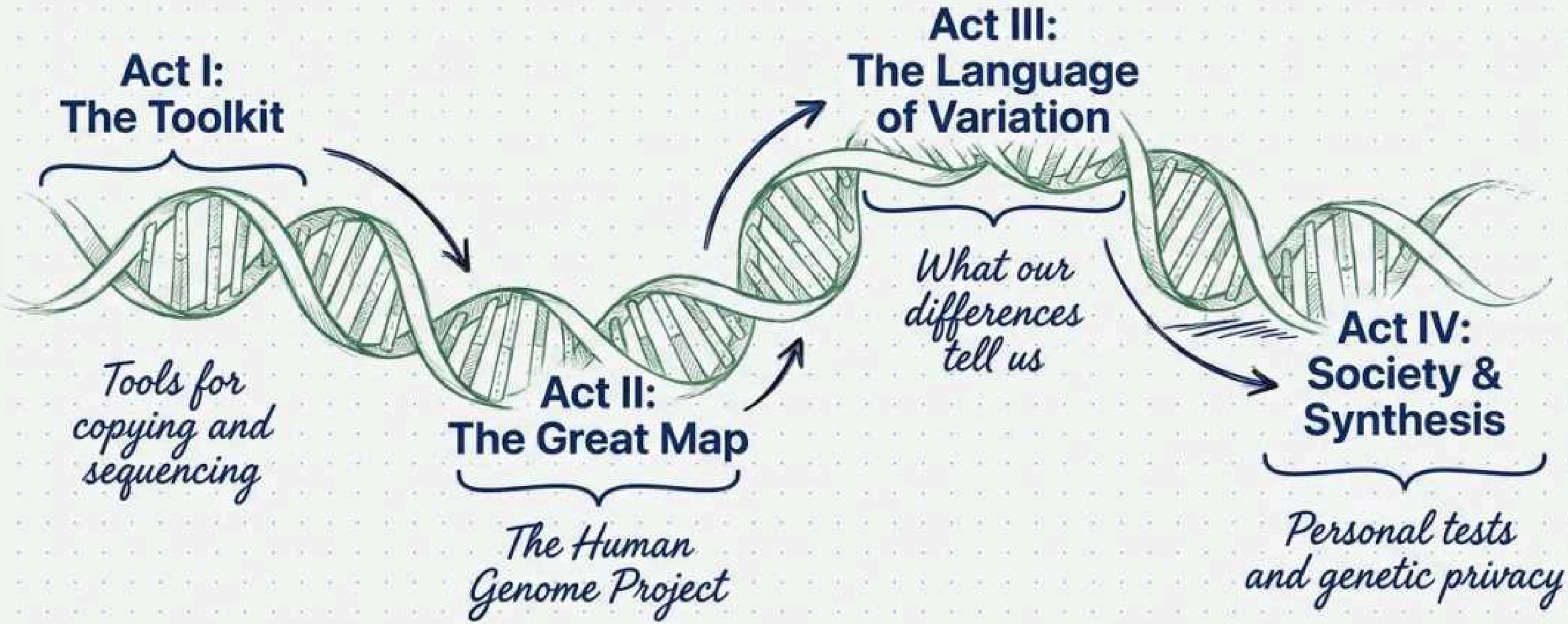
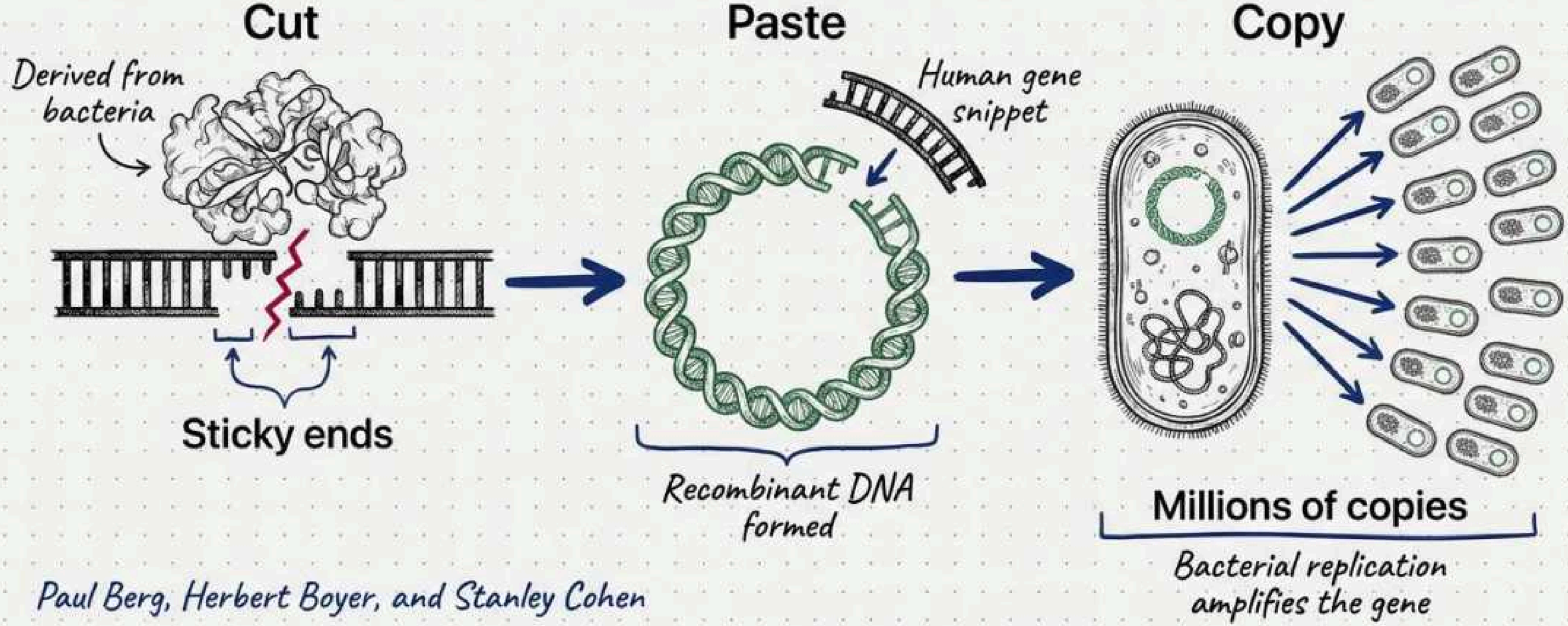
Reading the Genome: From Tools to Consequences

