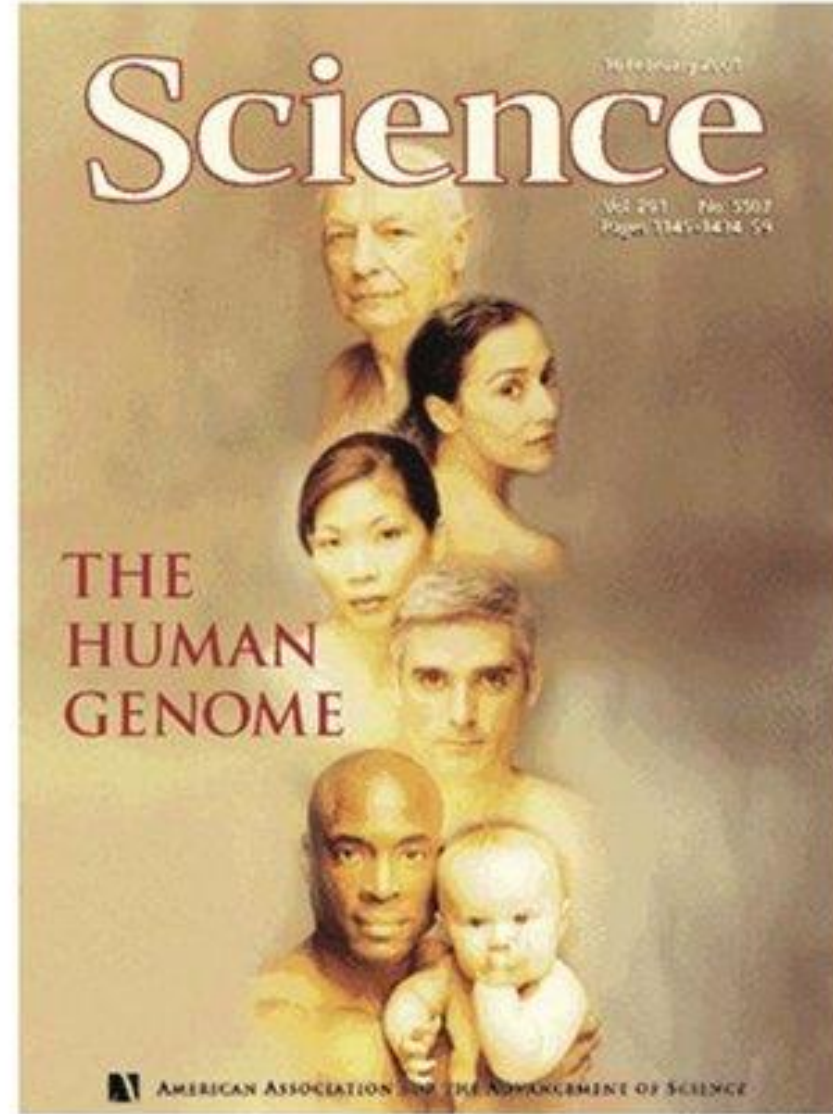
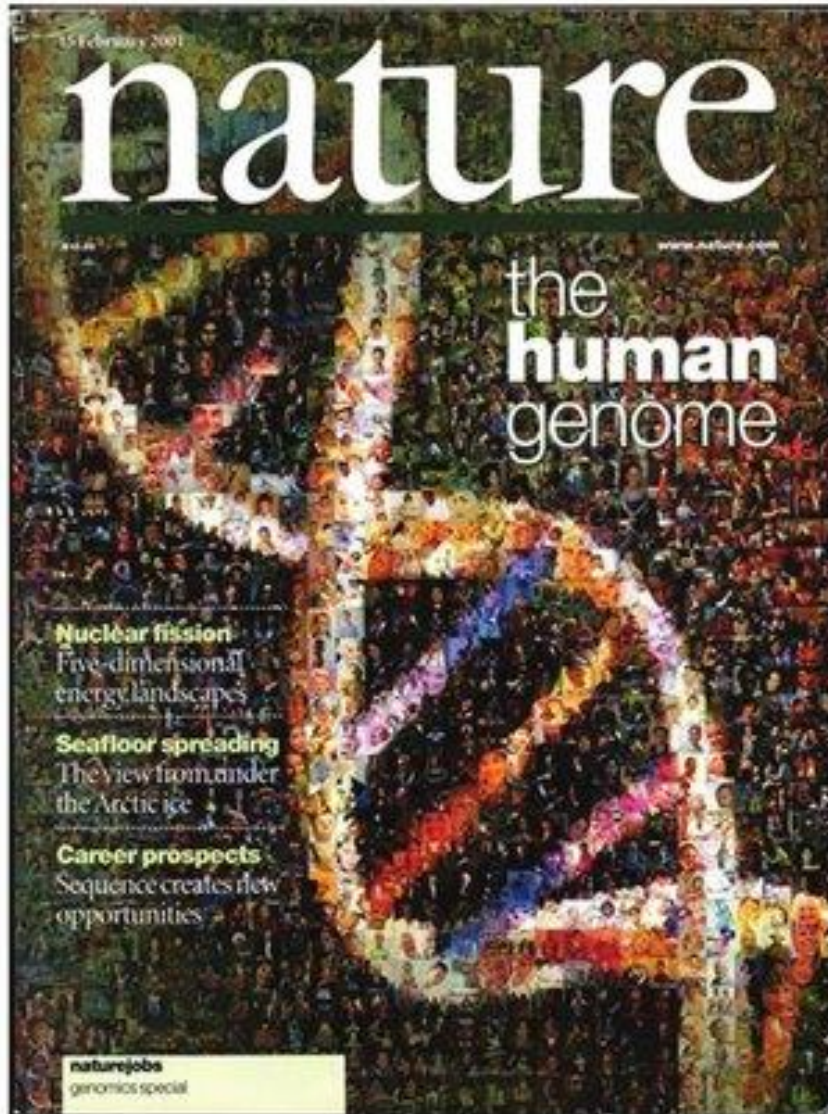


