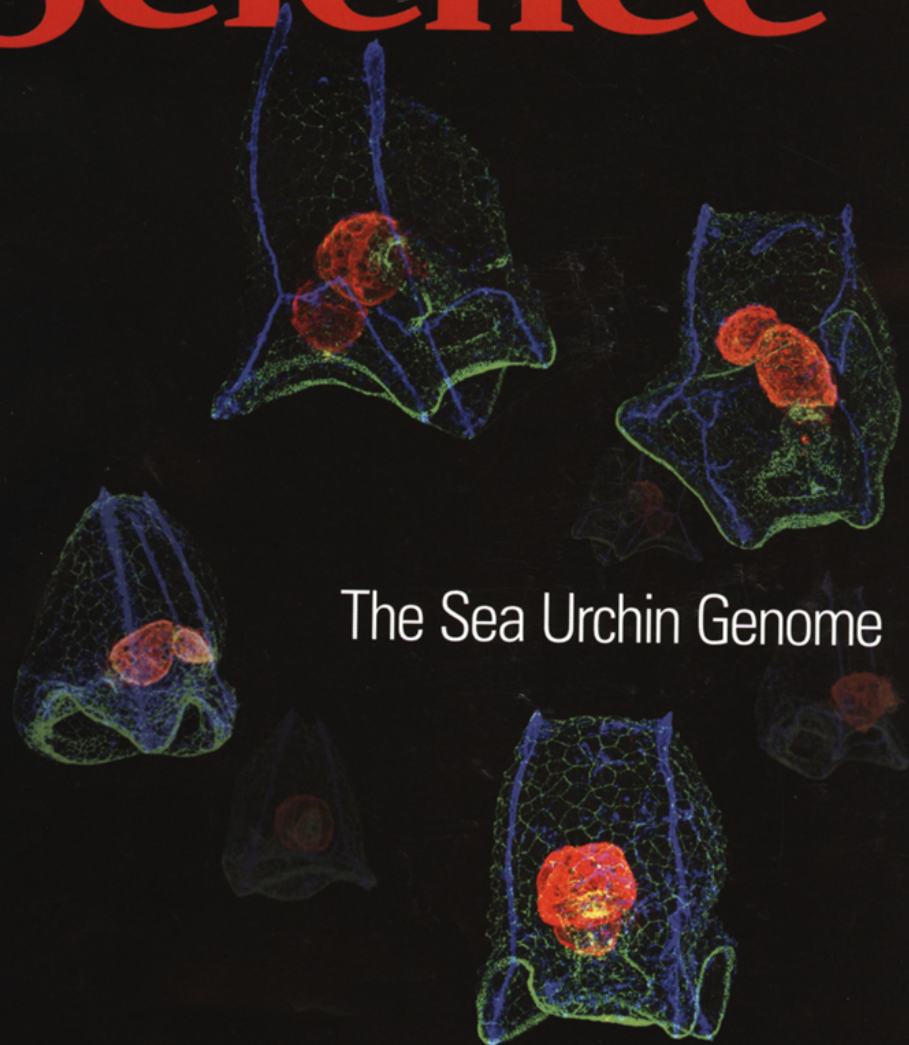
HONEYBEE GENOME

A blueprint for social organization

NATUREJOBS
Spotlight on
Northern England

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Science



The Sea Urchin Genome

 AAAS

8 May 2008 | www.nature.com/nature | \$10

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CARBON DIOXIDE CAPTURE

Cagey ZIFs for
emissions control

'FLIPPING' ENZYMES

Action mechanism of
HIV's Achilles' heel

SCIENCE AND MUSIC

First in a new series

THE PLATYPUS GENOME

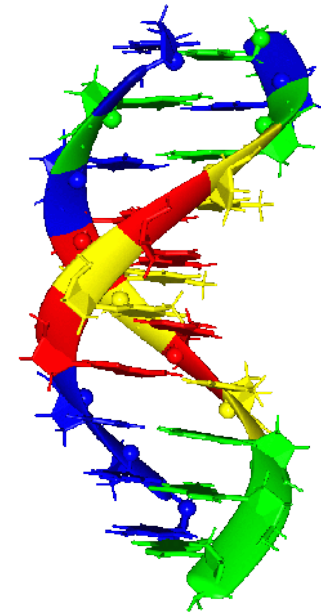
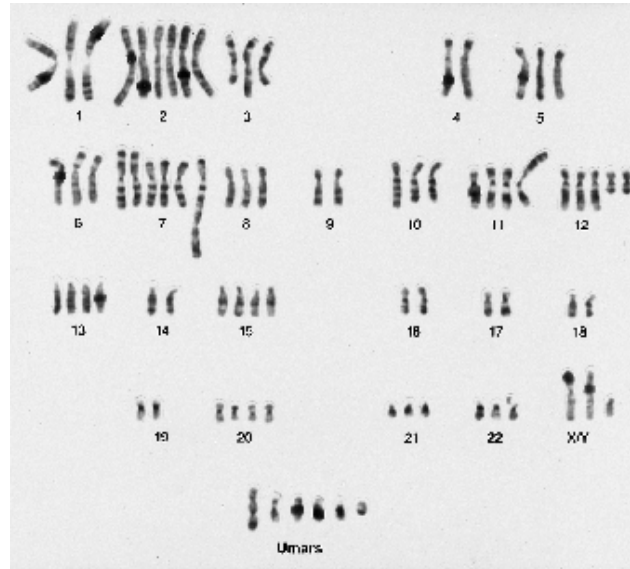
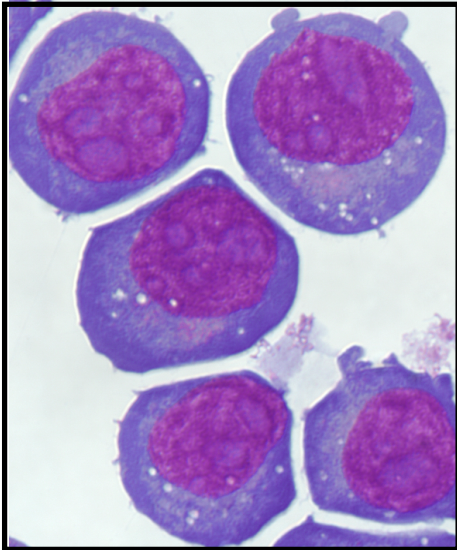
Sequence analysis reveals clues
to early mammalian evolution

NATUREJOBS
Up Canada way

Realities of New DNA Sequencing Technologies...



Cancer: A Disease of the Genome

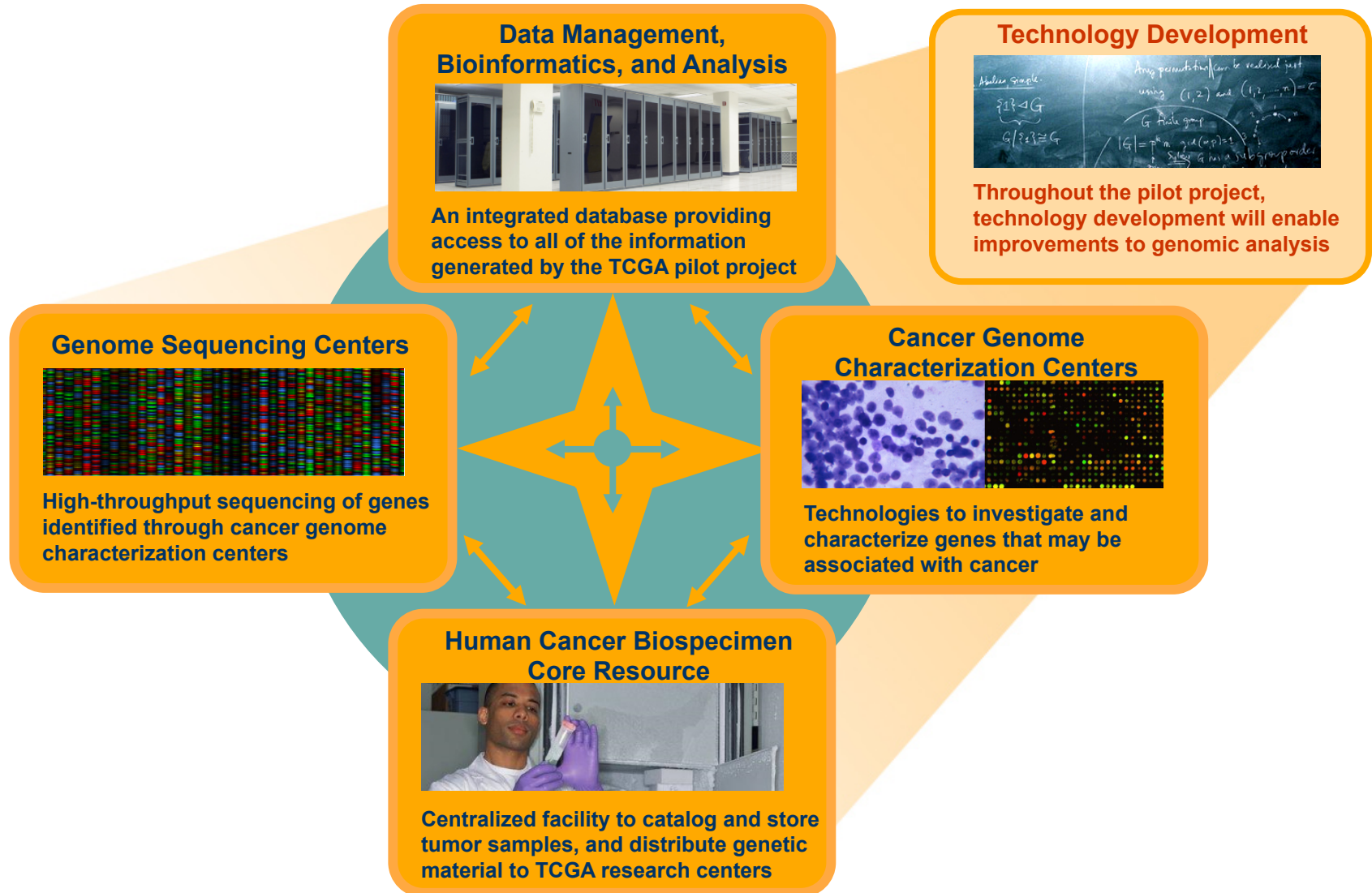


“If we wish to learn more about cancer, we must now concentrate on the cellular genome.”

