

Sociogenomics

ACADEMIC YEAR 2021/2022.

History of genetics

Nicola Barban



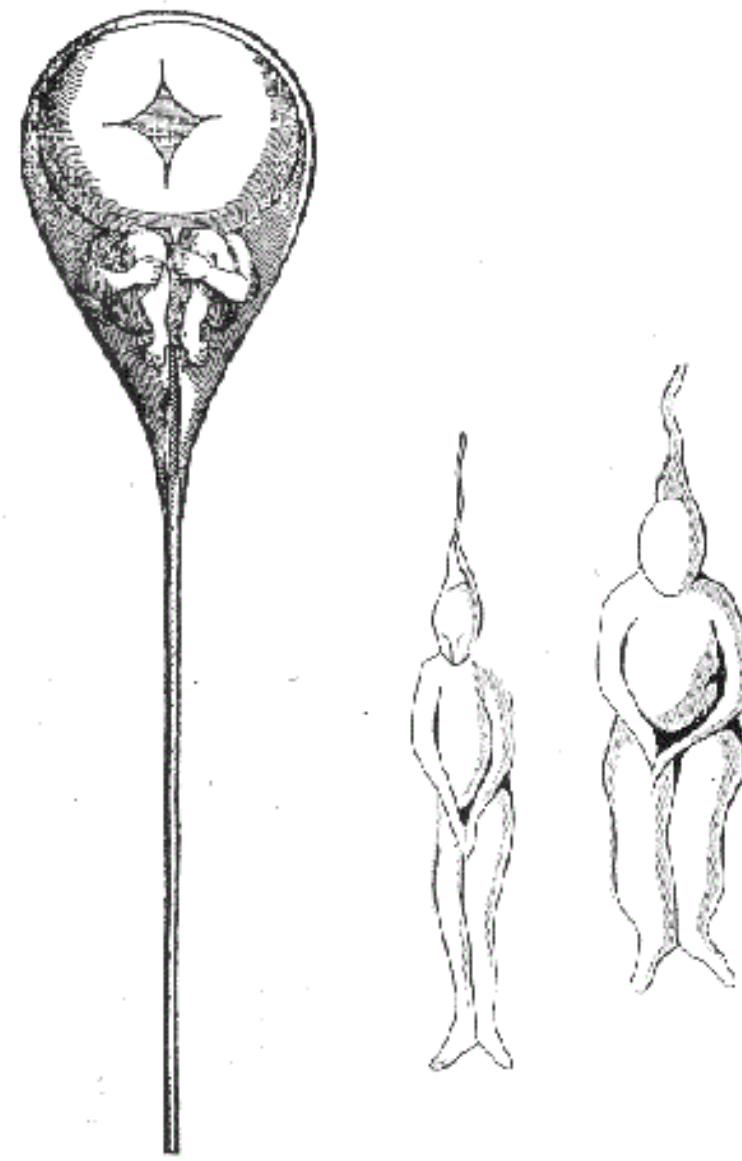
**Where do similarities and differences
between living organisms come from?**

Genetics in ancient times

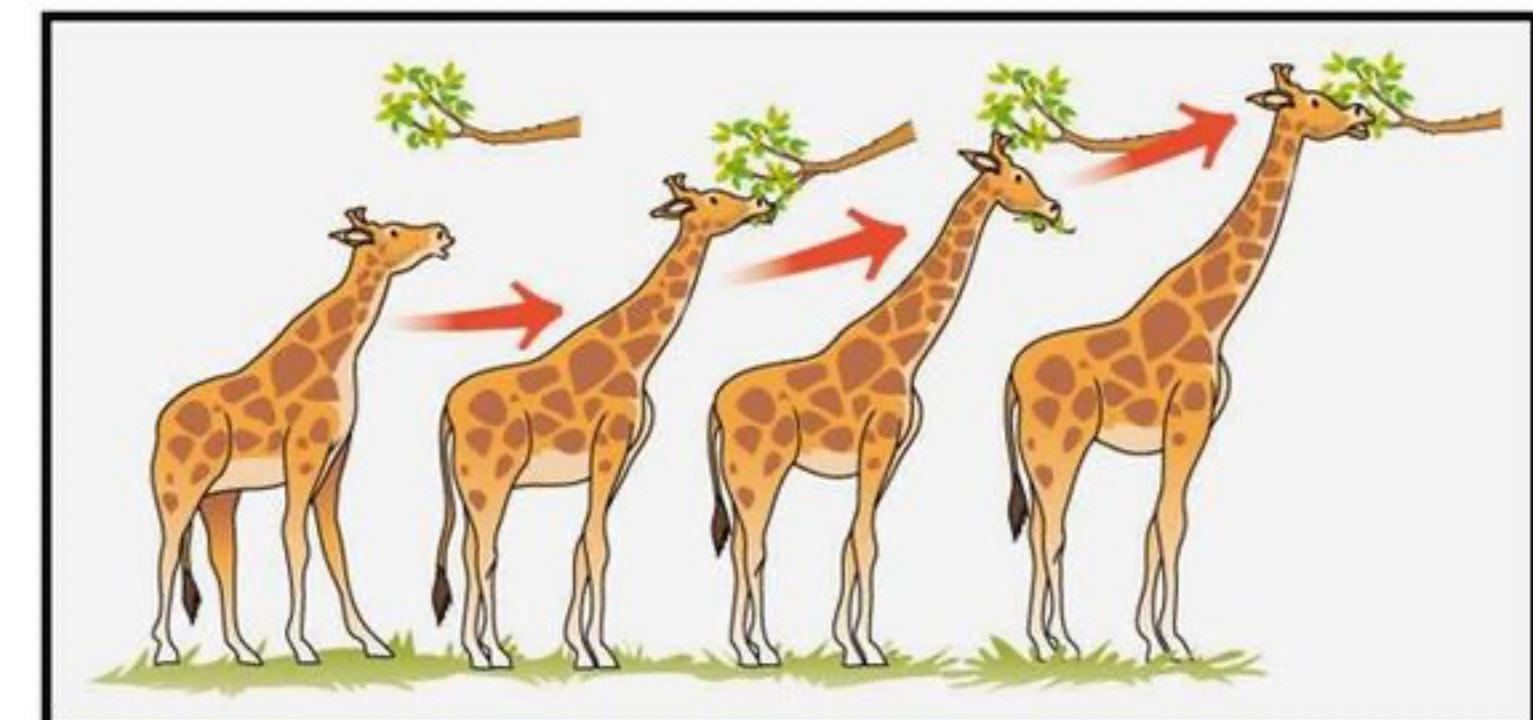
- Since the dawn of civilization, humankind has recognized the influence of heredity and applied its principles to the improvement of cultivated crops and domestic animals.
- Hippocrates (c. 460–c. 375 BCE), believed in the inheritance of acquired characteristics, and postulated that all organs of the body of **a parent gave off invisible “seeds,” which were like miniaturized building components and were transmitted during sexual intercourse**, reassembling themselves in the mother’s womb to form a baby.
- Aristotle (384–322 BCE) emphasized the importance of blood in heredity. He believed that the **male’s semen was purified blood and that a woman’s menstrual blood was her equivalent of semen. These male and female contributions united in the womb to produce a baby.** The blood contained some type of hereditary essences, but he believed that the baby would develop under the influence of these essences, rather than being built from the essences themselves.

Genetics during 17-18th century

During the 1600s, Dutch microscopist [Anton van Leeuwenhoek](#) (1632-1723) discovered "animalcules" in the sperm of humans and other animals. **Some scientists speculated they saw a "little man" (homunculus) inside each sperm.**



Jean-Baptiste Lamarck (1744-1829) invoked the idea of “the inheritance of acquired characters,” not as an explanation for heredity but as a model for [evolution](#). **He lived at a time when the fixity of species was taken for granted**, yet he maintained that this fixity was only found in a constant environment.

