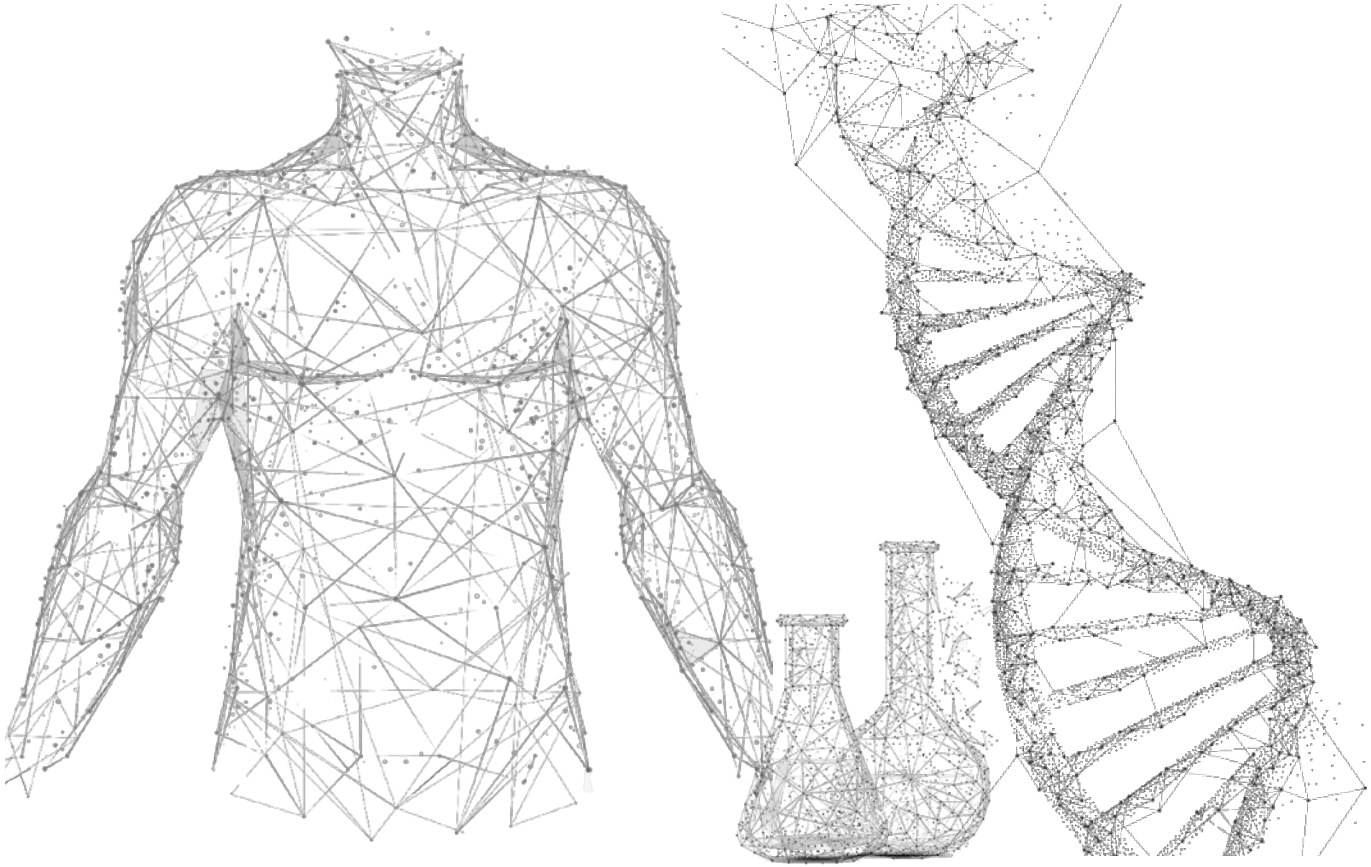


History and Dogma of Molecular Biology

San Luis Potosi State University (UASLP) Mexico
Molecular Biology Course, Faculty of Medicine graduate program

Dr. Christian A. García-Sepúlveda

Viral & Human Genomics BSL-3 Laboratory

Last updated January 21, 2025 v3

Genomes

Genomes must possess several key properties to effectively carry out their functions:

1. **Information Storage:** Must store genetic information in a stable and accessible form, including instructions needed for development, functioning, growth, & reproduction of organisms.

2. **Fidelity of Replication:** Must allow accurate replication during to ensure that genetic information is faithfully passed from one generation to the next.

3. **Capacity for Variation:** While maintaining stability, genomes must also have capacity for variation, allowing for evolution and adaptation (mutations, recombination, etc.)

4. **Regulation of Expression:** Must be able to vary expression of genes in response to internal and external signals.

Genomes

5. Compaction and Organization: Must allow condensation to fit within the nucleus or nucleoid while still being functional (replication, transcription & repair).

6. Repair and Maintenance: Must have mechanisms to maintain integrity and repair damage induced by replication or environmental factors (UV radiation or chemicals).

7. Transmission: Must allow transmission from one generation to the next, ensuring continuity of genetic information (replication and segregation)

8. Functional Redundancy: Might allow for multiple backup copies of essential genes to ensure that critical functions can still be performed.

These properties are crucial for the survival, adaptation, and evolution of living organisms.

Selfish gene theory

Teleology

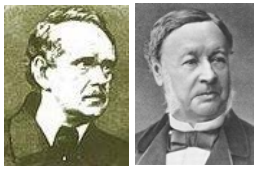
From Greek τέλος, -εος télos, -eos 'end' and -logy.

1. feminine. Philosophy. Doctrine of final causes.

Branch of metaphysics that refers to the study of the ends or purposes of an object or being, or literally, to the philosophical doctrine of final causes.

Reference here

History



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Fin inquisición
(1834)

Invasion Francesa
(1861-67)

I GM
(1914-18)

IIGM
(1939-45)

Apollo
(1969)

Today

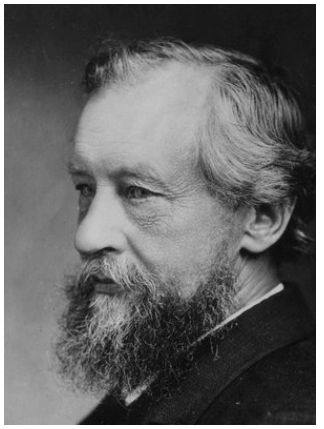
Gregor Johann Mendel (1822-1884)