¶ 5.1



1970s: The Dawn of Genetic Engineering

The Molecular Scissors



Paul Berg, Herbert Boyer, and Stanley Cohen

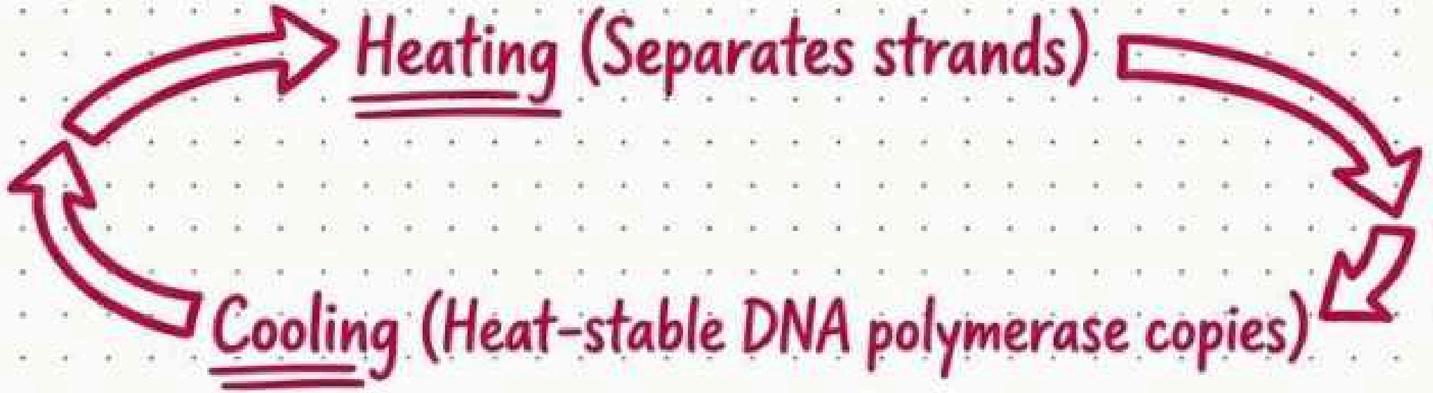
1983: Polymerase Chain Reaction (PCR)

¶ 5.3

$$N = N_0 \times 2^n$$

n ← cycles

N_0 ← 1 starting molecule

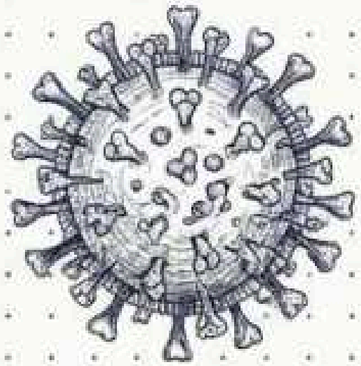


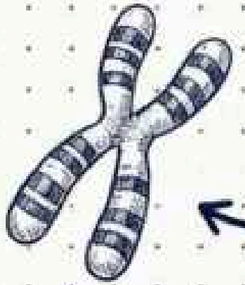
2^{30} cycles $\approx$ 1,000,000,000 (One Billion) copies

Kary Mullis (1993 Nobel Prize in Chemistry).

The Impact of Amplification

¶ 5.4



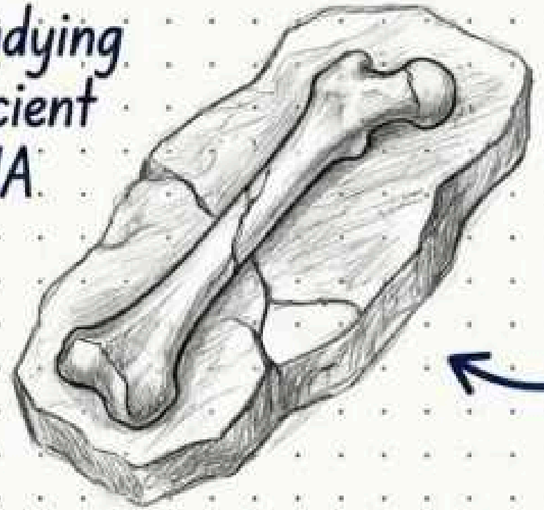


Diagnosing inherited diseases

Medicine

Detecting viruses from tiny samples

PCR

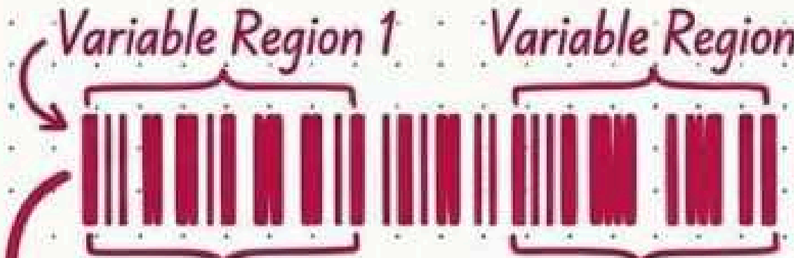


Studying Ancient DNA

History / Anthropology

The Law: DNA Fingerprinting

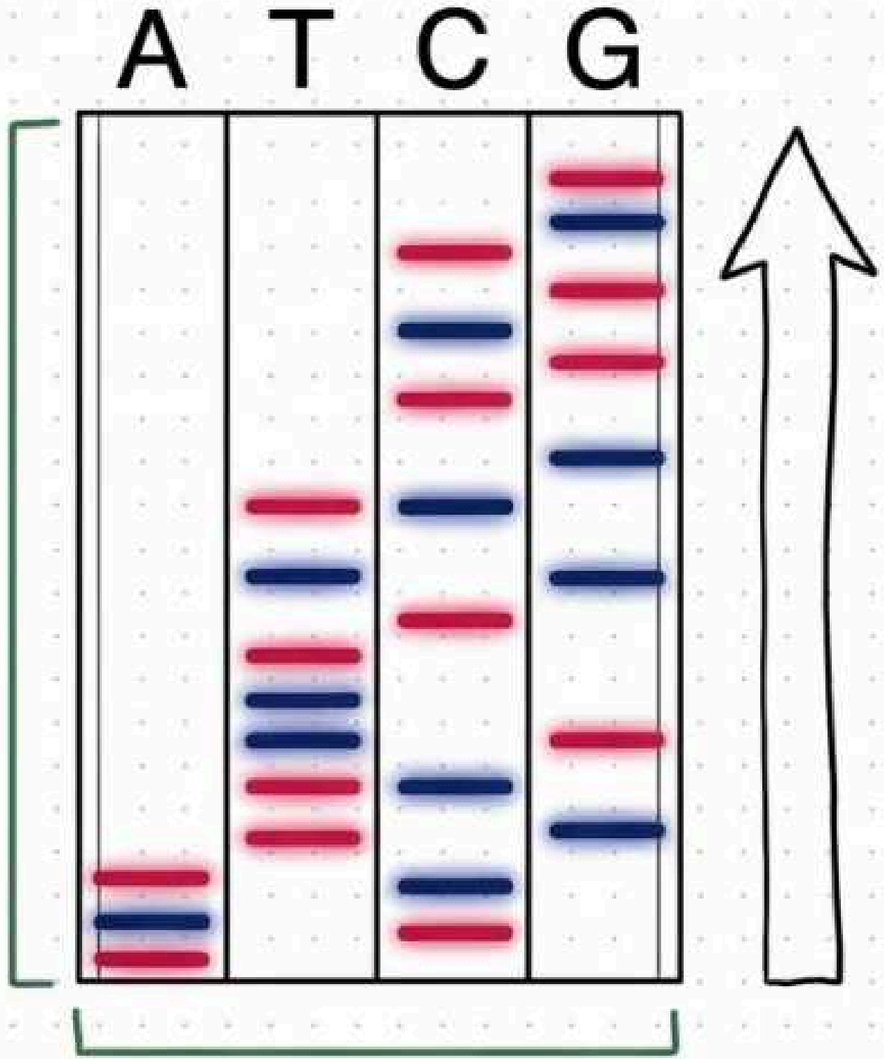
1984: Alec Jeffreys



- Solving Crimes
- Freeing the Wrongly Convicted
- Settling Parentage

1977: Reading the Letters (Sanger Sequencing)