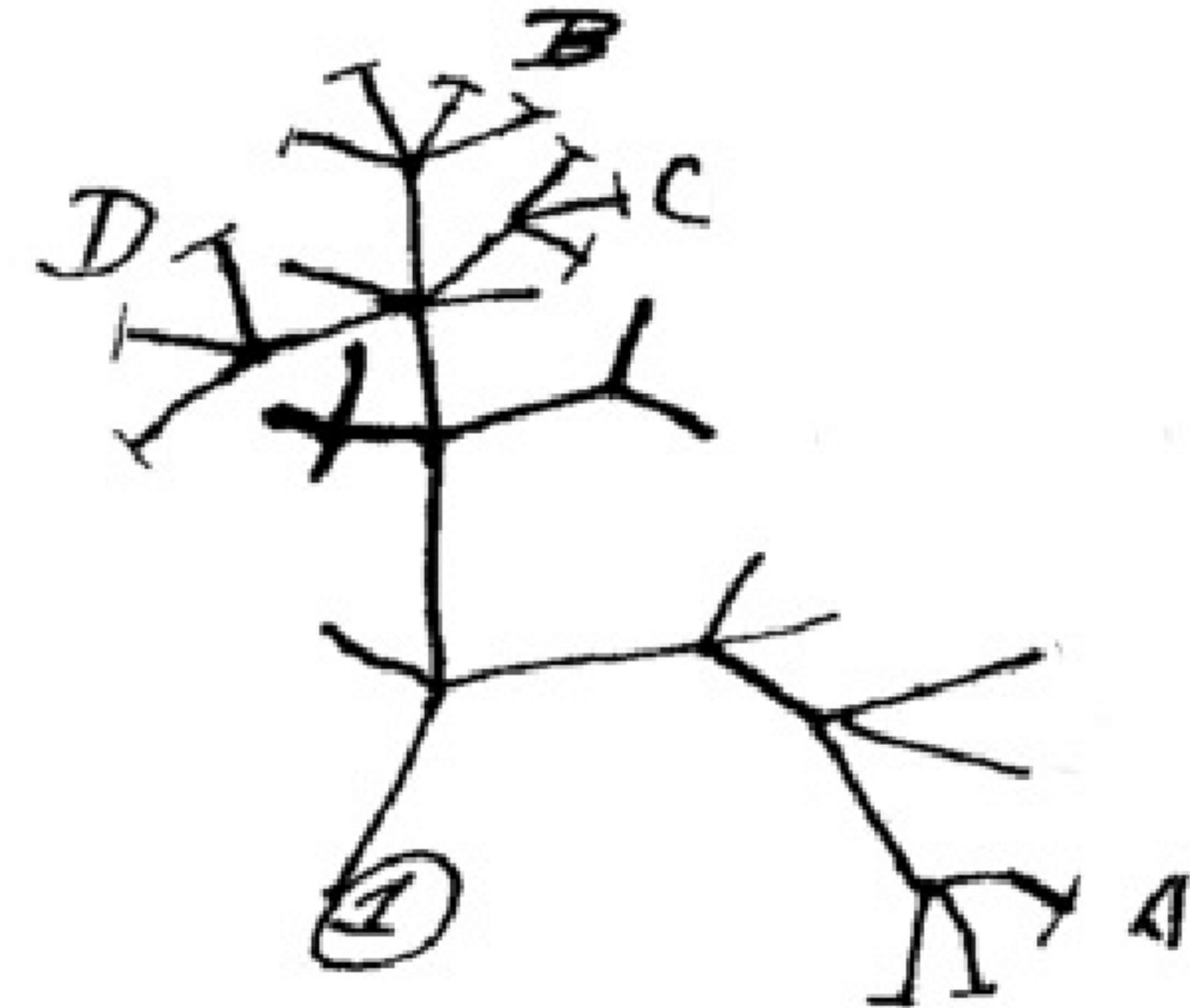


1859 Darwin publishes “On the origin of Species”

Theory of evolution: all species arose through the natural selection of small, inherited variations that increase the individual's ability to compete, survive, and reproduce.

Darwin's observations during his circumnavigation of the globe aboard the HMS *Beagle* (1831–36) provided evidence for natural selection and his suggestion that humans and animals shared a common ancestry.