-- Renato Dulbecco, 1986

The Cancer Genome Atlas:

<http://cancergenome.nih.gov>



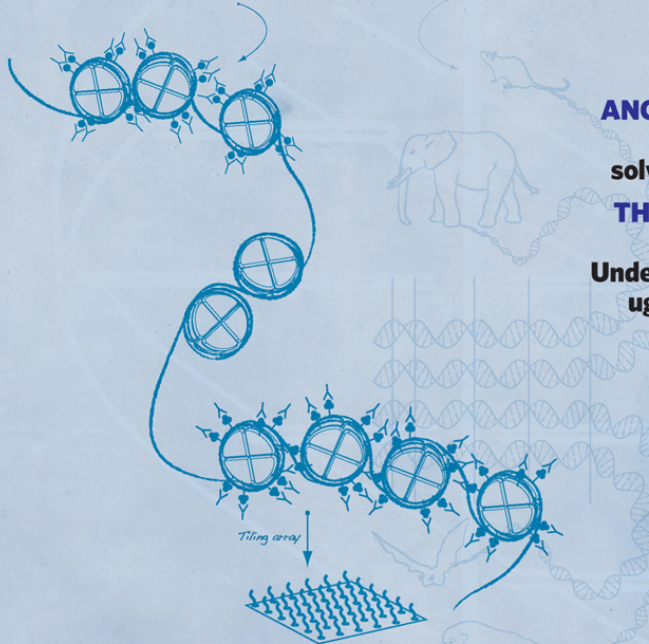
14 June 2007 | www.nature.com/nature | \$10

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nature

Histone-modification chromatin IP

Comparative-sequence alignment



DECODING THE BLUEPRINT

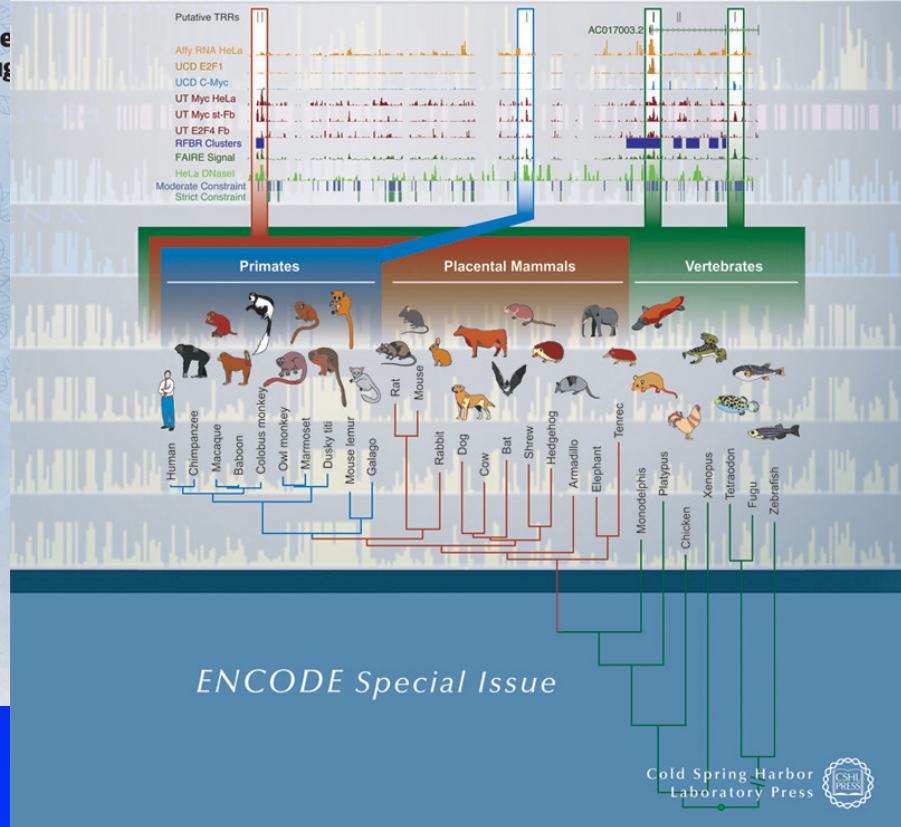
The ENCODE pilot maps human genome function

ISSN 1088-9051

June 2007

GENOME RESEARCH

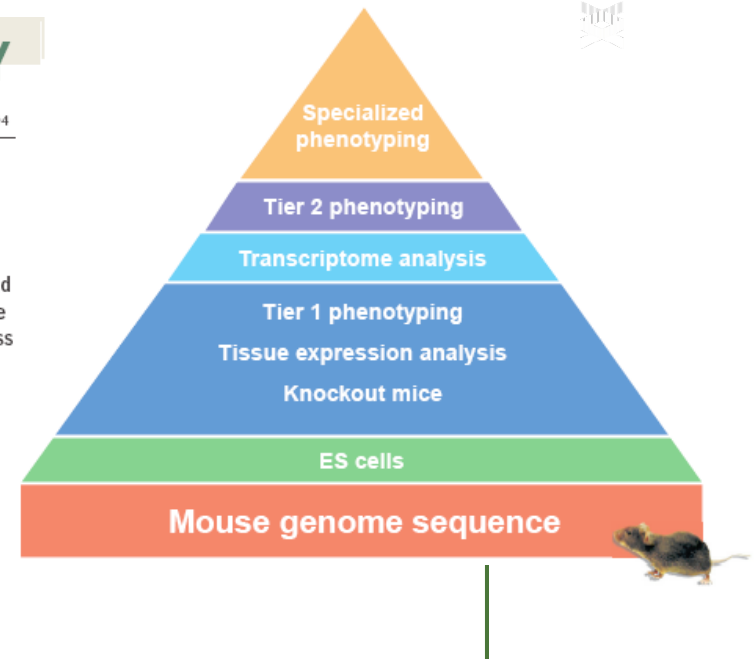
Volume 17 Number 6





The Knockout Mouse Project

Mouse knockout technology provides a powerful means of elucidating gene function *in vivo*, and a publicly available genome-wide collection of mouse knockouts would be significantly enabling for biomedical discovery. To date, published knockouts exist for only about 10% of mouse genes. Furthermore, many of these are limited in utility because they have not been made or phenotyped in standardized ways, and many are not freely available to researchers. It is time to harness new technologies and efficiencies of production to mount a high-throughput international effort to produce and phenotype knockouts for all mouse genes, and place these resources into the public domain.



Leading Edge

Commentary

A Mouse for All Reasons

The International Mouse Knockout Consortium^{1,2,*}

¹Communicating authors: Francis S. Collins, National Human Genome Research Institute, National Institutes of Health, USA; Janet Rossant, Hospital for Sick Children, University of Toronto, Canada; Wolfgang Wurst, GSF-National Research Center for Environment and Health, Technical University, Munich, Germany

²For a full list of International Mouse Knockout Consortium members, please see <http://www.cell.com/cgi/content/full/128/1/9/DC1/>.

*Correspondence: francisc@mail.nih.gov

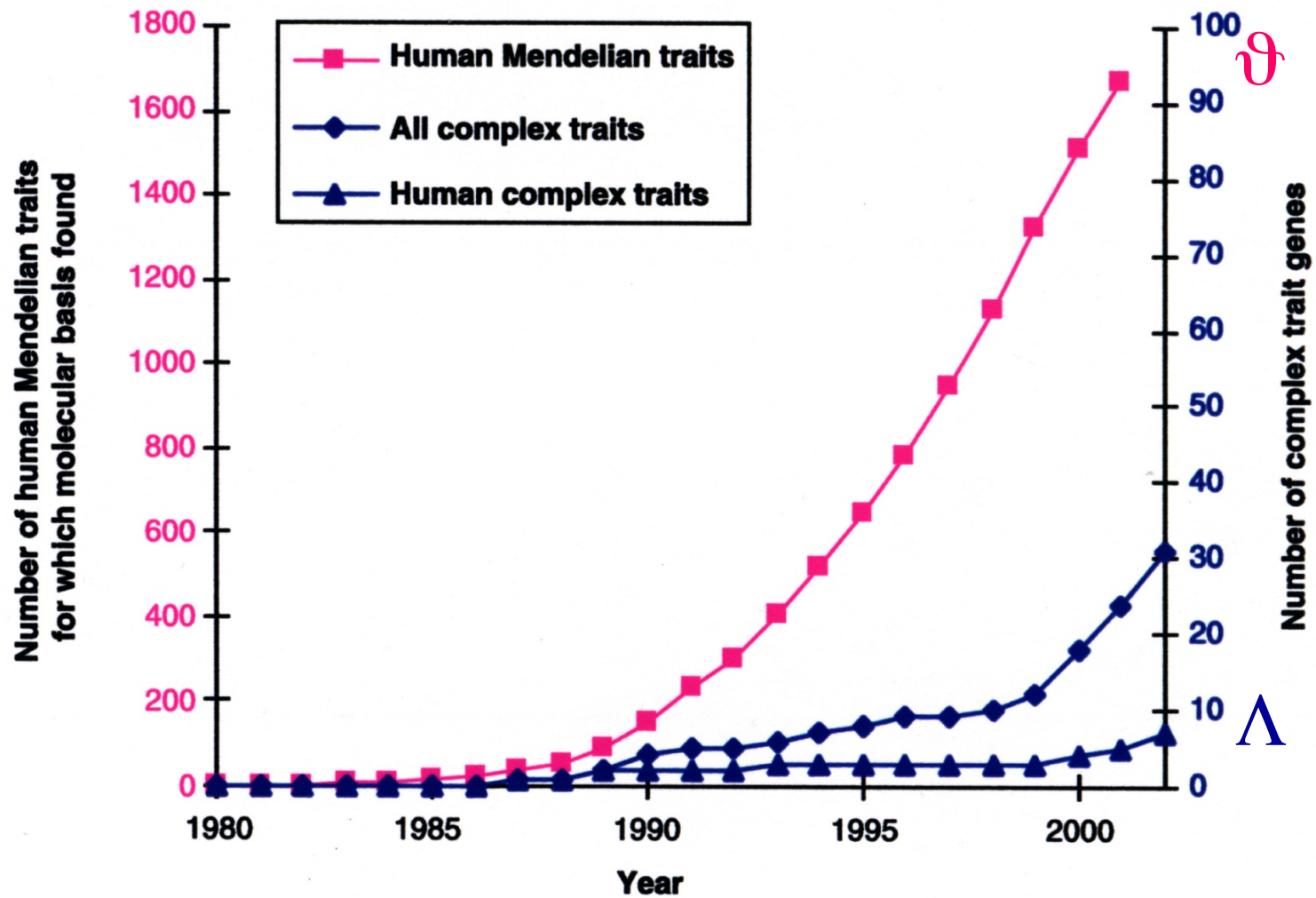
DOI 10.1016/j.cell.2006.12.018

Three major mouse knockout programs are underway worldwide, working together to mutate all protein-encoding genes in the mouse using a combination of gene trapping and gene targeting in mouse embryonic stem (ES) cells. Although the current emphasis is on production of this valuable resource, there are significant efforts to facilitate program coordination, to enhance the availability of this resource, and to plan for future efforts in mouse genetics research.