# Scientific Reading and Presentation

## III. Human Genome Project

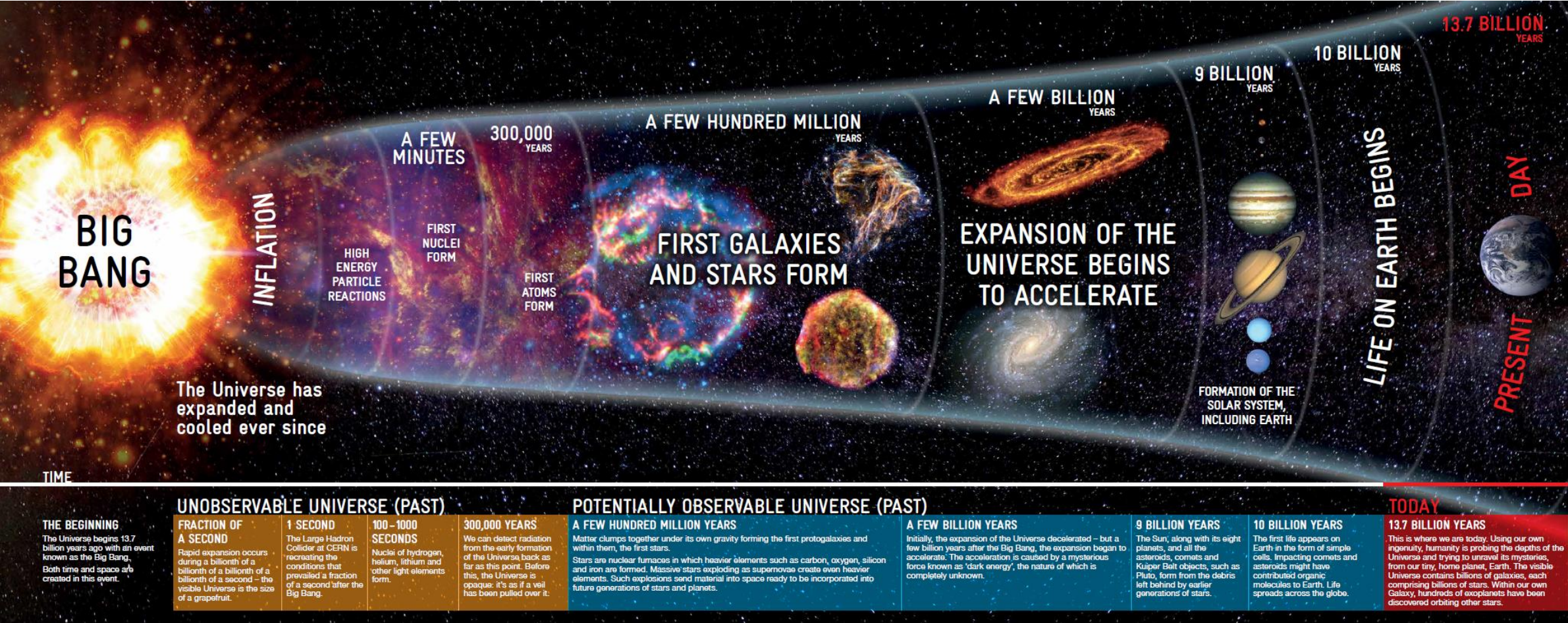
魏桐 10/16





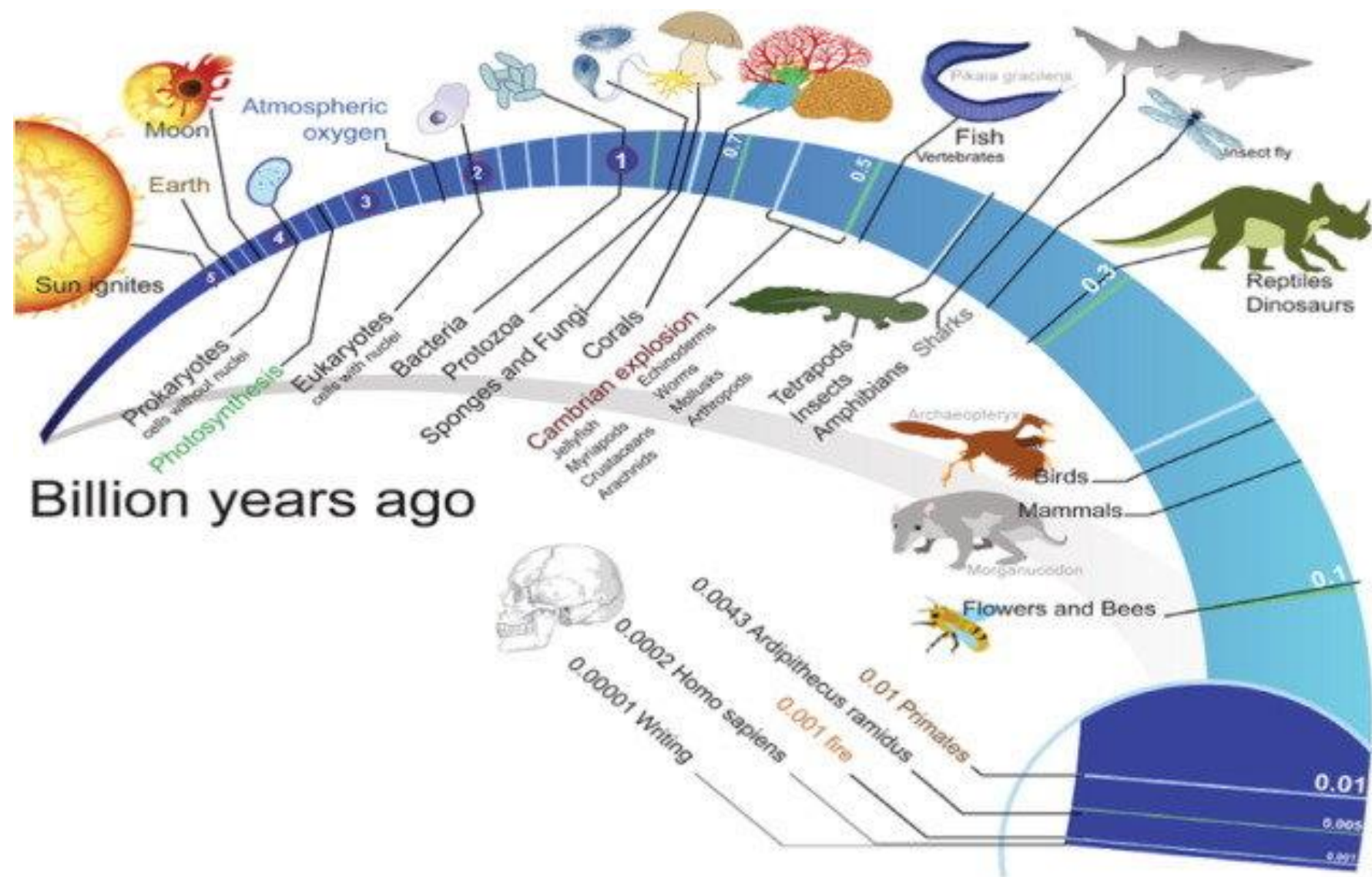


# The history of Universe





# The evolution of life



# Ancient hunter-gatherer life

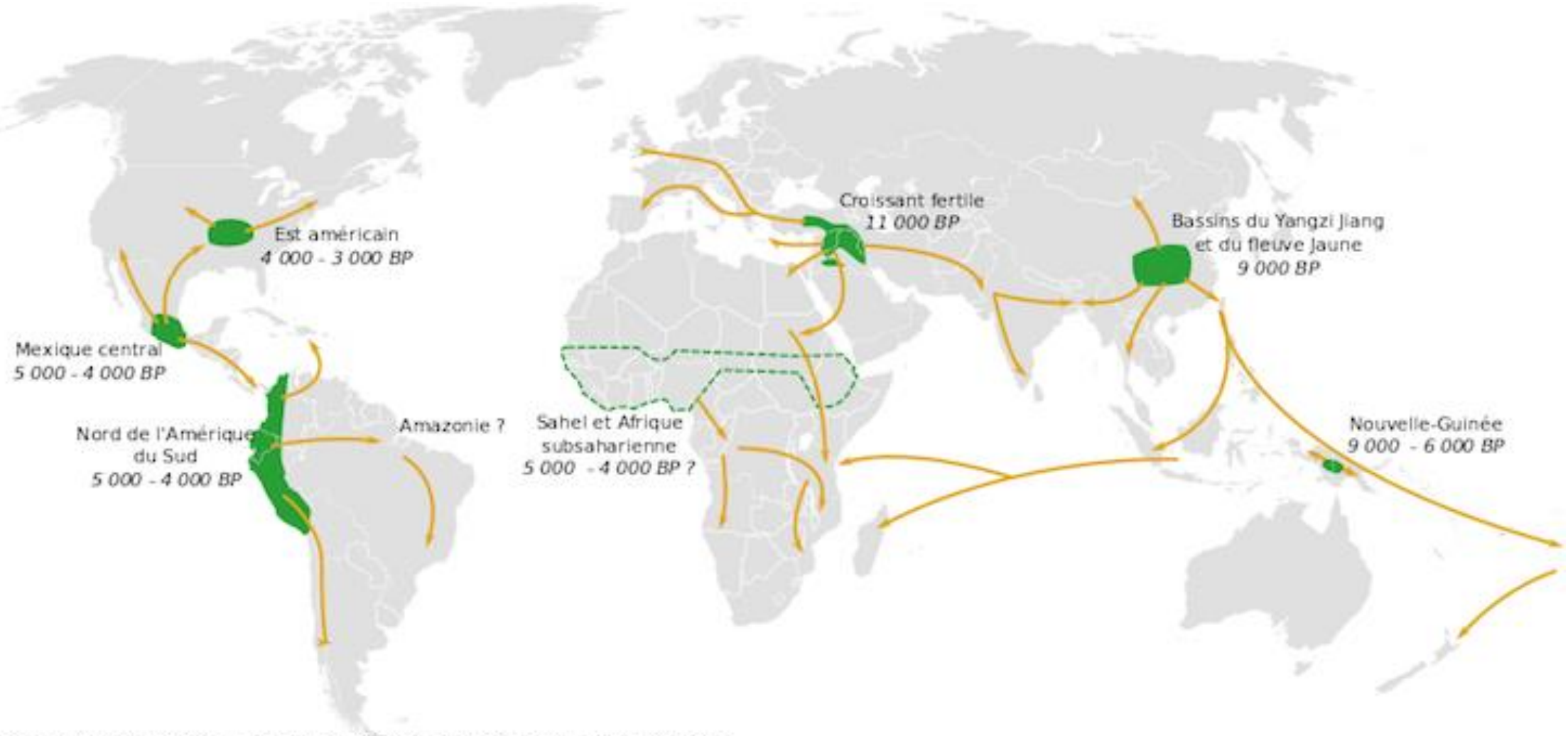




# The dawn of agriculture



# The origin of agriculture



D'après J. Diamond et al. (2003) "Farmers and Their Languages: The First Expansions", Science



# Aristotle (384-322 BC)



Aristotle (384-322 BC)  
Ancient Greek Philosopher

Aristotle's *Scala naturae* (highest to lowest)

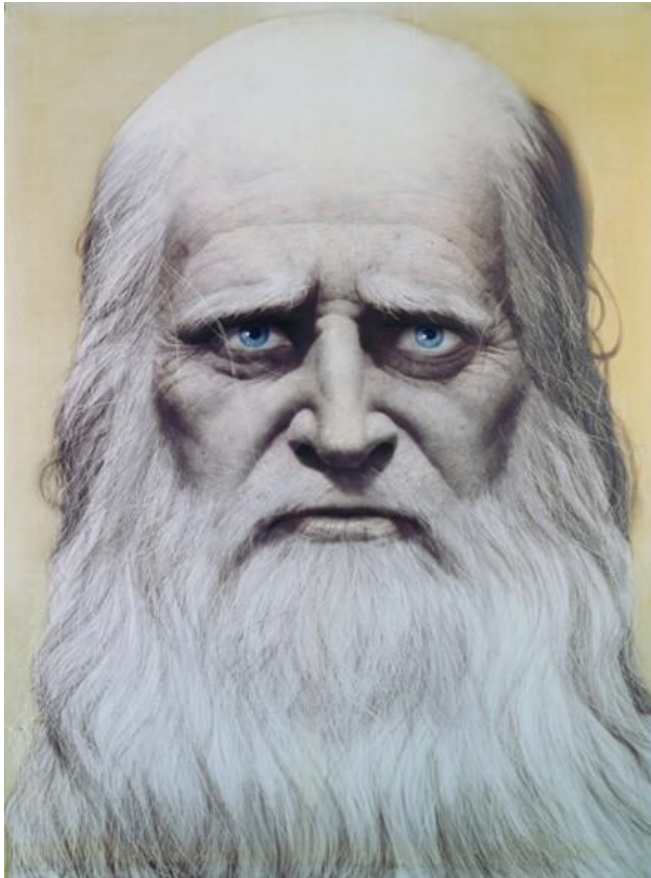
Group	Examples (given by Aristotle)	Blood	Legs	Souls (Rational, Sensitive, Vegetative)	Qualities (Hot–Cold, Wet–Dry)
Man	Man	with blood	2 legs	R, S, V	Hot, Wet
Live-bearing tetrapods	Cat, hare	with blood	4 legs	S, V	Hot, Wet
Cetaceans	Dolphin, whale	with blood	none	S, V	Hot, Wet
Birds	Bee-eater, nightjar	with blood	2 legs	S, V	Hot, Wet, except Dry eggs
Egg-laying tetrapods	Chameleon, crocodile	with blood	4 legs	S, V	Cold, Wet except scales, eggs
Snakes	Water snake, Ottoman viper	with blood	none	S, V	Cold, Wet except scales, eggs
Egg-laying fishes	Sea bass, parrotfish	with blood	none	S, V	Cold, Wet, including eggs
(Among the egg-laying fishes): placental selachians	Shark, skate	with blood	none	S, V	Cold, Wet, but placenta like tetrapods
Crustaceans	Shrimp, crab	without	many legs	S, V	Cold, Wet except shell
Cephalopods	Squid, octopus	without	tentacles	S, V	Cold, Wet
Hard-shelled animals	Cockle, trumpet snail	without	none	S, V	Cold, Dry (mineral shell)
Larva-bearing insects	Ant, cicada	without	6 legs	S, V	Cold, Dry
Spontaneously-generating	Sponges, worms	without	none	S, V	Cold, Wet or Dry, from earth
Plants	Fig	without	none	V	Cold, Dry
Minerals	Iron	without	none	none	Cold, Dry



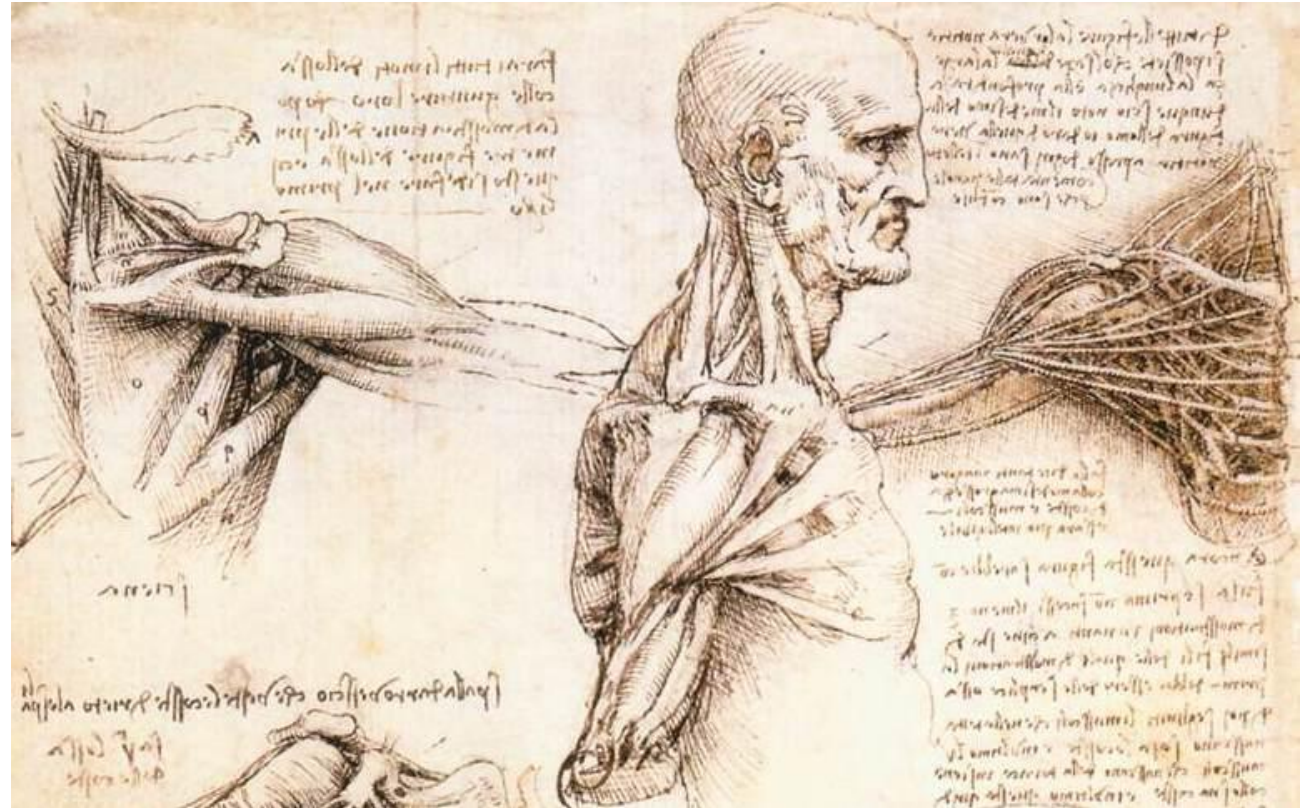
Aristotle's  
"Historia Animalium"  
~350 BC