I think

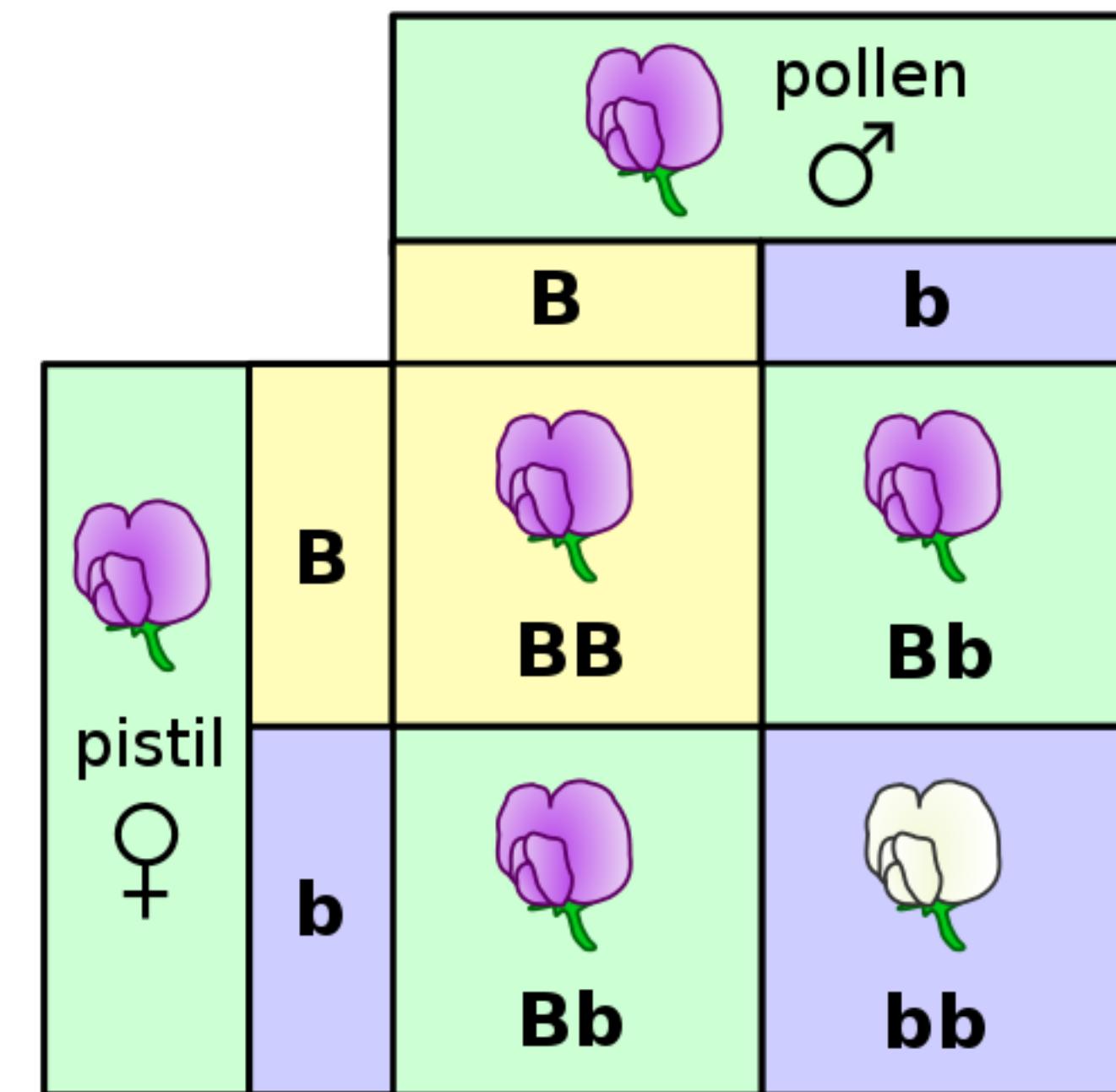


Mendel's laws of inheritance

Published in 1866, but largely ignored until early 1900

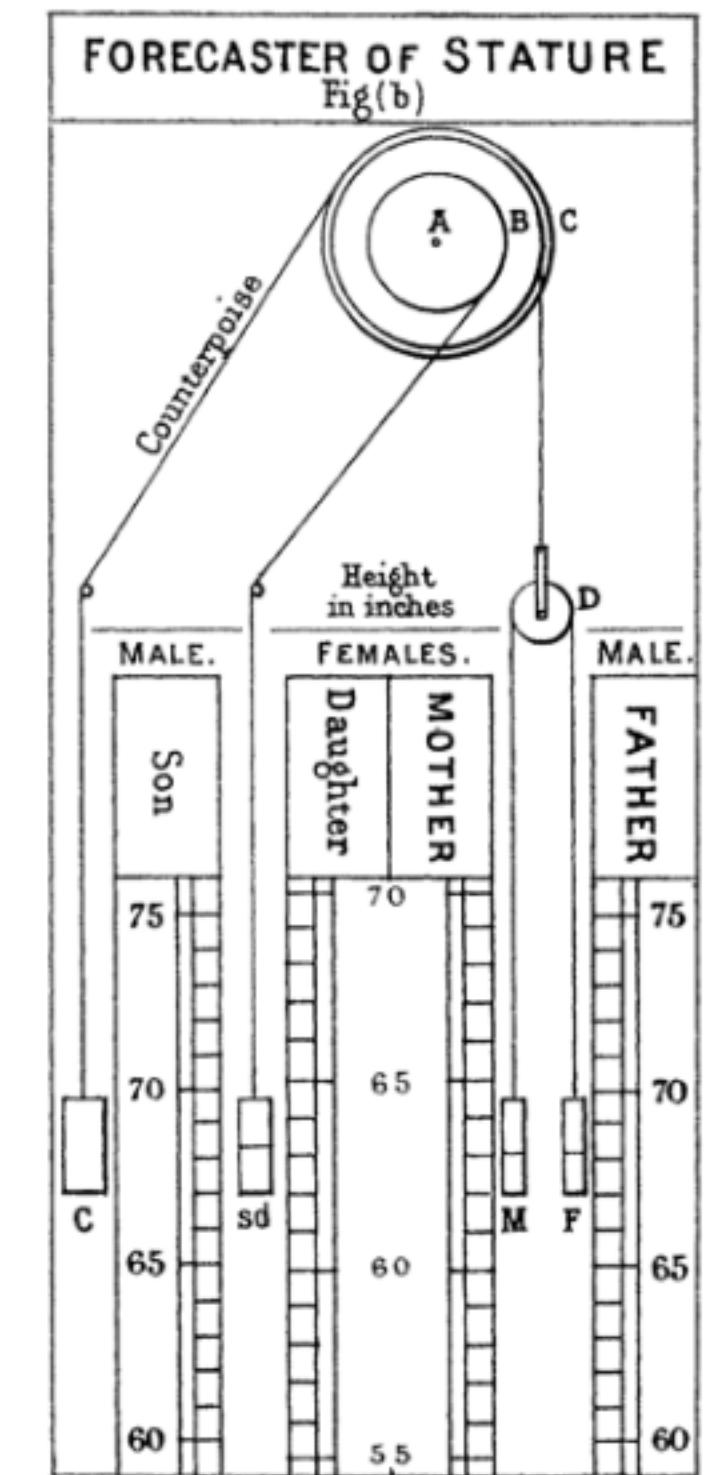
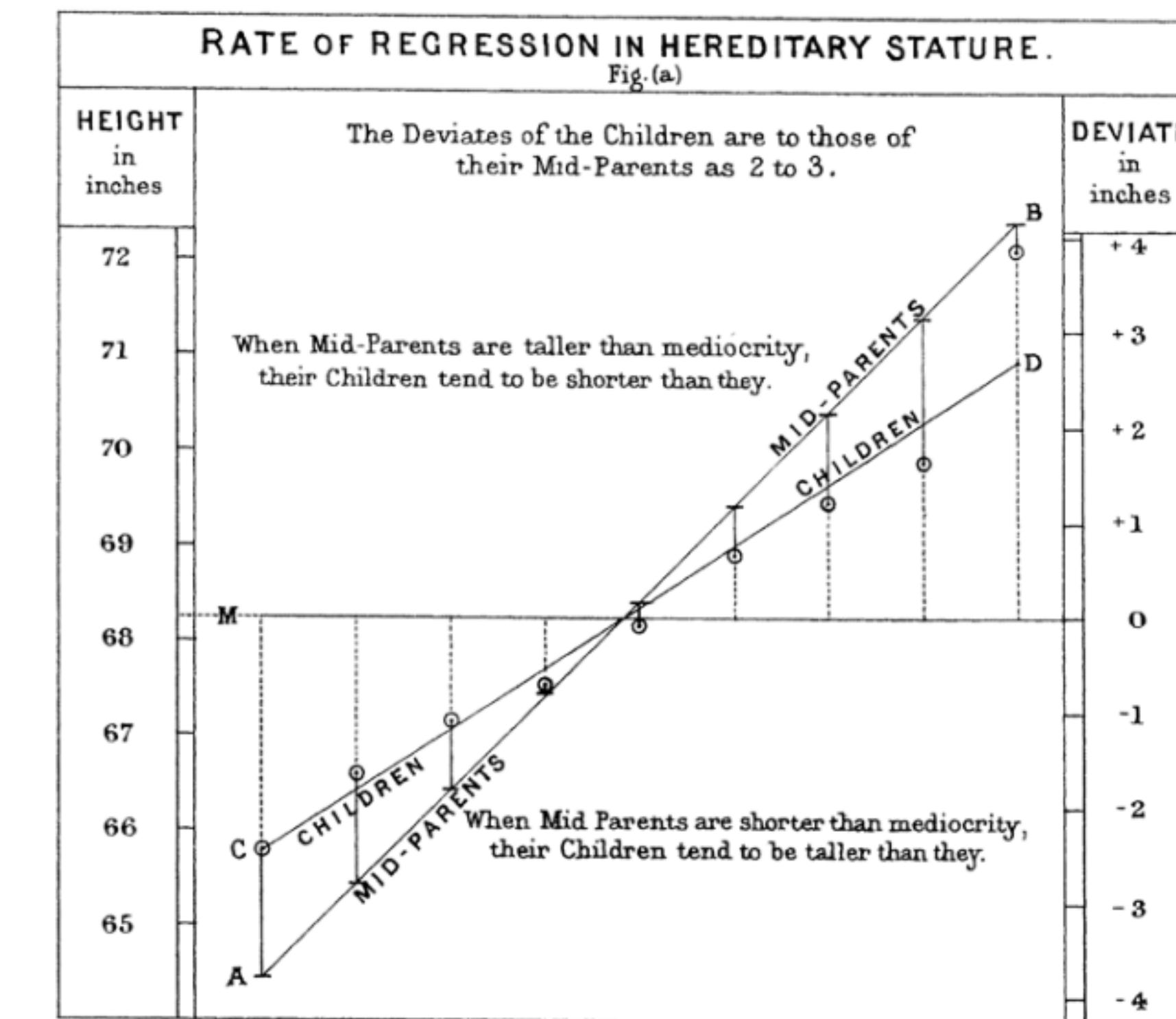


Law	Definition
Law of dominance and uniformity	Some alleles are dominant while others are recessive; an organism with at least one dominant allele will display the effect of the dominant allele.
Law of segregation	During gamete formation, the alleles for each gene segregate from each other so that each gamete carries only one allele for each gene.
Law of independent assortment	Genes of different traits can segregate independently during the formation of gametes.



