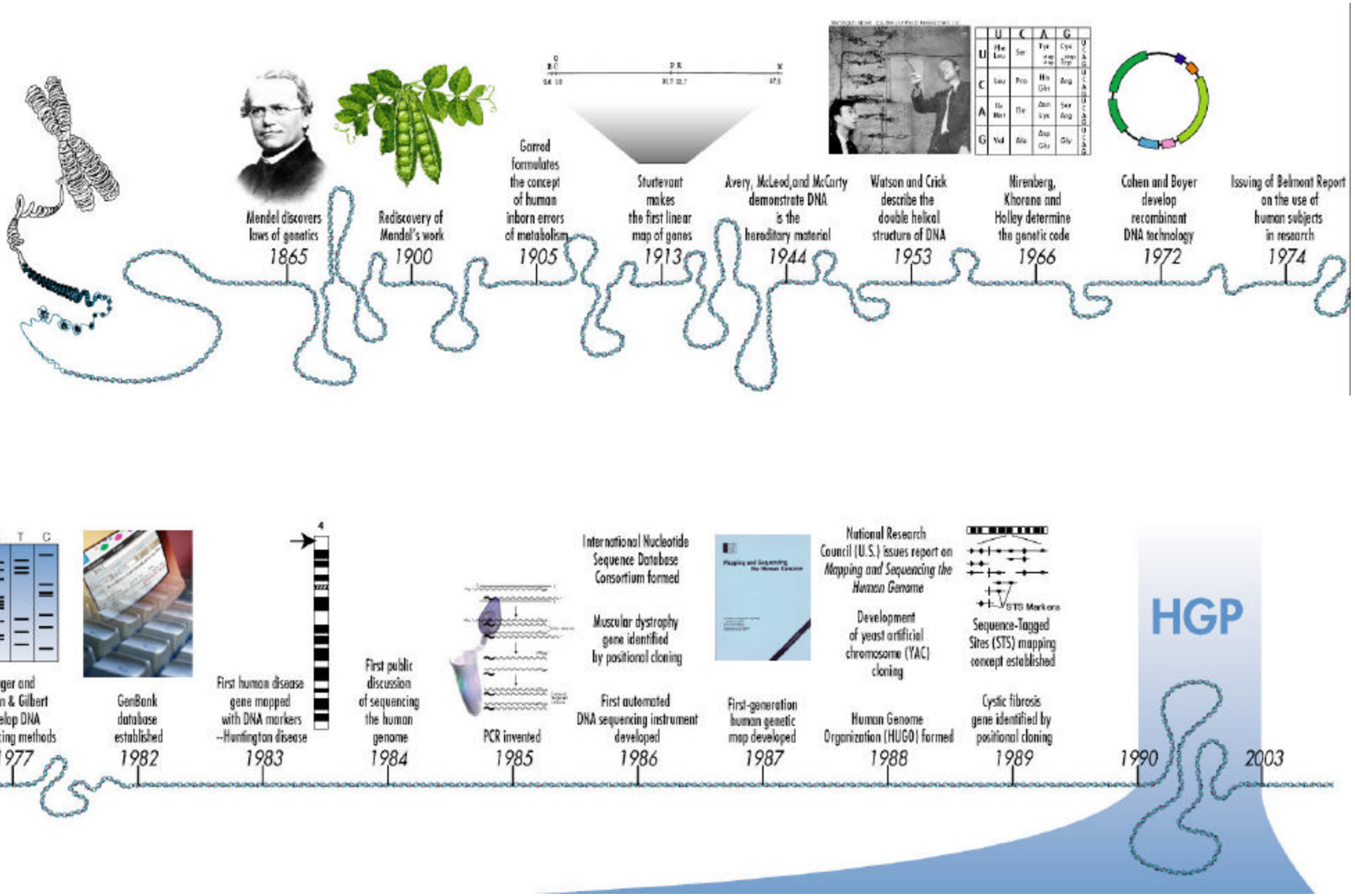
Future Directions in Genetic and Genomic Research