# Leonardo Da Vinci (1452-1519)

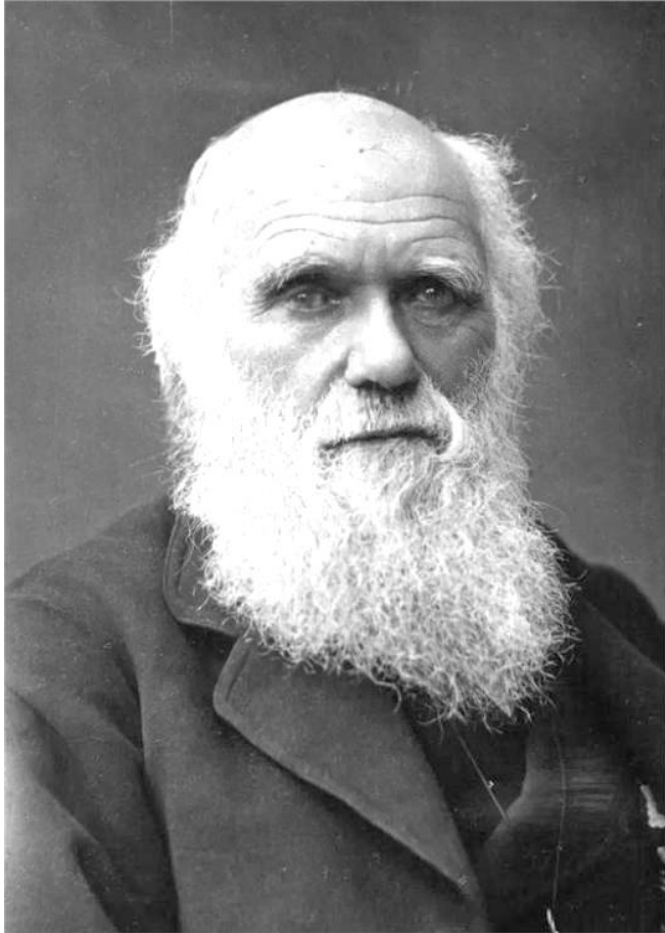


Da Vinci (1452-1519)  
Italian Polymath





# Charles Robert Darwin (1809-1882)

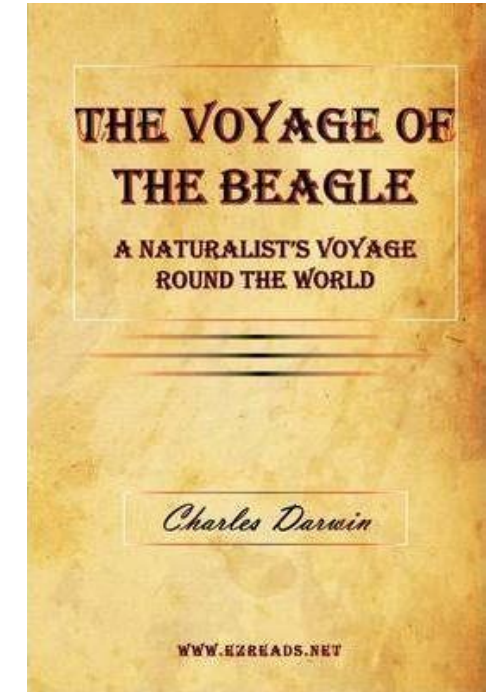
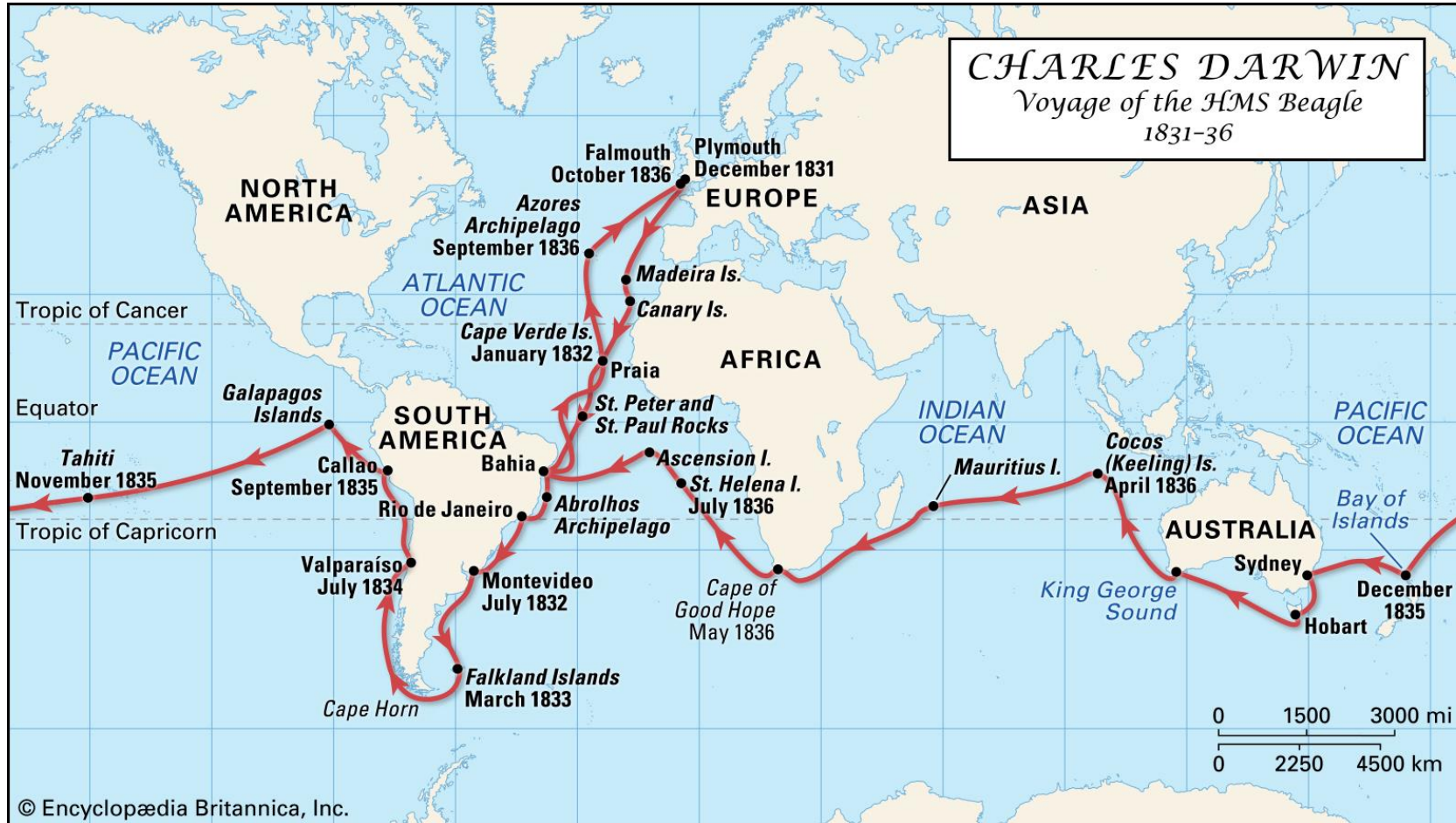


Darwin (1809-1882)  
English naturalist



Erasmus Darwin (1731-1802)  
English physician

# Charles Robert Darwin (1809-1882)

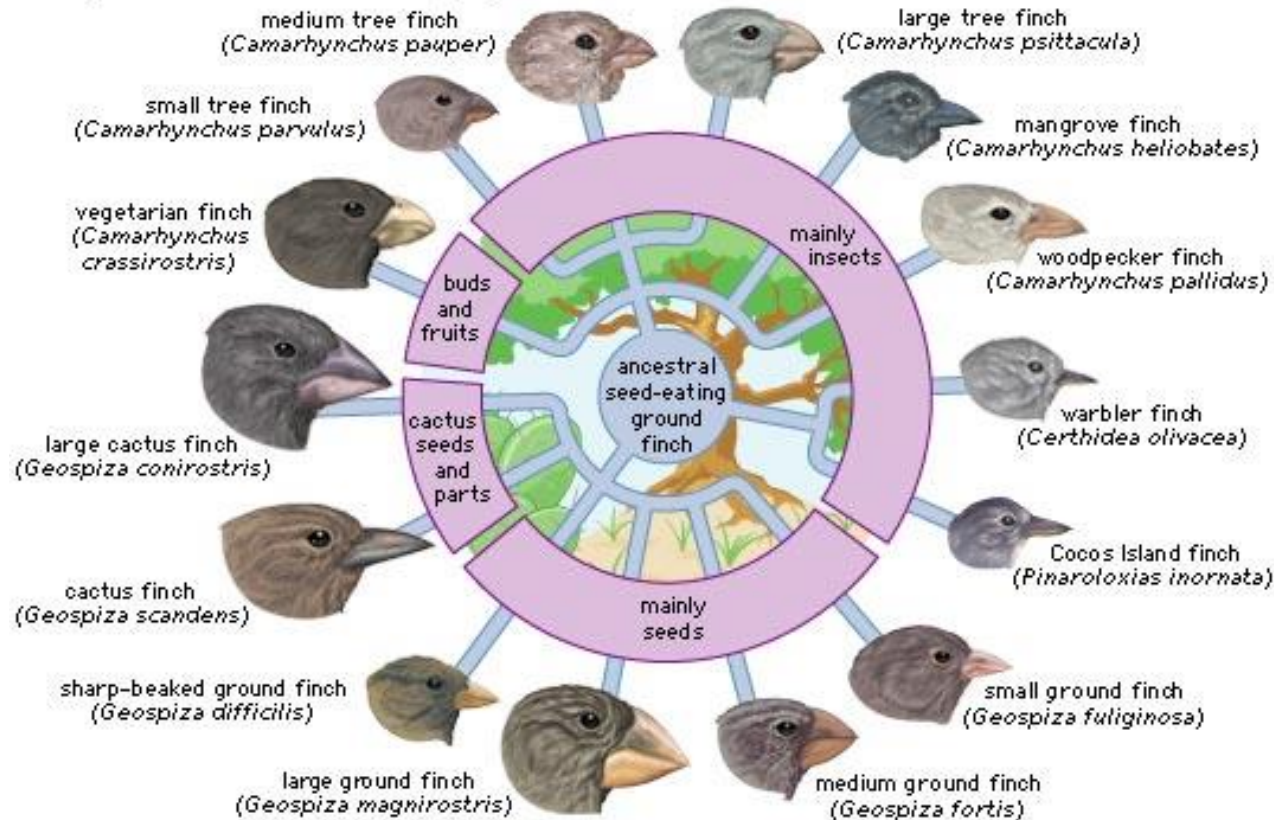


Voyage on the HMS Beagle (1831-1836)