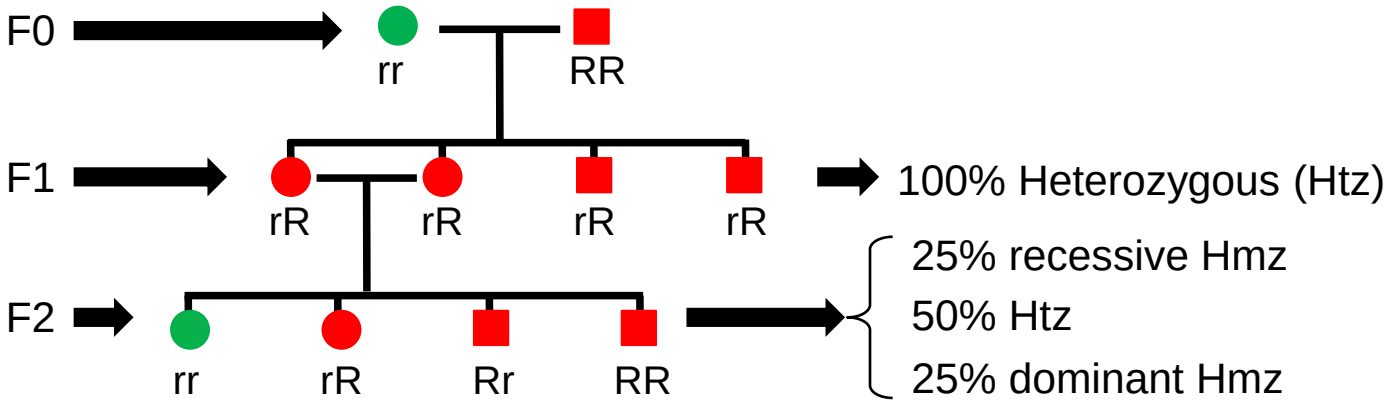
Monrovian Augustinian monk considered the father of modern genetics.

Described patterns of inheritance of traits from his selective breeding of peas (Mendelian laws).

Published his “Experiments on Plant Hybridization” in the Proceedings of the Natural History Society of Brünn.

Rediscovered in 1900 by Hugo de Vries and Carl Correns.





Gregor Johann Mendel (1822-1884)

His work laid the foundation for the field of genetics, and described main concepts:

1. Concept of Unit Factors (Genes):
   Mendel proposed "unit factors" (now known as genes) as genotype.

2. Alleles:
   Each individual has two alleles (gene variants) for a particular trait, one inherited from each parent

3. Law of Segregation:
   Alleles separate individually, each gamete carries only one allele for each trait.

4. Law of Independent Assortment:
   Different traits are inherited independently of each other.

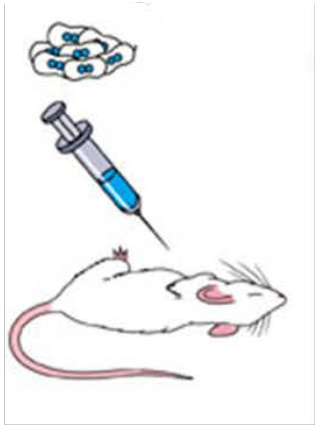
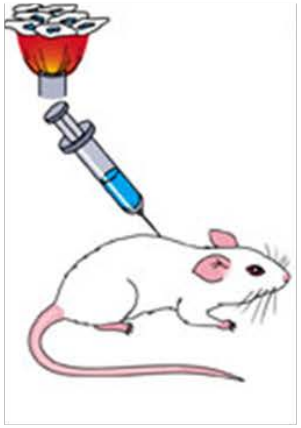
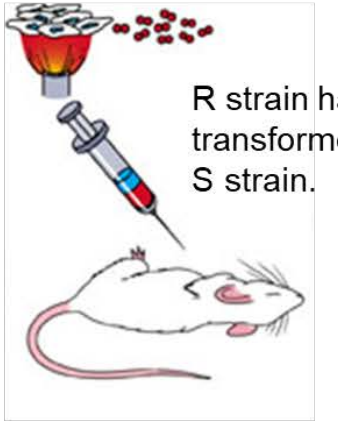
5. Dominance and Recessiveness:
   Dominant traits mask the expression of other traits, which are recessive.

Frederick Griffith (1879 - 1941)

British bacteriologist working on epidemiology and pathology of bacterial pneumonia.

Discovered an unidentified transforming principle (1928).

Griffith's experiment demonstrated that genetic material was transferable.

Live encapsulated virulent bacteria (S strain).	Live non-encapsulated avirulent bacteria (R strain).	Dead encapsulated virulent bacteria (S strain).	Dead virulent bacteria (S strain) mixed with live avirulent bacteria (R strain).
			 R strain has been transformed into S strain.

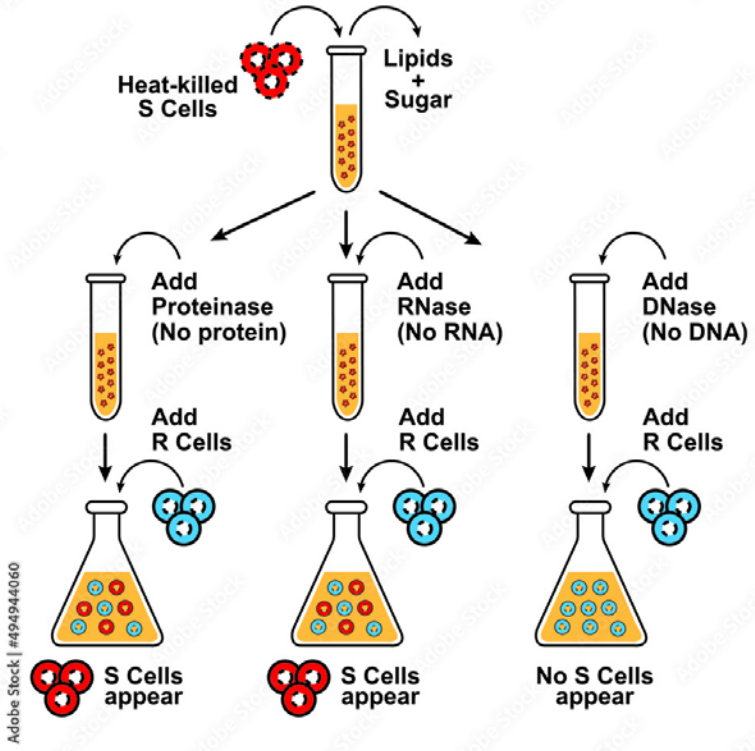
Avery-MacLeod-McCarty (1944)

Discovered that DNA is the bacterial transforming principle.

It had been widely believed that proteins carried genetic information.

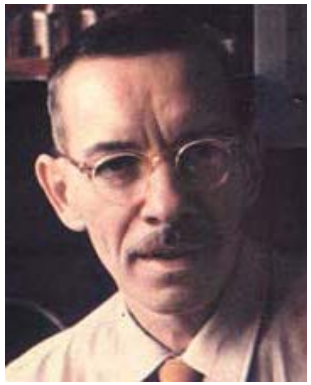
There was considerable reluctance to accept the conclusion that DNA was the genetic material.