Galton and quantitative genetics

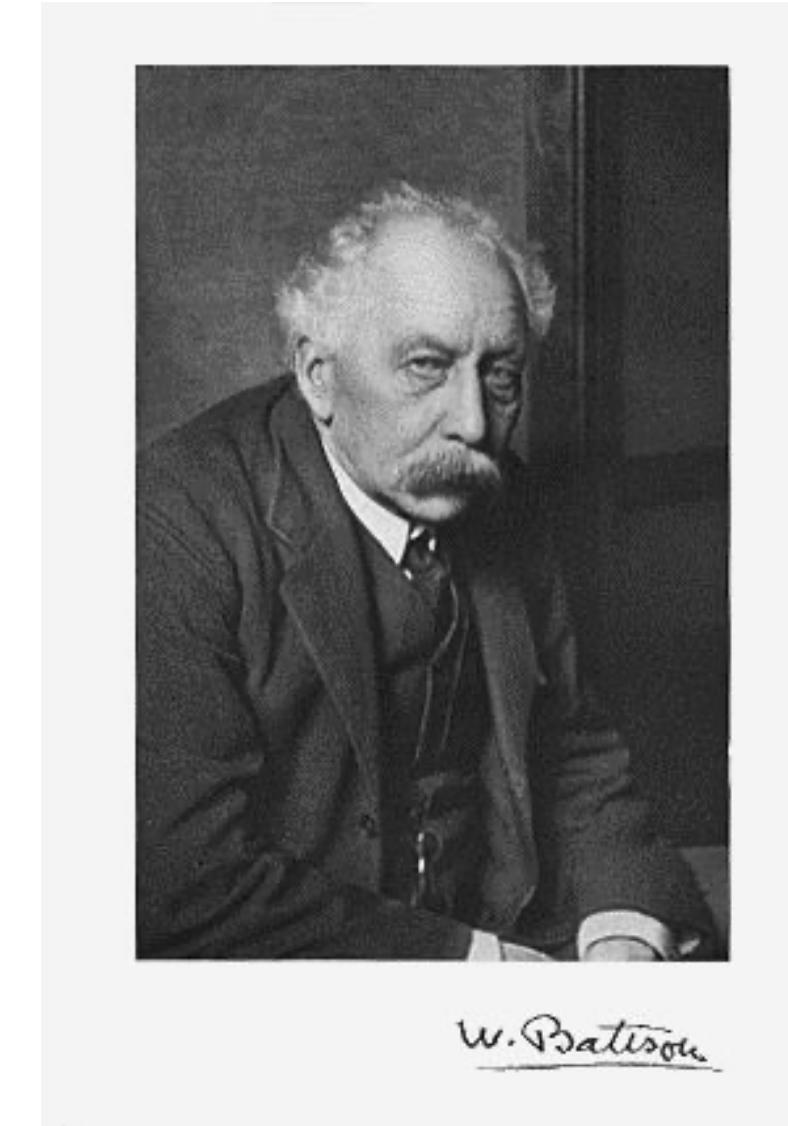
- Francis Galton (1889) was interested in the transmission of those characteristics that presented a continuous variation



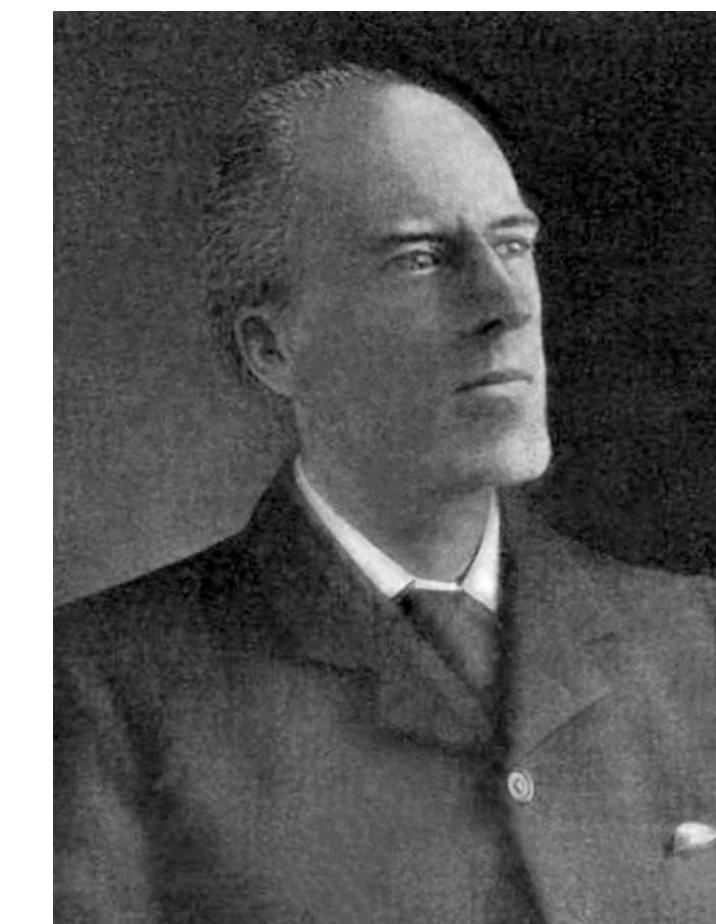
Mendelians and biometrists

In the beginning of the 1900s, controversy arose between:

- Mendelians: **qualitative traits** that show Mendelian patterns of inheritance. Quantitative traits reflect environmental differences.
- Biometrists: **quantitative traits that are normally distributed**. They doubted that mendelians laws could apply to continuous traits



William Bateson 1861-1923

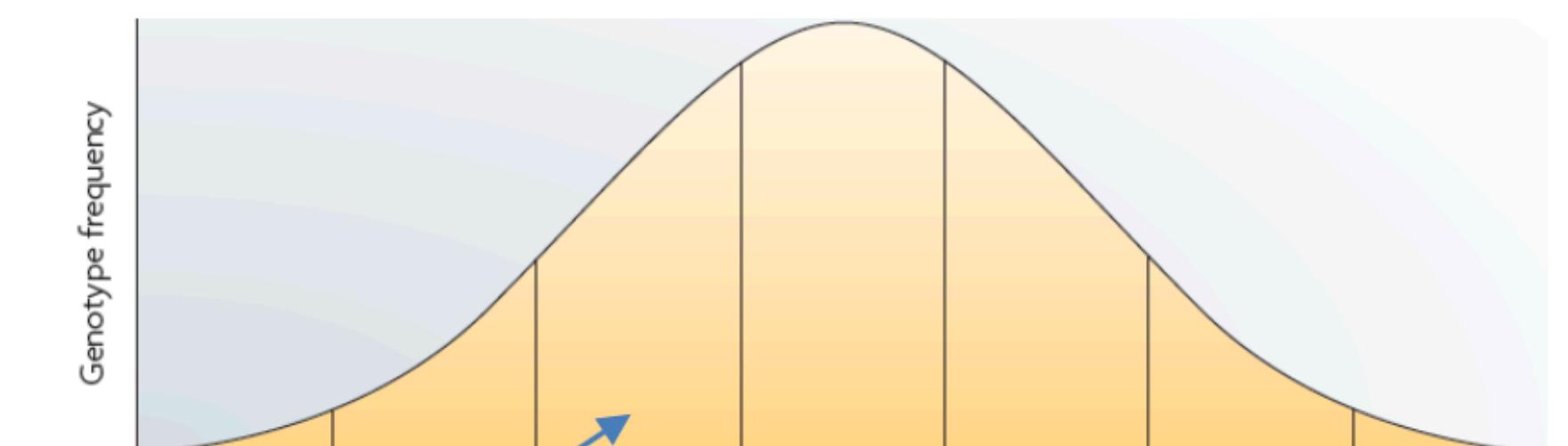
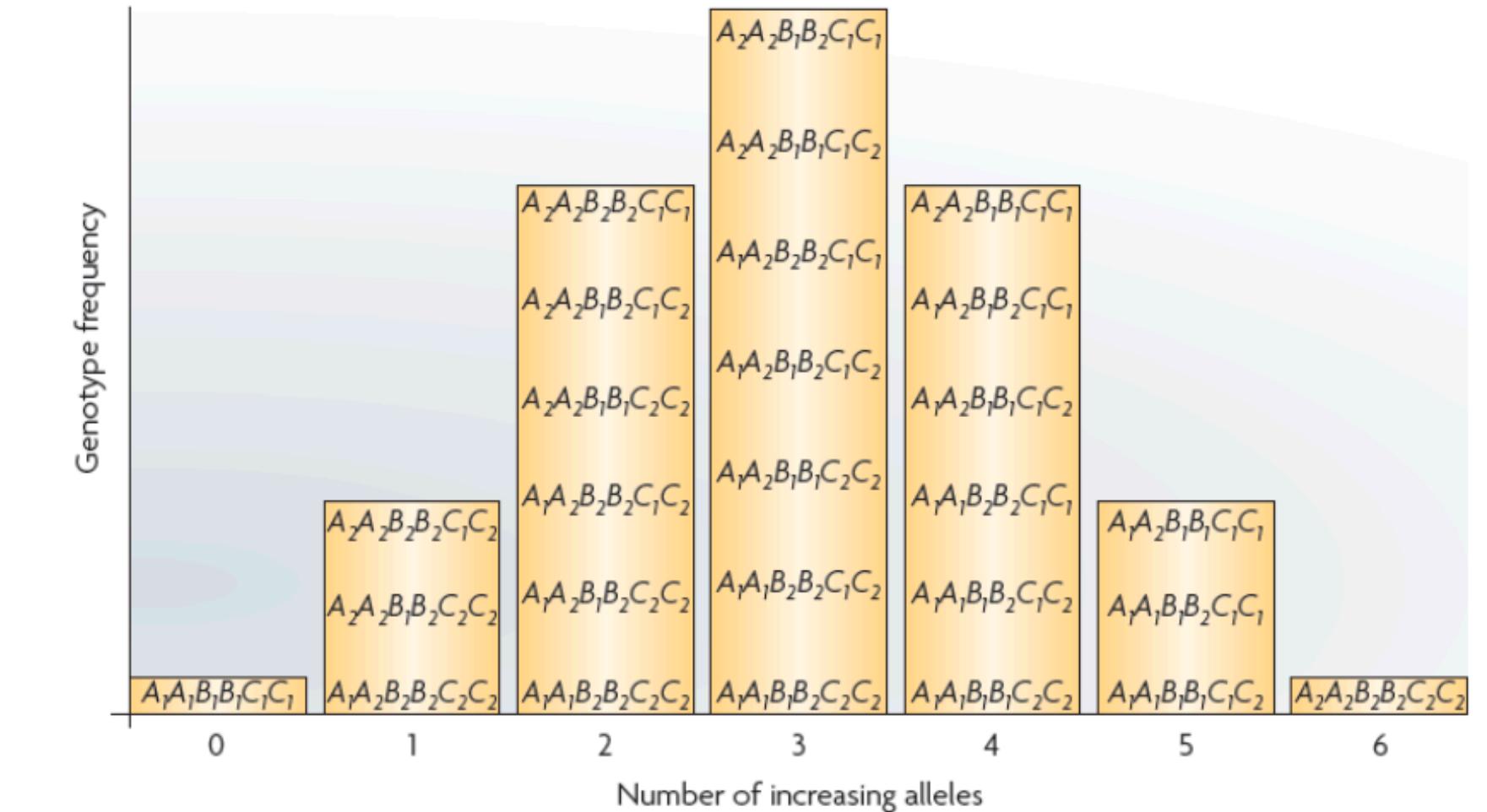
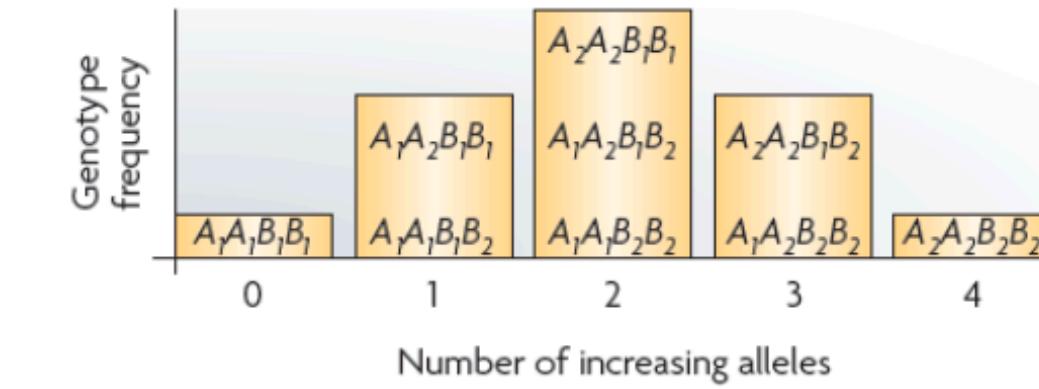
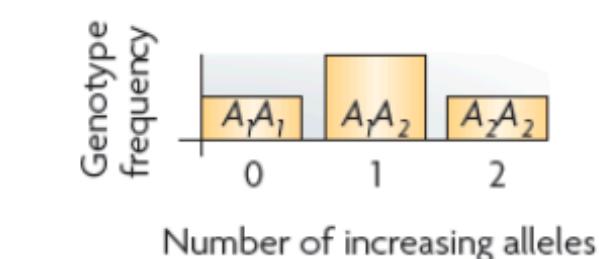