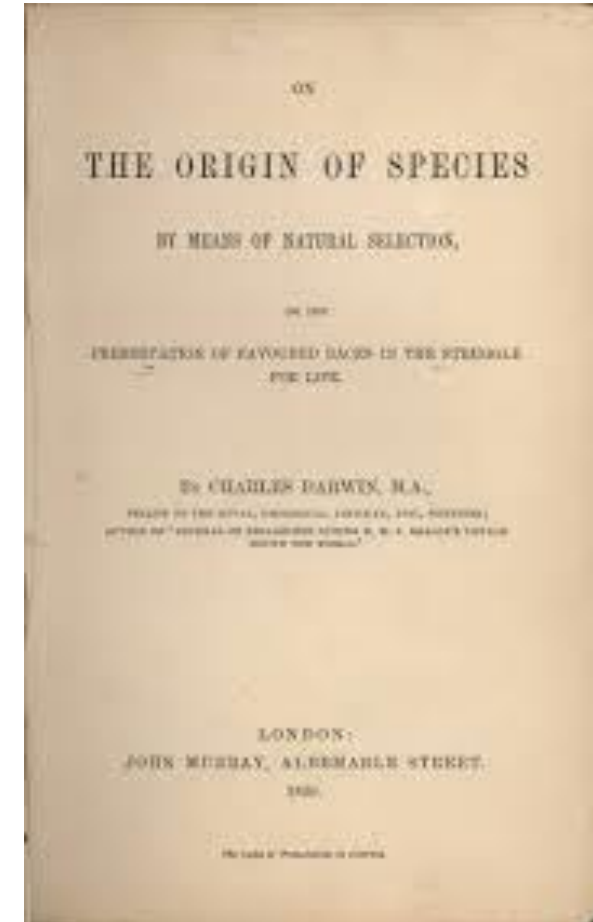


# Charles Robert Darwin (1809-1882)

## Adaptive radiation in Galapagos finches

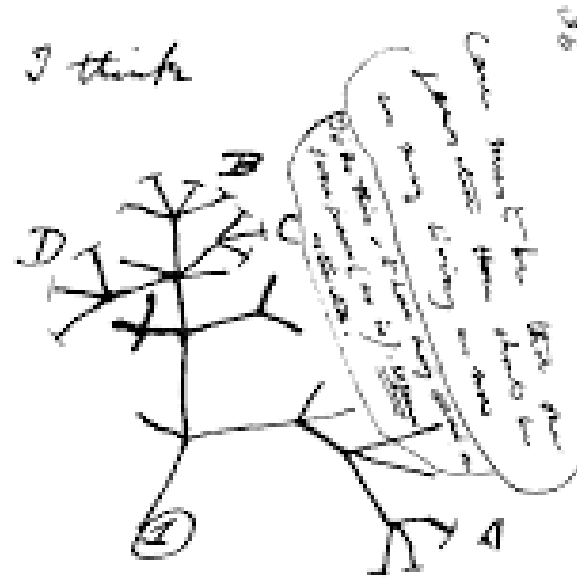


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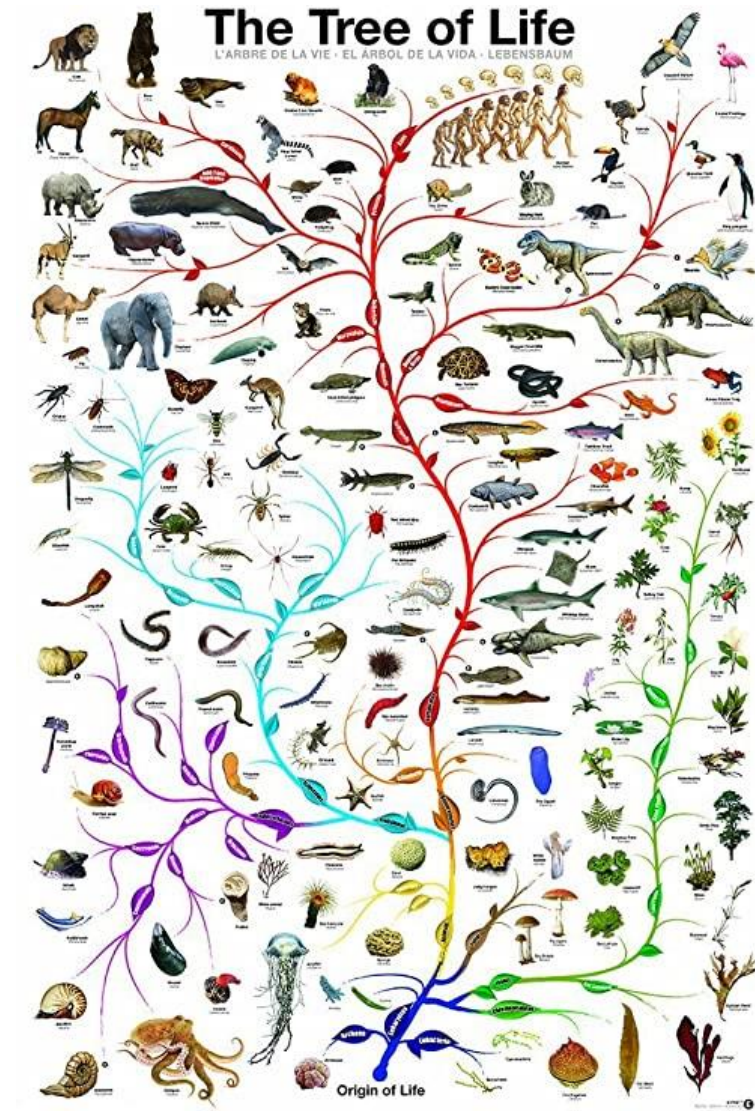
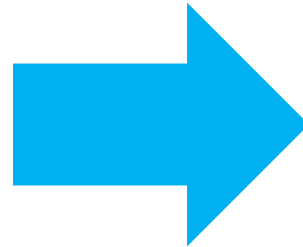


## The Origin of Species (1859)

# Darwin's tree of life



Then between A & B. various  
 sort of relation. C & B. the  
 first predation. B & D  
 rather greater distinction  
 Then form would be  
 formed. - binary relation





# Gregor Johann Mendel (1822-1884)

















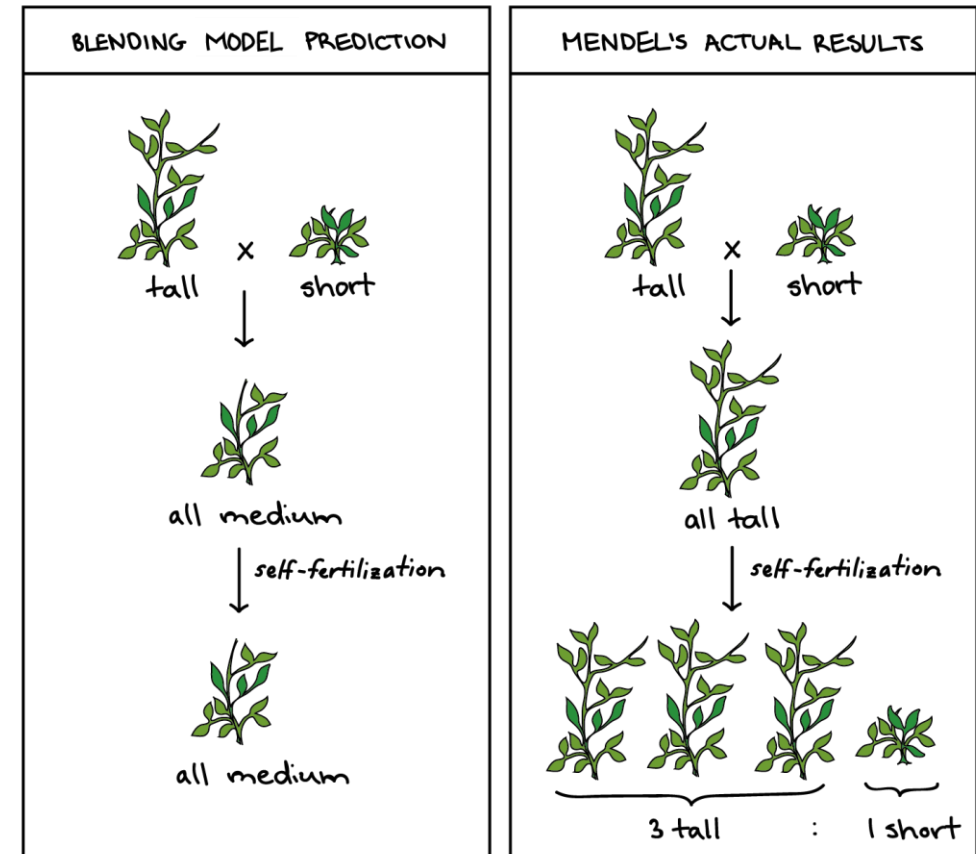
Mendel (1809-1882)  
Austrian Abbot



Pea plant experiment from 1856-1863

# Gregor Johann Mendel (1822-1884)

	Flower Colour	Plant Height	Seed Color	Seed Shape	Pod Colour	Pod Shape	Flower Position
<b>Dominant Trait</b>	 Purple	 Tall	 Yellow	 Round	 Green	 Inflated (full)	 Axial
<b>Recessive Trait</b>	 White	 Short	 Green	 Wrinkled	 Yellow	 Constricted (flat)	 Terminal