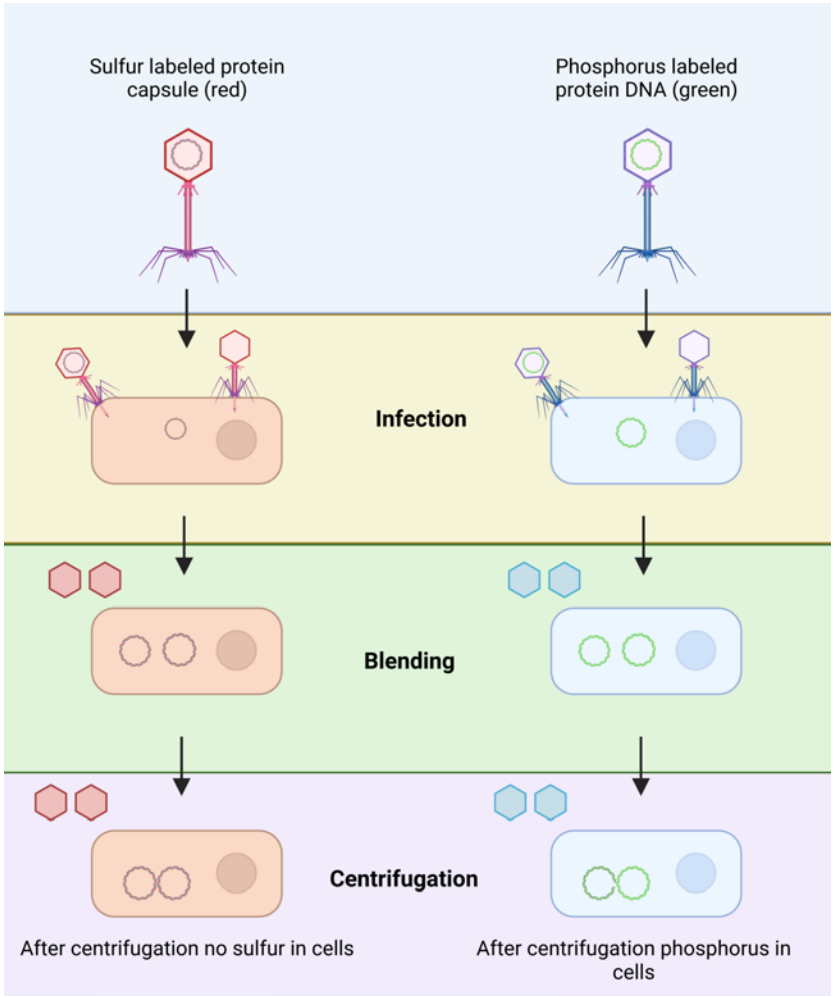
Largely neglected by much of the scientific community.



Rosalind Franklin–Maurice Wilkins (1953)


They provided further evidence that DNA was the transferable genetic material.



While DNA had been discovered in 1869, many scientists still assumed proteins carried inheritance information.

They used a model of bacteriophage T2 (a virus that infects bacteria) and radiolabels to show that DNA was transferred from the phage to the bacteria.

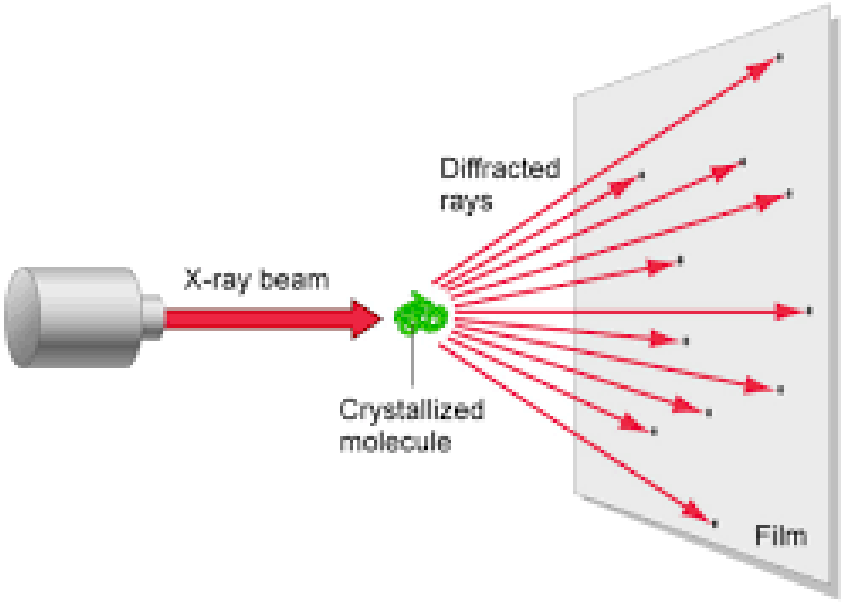
Rosalind Franklin–Maurice Wilkins (1953)

Worked with X-ray diffraction crystallography.

Produced clear "B form" X-shaped images from squid sperm.

Wilkins, Crick, and Watson were awarded the 1962 Nobel Prize for Physiology or Medicine.

Franklin died of ovarian cancer at the age of 37 in 1958.



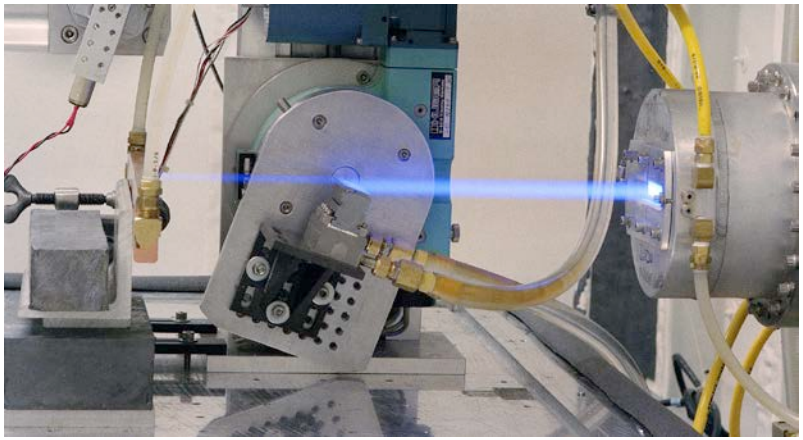
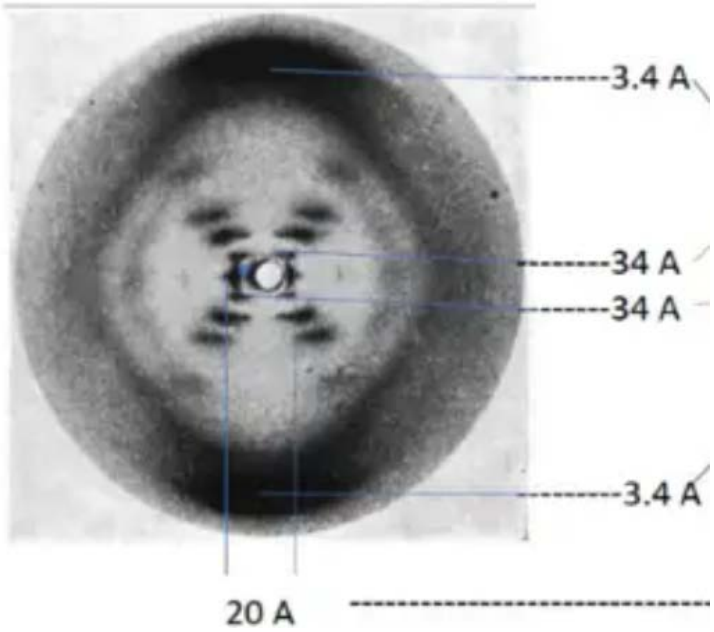