Karl Pearson 1857-1936

The infinitesimal model

Ronald Fisher (1918)

The **infinitesimal model**, also known as the **polygenic model**, is based on the idea that variation in a **quantitative trait** is influenced by an infinitely large number of **genes**, each of which makes an infinitely small (infinitesimal) contribution to the phenotype, as well as by environmental factors.

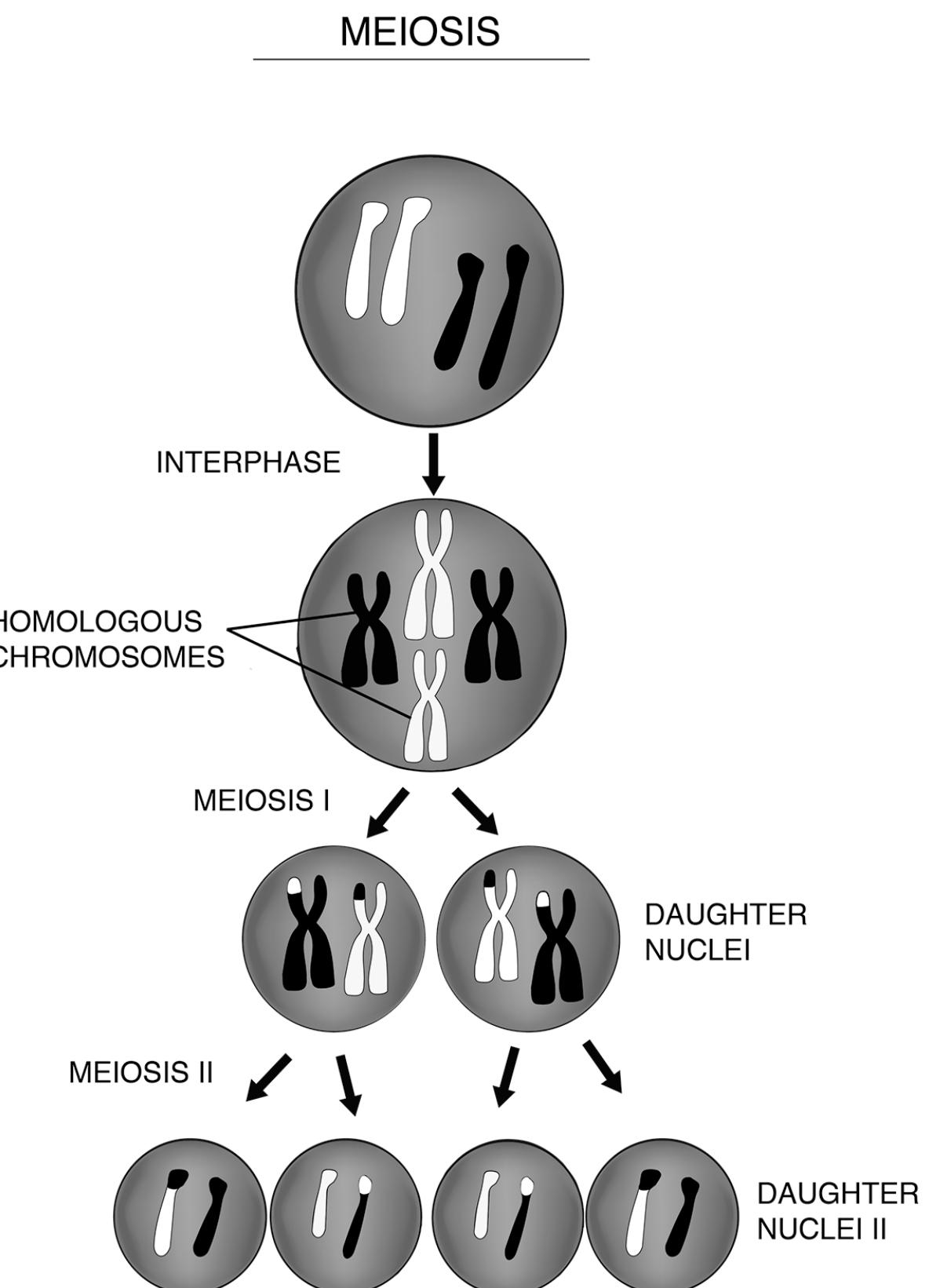


Most Human Traits (phenotypes) are polygenic!
Meaning that a very large number of genetic variants contributes in explaining phenotypic variation

Genes and heredity

Mendel's genes were only hypothetical entities, factors that could be inferred to exist in order to explain his results