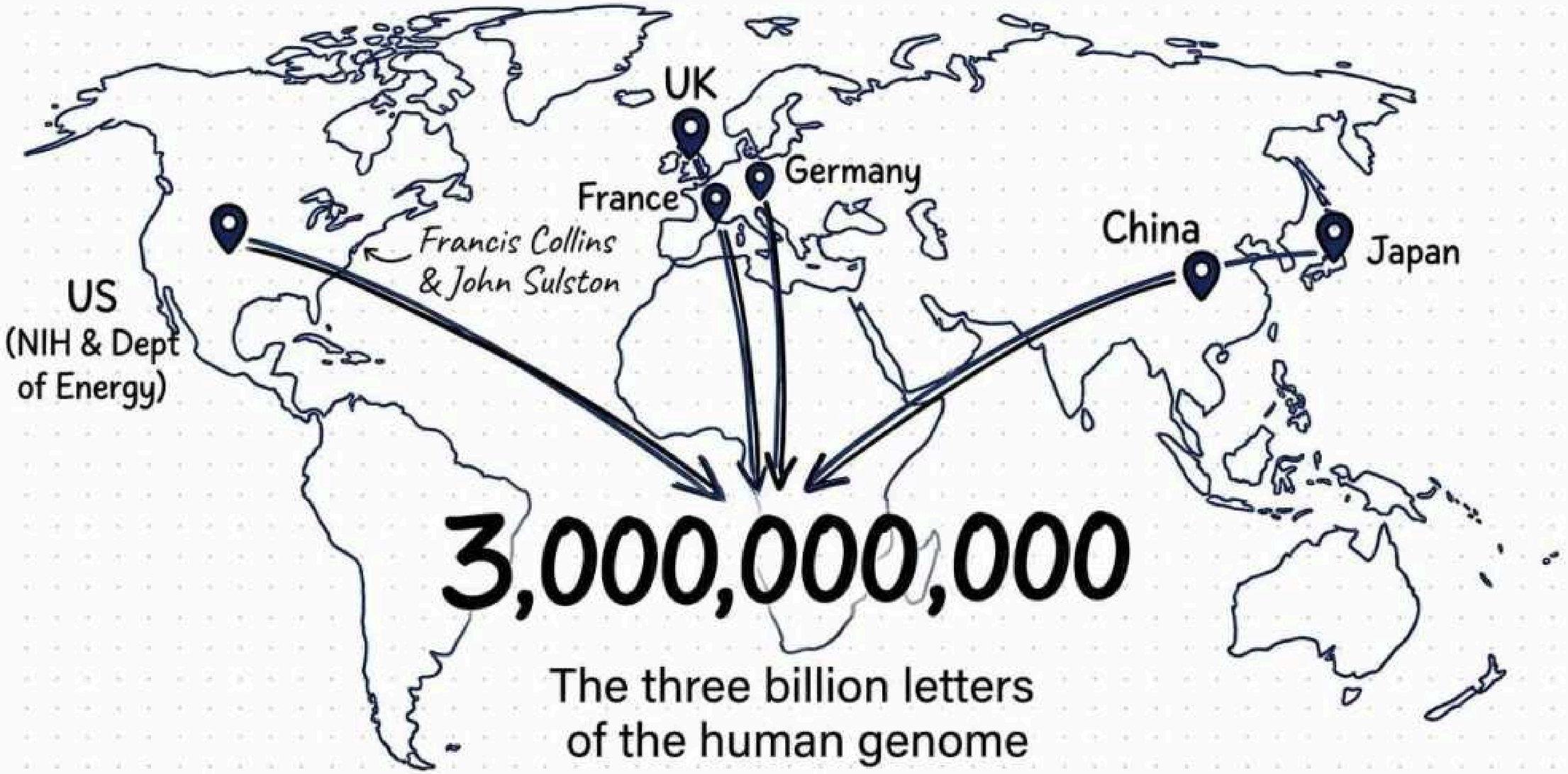
Frederick Sanger
(1980 Nobel Prize).



Reading the sequence of letters step-by-step by length

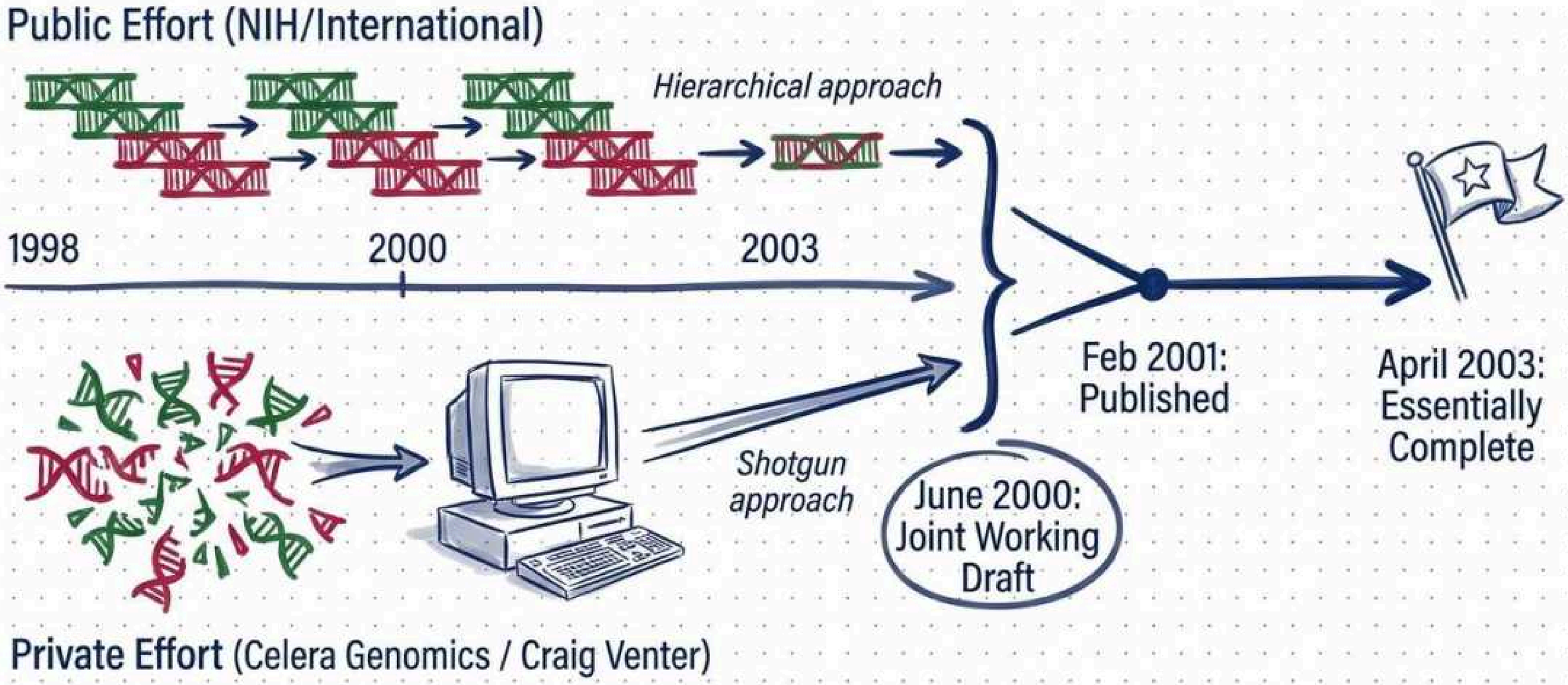
The gold standard for roughly thirty years.