MGC: Full Length cDNAs For Everyone



*Human and Mouse Goal = Total no. NM RefSeq genes



Glazier et al., Science 298:2345-9, 2002

27 October 2005 | www.nature.com/nature

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

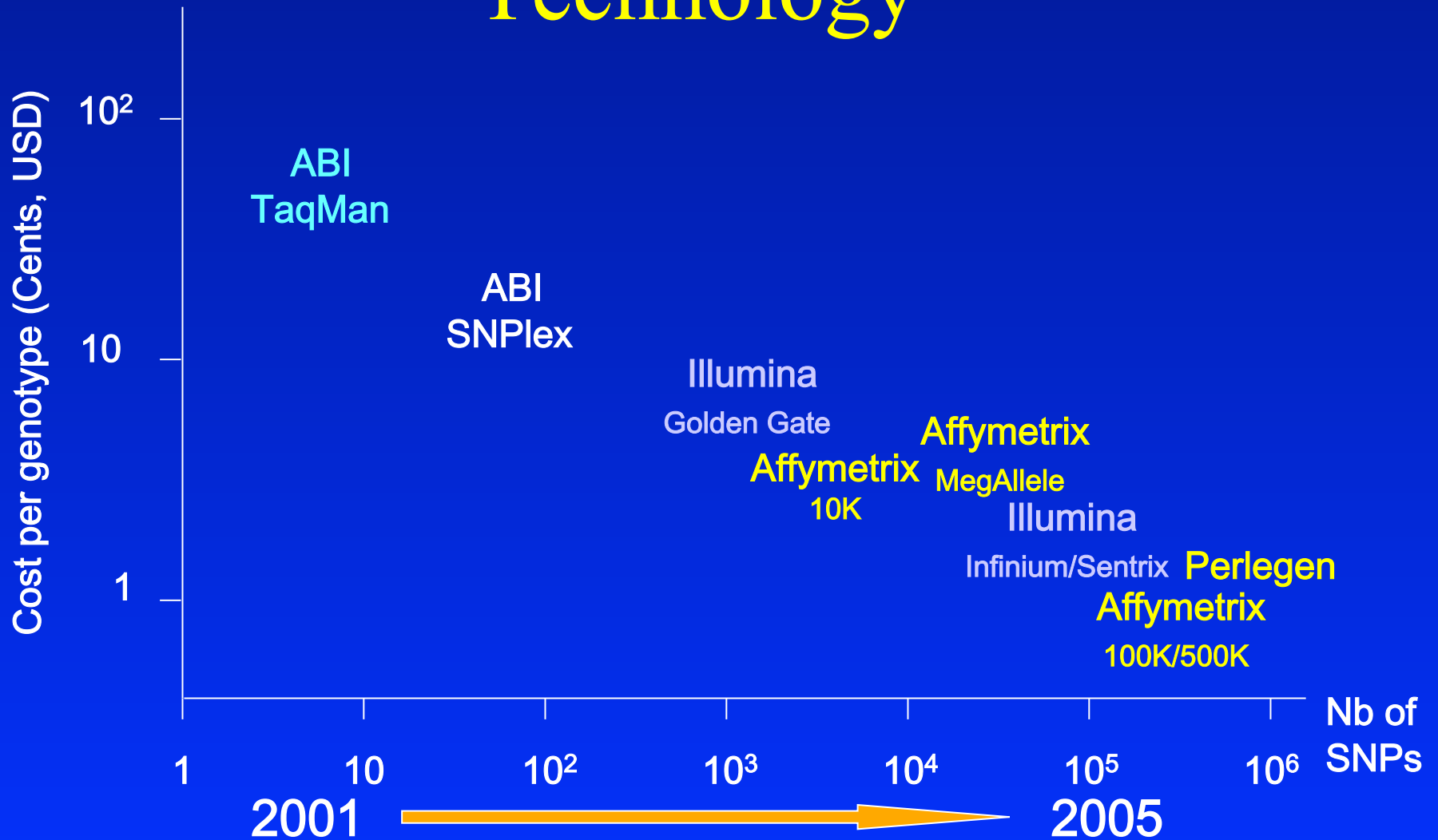
nature



THE HAPMAP PROJECT

Chapter and verse on
human genetic variation

Progress in Genotyping Technology

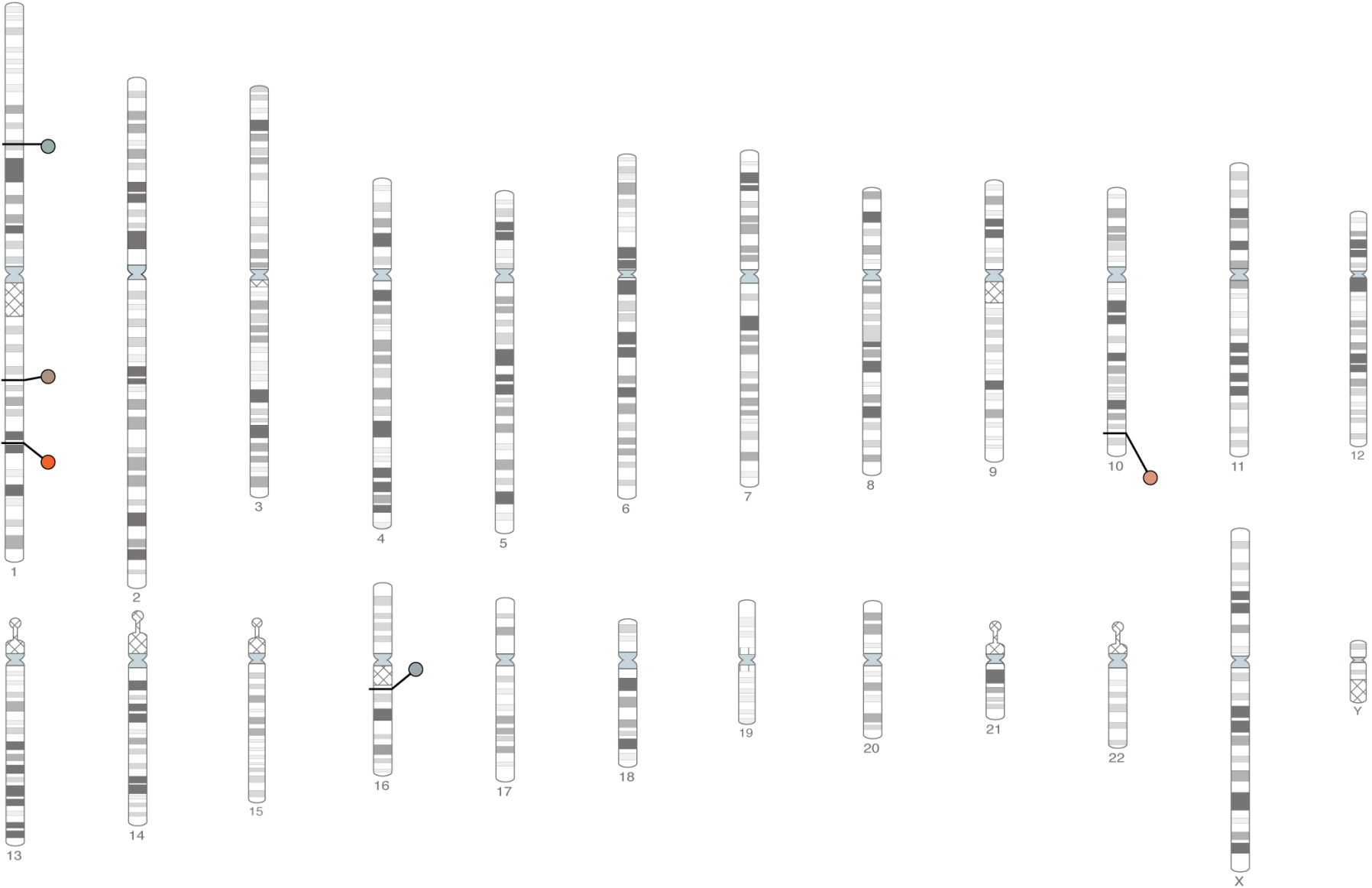


Courtesy S. Chanock, NCI

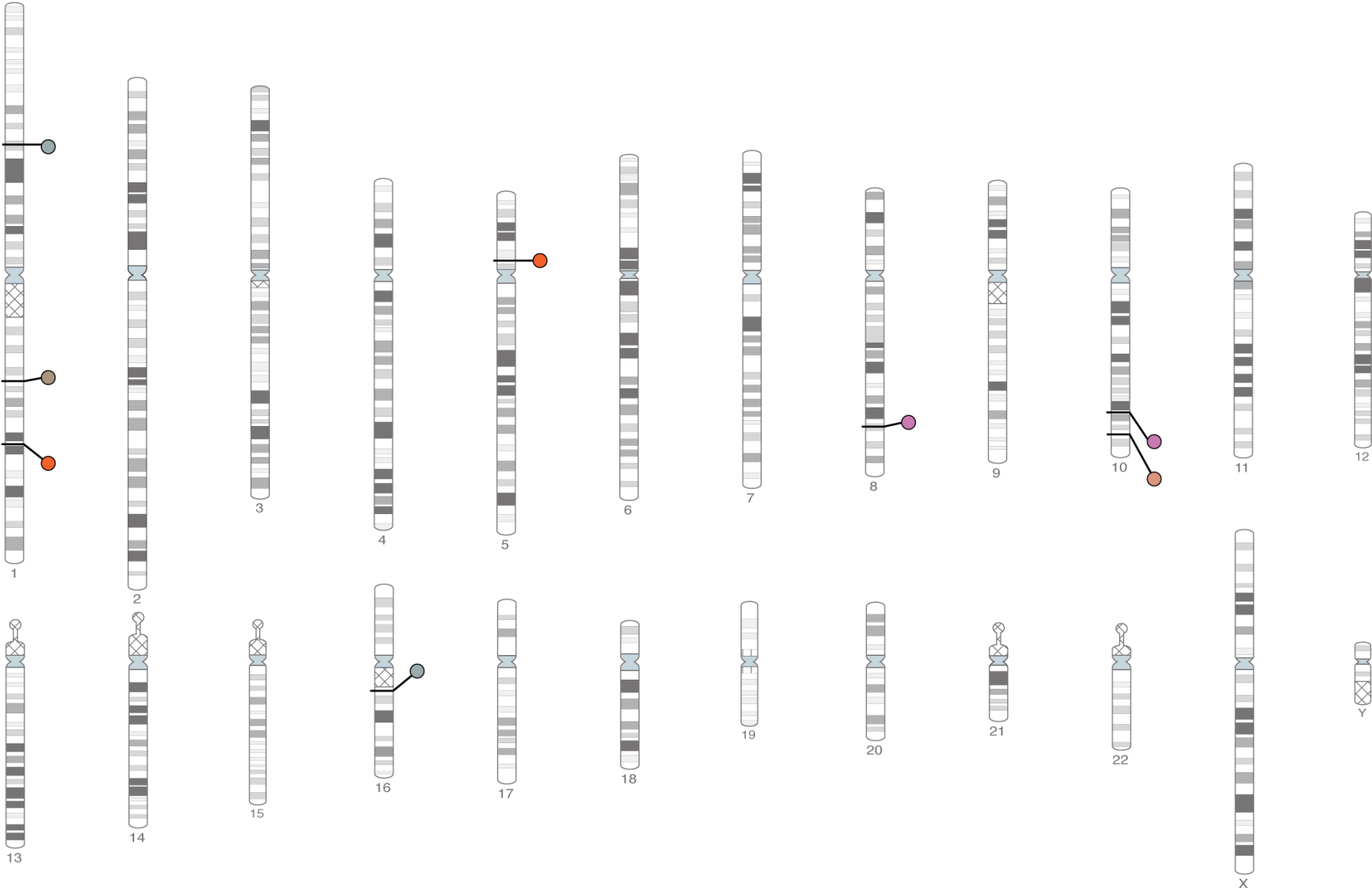