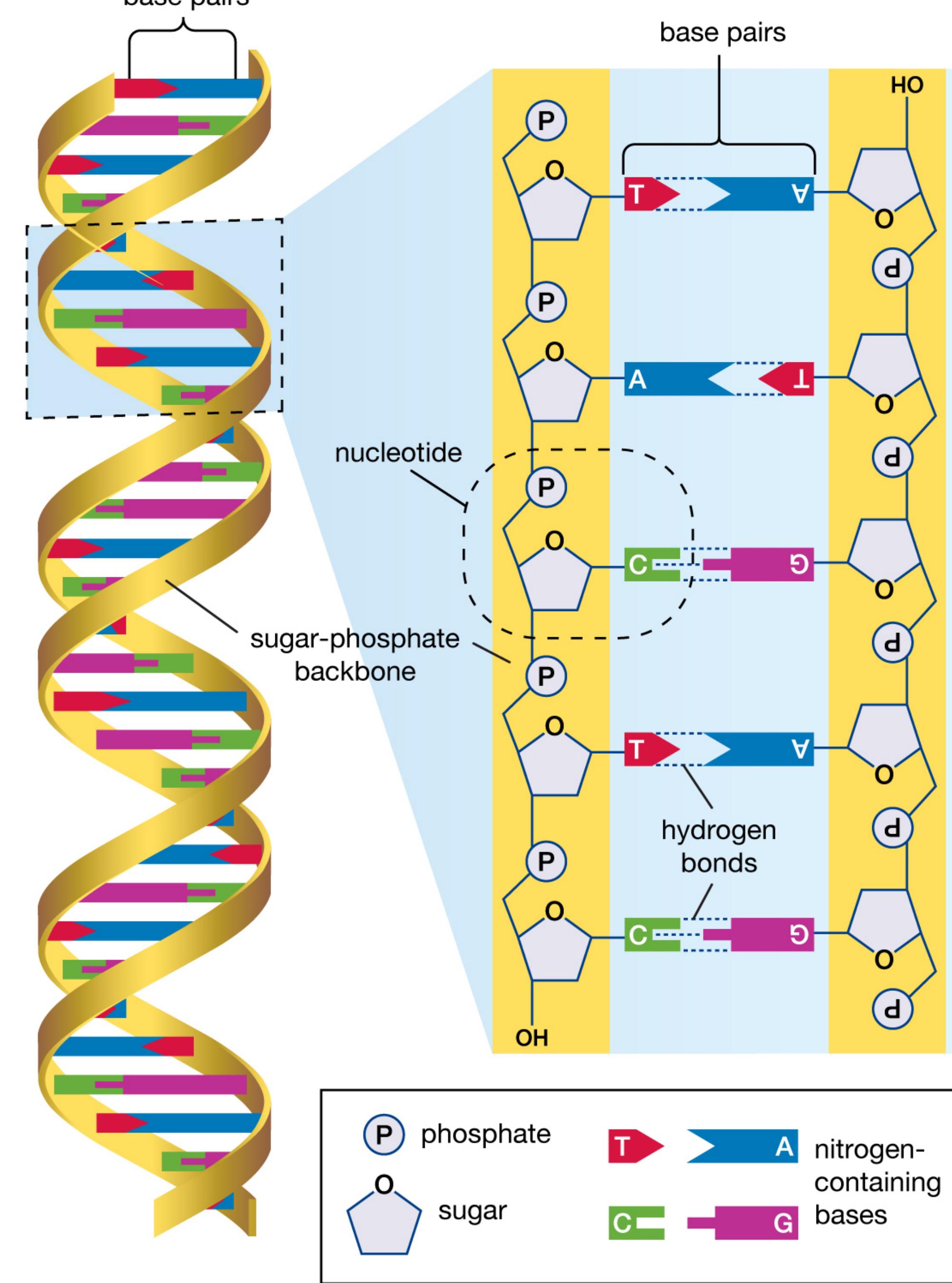
It seemed that genes were parts of chromosomes. In 1910 this idea was strengthened through the demonstration of parallel inheritance of certain Drosophila (a type of fruit fly) genes on sex-determining chromosomes by American zoologist and geneticist Thomas Hunt Morgan.



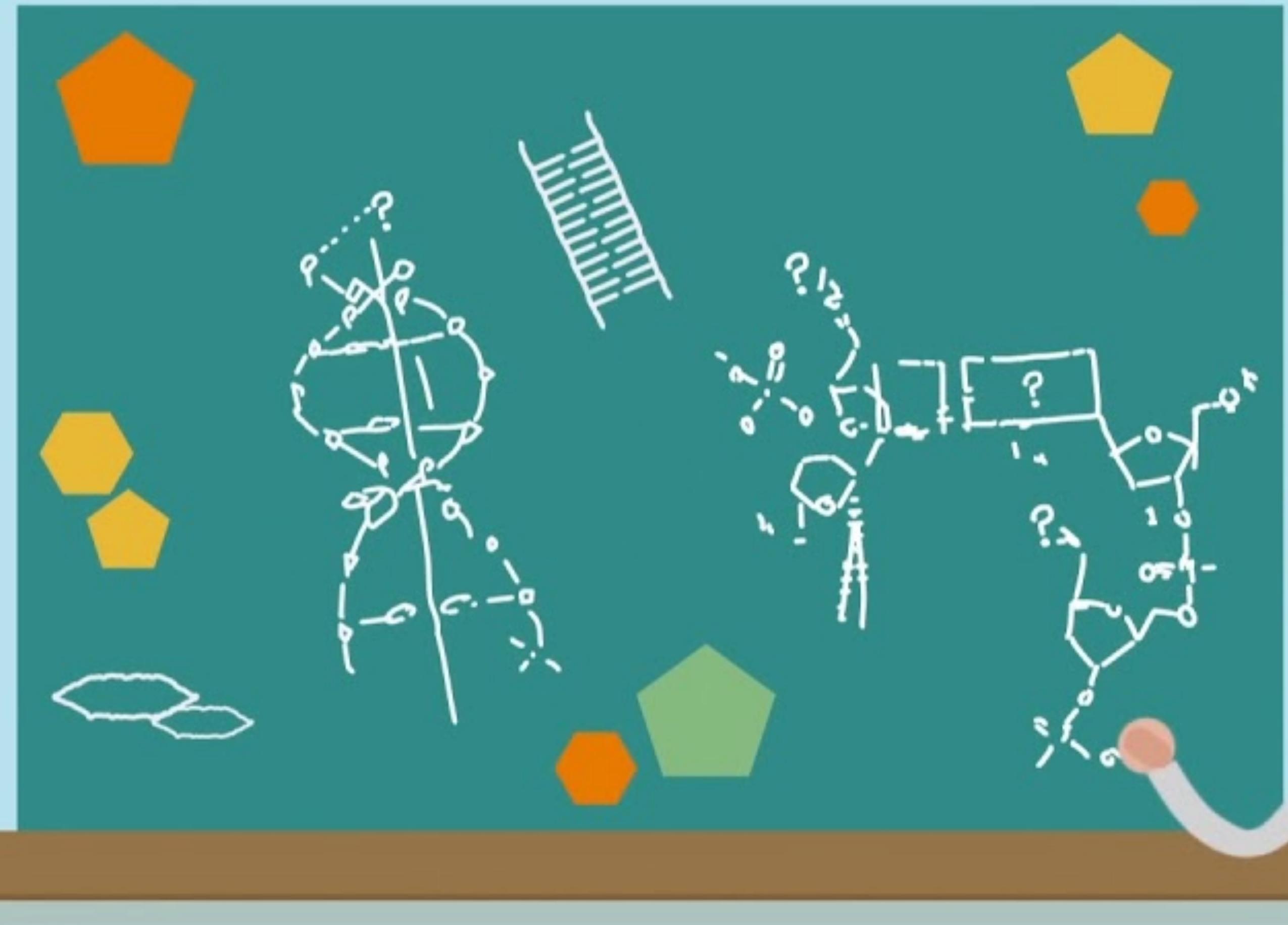
The discovery of DNA structure

A major landmark was attained in **1953** when James D. Watson and Francis Crick and Maurice Wilkins devised a double helix model for DNA structure.

Their breakthrough was made possible by the work of Rosalind Franklin, whose X-ray diffraction studies of the DNA molecule shed light on its helical structure.