1990: The Human Genome Project Begins



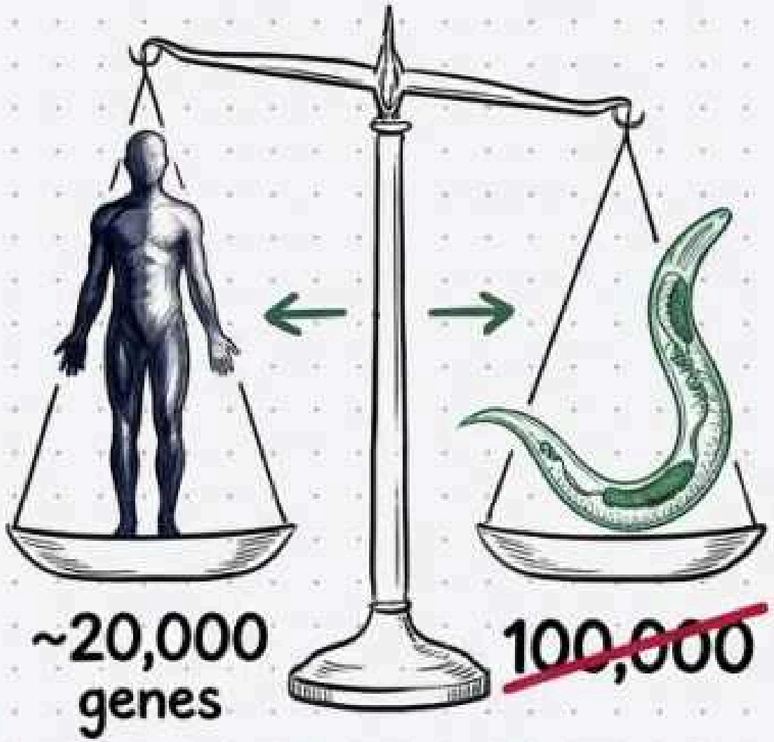
The Genome Race (1998 – 2003)