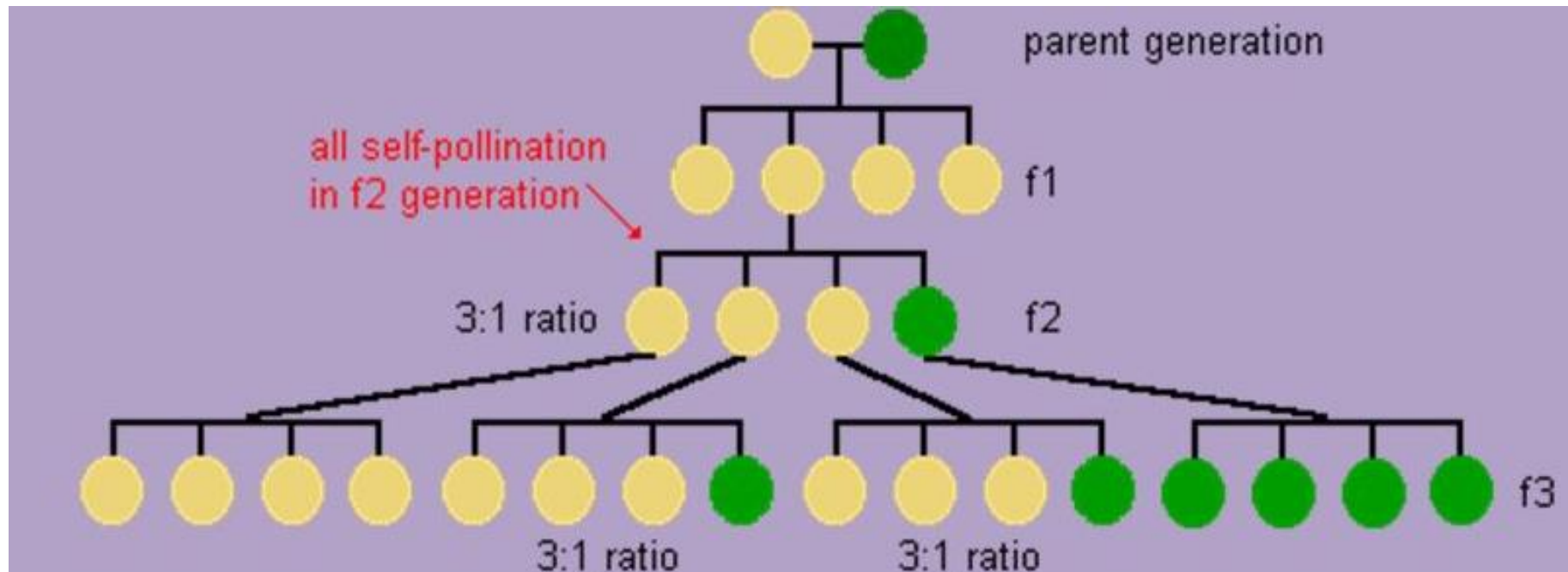


Pea plant experiment from 1856-1863



# Mendel's law of inheritance

- The law of segregation
- The law of independent assortment
- The law of dominance



# Friedrich Miescher (1844-1895)



Miescher (1844-1895)  
Swiss Physician

- Discovered DNA in 1869
- Experiment
  - Collected white blood cells
  - Lysed cells and isolated nuclei
  - Found a substance he called **nuclein**, which was presented in every tested cell type and high in phosphorus



# Albrecht Kossel (1853-1927)

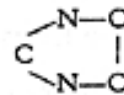


Kossel (1853-1927)  
German biochemist

- Isolated and described the **five organic compounds** that are present in nucleic acid: adenine, cytosine, guanine, thymine, and uracil.

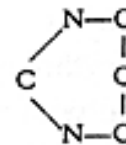
*Grouping of atoms in:*

Imidazole ring



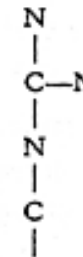
In adenine, guanine  
and histidine

Pyrimidine ring



In adenine, guanine  
thymine, cytosine

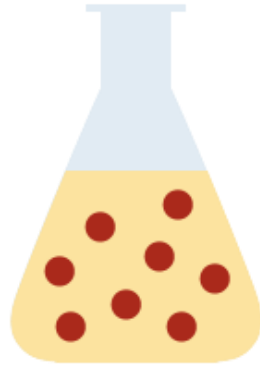
Arginine



Nobel Prize for Physiology or Medicine in 1910

# Avery-Macleod-McCarty experiment

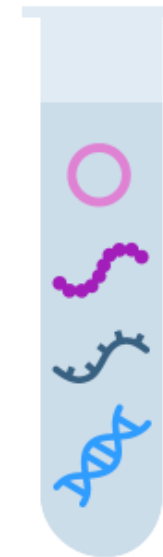
- smooth (S) bacteria strain pathogenic
- rough (R) bacteria strain non-pathogenic



S-strain



Detergent is used to break open heat-killed S-strain cells to separate the components



sugar coat

protein

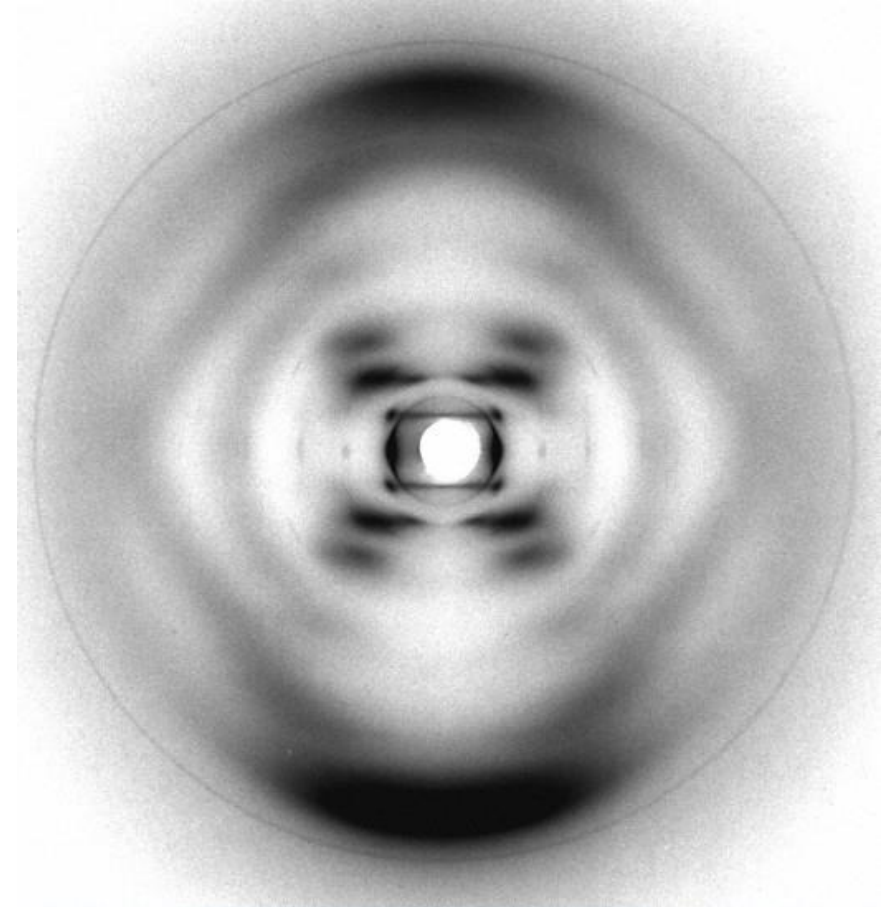
RNA

DNA

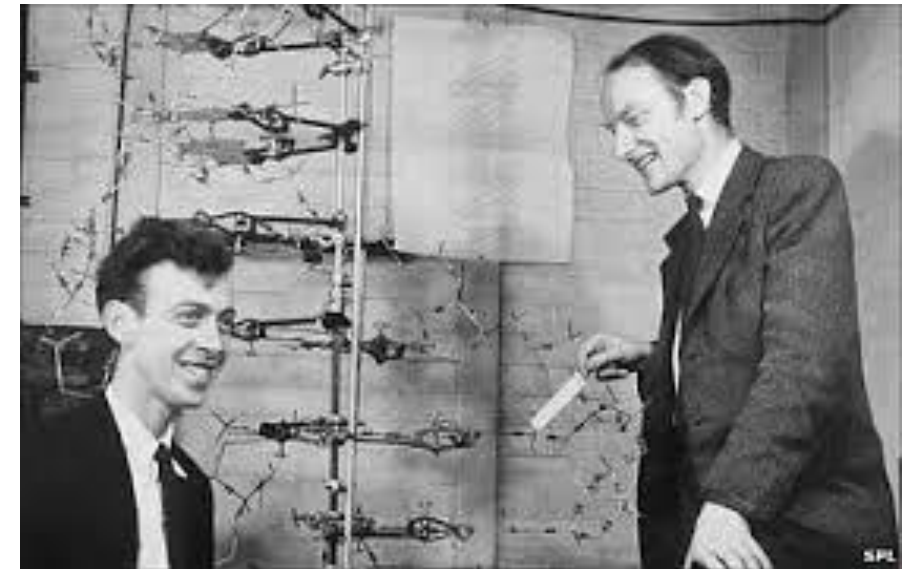
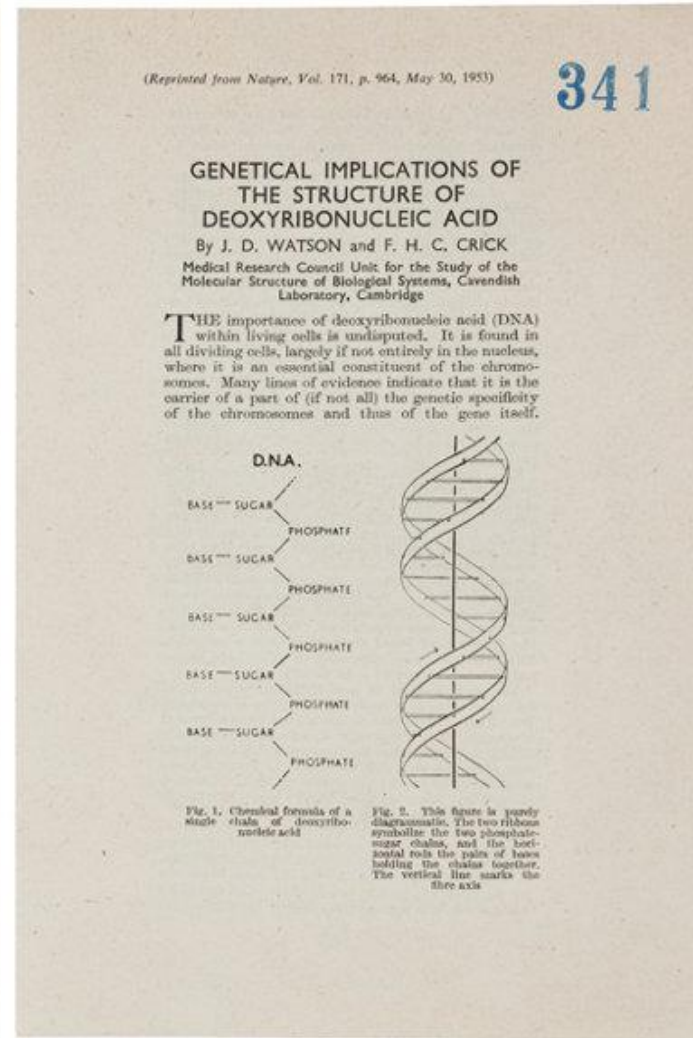
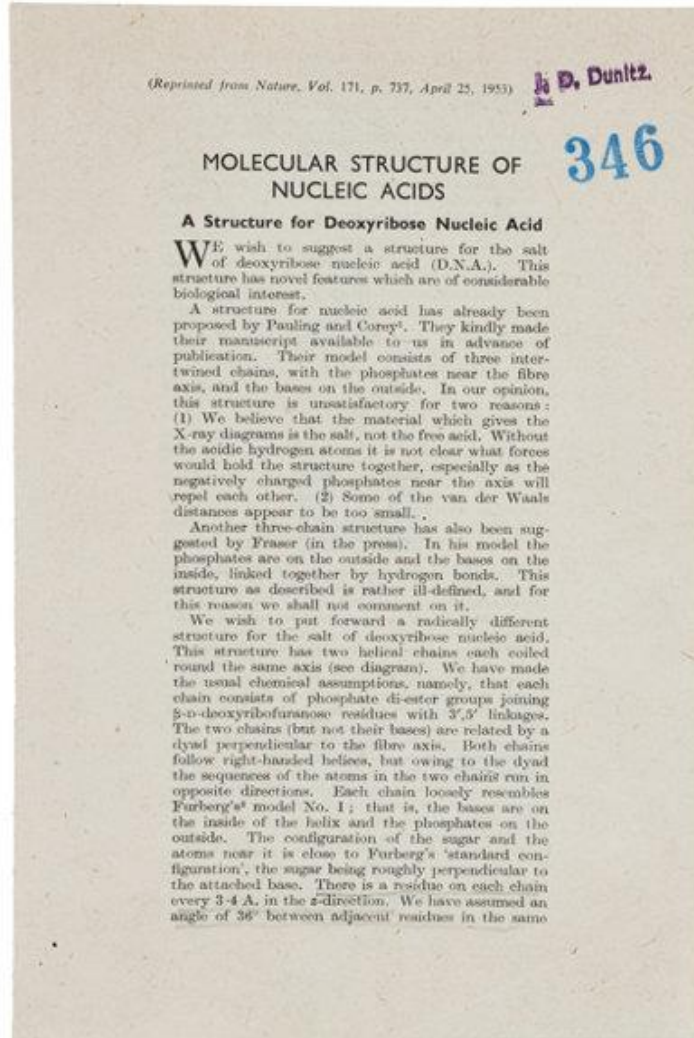