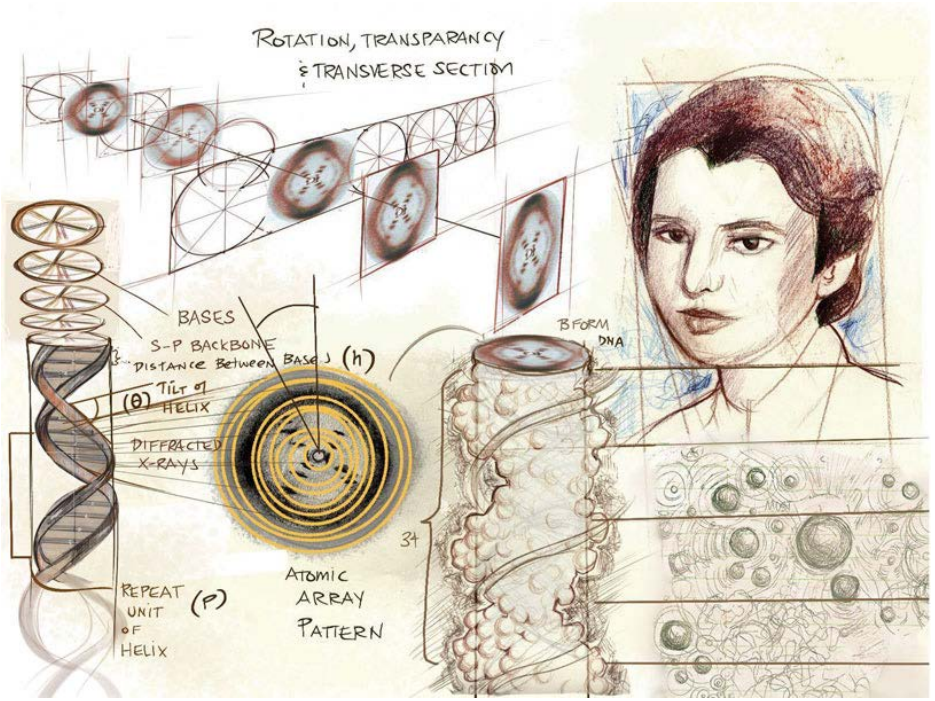
Photo 51

X-ray diffraction image of high-quality "B" form paracrystalline DNA gel.

Taken by Raymond Gosling, Wilkin's postgraduate student at King's College London.

Max Perutz, without Franklin's knowledge or permission, provided Watson an unpublished progress report containing X-ray diffraction images that proved crucial at allowing modelling of DNA's double-helix structure.





Caryn Babaian, Deconstructing DNA Beyond the Helix. American Scientist, March 2024

James Watson- Francis Crick (1952)

X-ray diffraction image of high-quality "B" form paracrystalline DNA gel.

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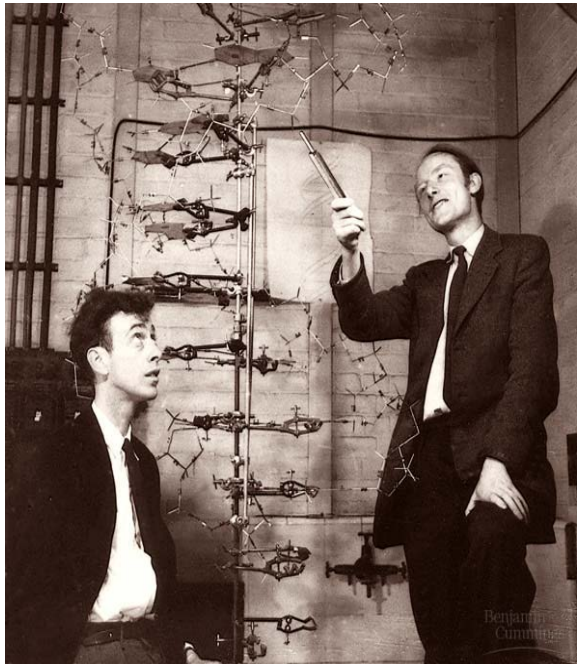
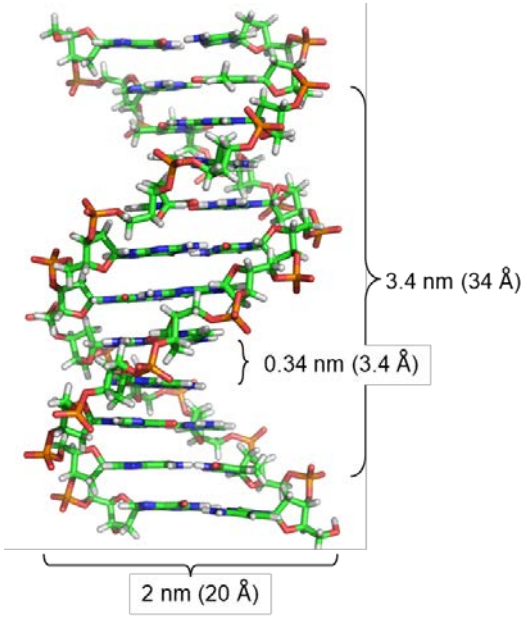
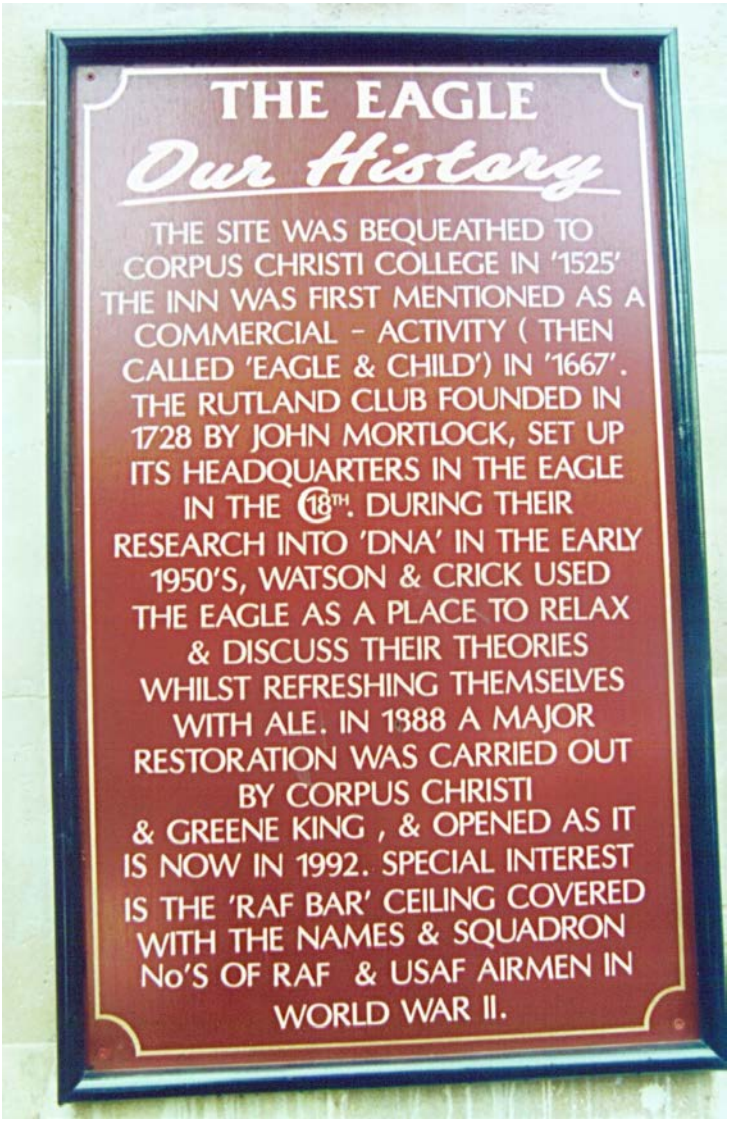
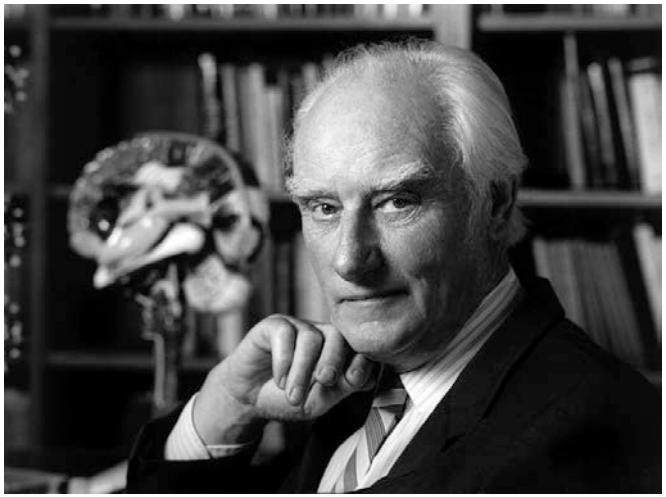