Francis Crick

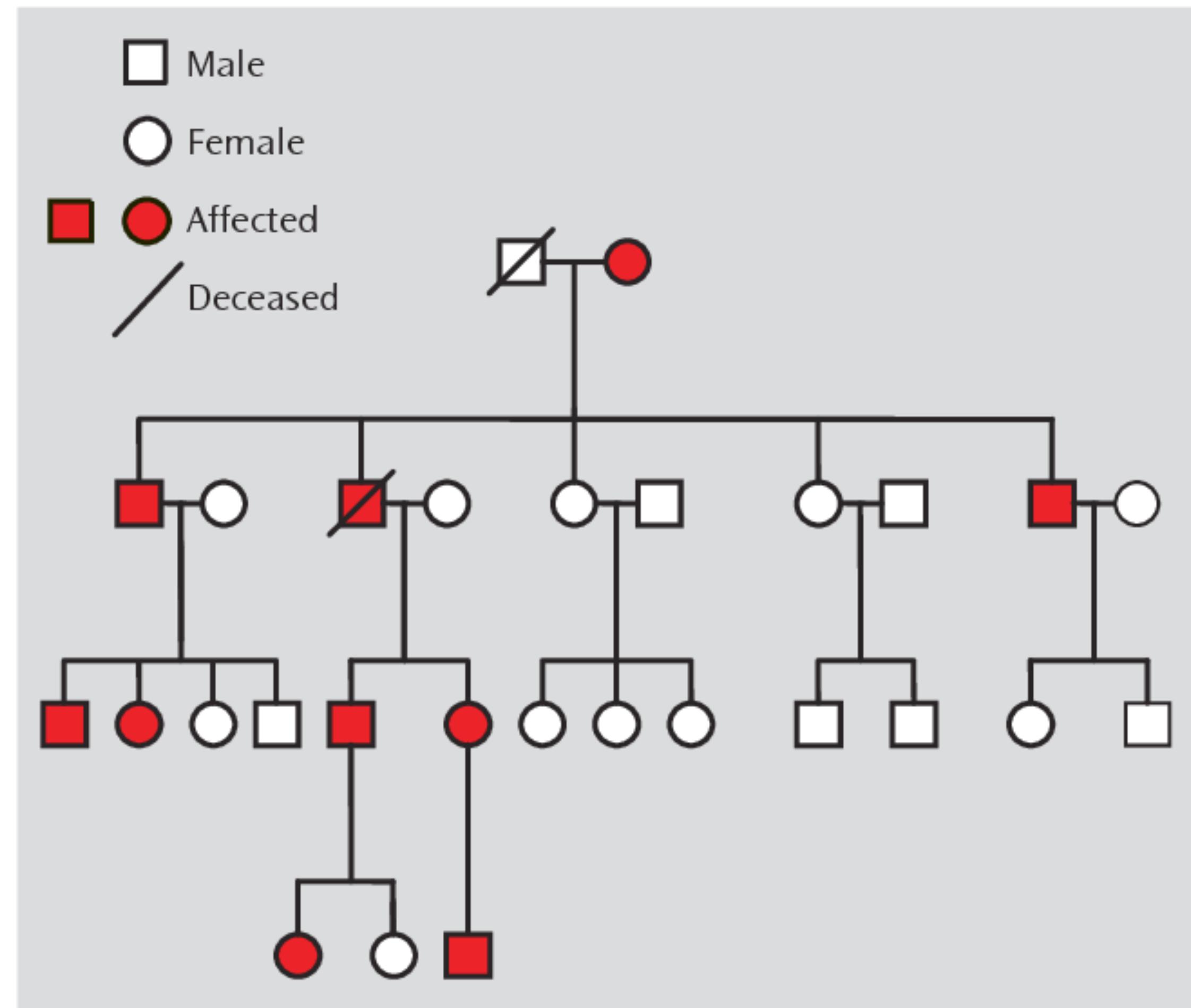


James D. Watson

Linkage Studies

A gene-hunting technique that traces patterns of disease in high-risk families. It attempts to locate a disease-causing gene by identifying genetic markers of known chromosomal location that are co-inherited with the trait of interest.

suitable for large effects: genes were found for many single gene disorders (Mendelian traits)



The Human Genome Project

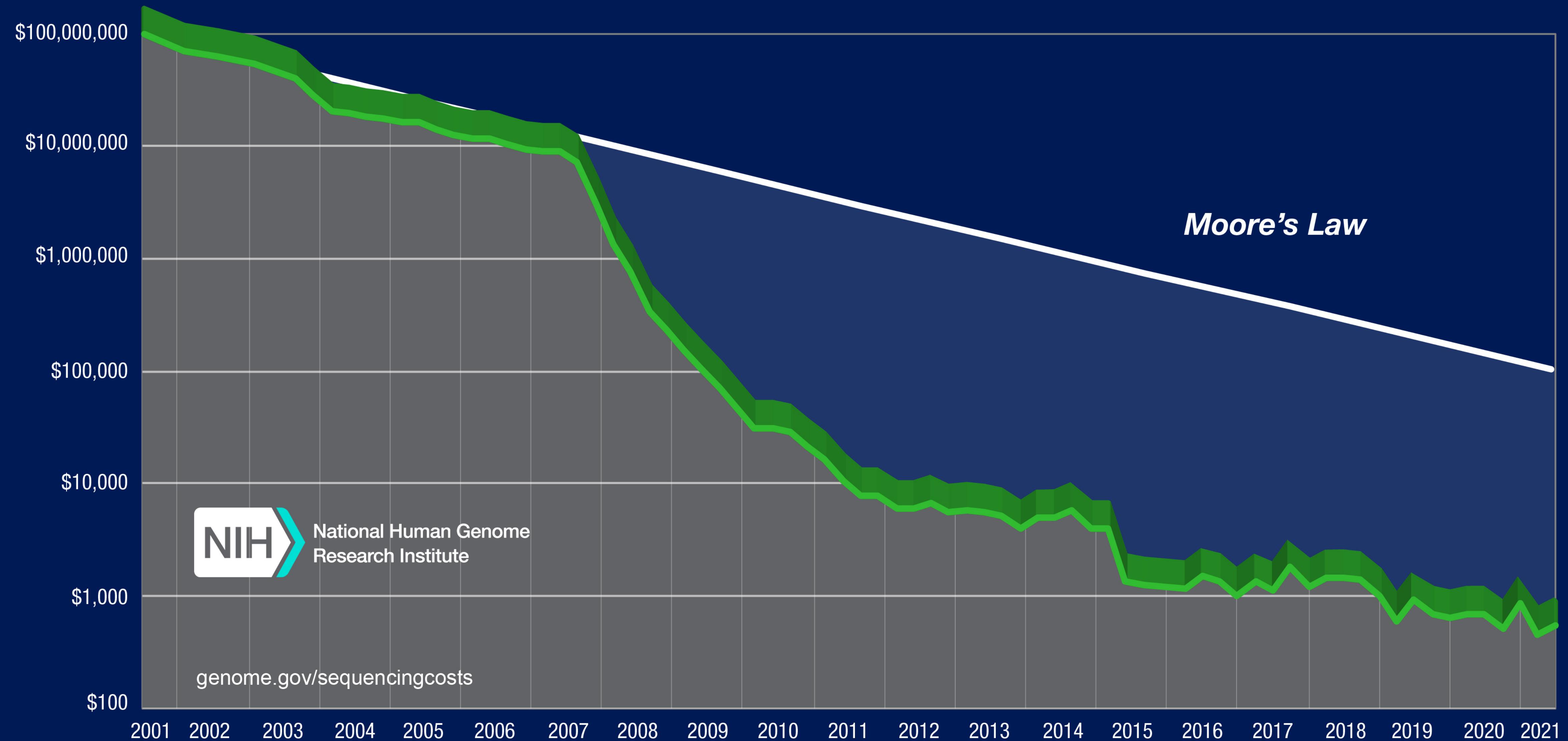
The Human Genome Project (HGP), which operated from 1990 to 2003, provided researchers with basic information about the sequences of the three billion chemical base pairs (i.e., [adenine \[A\]](#), [thymine \[T\]](#), [guanine \[G\]](#), and [cytosine \[C\]](#)) that make up human genomic [DNA](#) (deoxyribonucleic acid).

Announced on June 26, 2000 by Bill Clinton in a joint announcement with Tony Blair

Once significant human genome sequencing began for the HGP, a 'draft' human genome sequence (as described above) was produced over a 15-month period (from April 1999 to June 2000). The estimated cost for generating that initial 'draft' human genome sequence is **~\$300 million** worldwide.