¶ 5.7

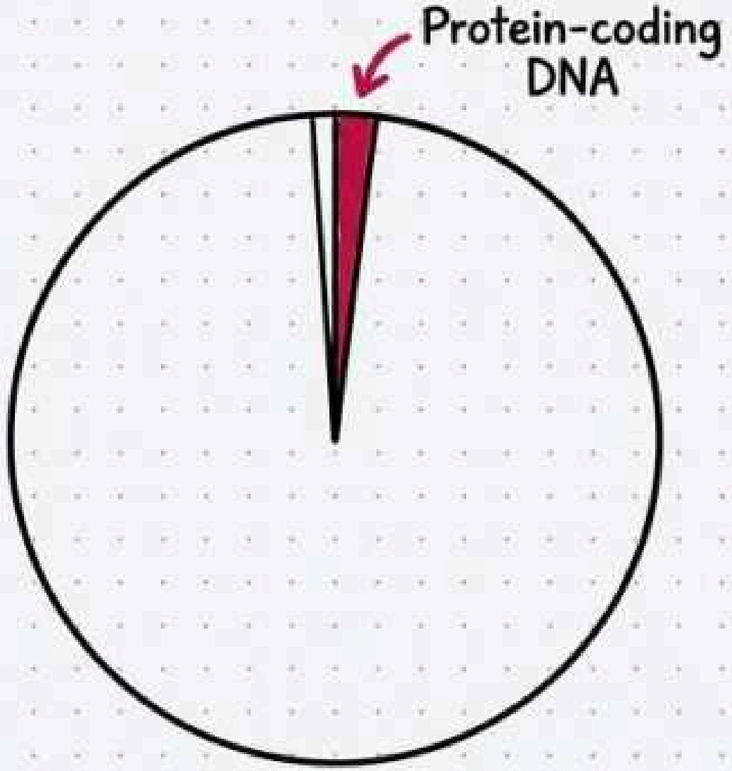


A Humbling Result

The Gene Count



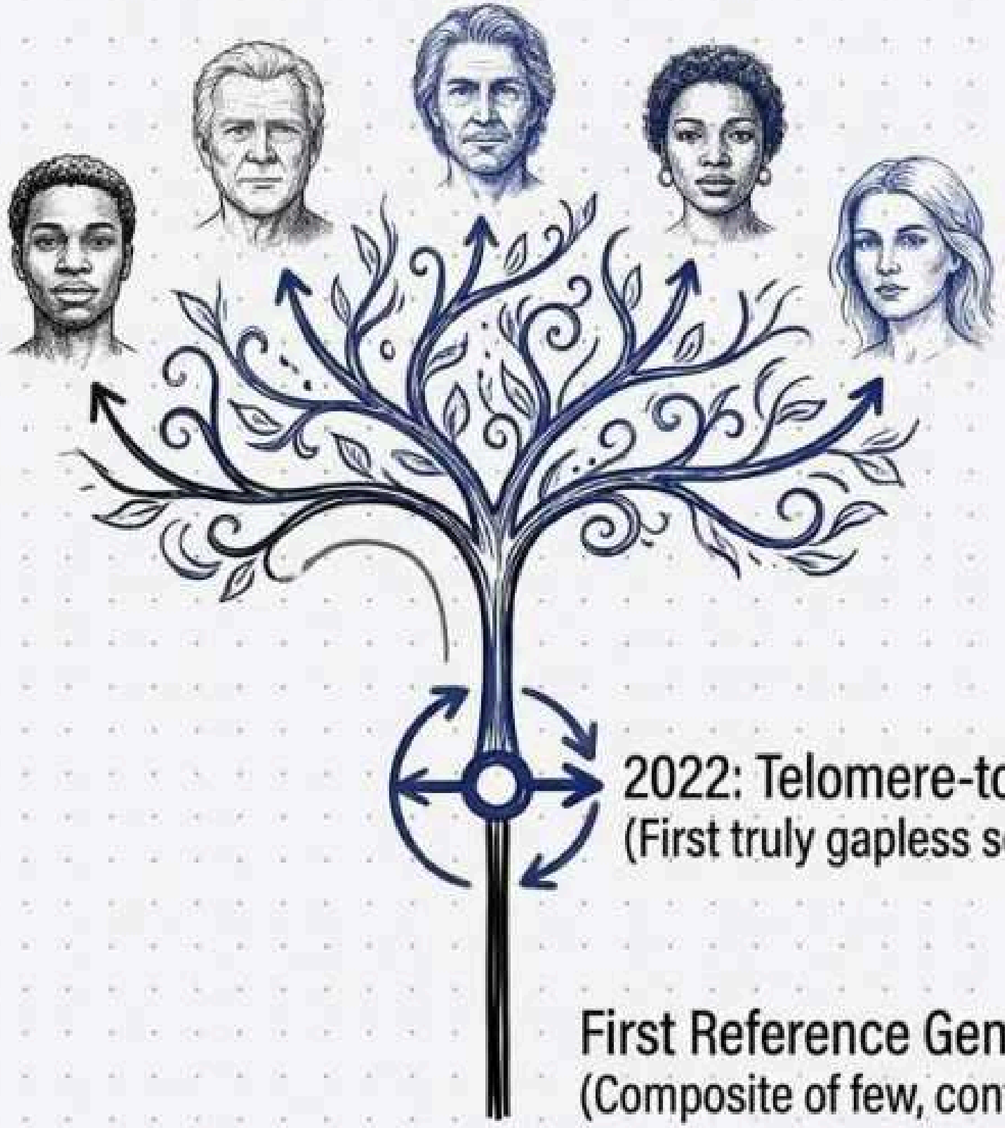
The Coding Slice



The Similarity



From Reference to Pangenome

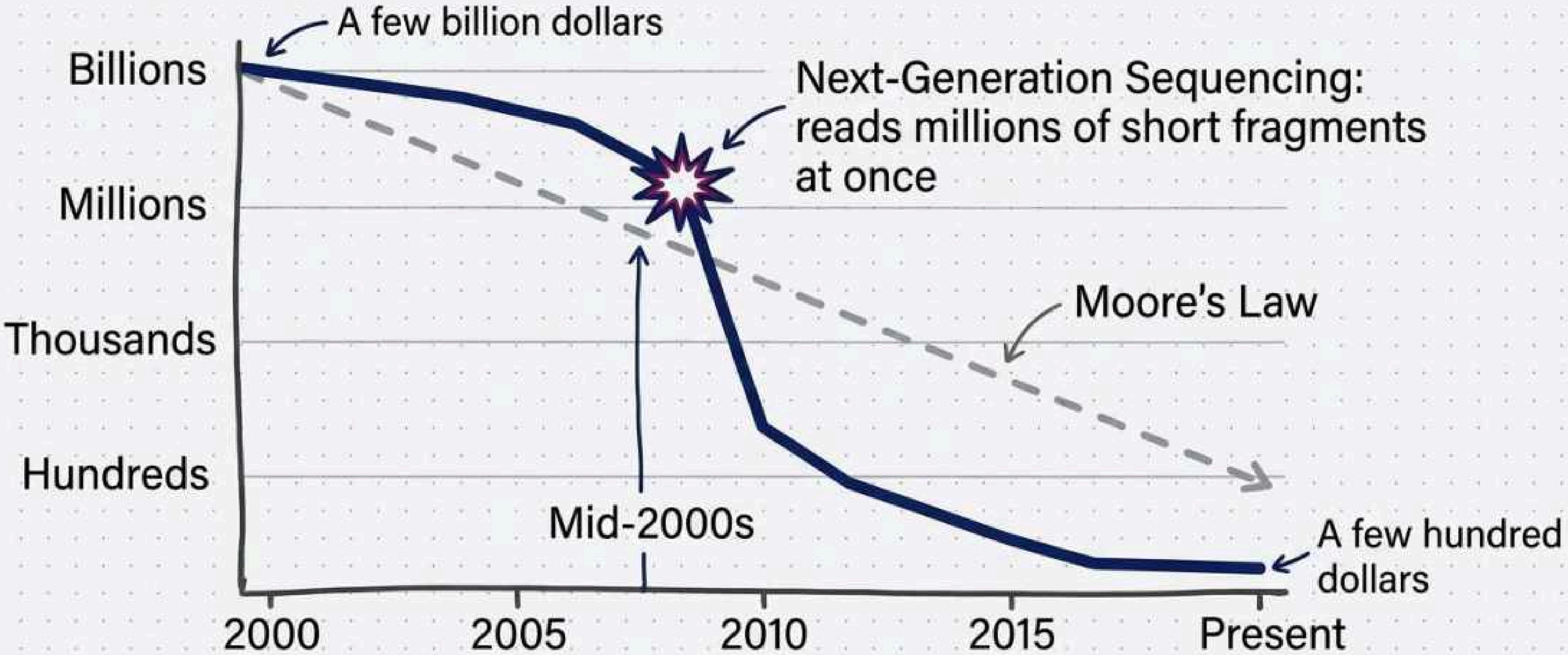


The Pangenome

2022: Telomere-to-Telomere Consortium
(First truly gapless sequence, 3.1 Billion letters)

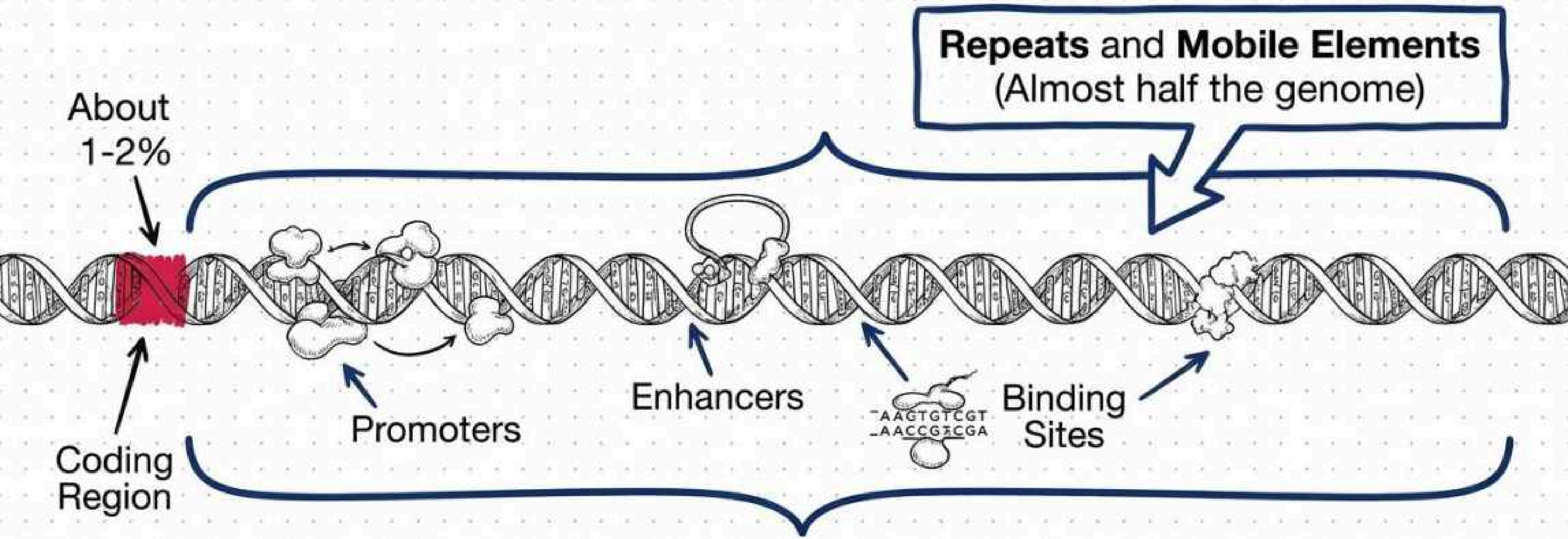
First Reference Genome
(Composite of few, contained gaps)

The Collapse of Sequencing Costs



Long-read technologies now complement short reads.

2003: The ENCODE Project & The Noncoding Genome



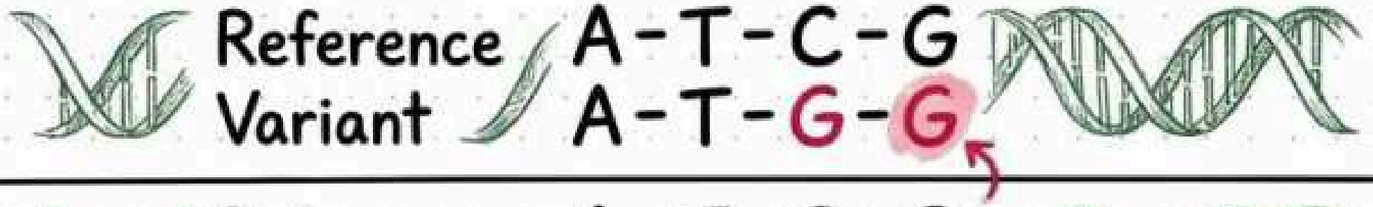
Biochemical activity confirmed, but scientists still debate how much is truly functional.