2005



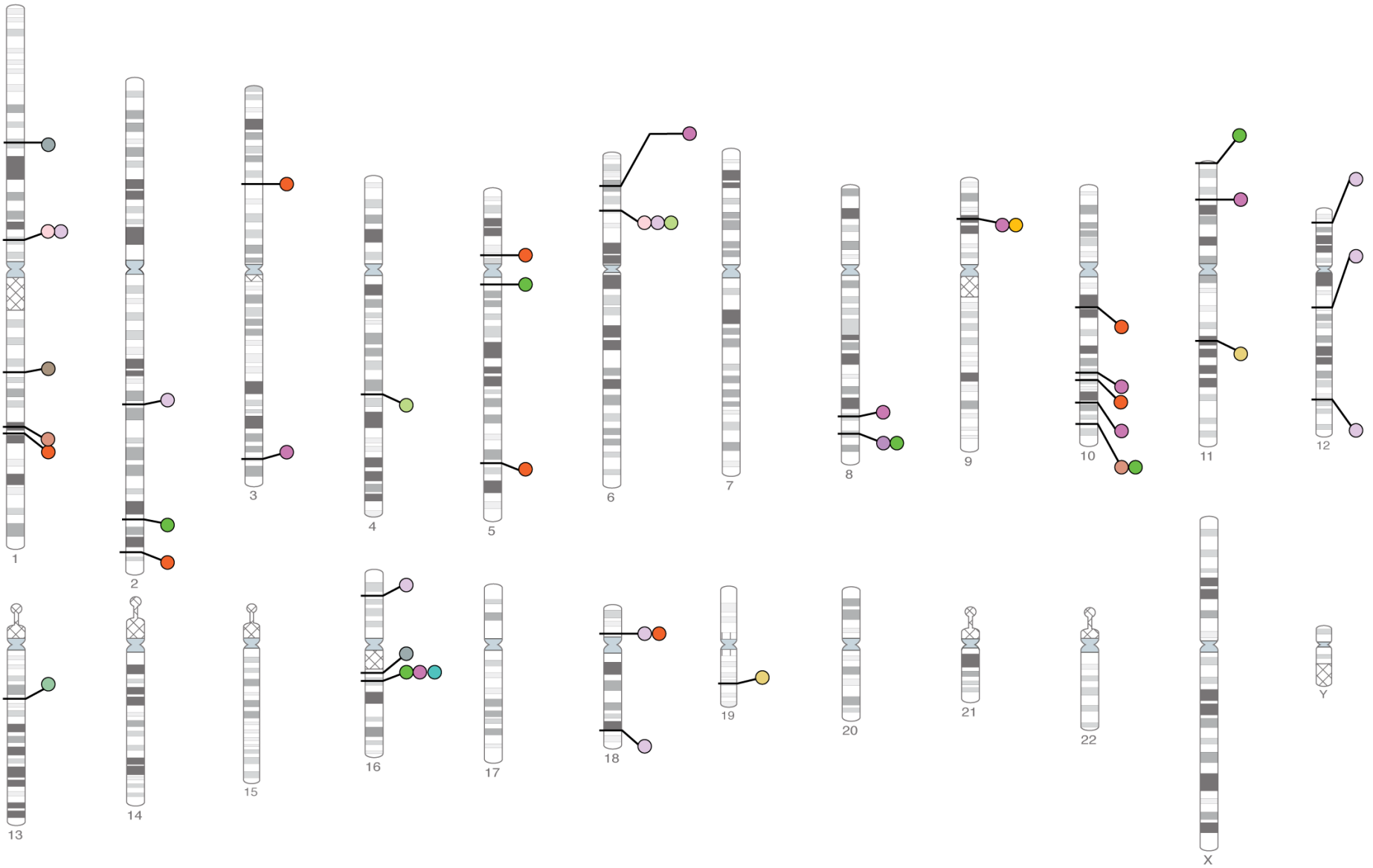
2006



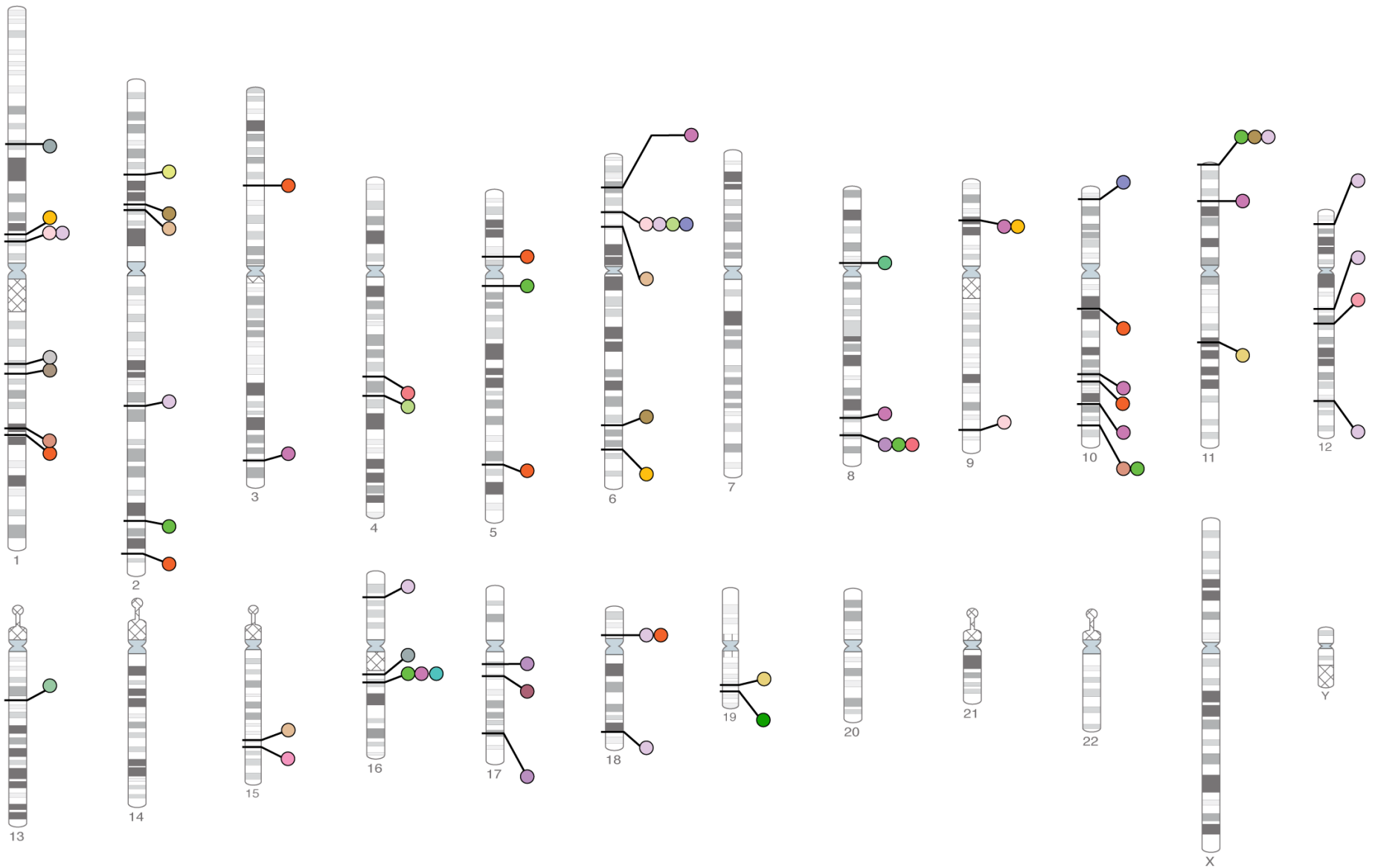
2007 1st quarter



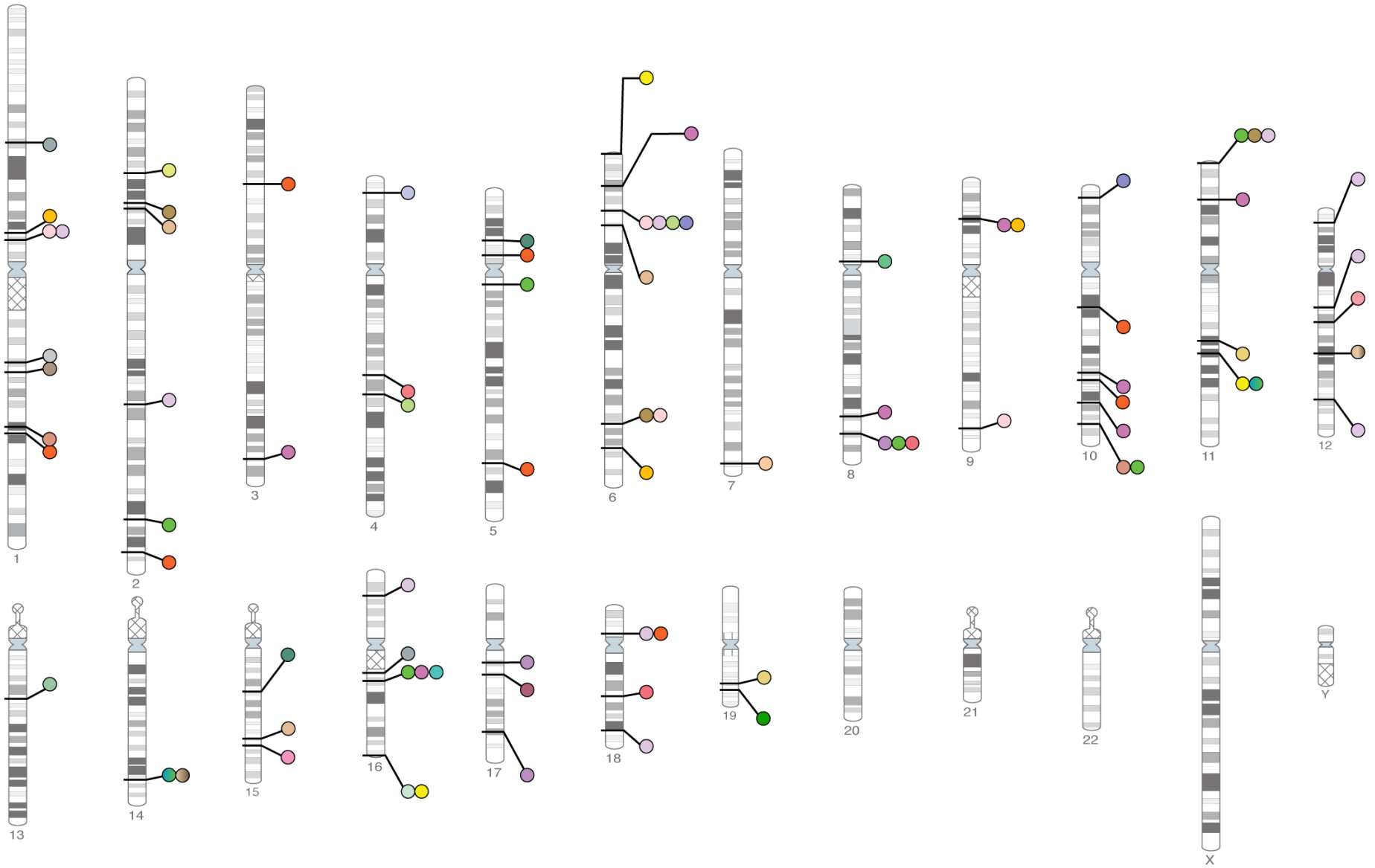
2007 2nd quarter



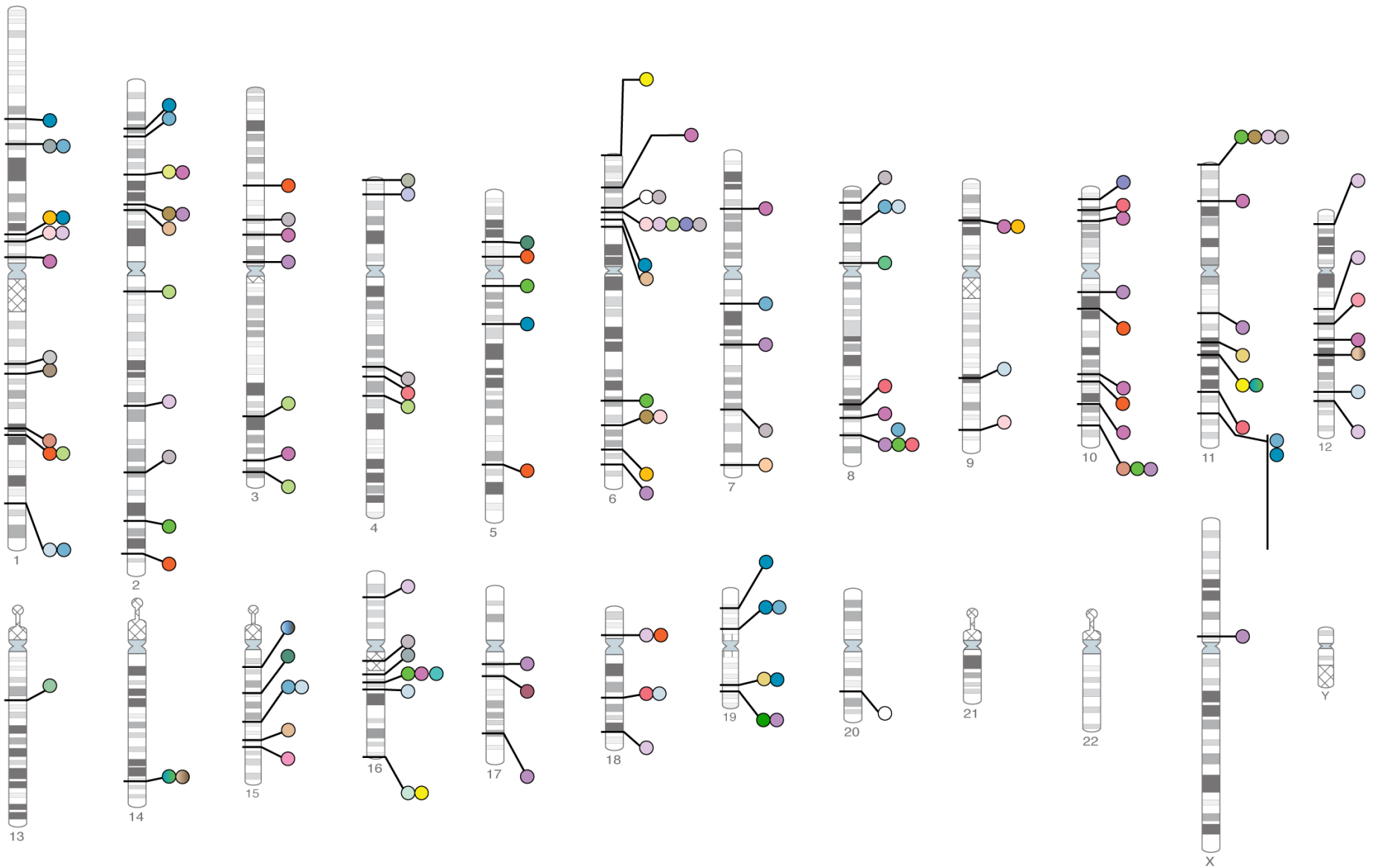
2007 3rd quarter



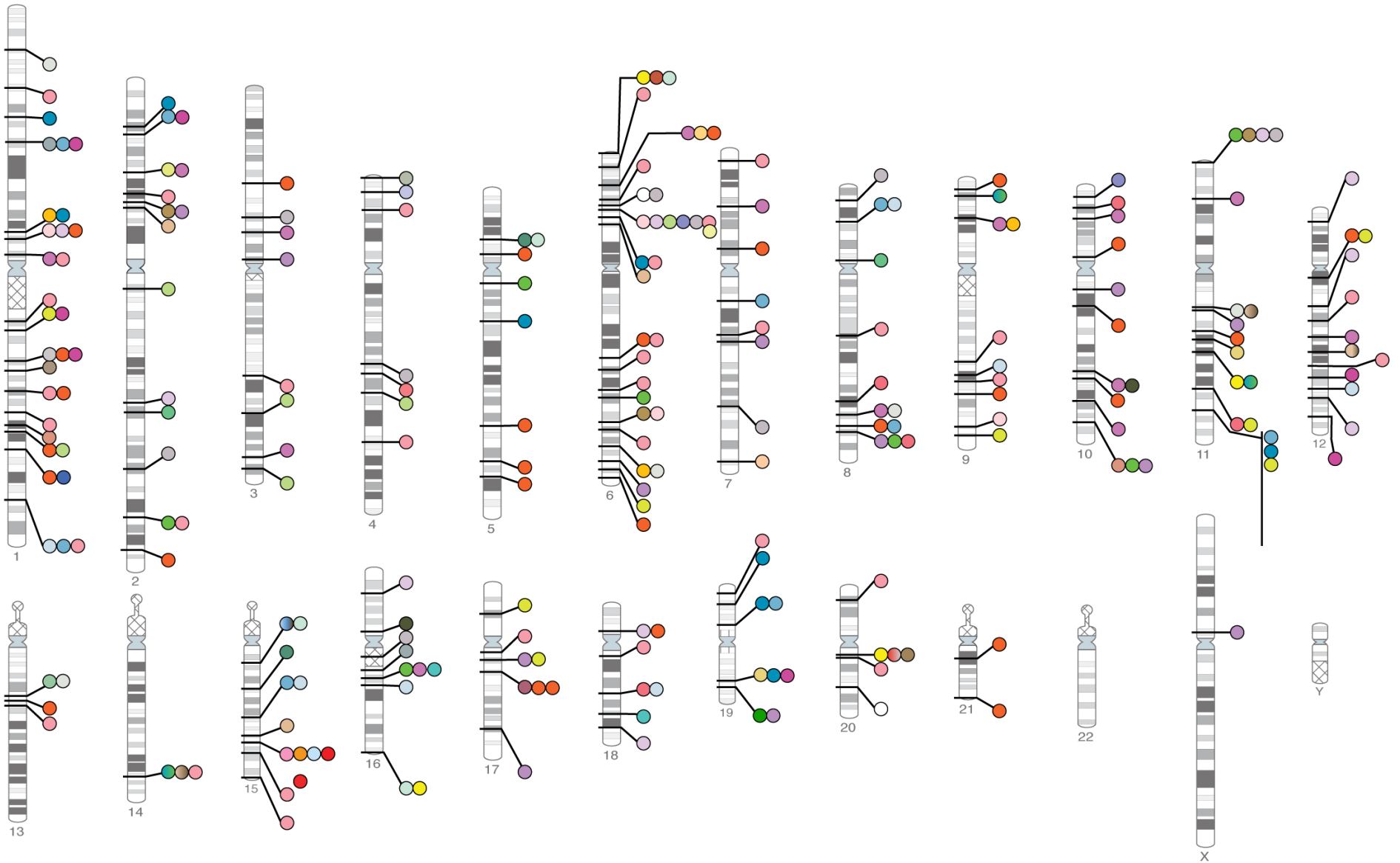
2007 4th quarter



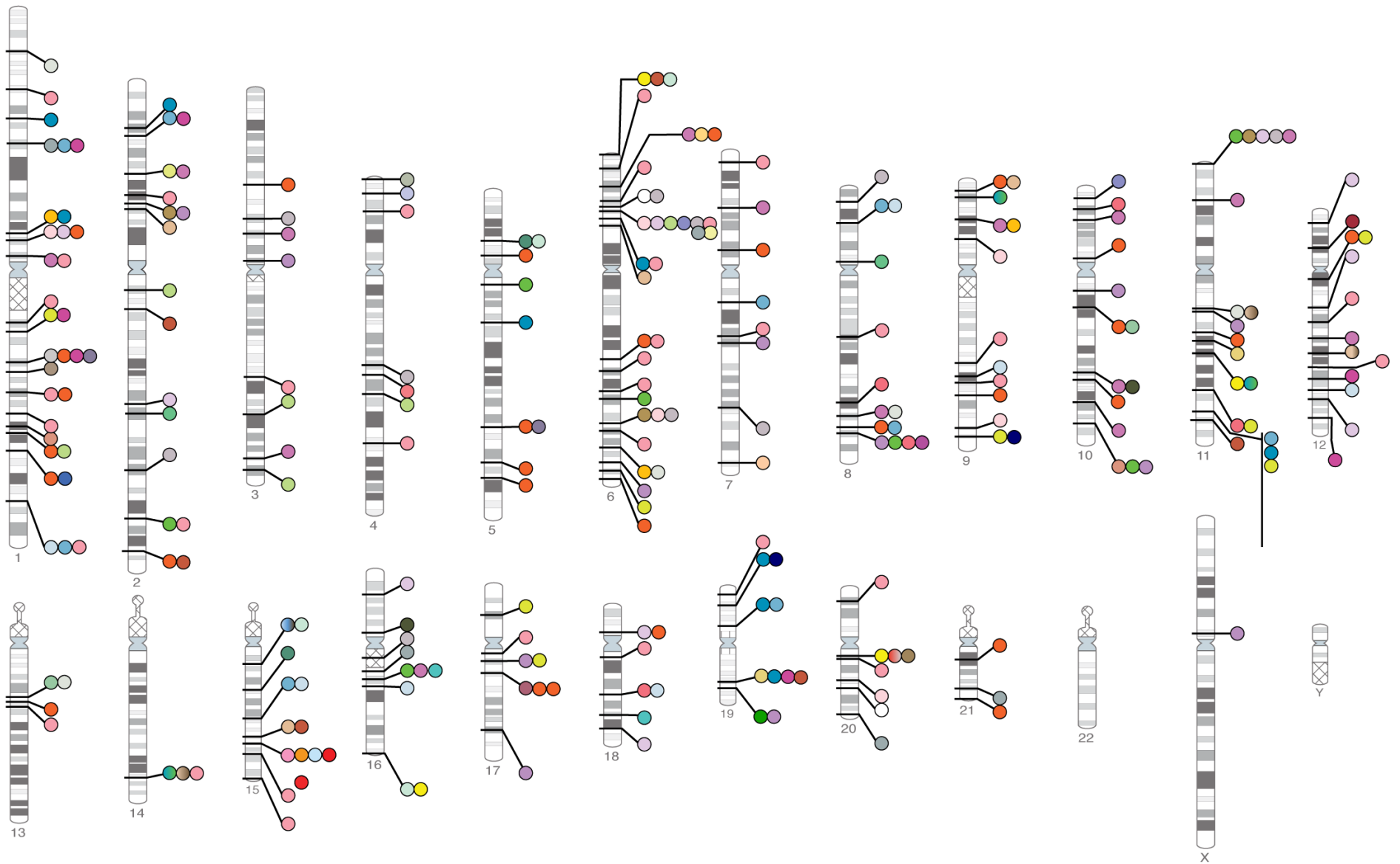
2008 1st quarter



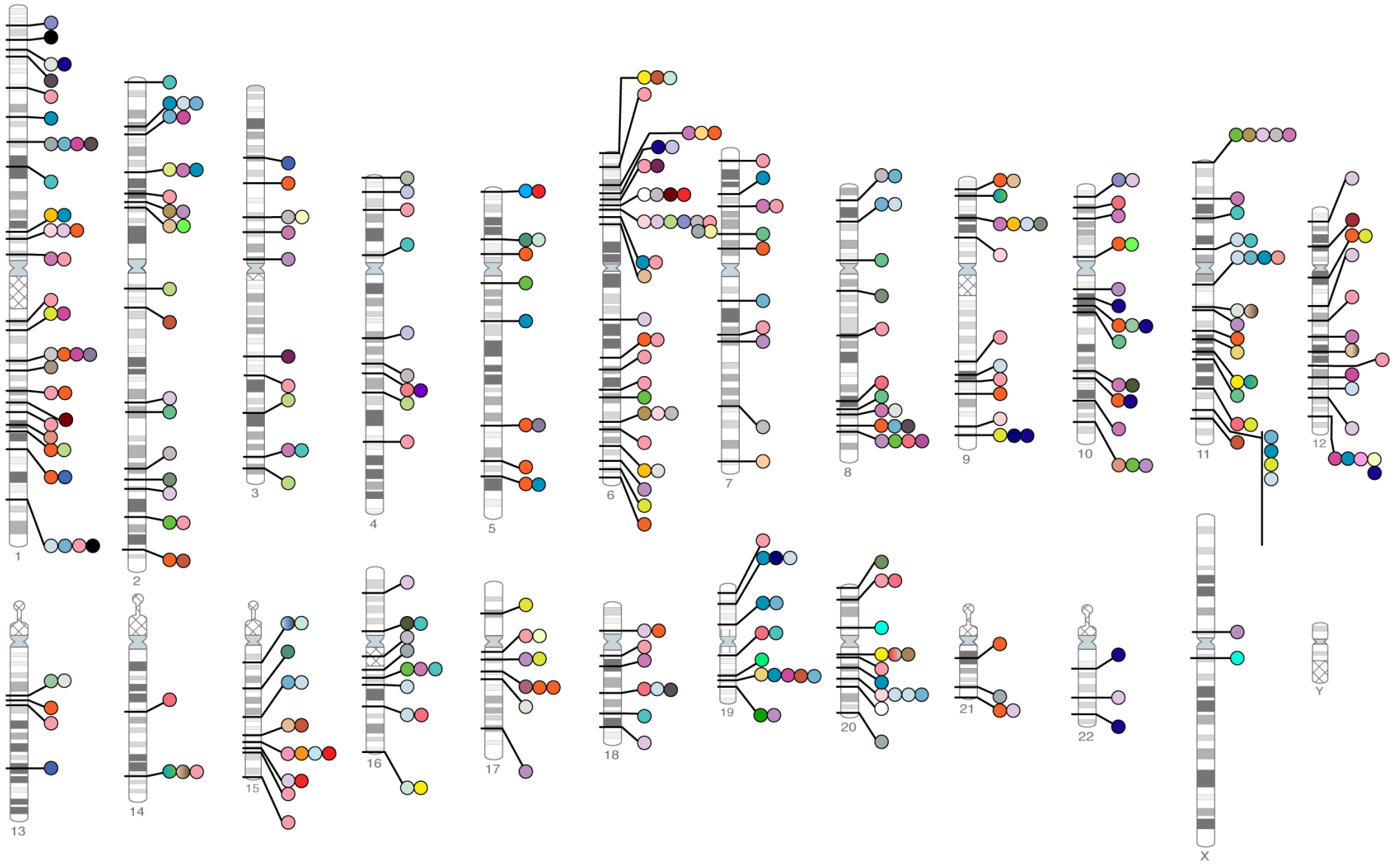
2008 2nd quarter



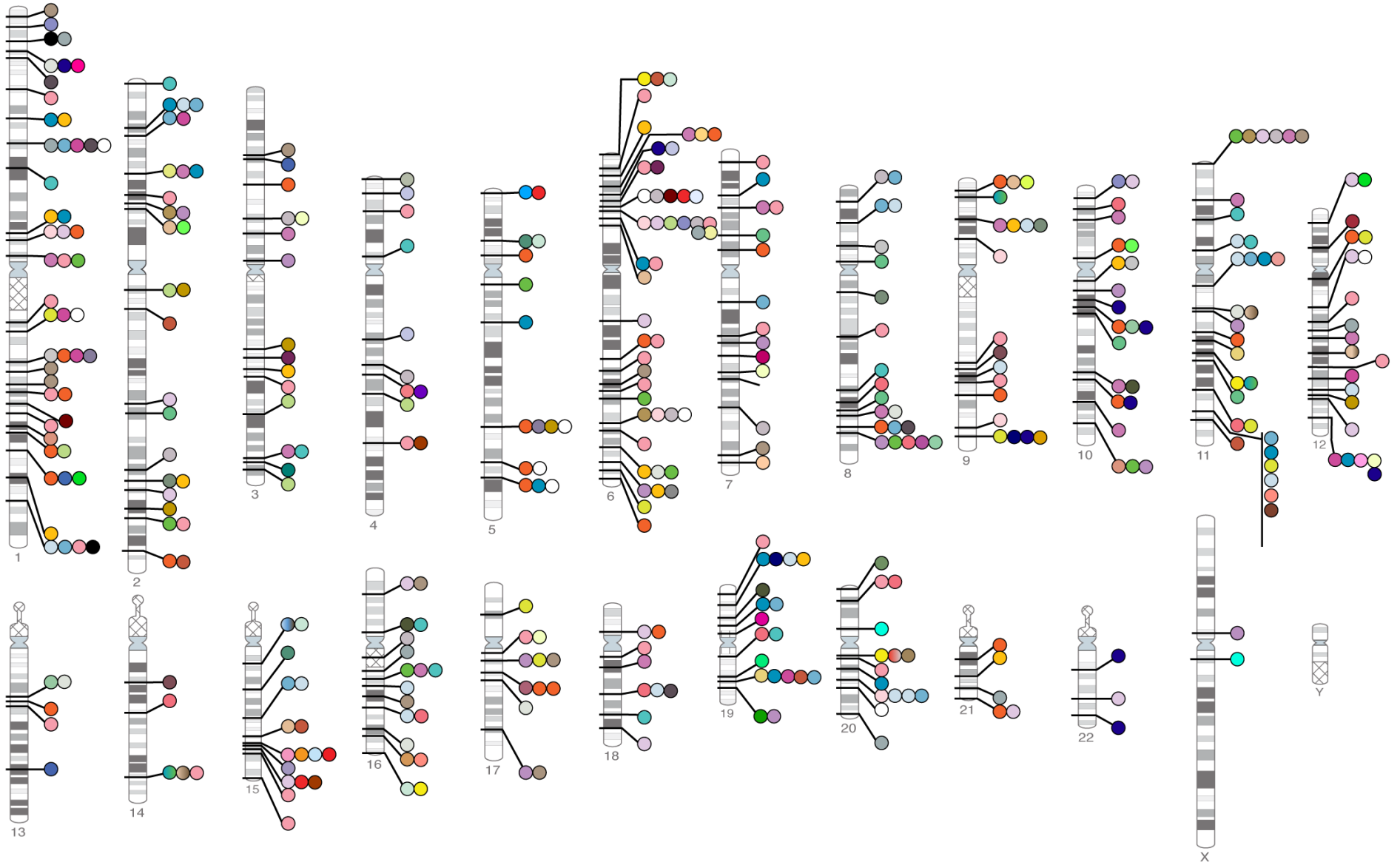