“The Eagle Pub” Cambridge, England UKGB



Sir Francis Crick



Important theoretical molecular biologist .

The genetic code.

Central dogma.

Important contributions to theoretical neurobiology

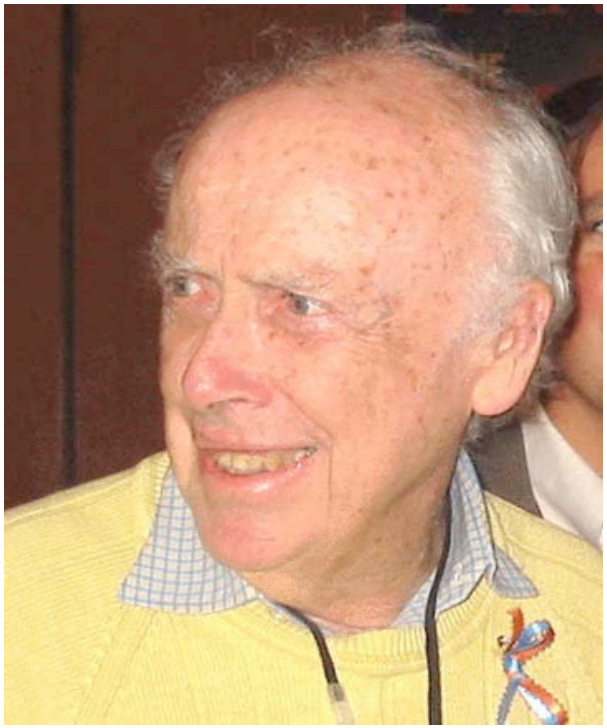
Advance the scientific study of human consciousness.

Icosahedral symetry of viruses.

Protein translation.

mRNA, tRNA

James Watson



• Genetic screening and genetic engineering to cure “stupidity” and “make all girls pretty”.

•“Gene defining homosexuality of a child and his mother right to abort him”

•“On the issue of obesity, Watson was quoted as saying: "Whenever you interview fat people, you feel bad, because you know you're not going to hire them.”

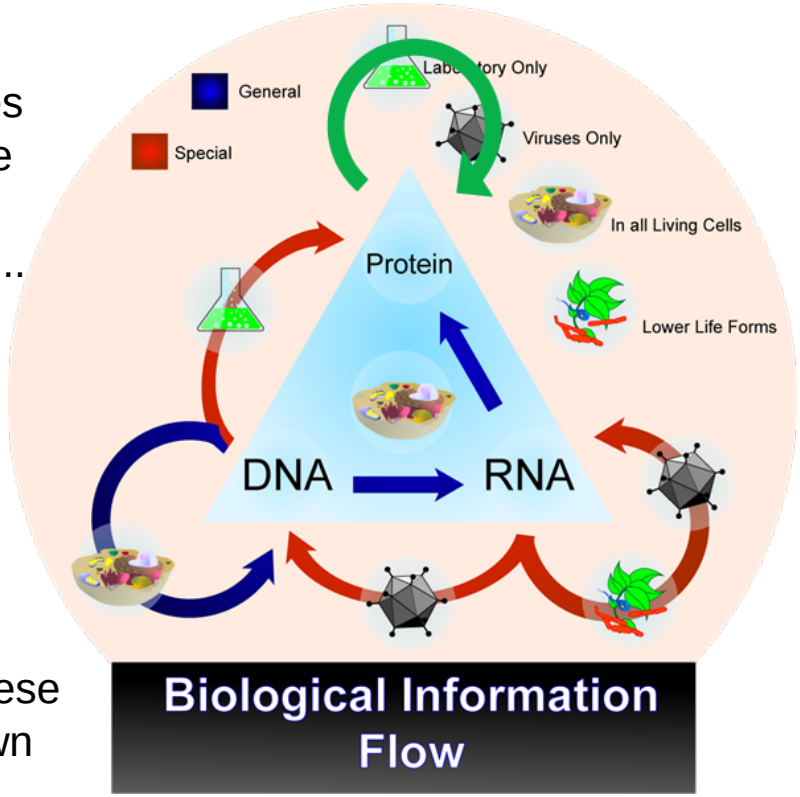
• Suggested a link between skin color and sex drive “Latin lovers vs English patients.”

• “I am gloomy about the prospect of Africa because our social policies are based on the fact that their intelligence is the same as ours

The dogma of molecular biology

Proposed by Francis Crick in 1958 and rethought in 1970.

As in the dogma of faith, it corresponds to a set of rules or beliefs essential to understanding the concept of the flow of genetic information through biopolymers and in living organisms (according to our current knowledge)...



3x3

Proposes **3** classes of **biopolymers**: DNA, RNA and polypeptides.

Proposes **3 modes** of information transfer between these biopolymers: general mode, special mode and unknown improbable mode.

Each mode has **3** transfer **directions**

The dogma of molecular biology

The three general directions are:
DNA to DNA (Replication).
DNA to RNA (Transcription).
RNA to AA (Translation).