Cost per Human Genome



Human Genetic Variation

- Human Genome consists of approx 3 billion base pairs
- 99.5% similarity among individuals
- Only about 1.5% of the genome codes for proteins
- Each person has the same set of genes - about 20,000 in all. The differences between people come from slight variations in these genes



Mapping genomic variations

Cells sometimes make mistakes during the copying process. These typos lead to variations in the DNA sequence at particular locations, called single nucleotide polymorphisms, or SNPs (pronounced “snips”).

Need to build a map of genetic variation



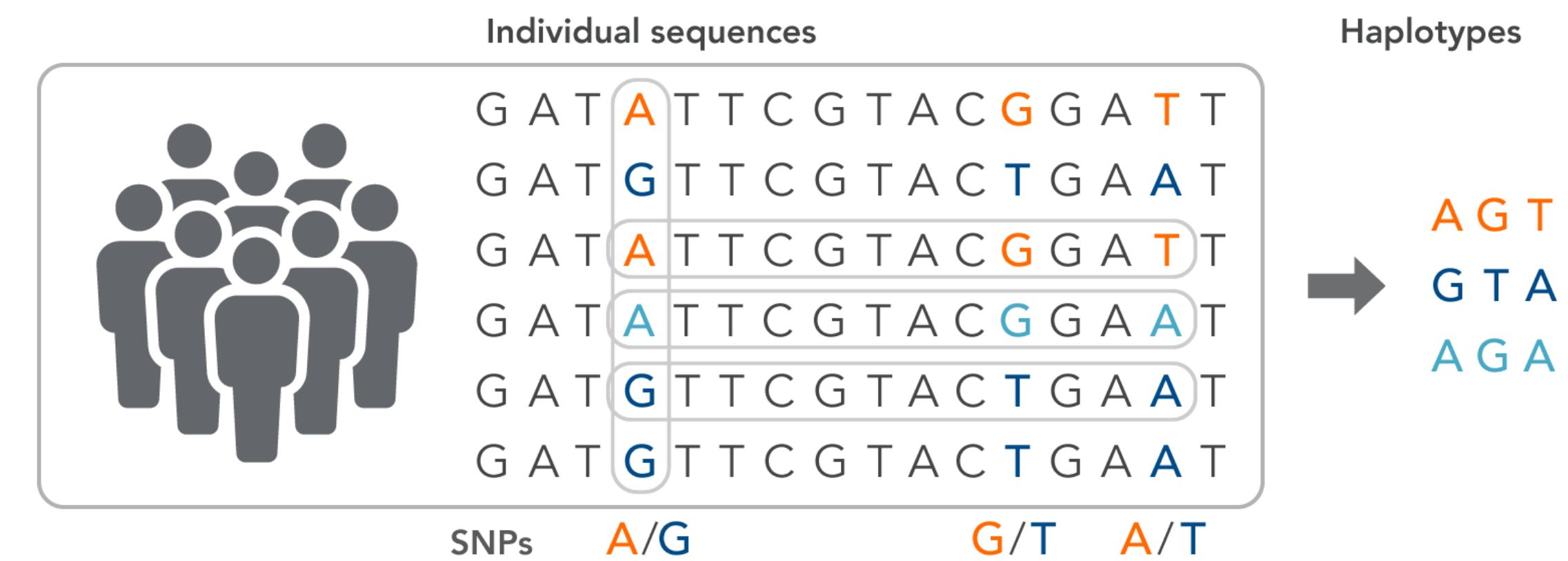
The HapMap Project

The International HapMap Project was an organization that aimed to develop a haplotype map (**HapMap**) of the human genome

The HapMap project focuses only on common SNPs, those where each allele occurs in at least 1% of the population.

The complete data obtained in Phase I were published on 27 October 2005

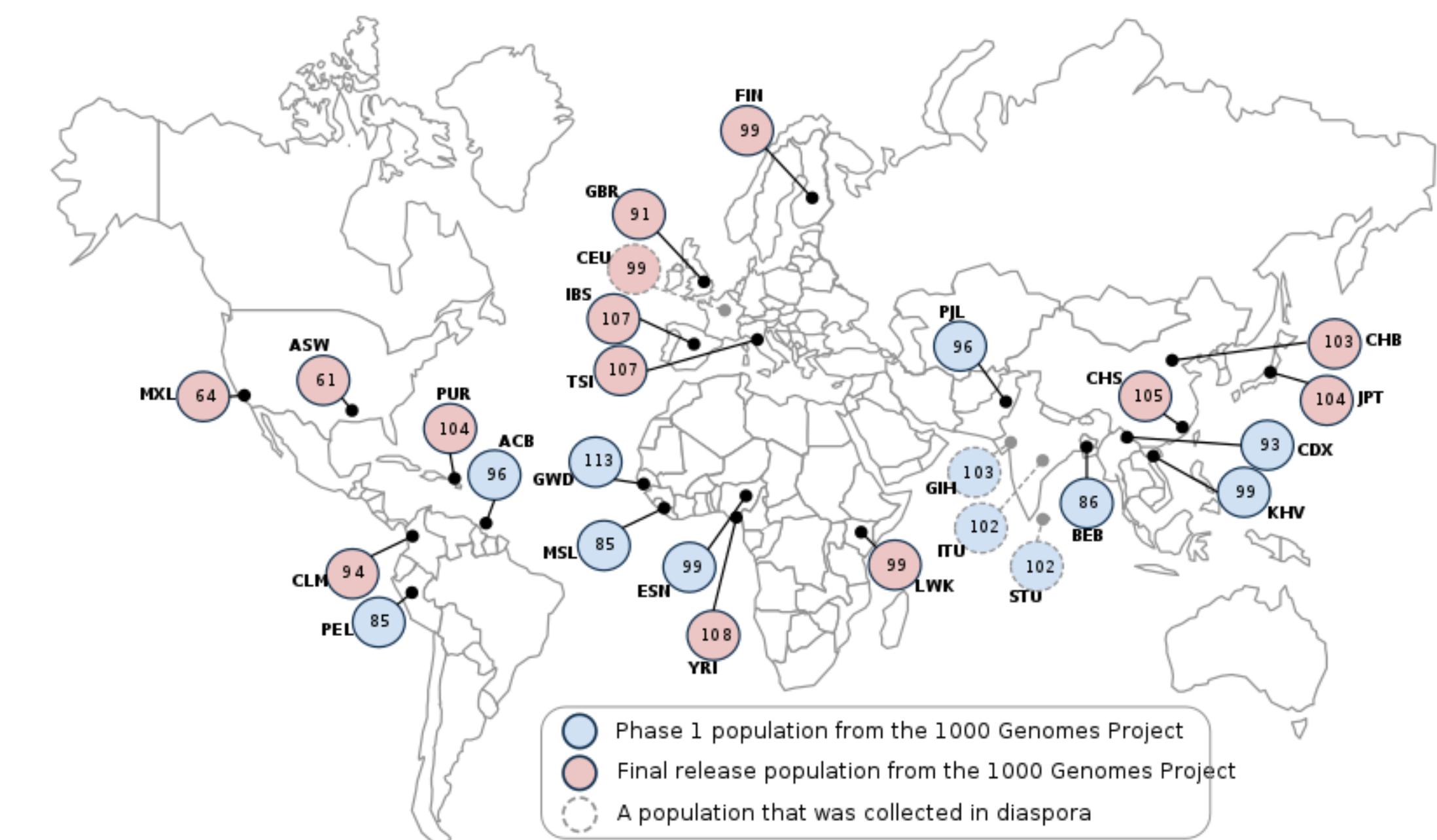
The HapMap project chose a sample of 269 individuals and selected several million well-defined SNPs, genotyped the individuals for these SNPs, and published the results.



The 1000 Genome Project

Launched in 2008, to extend the HapMap

goal to create a complete and **detailed catalogue of human genetic variations**



Genome Wide association Studies

- Data from HapMap and 1000Genomes help scientists to go from linkage to association studies
- A Genome Wide Association Study is the “gold standard” techniques to find association between a genetic variant and a trait/disease
- <https://www.ebi.ac.uk/gwas/diagram>

What's next?

- Understanding interaction between **environment and genetics**
- **Genetic editing (CRISPR)**
- **Epigenetic**
- **Precision medicine**
- **Genomic privacy**