2008 3rd quarter



2008 4th quarter



2009 1st quarter



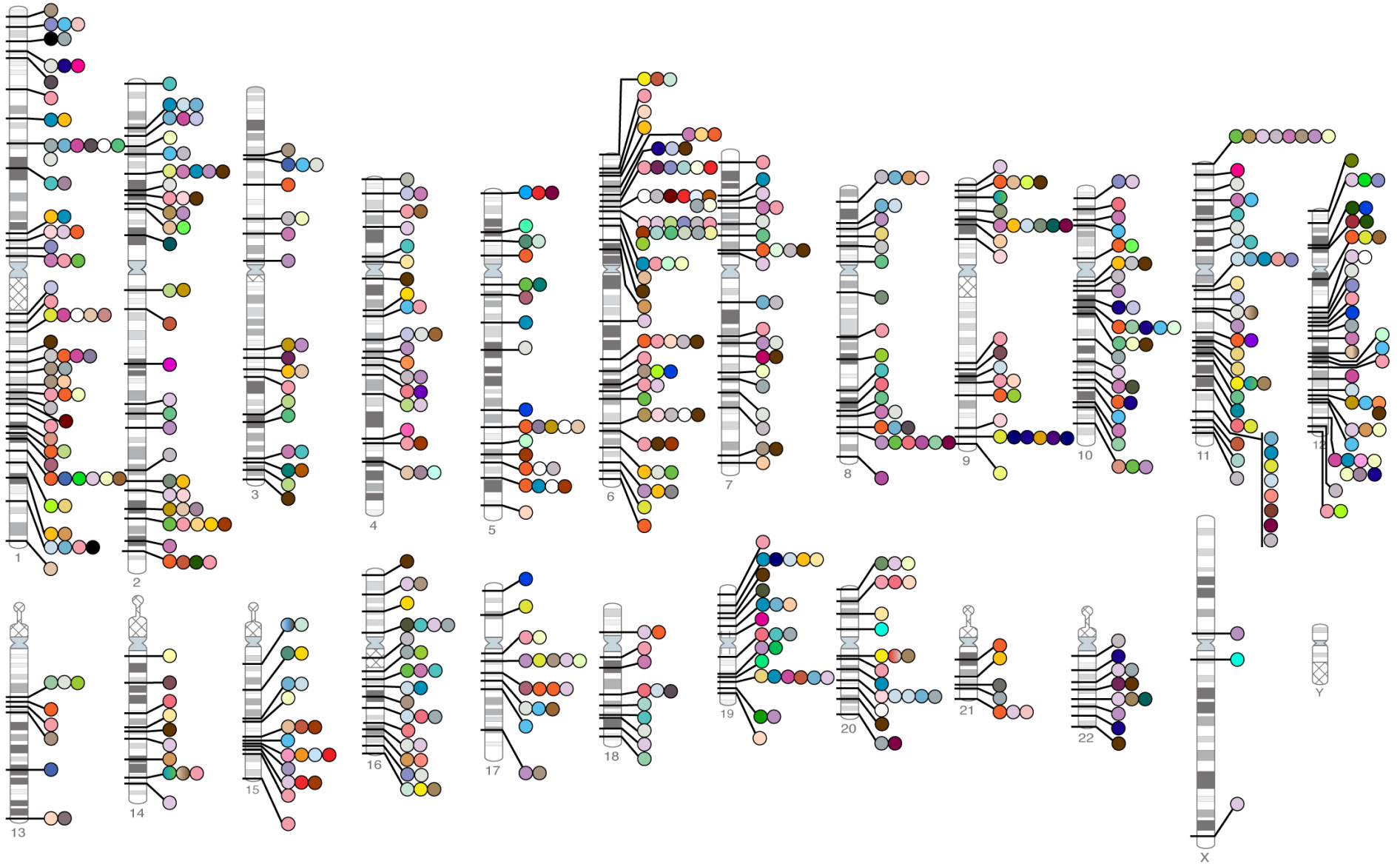
2009 2nd quarter



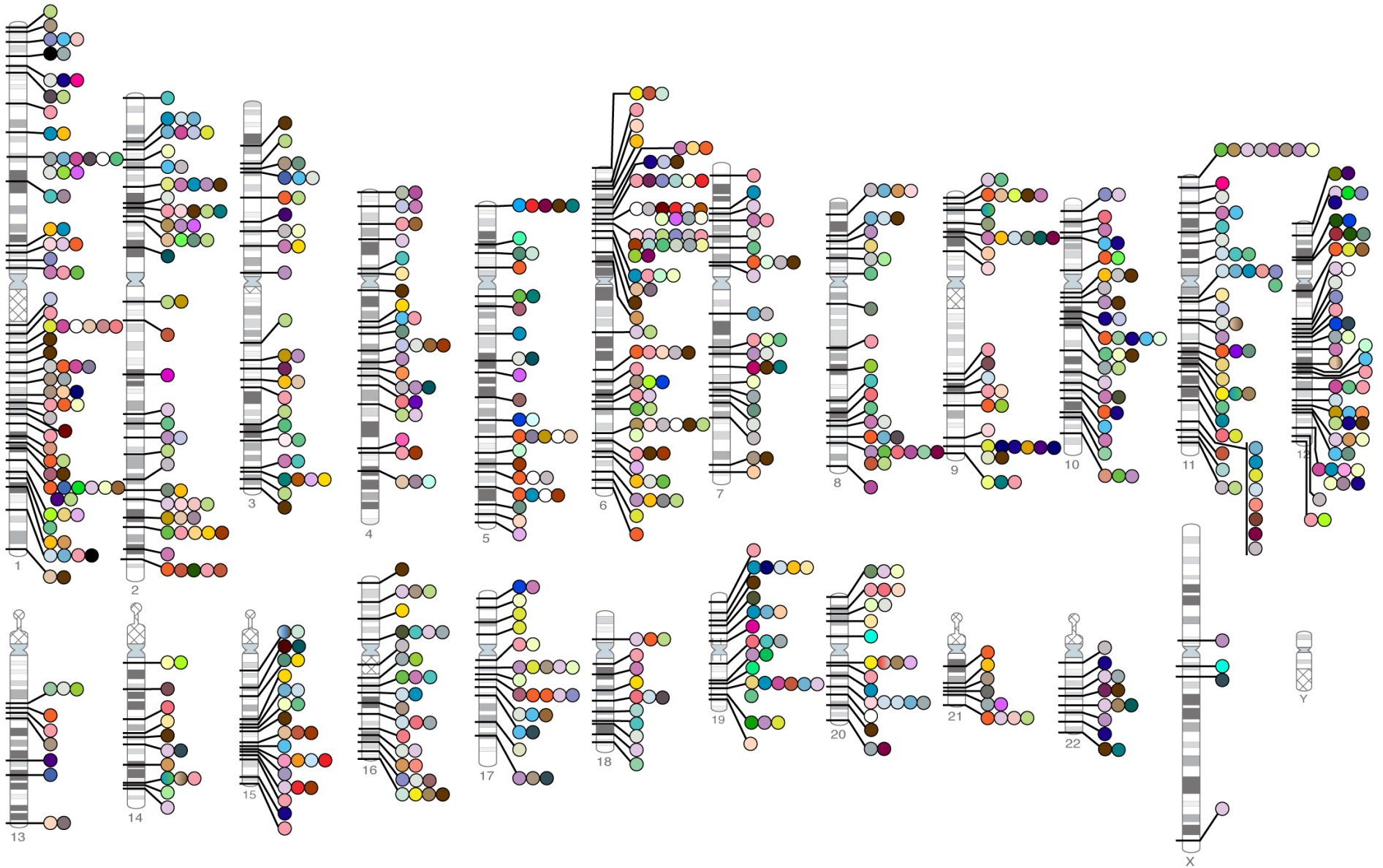
2009 3rd quarter



2009 4th quarter



2010 1st quarter







Home

What is deCODEme?



deCODE genetics
the pioneers in gene discovery

deCODEme
the most comprehensive genome scan
with information on more diseases and genes

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Navigenics

About

Leadership

Policies