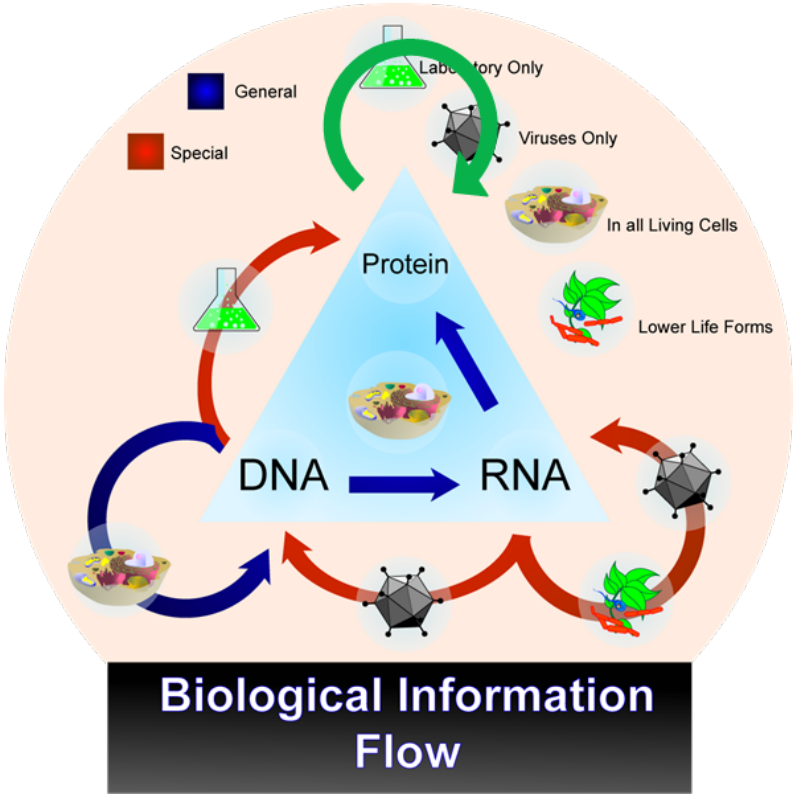
They occur normally in most cells.

The three special directions are:
RNA to RNA (RNA Replication).
RNA to DNA (Reverse transcription).
DNA to AA (Only in vitro).

They occur in extraordinary ways, but they do occur.

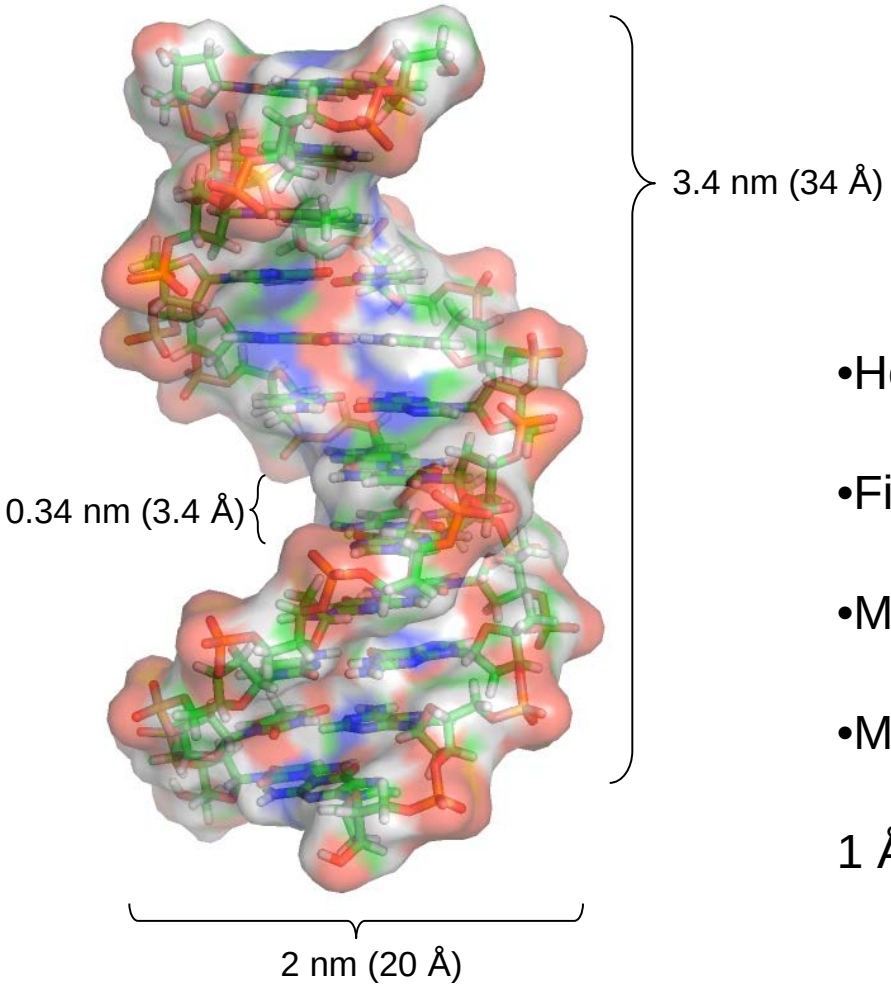
The three unknown directions are:
AA to DNA (Intelligent evolution).
AA to RNA (Another form of intelligent evolution).
AA to AA (NOTE: prions).

It is currently thought that they never occur.



James Watson & Francis Crick

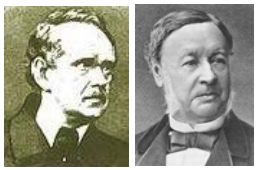
Refined DNA duplex model (dodecamer)



- Helicoidal structure
- Filamentous molecule
- Minor repeat units 0.34 nm (3.4 Å)
- Major repeat unit 3.4 nm (34 Å)

1 Ångström = 0.1 nanometer

Timeline update



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I GM
(1914-18)

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Apollo
(1969)

Today

Sir Fred Sanger (1918-2013)

One of five researchers to have received two Nobel Prizes

Commander of the Order of the British Empire (CBE)

Fred Sanger	Chem 1958	Chem 1980
	Insulin aa sequence	DNA sequencing method

Introduced "dideoxy" chain-termination method for DNA sequencing.

First researcher to sequence a complete genome (Phage φ-X174).

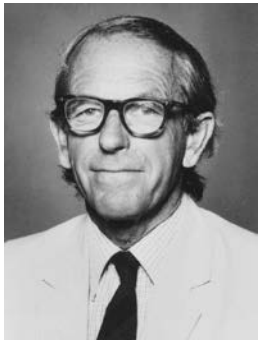
Sangers rule “... anytime you get technical development that’s two to threefold or more efficient, accurate, cheaper, a whole range of experiments opens up.”

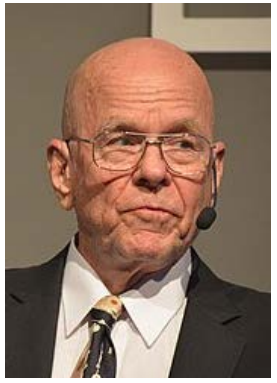
The Wellcome Trust Sanger Institute (formerly the Sanger Centre) is named in his honour.