Watson (center), Crick (right) met McCartney (left)



Photograph 51, Maurice Wilkins showed





# Watson, Crick & Wilkins



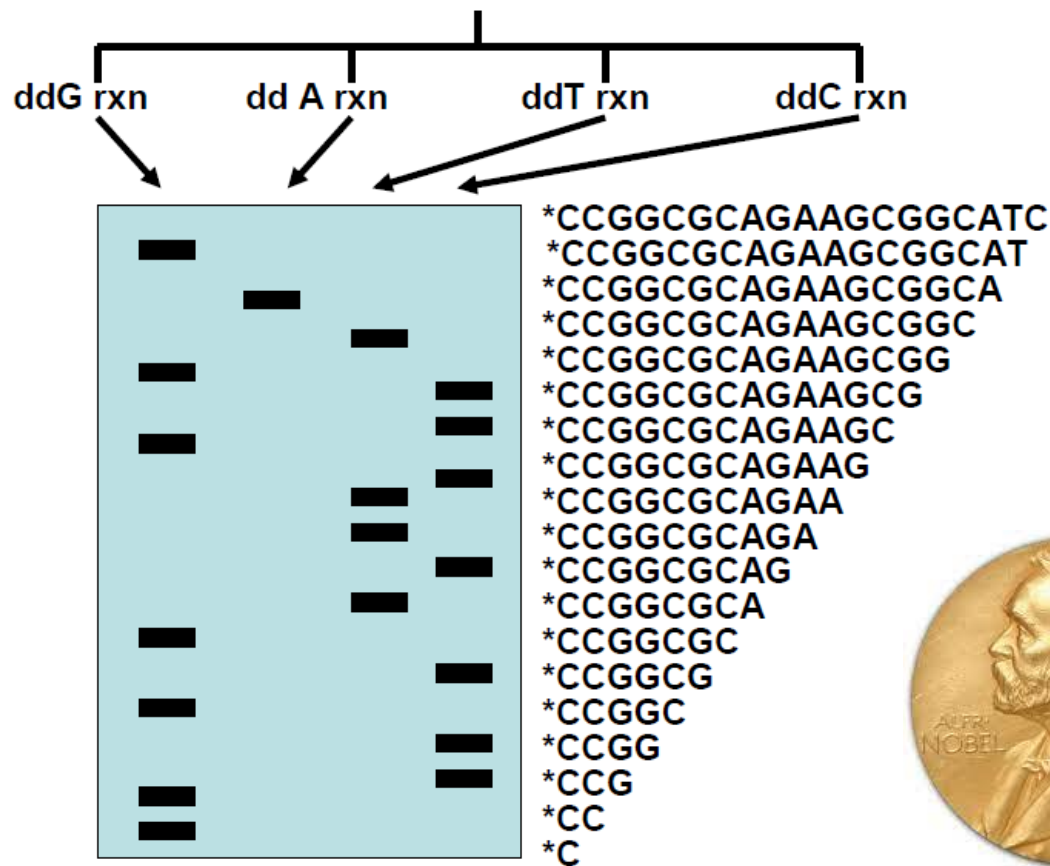
Nobel Prize for Physiology or Medicine in 1962

# Frederick Sanger (1918-2013)



Sanger (1844-1895)  
British Biochemist

5' pCpCpGpGpCpGpCpApGpApApGpCpGpGpCpApTpCpApGpCpApApA 3'

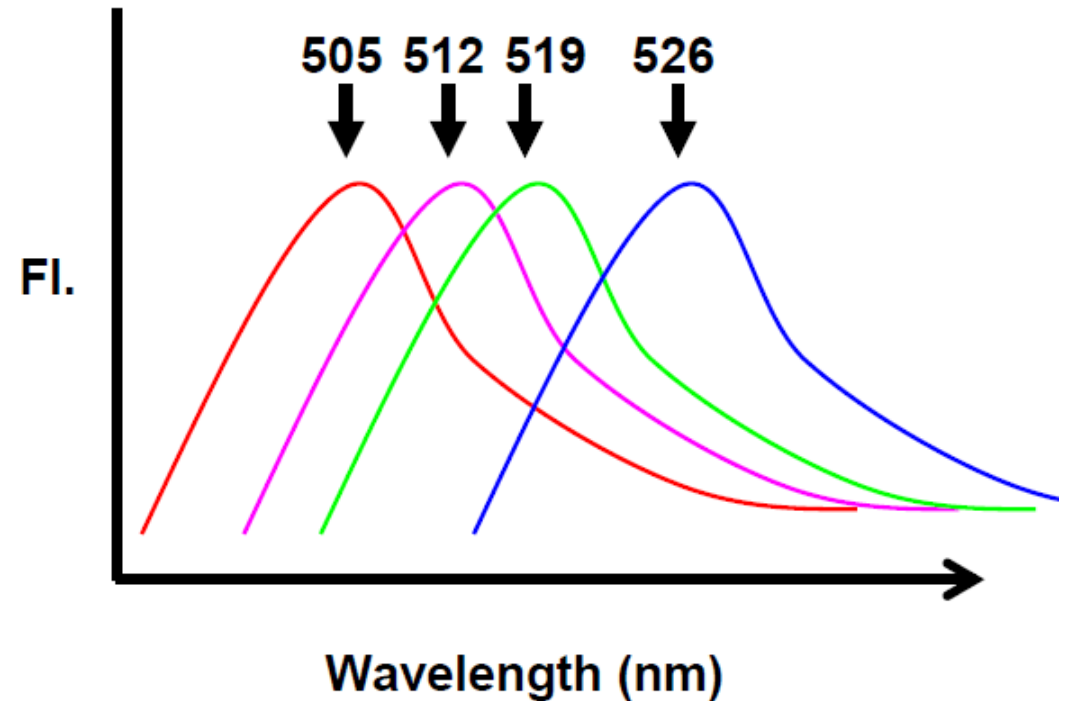


Sanger chain-termination sequencing in 1977  
Nobel Prize in Chemistry in 1980



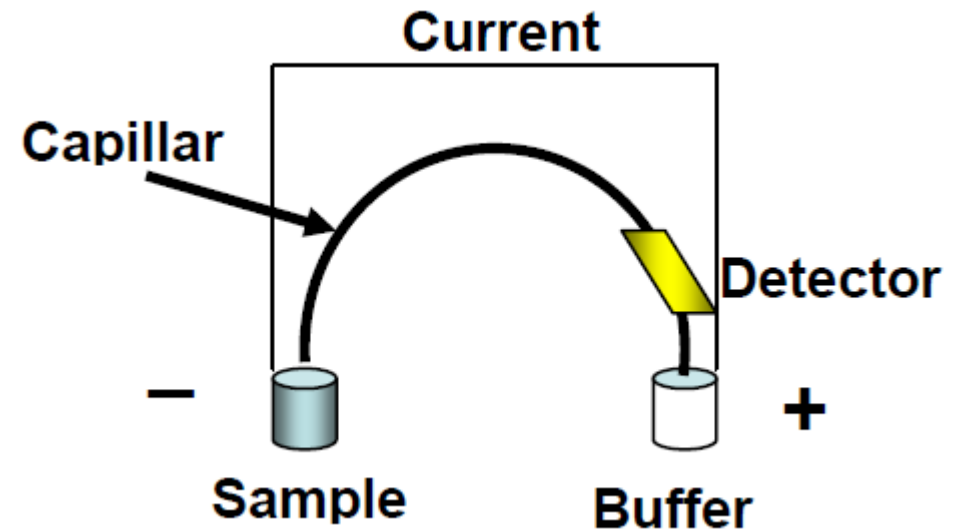
# Sanger sequencing: chemicals

- In 1986, Leroy Hood replaced radioactive labels with **fluorescent labels** in primers, which was commercialized in 1987 by Applied Biosystems (Nature, 321: 674–679).
- James Prober at DuPont labeled **the terminators** and improved dye sets, which were sold to Applied Biosystems later (Science, 238: 336–341).



# Sanger sequencing: gel system

- In 1990, Harold Swerdlow used **capillaries** to separate DNA (J Chromatogr, 516: 61–67), which was established in analytical chemistry in the late 1980s.
- In 1993, B.L. Karger et. al. used **a low viscosity non-cross-linked separation matrix** in capillaries (Anal Chem, 65: 2851–2858).