The Mechanics of Variation

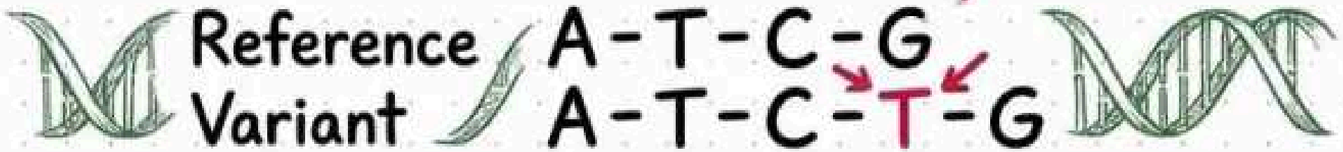
¶ 5.12

Visual Sequence Alignment Glossary

SNP
(Single Nucleotide Polymorphism)



Insertion



Deletion

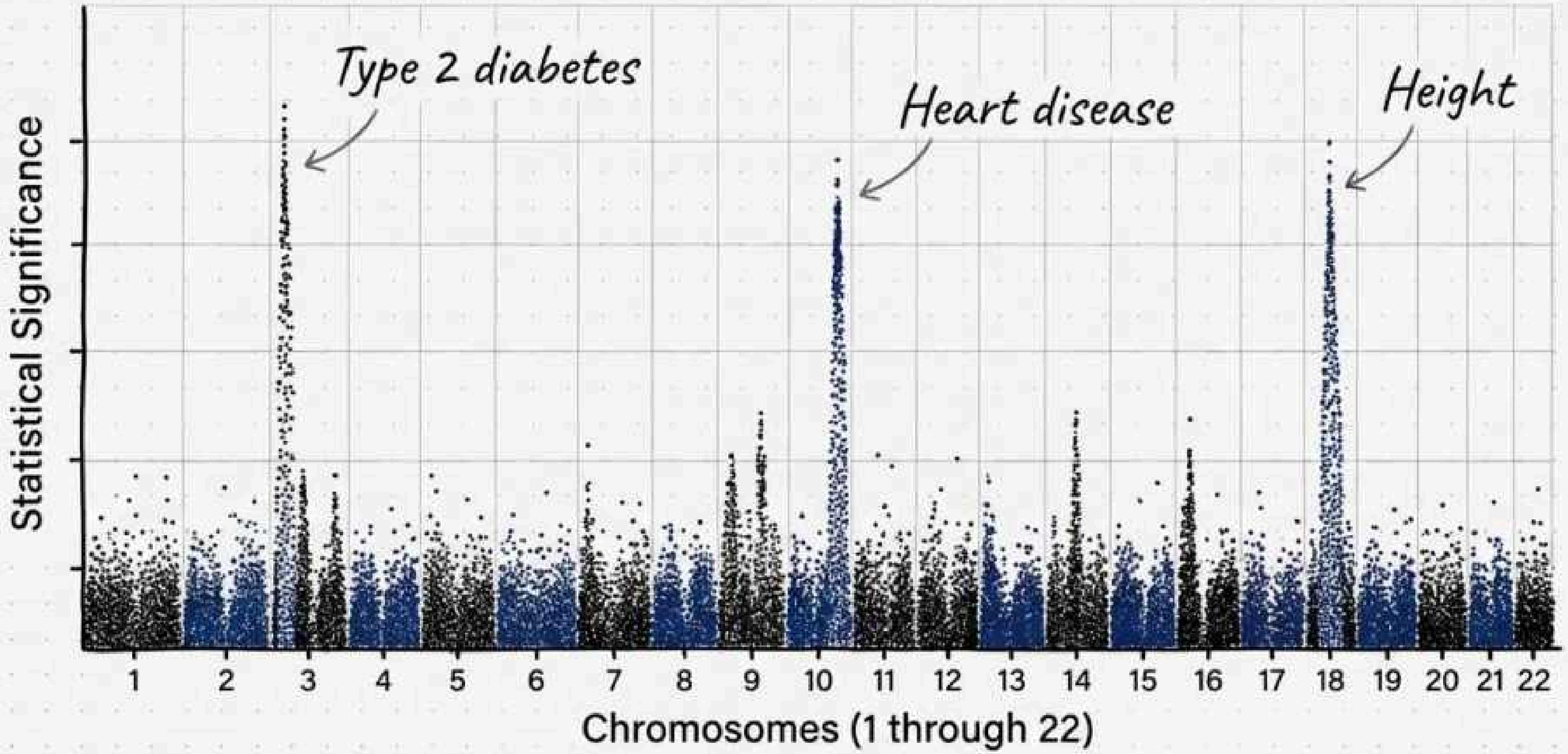


CNV
(Copy Number Variant)



Typical people differ at roughly 4 to 5 million places across the genome.

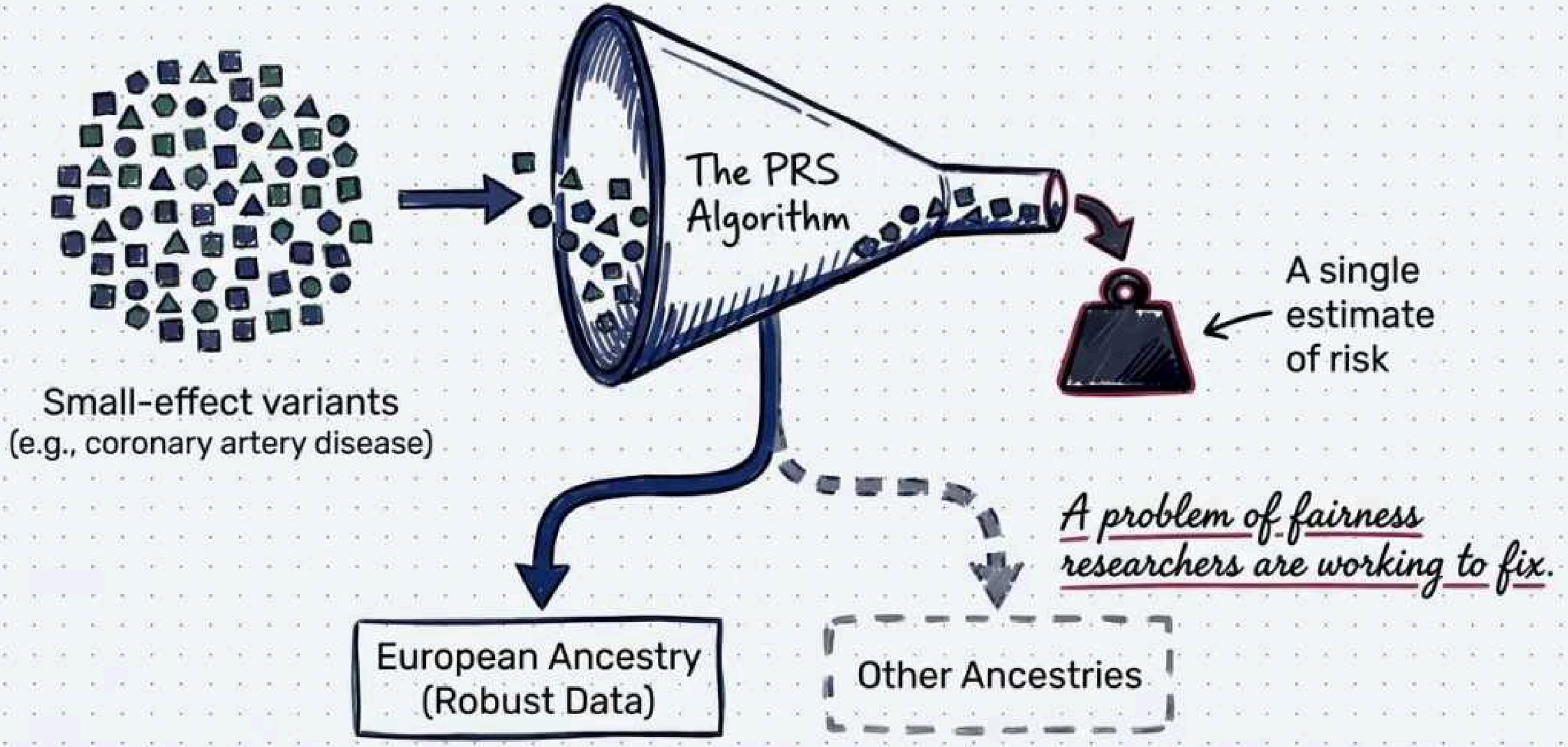
Genome-Wide Association Studies (GWAS)



CAUTION: Most variants have a TINY effect. No single variant predicts your risk.