Double Nobel Laureates

One of five researchers to have received two Nobel Prizes

Marie Curie:	Phys 1903 Radioactivity	Chem 1911 Radium/Polonium
Linus Pauling	Phys 1954 Chemical Bonds	Peace 1962 Anti-nuclear proliferation
John Bardeen	Phys 1956 Transistor	Chem 1972 Superconductivity
Fred Sanger	Chem 1958 Insulin aa sequence	Chem 1980 DNA sequencing
Kary Sharpless	Chem 2001 Stereoselective Rx.	Chem 2022 Click chemistry





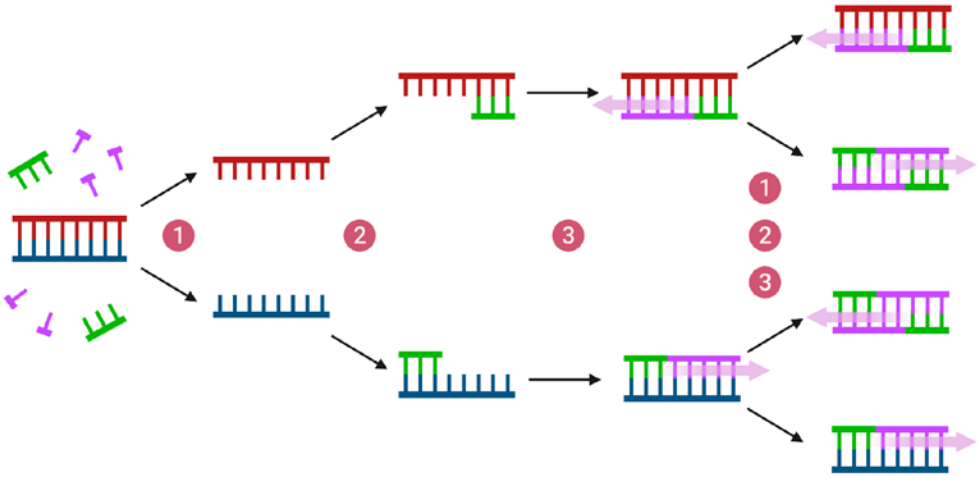
Kary Mullis (1944 – 2019)

American biochemist won the Nobel Prize (1993).

Invention of Polymerase Chain Reaction (PCR) based DNA amplification in 1983.

PCR became a critical tool for biochemistry and molecular biology.

Also suffered from Nobel disease: Mullis downplayed humans' role in climate change, doubted HIV caused AIDS, and believed in astrology/paranormal.



Credited his 1960's LSD experiences as having a significant impact on his creativity and problem-solving abilities.

Haemophilus influenza (1995)

First bacteria to be sequenced

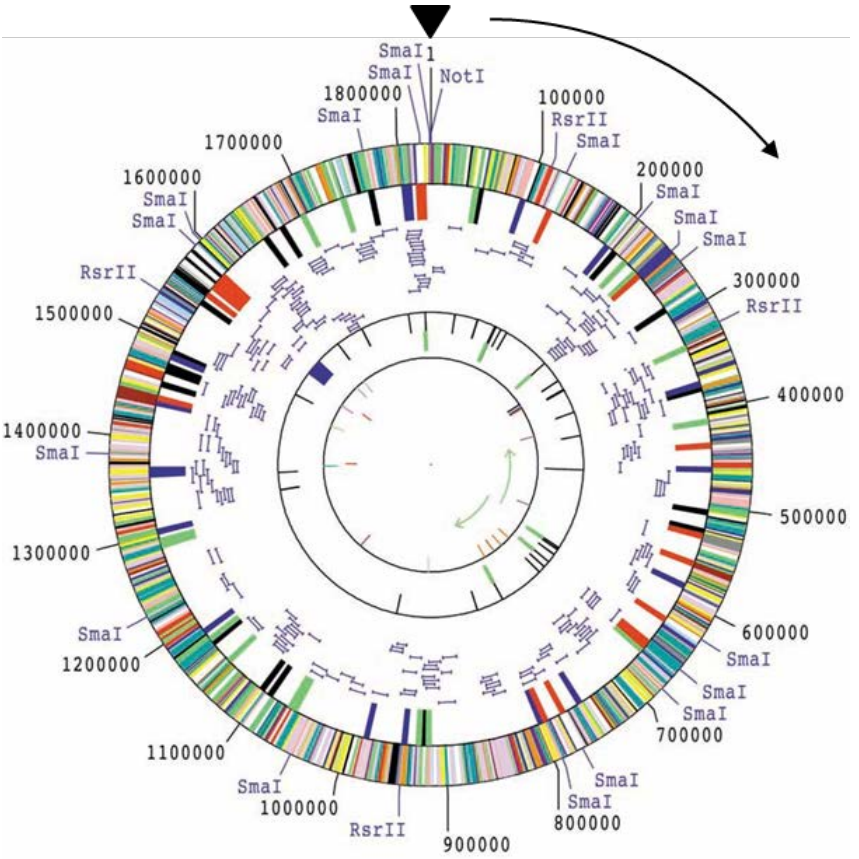
Non-motile Coccobacillus G-Neg

Discovered in 1892 Pfeiffer

Thought to be responsible for influenza

Causes bacteremia, meningitis, cellulitis, osteomyelitis, epiglottitis.

First free-living organism to be sequenced



Small genome:

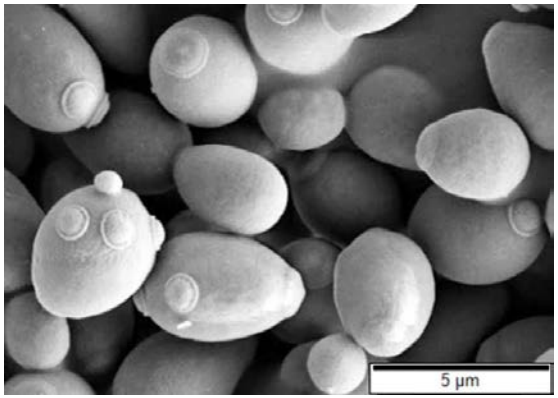
1,830,140 bases

1740 genes

Institute for Genomic Research

Published in Science

Saccharomyces cerevisiae (1996)



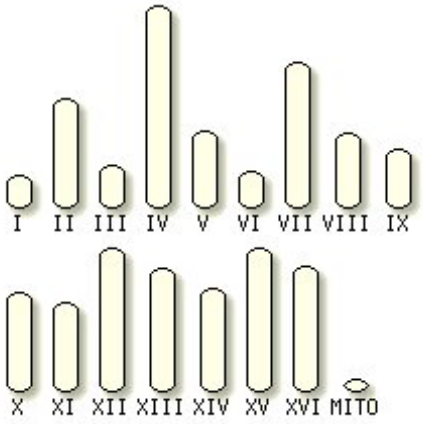
First eukaryote to be sequenced

Saccharomyces cerevisiae (5-10 µM)

Dust that covers grapes

Most studied eukaryotic organism by MolBio and CellBio (E. coli is the most studied prokaryote).

Forms buds.



Complex genome:

13,000,000 bases

6,275 genes (only 5,800 functional)

23% Genomic homology with HoSa

And the most important of course...Beer, Biere, Birra, Brujaja, Cheve.

Common taxonomic abbreviations

Homo sapiens – HoSa

Escherichia coli – EcCo

Saccharomyces cerevisiae – SaCe

Mus musculus – MuMu

Caenorhabditis elegans – CaEl

Drosophila melanogaster – DrMe

Arabidopsis thaliana – ArTh

Danio rerio – DaRe

Bos taurus – BoTa

Rattus norvegicus – RaNo

Pan troglodytes – PaTr

Gorilla gorilla – GoGo

Pongo pygmaeus – PoPy

Macaca mulatta – MaMu

Pan paniscus (bonobo) – PaPa

Callithrix jacchus (marmoset) – CaJa

Papio anubis (baboon) – PaAn

Saimiri sciureus (squirrel monkey) – SaSc

Aotus nancymaae (night monkey) – AoNa

Gallus gallus – GaGa

Canis lupus familiaris – CaLu

FaFelis catus – FeCa

Oryctolagus cuniculus (rabbit) – OrCu

Sus scrofa – SuSc

Equus caballus – EqCa

Ceanorhabditis elegans (1998)

First nematode & metazoan to be sequenced

1 mm length

Model CellBio, MolBio, DevBio.