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

Inaugural Meeting of SACGHS

June 11, 2003


Mendel discovers laws of genetics
1865
Rediscovery of Mendel's work
1900
Garrod formulates the concept of human inborn errors of metabolism
1905
Sturtevant makes the first linear map of genes
1913
Avery, McLeod, and McCarty demonstrate DNA is the hereditary material
1944
Watson and Crick describe the double helical structure of DNA
1953
Nirenberg, Khorana and Holley determine the genetic code
1966
Cohen and Boyer develop recombinant DNA technology
1972
Issuing of Belmont Report on the use of human subjects in research
1974
Sanger and Maxam & Gilbert develop DNA sequencing methods
1977
GenBank database established
1982
First human disease gene mapped with DNA markers --Huntington disease
1983
First public discussion of sequencing the human genome
1984
PCR invented
1985
International Nucleotide Sequence Database Consortium formed
Muscular dystrophy gene identified by positional cloning
First automated DNA sequencing instrument developed
1986
First-generation human genetic map developed
1987
National Research Council (U.S.) issues report on Mapping and Sequencing the Human Genome
Development of yeast artificial chromosome (YAC) cloning
Human Genome Organization (HUGO) formed
1988
STS Markers
Sequence-Tagged Sites (STS) mapping concept established
Cystic fibrosis gene identified by positional cloning
1989
1990
2003
HGP

1990

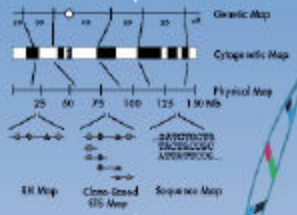
Human Genome Project (HGP) launched in the U.S.

Ethical, Legal, and Social Implications (ELSI) programs founded at NIH and DOE

First gene for breast cancer (BRCA1) mapped

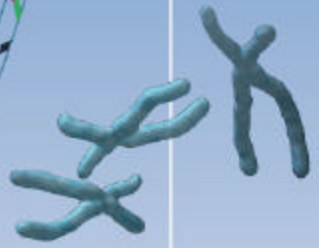
1991

First U.S. Genome Centers established



1992

Second-generation human genetic map developed



Rapid data release guidelines established by NIH and DOE

1993

New five-year plan for the HGP in the U.S. published

Sanger Centre founded (later renamed Wellcome Trust Sanger Institute)

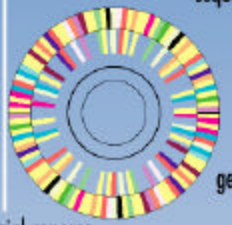
The Wellcome Trust

1994

HGP's human genetic mapping goal achieved

1995

HGP's human physical mapping goal achieved



First bacterial genome (*H. influenzae*) sequenced

U.S. Equal Employment Opportunity Commission issues policy on genetic discrimination in the workplace

1996

First human gene map established

Pilot projects for human genome sequencing begin in U.S.

First archael genome sequenced

Yeast (*S. cerevisiae*) genome sequenced

HGP's mouse genetic mapping goal achieved

Bermuda principles for rapid and open data release established

1997

DOE forms Joint Genome Institute

NCHGR becomes NHGRI

E. coli genome sequenced

Genoscope (French National Genome Sequencing Center) founded

1998

Incorporation of 30,000 genes into human genome map

New five-year plan for the HGP in the U.S. published

RIKEN Genomic Sciences Center (Japan) established

Roundworm (*C. elegans*) genome sequenced

SNP initiative begins

GTGCT
GTCCT

Chinese National Human Genome Centers (in Beijing and Shanghai) established

1999

Full-scale human sequencing begins

Sequence of first human chromosome (chromosome 22) completed

2000

Draft version of human genome sequence completed

President Clinton and Prime Minister Blair support free access to genome information