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My Genes.
My Health.
My Life.
My Guide.

Play Video

Welcome to Navigenics

We are in the midst of an exciting era of discoveries about the connections between our individual genetic composition and our personal health and wellness. These discoveries are providing a detailed map of thousands of genes that instruct the body how to grow, live and thrive – and a better understanding of how variations in these genes may influence our health over time.

and traits

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Your genes offer a road map to optimal health

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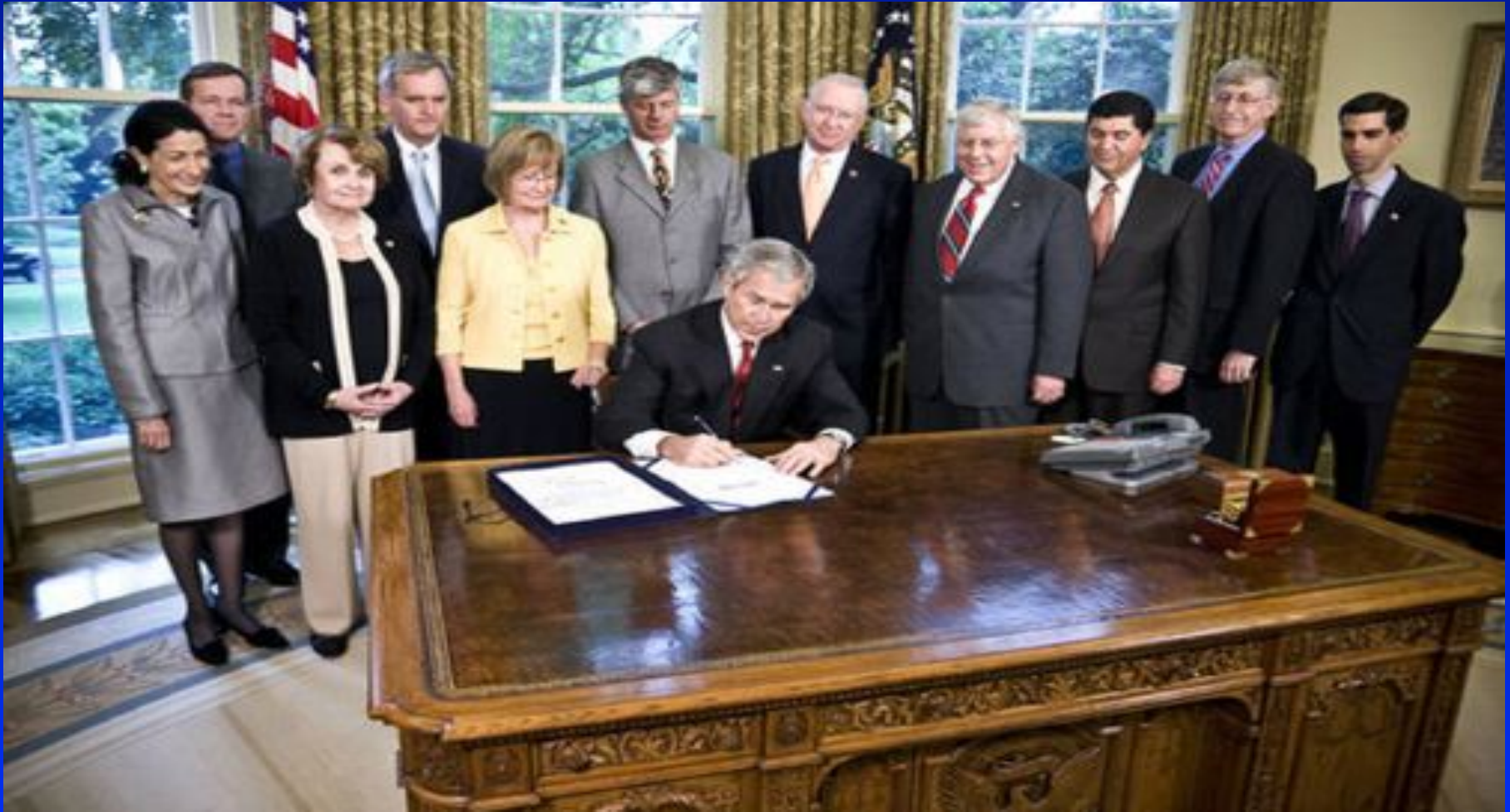
2007: 23andMe introduces the first Personal Genome Service.
Unlock the secrets of your own DNA. Today.

175,000 years ago: The mother of all present-day humans is born in Africa.

1953: Watson and Crick uncover the double-helix structure of DNA.