# The 1<sup>st</sup> automated sequencer



Model 370A launched in 1986  
by Applied Biosystems



Model 3700 launched in 1998  
by PE Biosystems

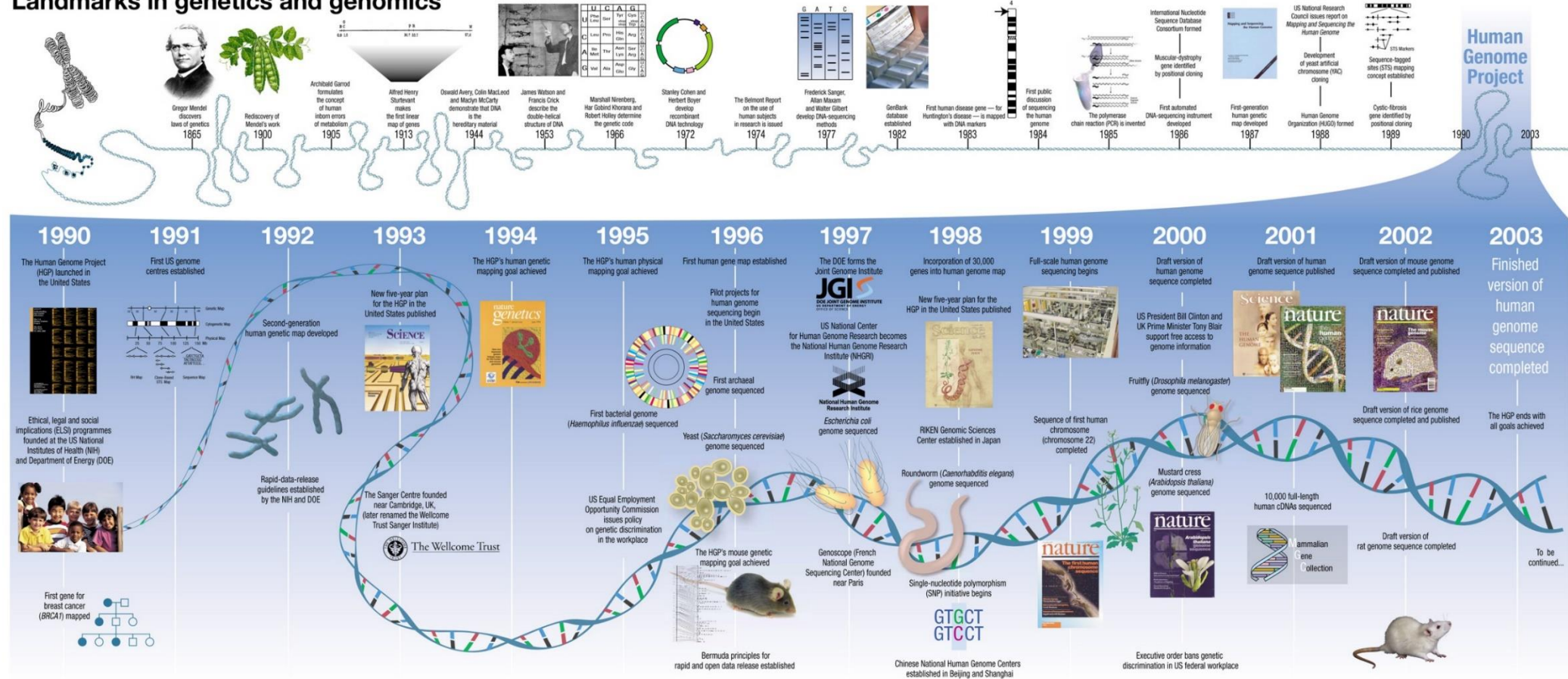
# Section II

# Human Genome Project



# Human Genome Project (1990-2003)

## Landmarks in genetics and genomics



DESIGN BY DARRYL LEA  
PLAN COURTESY J. BLAMIRE, CITY UNIV, NEW YORK; WATSON & CRICK COURTESY A. BARRINGTON BROWN/NPL; SCIENCE COVERS COURTESY AAAS

© 2003 Nature Publishing Group



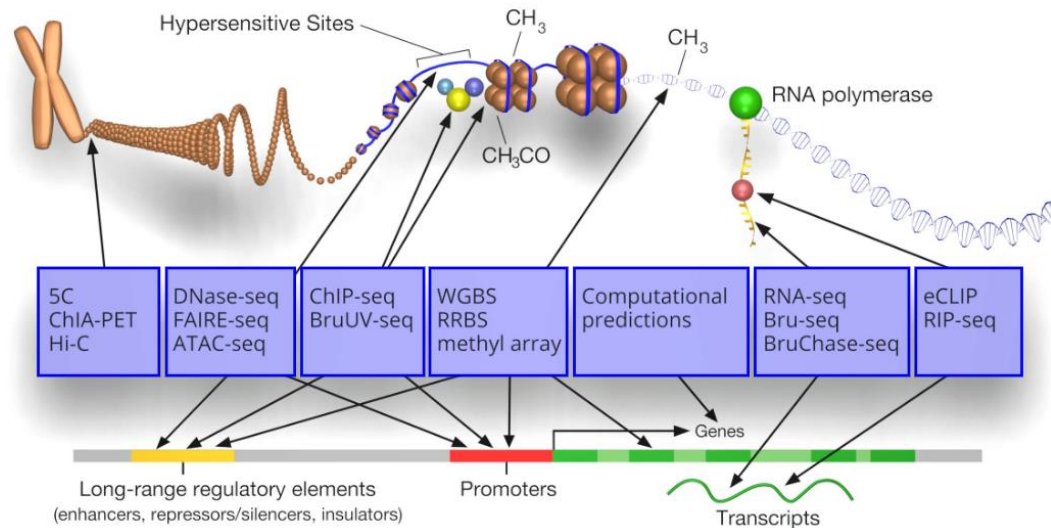
- A map of **haplotype blocks** and the tag SNPs that identify the haplotypes
- Enable to find genes and genetic variations that **affect health and disease**
- Associate a phenotype from the 10 million SNPs to roughly **500,000 tag SNPs**



# Human ENCODE project



- There have been genetic, evolutionary and **biochemical** approaches.
- The **ENCyclopedia Of DNA Elements** (ENCODE) launched by the US National Human Genome Research Institute (NHGRI) in September 2003
- ENCODE aims **to identify all functional, in a sense of genetic, evolutionary, or biochemical, elements** in the human genome.

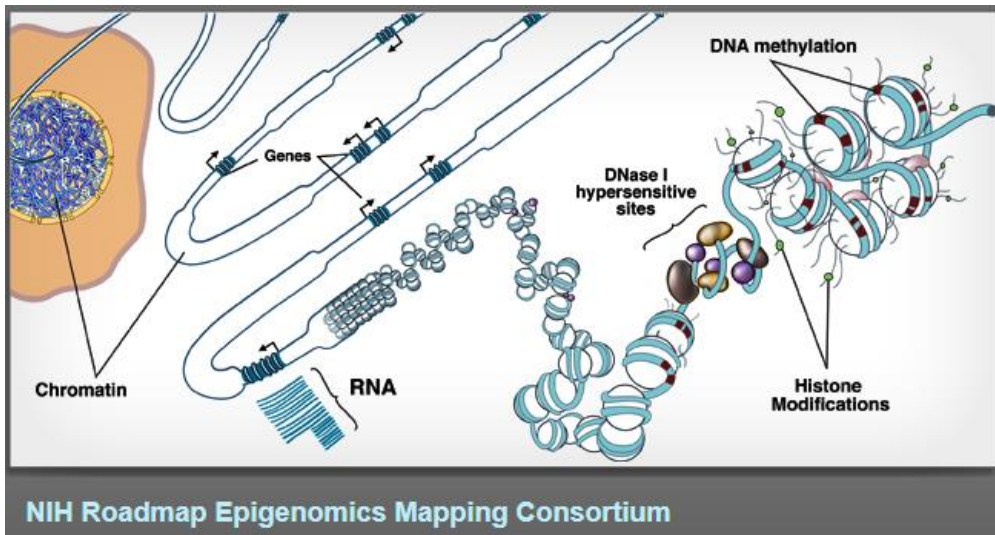


- The human genome is **pervasively transcribed**.
- Numerous previously unrecognized **transcription start sites** have been identified.
- DNA replication timing is correlated with **chromatin structure**.
- A total of 5% of the bases in the genome are under **evolutionary constraint** in mammals.
- Different functional elements vary greatly in their **sequence variability** across the human population.

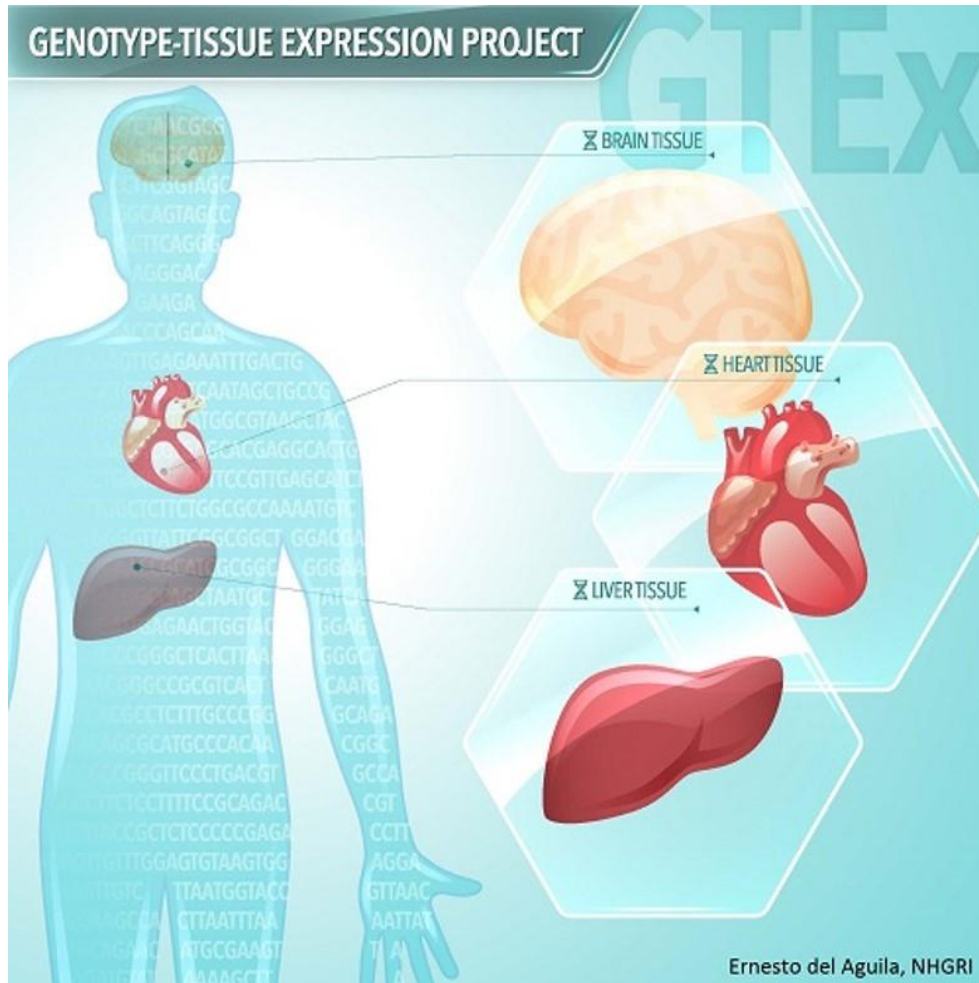


# Roadmap Epigenomics Project

- The NIH Roadmap Epigenomics Mapping Consortium was launched with the goal of producing a public resource of human epigenomic data to catalyze basic biology and disease-oriented research.