Fruit fly (*D. melanogaster*) genome sequenced

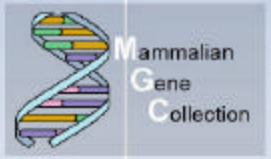
Mustard cress (*A. thaliana*) genome sequenced

Executive order bans genetic discrimination in U.S. federal workplace

2001

Draft version of human genome sequence published

10,000 full-length human cDNAs sequenced



2002

Draft version of mouse genome sequence completed and published

Draft version of rat genome sequence completed

Draft version of rice genome sequence completed and published

2003

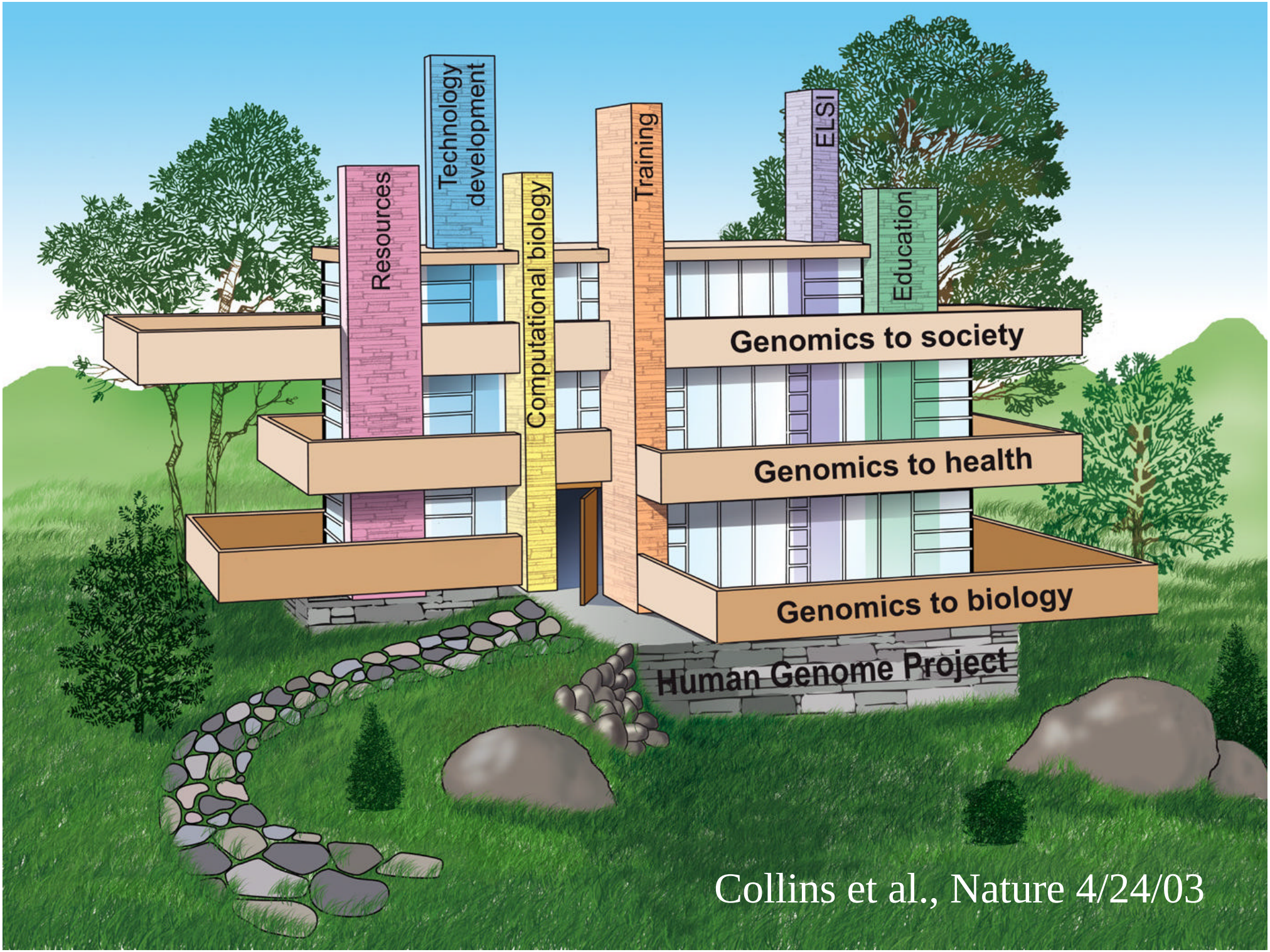
Finished version of human genome sequence completed

HGP ends with all goals achieved

to be continued..