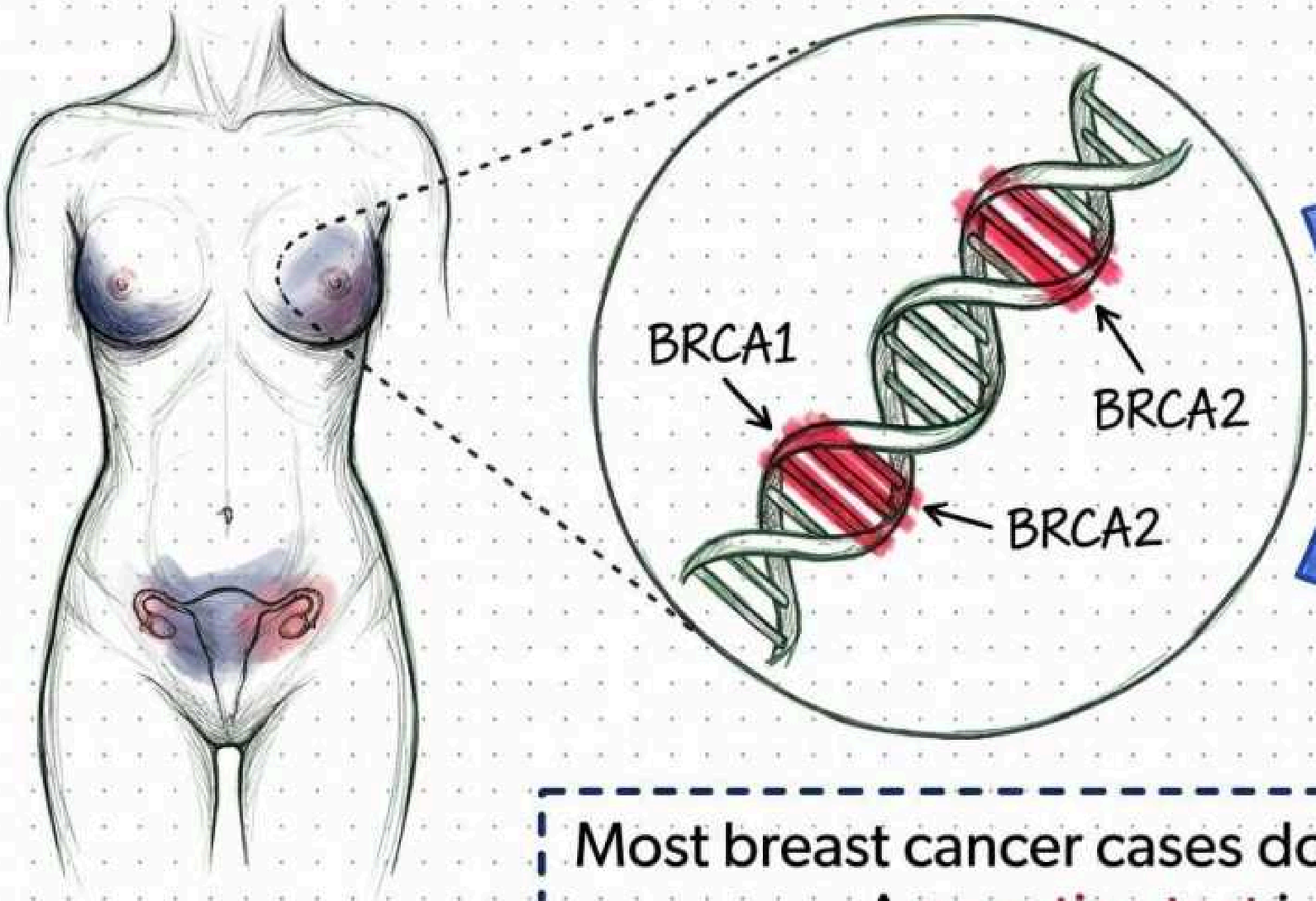
Polygenic Risk Scores (PRS)

¶ 5.14



Monogenic Risk: Single Genes, Large Effects

¶ 5.15



Closer Screening

↓

Angelina Jolie's public decision in 2013

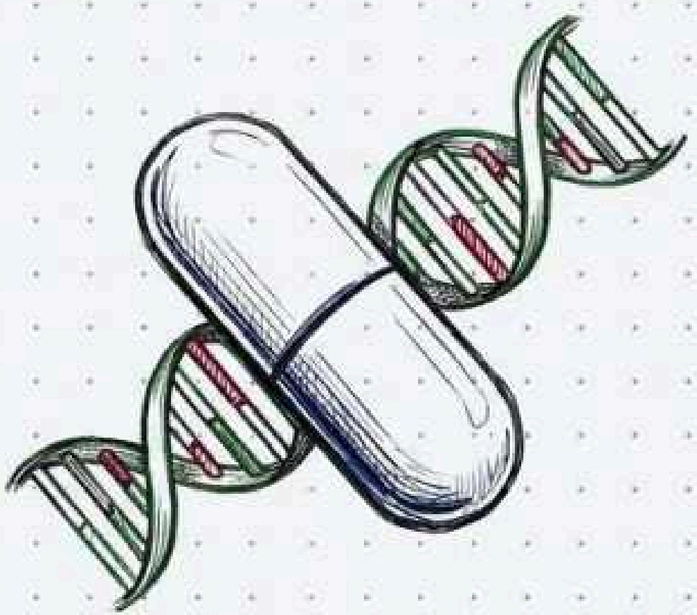
↓

Preventive Surgery

Most breast cancer cases do not involve these genes.
A negative test is no guarantee.

Precision Medicine in Practice

Pharmacogenomics



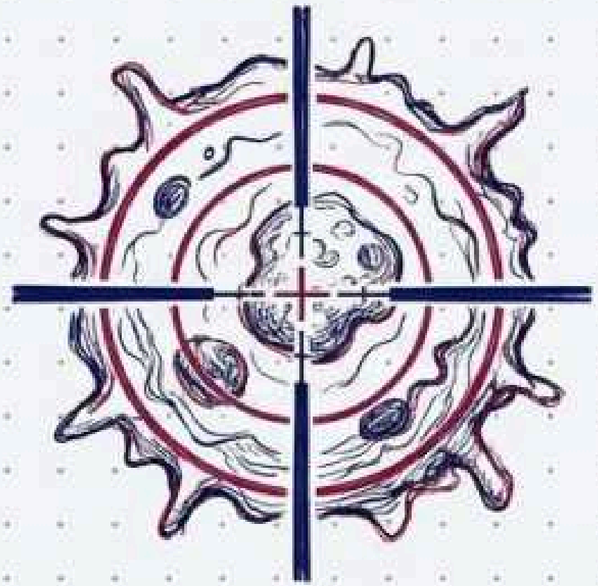
Using genes to guide drug choice and dosage based on breakdown speed.