Welcome to 23andMe, a web-based service that helps you read and understand your DNA. After providing a saliva sample using an at-

GINA Becomes Law



May 21, 2008 – The Oval Office

Genetics and Drug Response: The case of Plavix

- Drug Functions:
 - Works by preventing platelets from forming clots
 - Must be activated by specific enzymes (P450)
- Clinical Observations:
 - Commonly used in patients at risk for heart attacks and strokes
 - *However*, it does **not** work for about **30%** of the U.S. population
- **Mystery solved: Variations in the CYP2C19 gene account for lack of response**
- **FDA adds a “black box” warning**

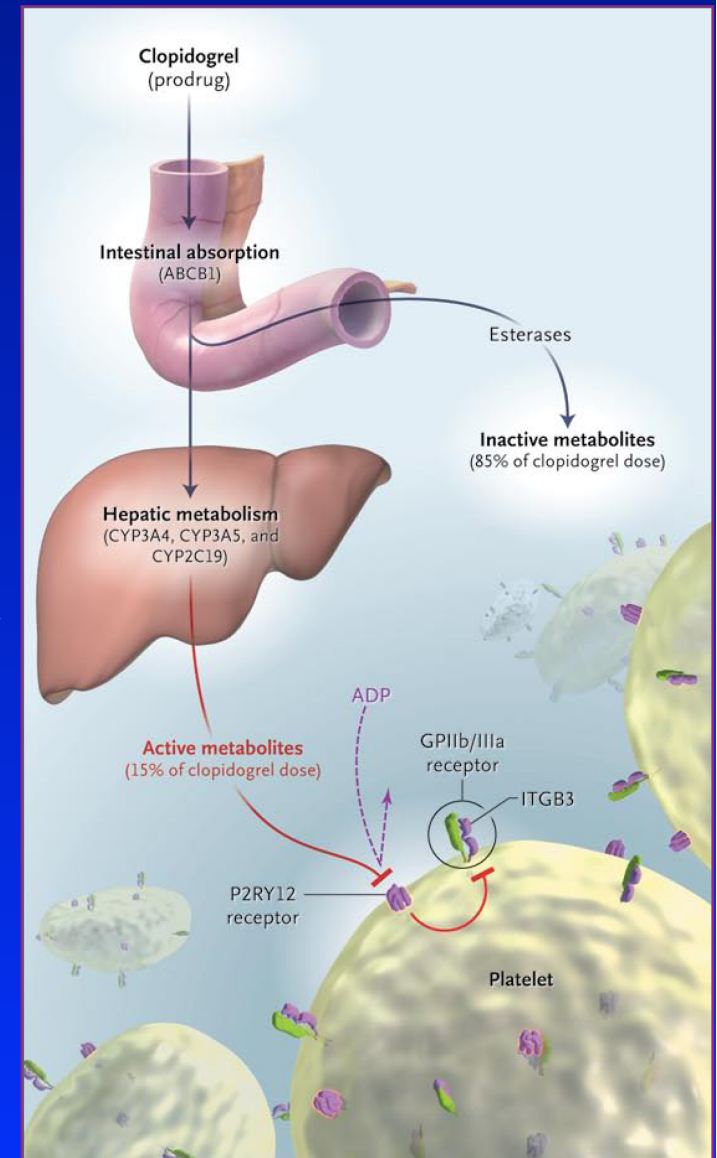


Image: T. Simon, C. Verstuyf, et. al, NEJM

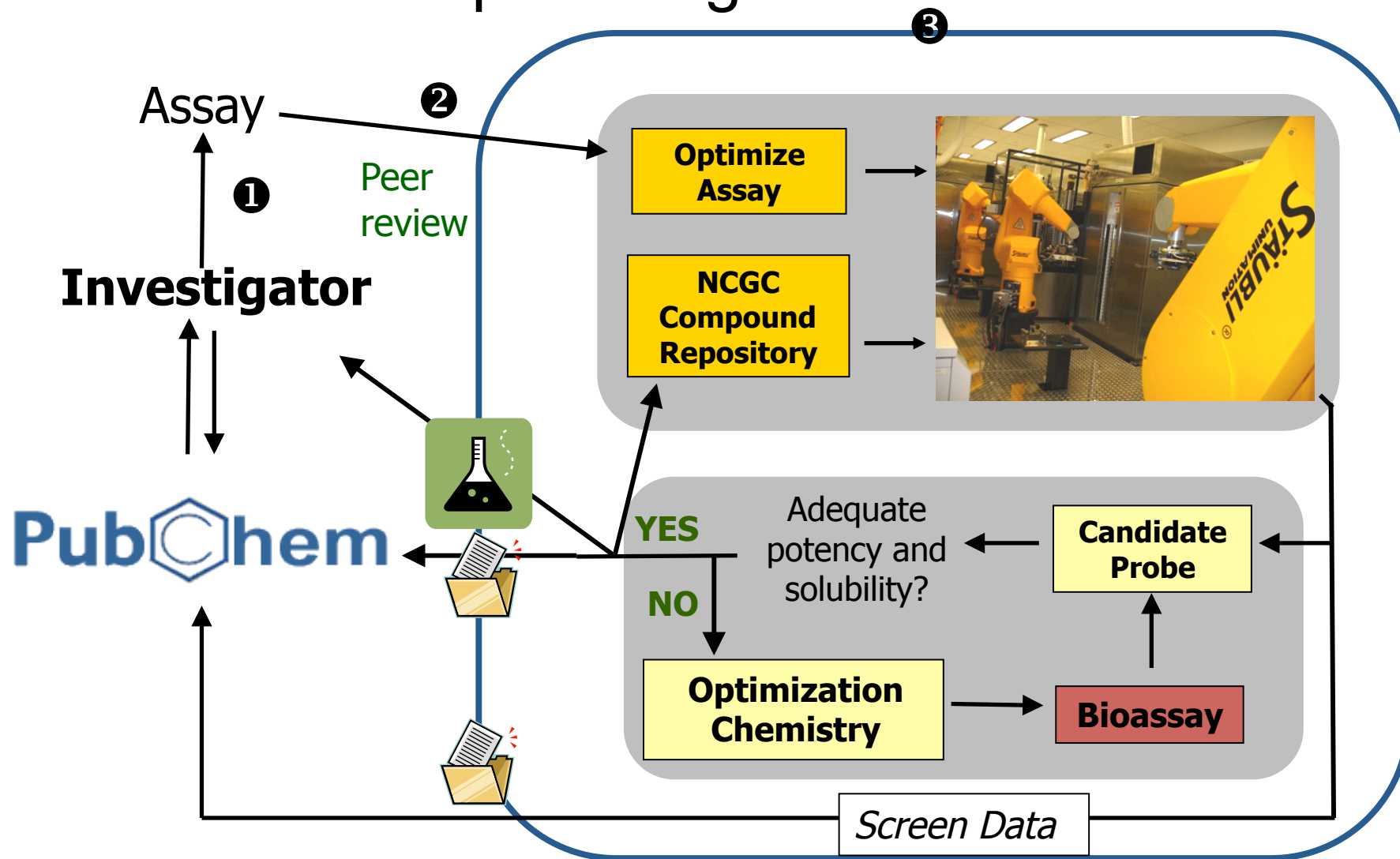
Two common misconceptions about gene discovery and validation of drug targets

- **A modest odds ratio means it's not a good target**
- **If a drug is developed against that target, it will only work for those with the risk allele**

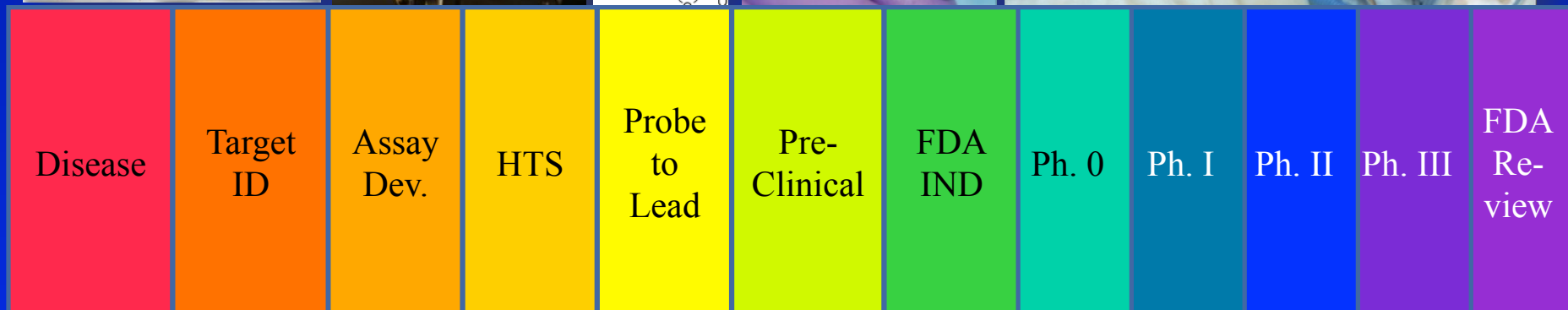
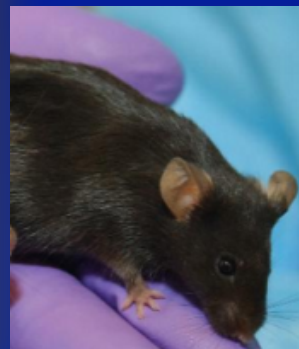
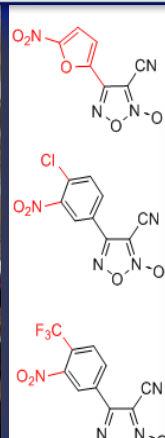
The First Nine GWAS Loci for Type 2 Diabetes

- *TCF7L2*
- *IGF2BP2*
- *CDKN2A/B*
- *FTO*
- *CDKAL1*
- *KCNJ11*
- *HHEX/IDE*
- *SLC30A8*
- *PPARG*

NIH Roadmap “Small Molecule” Initiative: Empowering Translation



Cures Acceleration Network



NIH Molecular Libraries Initiative

NIH TRND

NIH RAID

Pharma, Biotech, NIH Clinical Center, CTSA

New NIH FDA Partnerships

Prediction is difficult.
Especially about the future.

- Yogi Berra?
- Dan Quayle?
- Niels Bohr?

2010

- Predictive genetic tests available for a dozen conditions
- Interventions to reduce risk available for several of these
- Many primary care providers begin to practice genetic medicine
- Preimplantation diagnosis widely available, limits being fiercely debated
- Reasonably effective federal legislative solutions to genetic discrimination and privacy in place in US
- Access remains inequitable, especially in developing world

2020

- **Gene-based designer drugs for diabetes, hypertension, etc.,
coming on the market**
- **Cancer therapy is precisely targeted to molecular
fingerprint of tumor**
- **Dx/Rx pharmacogenomic approach is standard practice
for many drugs**
- **Mental illness diagnosis transformed, new therapies
under study, societal views shifting**
- **Homologous recombination technology suggests
germline gene therapy could be safe**

2030

- **Comprehensive genomics-based health care is the norm**
Individualized preventive medicine available
Environmental factors, and their interaction with
genotype, pinpointed for many diseases
Illnesses are detected early by molecular surveillance
Gene therapy and gene-based drug therapy available
for many diseases
- **Full computer model of human cell replaces many**
laboratory experiments
- **Average life span reaches 90 years, stressing prior**
socioeconomic norms
- **Major anti-technology movements active in US,**
elsewhere
- **Serious debate is underway about humans possibly**
“taking charge” of their own evolution