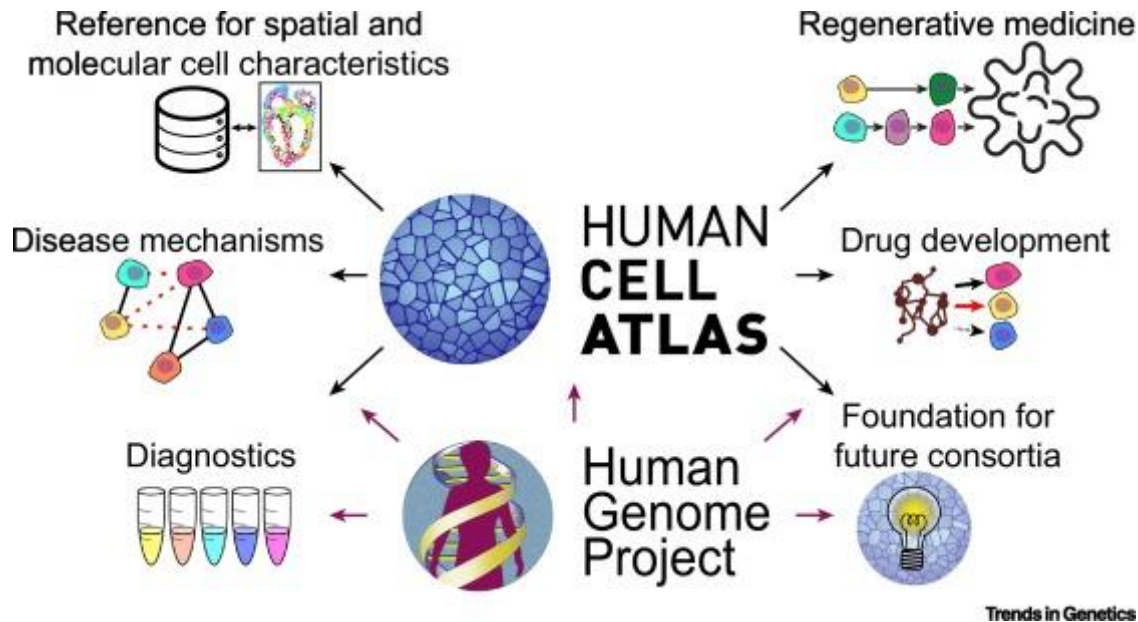
# BGI华大 Genotype-Tissue Expression Project (GTEx)



- The aim is to increase our understanding of how changes in our genes contribute to common human diseases, in order to improve health care for future generations.
- On Sept. 11, 2020, the final set of analyses from the GTEx Consortium were published in Science.

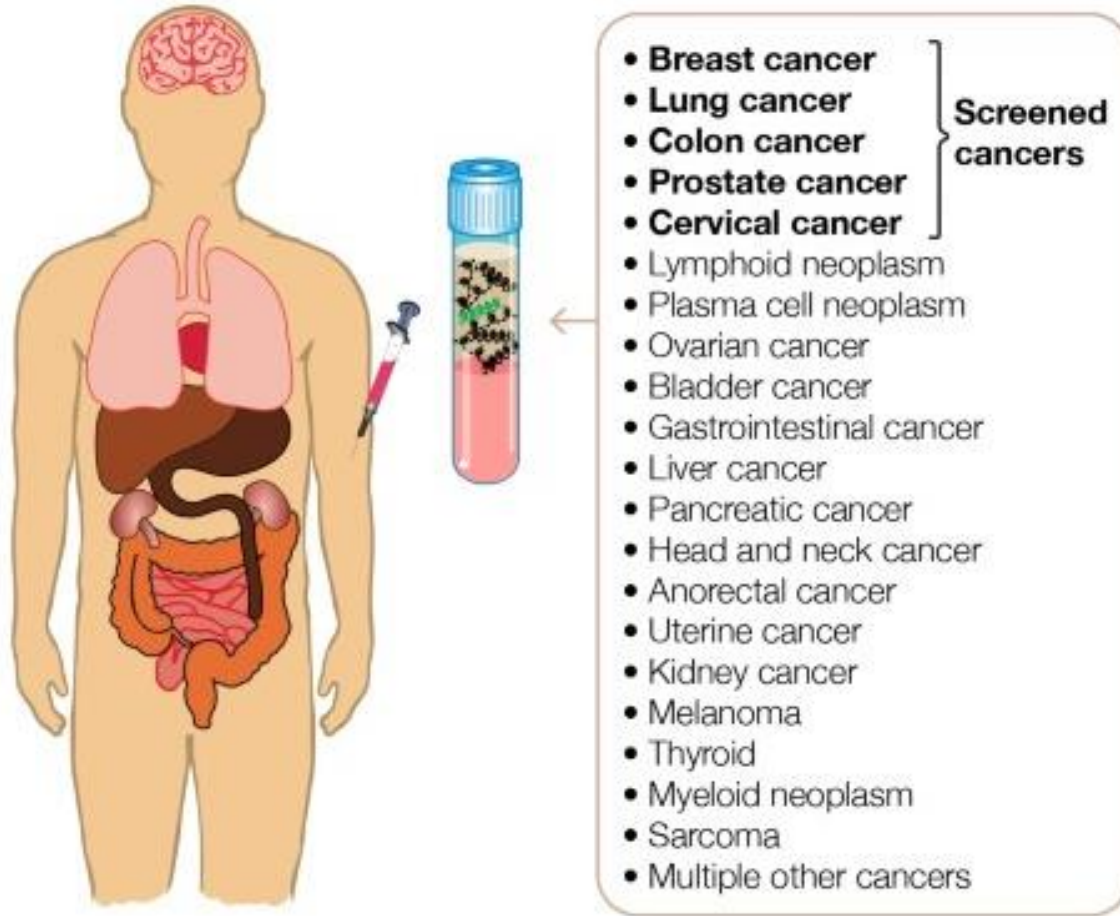


# Human Cell Atlas Project

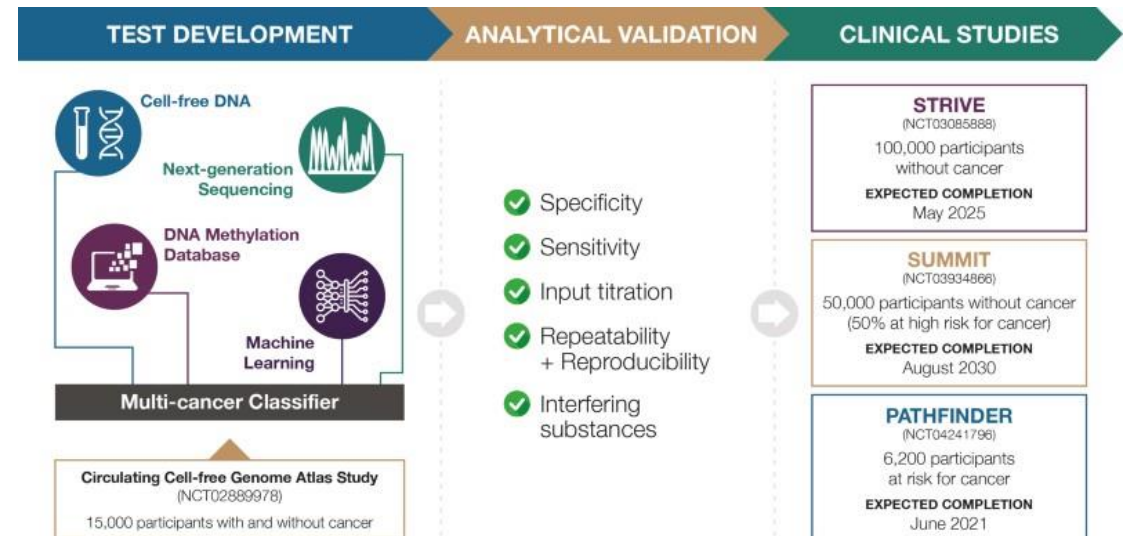


- To create cellular reference maps with **the position, function and characteristics** of every cell type in the body.
- Co-founded in 2016 by Dr Aviv Regev at the Broad Institute of MIT and Harvard (USA), and Dr Sarah Teichmann at the Wellcome Sanger Institute (UK). Now the global initiative has grown to encompass more than 2,200 members from over 75 countries around the world.

“One test-many cancers” approach

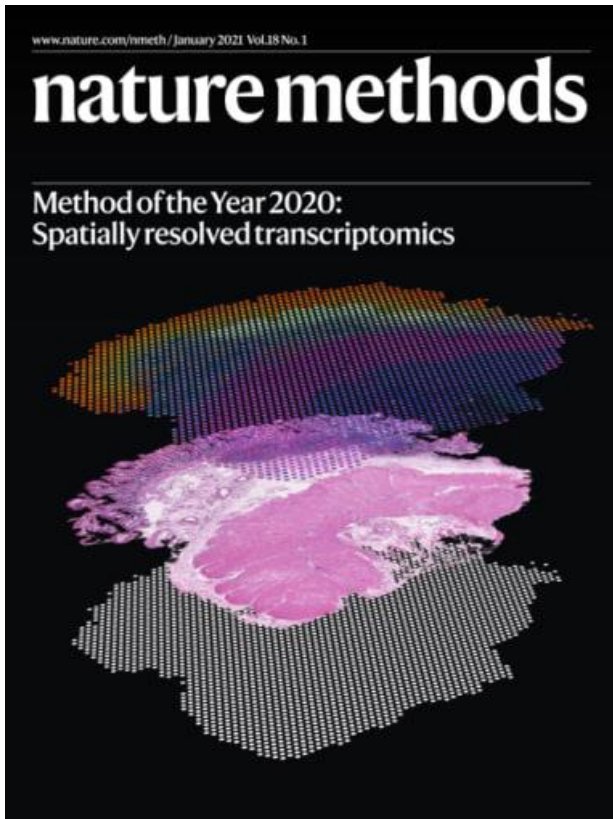


- The mission of the company is to detect cancer early, when it can be cured.
- Galleri™, a simple blood test that can detect over 50 types of cancers.





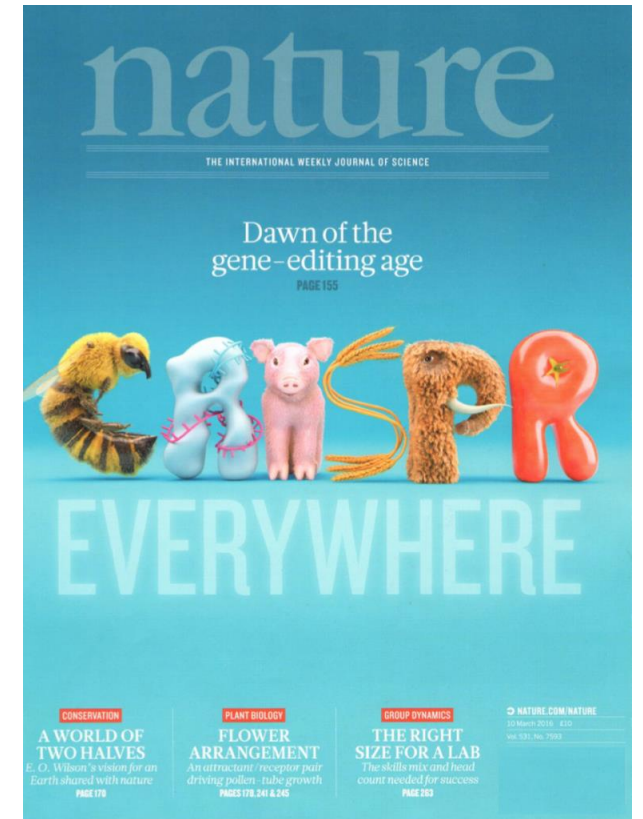
# Human genomics nowadays



Tempo-spatial omics



Large population



Genome editing

# Questions?

OMICS FOR ALL  
基因科技造福人类

华大生命科学研究院  
**BGI** • research