Newborn Screening



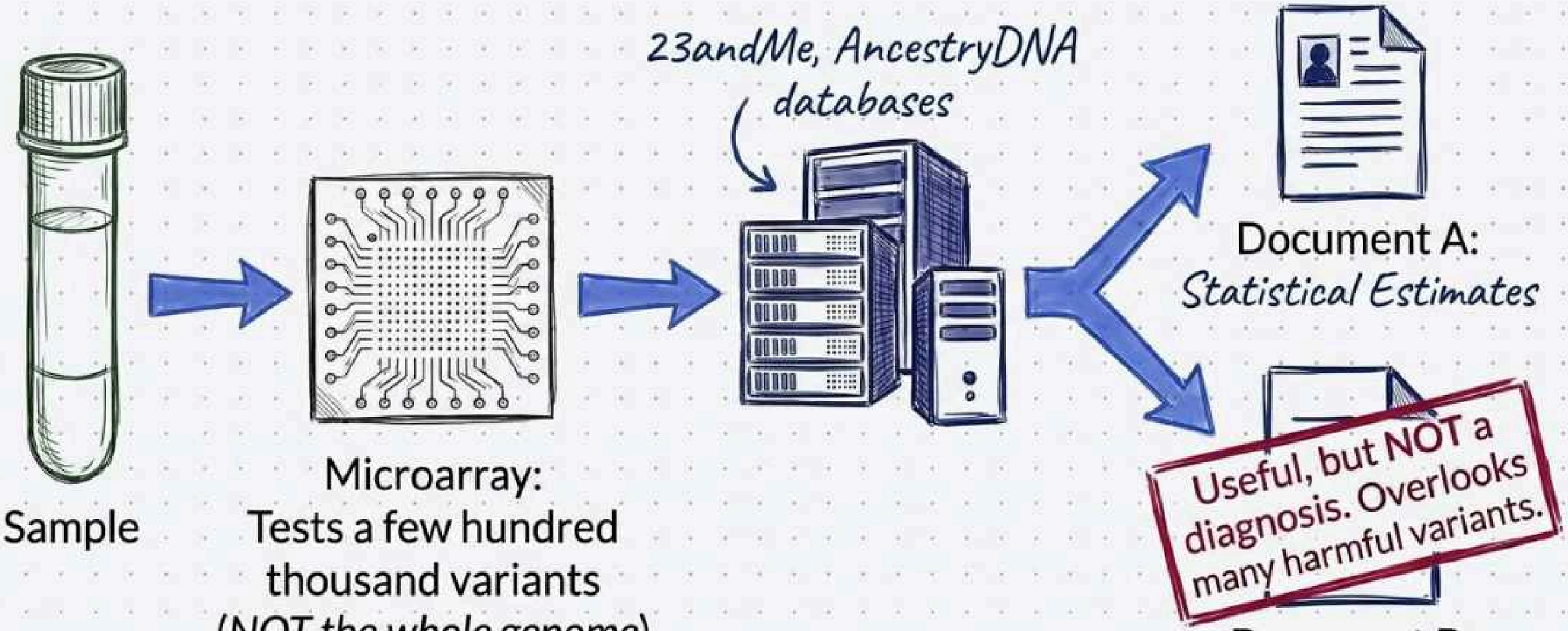
Catching treatable conditions early.

Cancer Therapeutics



Sequencing a tumor to reveal driver mutations and choose targeted therapies.

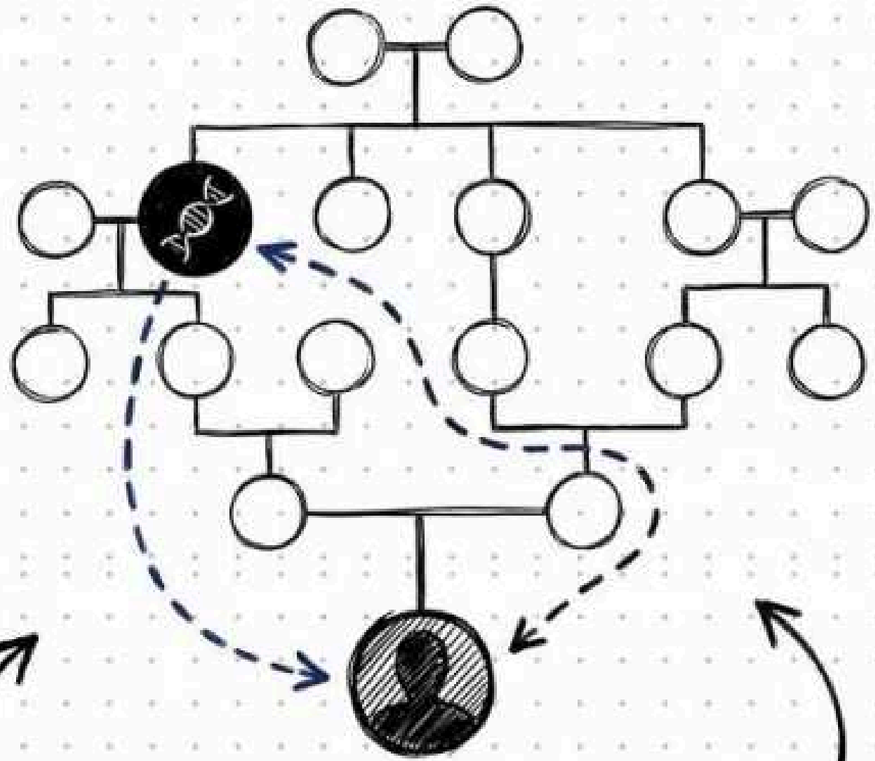
The Consumer Genetics Boom



The Stakes of Genetic Privacy

¶ 5.18

Law Enforcement



Your DNA reveals relatives.
(e.g., 2018 Golden State Killer arrest via consumer database).

The Law

GINA (Genetic Information Nondiscrimination Act of 2008)



1

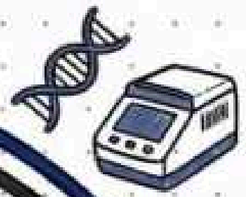
Protected:
Health Insurers, Employers

2

Unprotected:
Life Insurance, Long-term Care Insurance

Synthesis: The Power and the Probability

1. The Tools
Recombinant DNA, PCR, Sequencing.

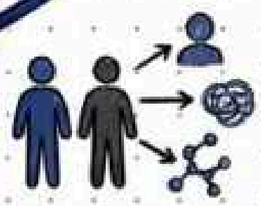


2. The Map
HGP delivers full draft (early 2000s).





3. The Insight
We are nearly identical; non-coding DNA rules; traits depend on many small effects.



4. The Responsibility
Genetic info is powerful but probabilistic. Needs protection.





Reading the genome gave us the map. Navigating it requires careful ethical stewardship.

Applying the Knowledge: Assessing Genetic Risk

	Type 2 Diabetes (Polygenic)	BRCA1 (Monogenic)
Variants Involved	Thousands of tiny variants	A single, specific gene mutation
Effect Size	Each variant has a tiny effect (Risk Score)	Mutation carries massive deterministic weight
Predictability / Certainty	Probabilistic, heavily influenced by outside factors	High lifetime chance, though still no absolute guarantee
Real-World Meaning	"Slightly higher than average" risk; focus on lifestyle	Actionable clinical risk; consider preventive screening/surgery

What does your result actually mean?