All of the original goals of the Human Genome Project have been accomplished

What's next?



Collins et al., Nature 4/24/03

Genomics to Biology

- Define the structure of human variation
- Sequence lots of additional genomes
- Reduce the cost of sequencing a mammalian genome to $1000 or less
- Identify all functional elements of the genome
- Identify all the proteins of the cell, and their interactions
- Develop a computational model of the cell

Genomics to Health

- Identify the genetic and environmental risk factors for all common disease
- Develop “sentinel systems” for early detection of disease and molecular taxonomy of illness
- Develop and deploy high-throughput robotic screening of small molecules for academic researchers
- Catalyze development of large human cohorts for genotype-phenotype correlations
- Elucidate the role that genomics can play in reducing health disparities
- Utilize genomics to improve health in the developing world

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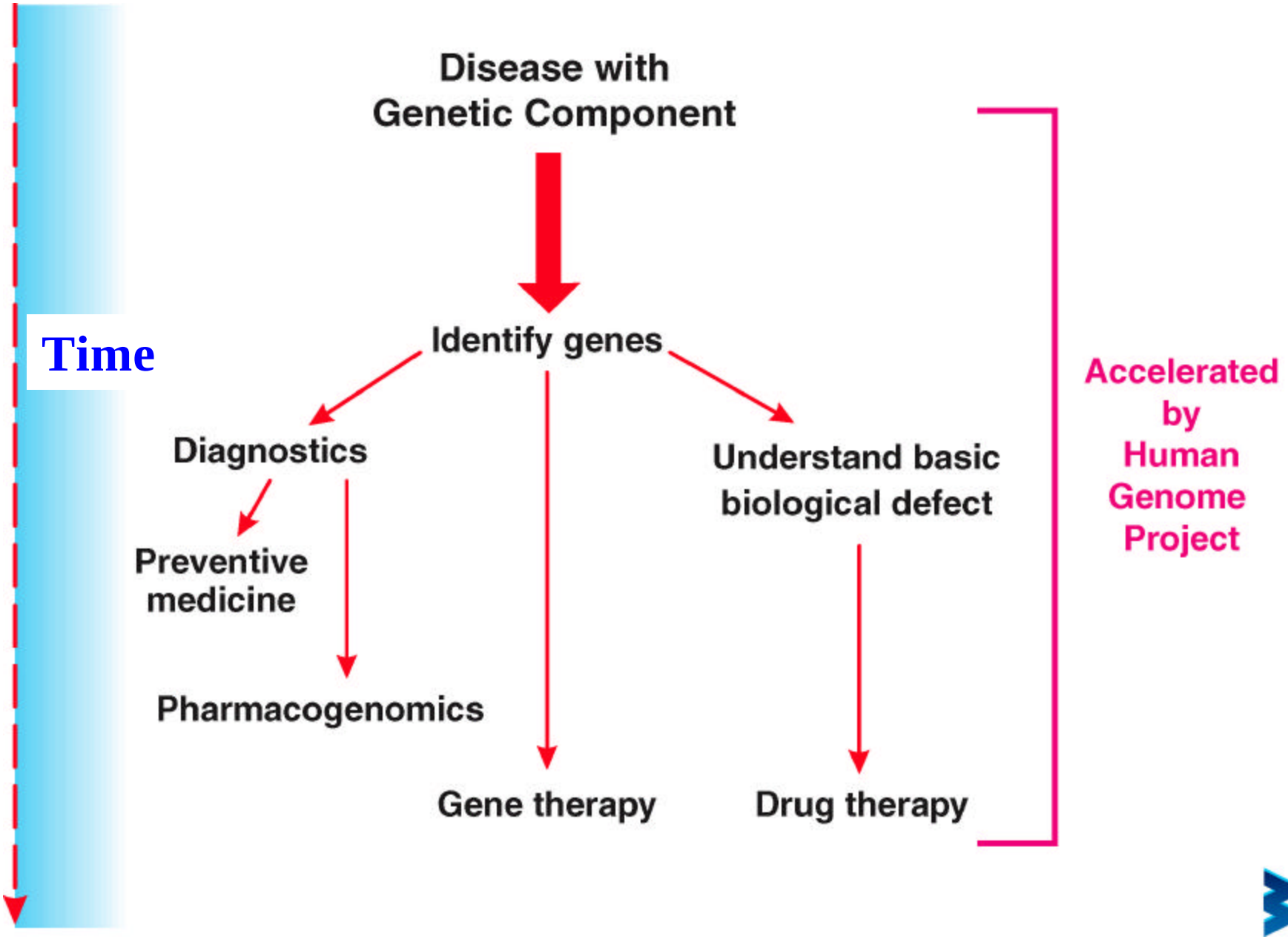
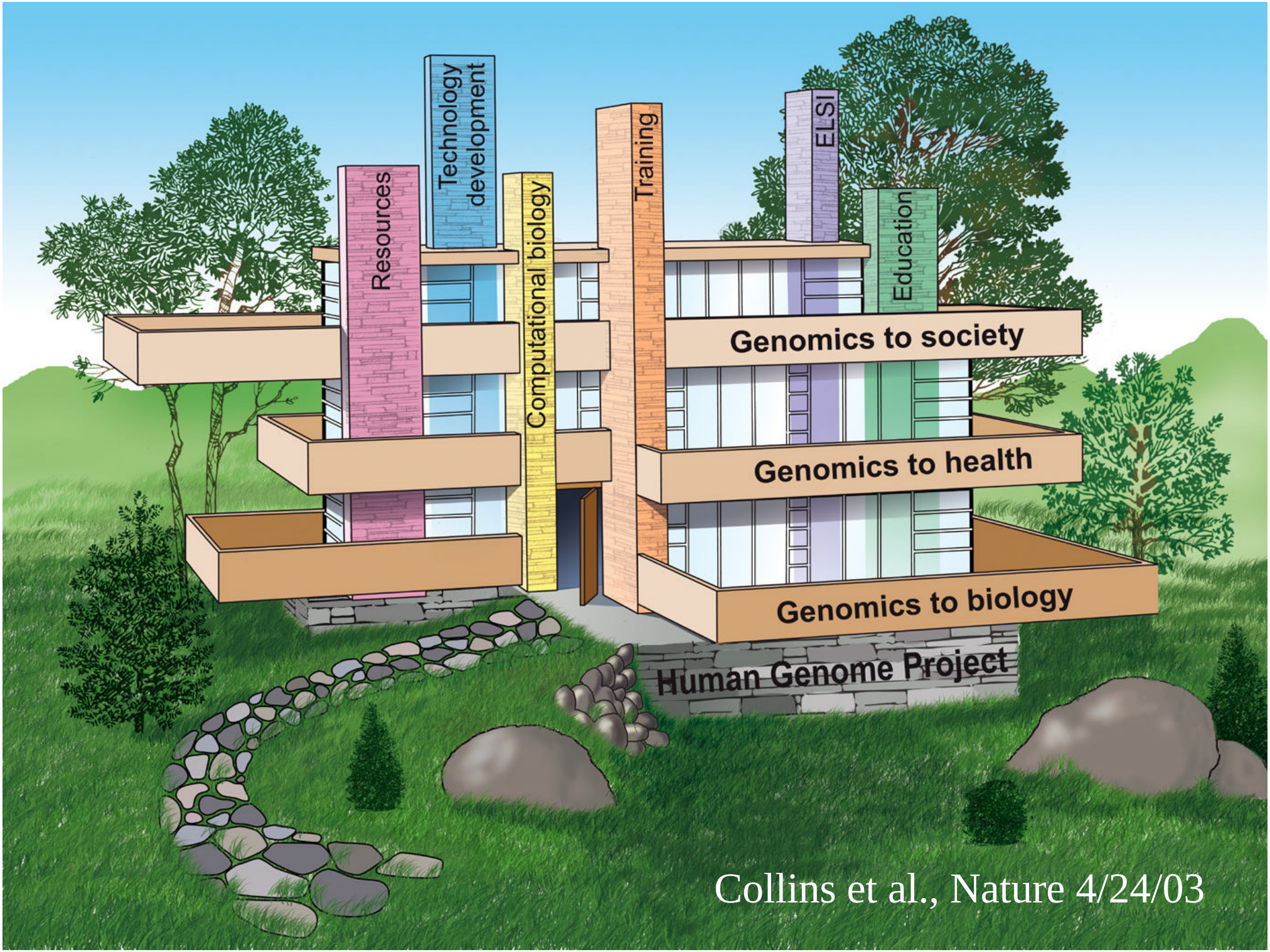
What's needed to identify the causes of common disease