5 pairs of autosomes and one sexual pair

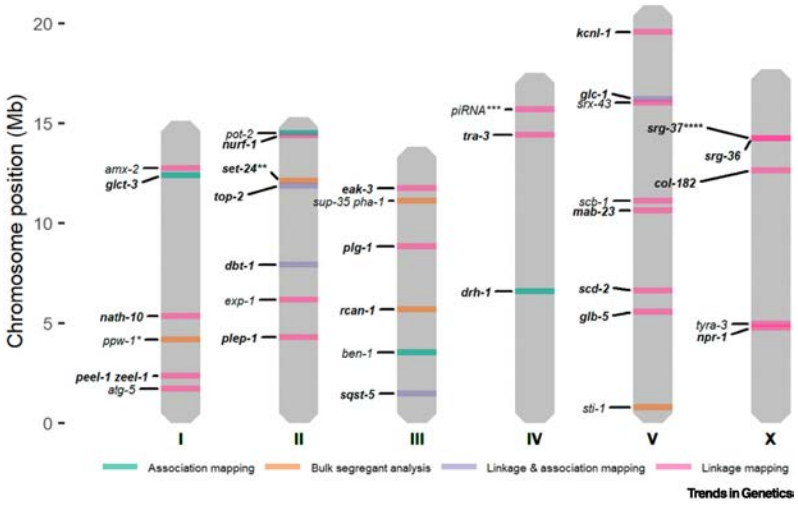
Easy reproduction and freezable

The development of its 1031 somatic cells has been mapped and the network of its 302 neurons as well.

Model for the study of nicotine dependence

100'000,000 bases and 20,000 genes

Only survivor of 2003 STS-107 (Columbia) re-entry.



Human Genome Project: Chromsome 22

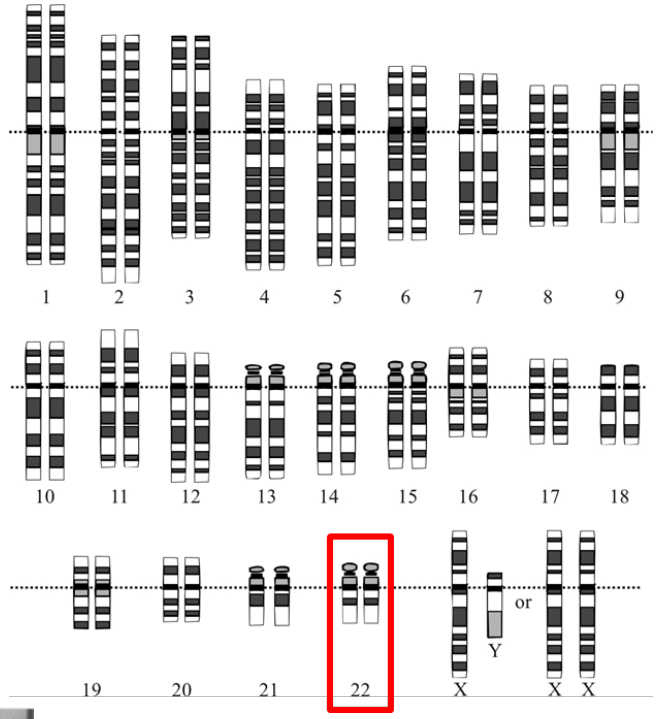
First human chromosome to be sequenced

Second smallest chromosome (see 21)

49 x10^6 bases

1.5 – 2.0 % total human DNA

Contains between 500 and 800 genes



Mutations in this chromosome cause:

- Amyotrophic Lateral Sclerosis
- Breast Cancer
- Neurofibromatosis type 2
- Possibly autism

Drosophila melanogaster (2000)

First insect to be sequenced

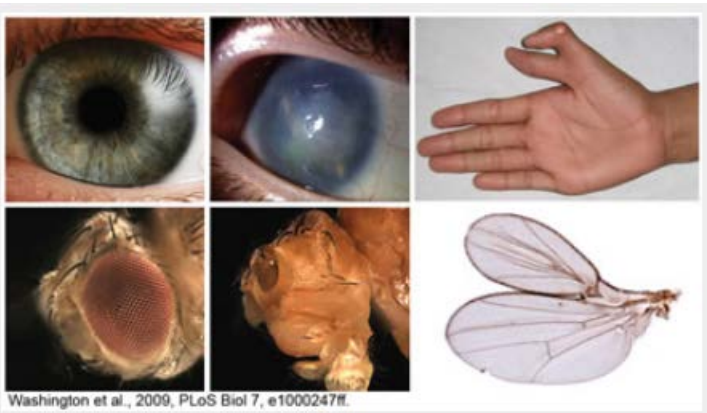
Drosophila melanogaster (2.5 mm)

BioMol, BioCel, Gene, Physio, BioDes model:

- Small
- Propagatable (>800 eggs/day)
- Short incubation (2 weeks)
- Giant chromosomes (puffs)
- Three autosomes and one sexual pair
- 132 x10^6 bases

13,767 protein-coding genes (20% of its genome)

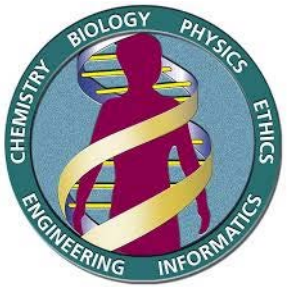
More than 60% of its genome encodes non-expressed functional DNA (regulator of gene expression).



Related genes of flies and humans link to related diseases (*left: loss of retina/eye upon loss of Pax6; right: upregulation of hedgehog in the anterior limb causes duplications*)

droso4public.wordpress.com

Human Genome Project



In 1984, the US DOE proposes HGP.

In 1990, the US government grants 3 x 10^9 USD.

International effort (EU, UK, Germany, France, Japan and China).

Objective of the project: map location of the 100,000 human genes thought to exist.

First draft ready by 2000, final version ready in 2006.

3x10^9 nucleotide bases.

20,000–25,000 genes not 100,000.

92% of the genome (telomeres and centromeres not included).

Humans share about 99.9% of their DNA.

Human Genome Project

The most extraordinary promise of the project: A MEDICAL REVOLUTION!

Knowing the sequence of the human genome would allow us to eliminate most of the diseases that plague humanity.

Let us remember that genetics intervenes in every pathology as part of the ecological triad.

Furthermore, the economic benefits would be immeasurable, reducing the cost of medical care, treatment, prevention and rehabilitation of diseases.


SPECIAL SECTION COMPLETING THE HUMAN GENOME

RESEARCH ARTICLE

HUMAN GENOMICS

The complete sequence of a human genome

www.science.org/doi/pdf/10.1126/science.abj6987

Laboratorio de Genómica Viral y Humana

Instalaciones de Alta Contención Biológica Nivel de Bioseguridad 3 (BSL-3) CDC-certificadas

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