- A catalog of human variation
- A map of how that variation is organized across chromosomes
- Improved technology for genotyping and DNA sequencing
- Advanced methods for collecting environmental exposure data
- Large numbers of well-characterized individuals, followed prospectively – including healthy people

If we do this right, the major contributing genes for diabetes, heart disease, cancer, mental illness, Alzheimer's and Parkinson's disease, asthma, and response to major drug classes will be identified within the next 5 – 10 years.


Disease with
Genetic Component
Time
Identify genes
Diagnostics
Understand basic
biological defect
Preventive
medicine
Pharmacogenomics
Gene therapy
Drug therapy
Accelerated
by
Human
Genome
Project



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Genomics to Society

- Enhance genetic privacy and protection against genetic discrimination
- Encourage appropriate patenting and licensing practices to benefit the public
- Understand the relationship of genomics, race, and ethnicity, and bring this to bear usefully on the often contentious dialog about race
- Assess the ramifications of advances in understanding genetic factors that influence behavior
- Define boundaries of the appropriate application of genomics in the non-medical arena

Possible Areas for Focus by SACGHS

- Genetic discrimination
  - Achieving a legislative solution for health insurance and the workplace
  - Developing options for life, disability, and long term care insurance
  - Need for exploration of potential discriminatory uses of genetics in adoption, education, the military…
- Genetic testing
  - Oversight to ensure clinical validity
  - Special concern: direct to consumer marketing

Genetic services on the internet?

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understand and manage a child's behavior before it gets out of c

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addictions. The Reward product line is then available to treat the
towards RDS.

Imagene is an at home genetic testing kit that is simple to use.
instructions.

1. Take Foam tipped applicator and rub the inside of left cheek 25 times. Repeat with second applicator.
2. Take foam tipped applicator and rub inside of right cheek 25 times.
3. Take applicator and place inside circle of the indicator card.
4. Press and hold for 1 minute.
5. Flip and reverse Applicator and repeat step 3 within the same circle of the indicator card.
6. The pink circle turns white when the test is complete

"Are you concerned about your children's future? Does your child have the genetic trait that leads to disruptive and addictive personalities? DNA testing can help you to understand and manage a child's behavior before it gets out of control."

Possible Areas for Focus by SACGHS (cont.)

- Minimizing roadblocks to genetic research while protecting human subjects
- Optimizing delivery of genetic services in the future
  - Workforce issues
  - Access issues
  - Cross-cultural issues
  - Reimbursement issues

Plans fail for lack of counsel,
but with many advisers they succeed.

Proverbs 14:22