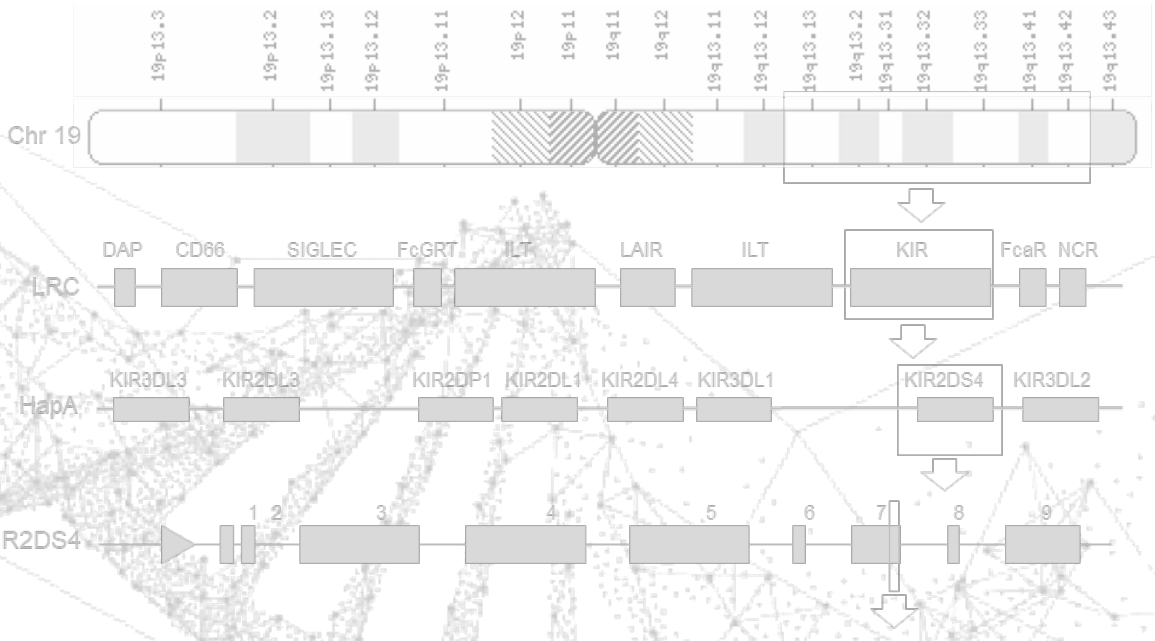


History of Molecular Biology

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

Dr. Christian A. García-Sepúlveda

Viral & Human Genomics BSL-3 Laboratory

Last updated October 18, 2024 v1

Timeline

Shleiden / Schwann
Cellular biology
(1839)


Brown
Nucleous
(1833)


Mendel
Inheritance
(1866)


Miescher
Nuclein
(1869)


Morgan
Cromosomas
Drosophila
(1911)


Levene
A, G, C, T
(1910)

Mendel (de Vries)
Rediscovery
(1900)


Avery-MacLeod-McCarty
Transforming principle DNA
(1944)


Astbury
Crystallography
(1943)


Griffith
Transforming principle
(1928)


Chargaff
A=T
(1948)


Franklin-Wilkins
DNA structure
(1952)


Hershey-Chase
Phage
(1952)


Kornberg
DNA Pol
(1955)


Watson-Crick
DNA 3D
(1953)


Cohen & Boyer
Cloning
(1973)


Sanger
Sequencing
(1975)


Mullis
PCR
(1983)

Phage FX174
(1980)

DOE HUGO
(1986)

H. influenza
(1995)

S. cervisiae
(1996)

C. elegans
(1998)

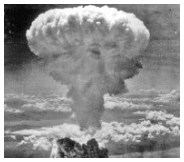
Chrom. 22
(1999)

D. melanogaster
(2000)

H. sapiens
(2001/3)

1840 1850 1860 1870 1880 1890 1900 1910 1920 1930 1940 1950 1960 1970 1980 1990 2000 2010 2020 2030



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Gregor Mendel

(1822–1884)

Monrovian (Czech Republic) monk

Father of modern genetics

Plant hybridization (Pisum sativum)

Observed the transmission of 7 traits.

Methodical statistical analysis, novel for biological research at the time.

Fundamental laws of inheritance
- Law of Segregation
- Law of Independent Assortment
- Law of Dominance

Published findings in the Natural History Society of Brno (1865).

Largely unrecognized during his lifetime.

Rediscovered by Hugo de Vries, Carl Correns, and Erich von Tschermak (1900).

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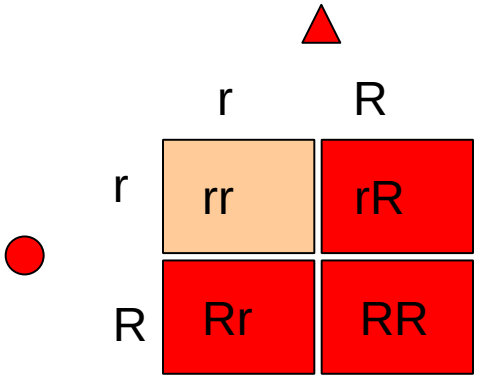
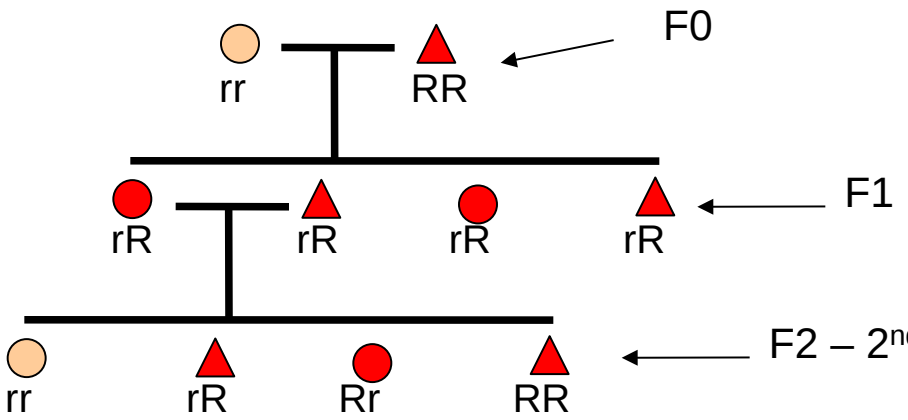


Seed		Flower	Pod		Stem	
Form	Cotyledons	Color	Form	Color	Place	Size
Grey & Round	Yellow	White	Full	Yellow	Axial pods, Flowers along	Long (6-7ft)
White & Wrinkled	Green	Violet	Constricted	Green	Terminal pods, Flowers top	Short (~1ft)
1	2	3	4	5	6	7



- 25% Recesive Hmzyg
- 50% Htzyg
- 25% Dominant Hmzyg

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Johann Friedrich Miescher

(1844-1895)

Swiss physician and biologist

Discovered nucleic acids in 1869 while studying leukocytes.

Named the substance "nuclein" due to its location in the cell nucleus.

Used pus-soaked bandages from surgical wards as source material.

Laid the foundation for later discoveries in genetics and molecular biology.

Initially focused on proteins, but his discovery of nuclein highlighted a new class of biological molecule.

Not fully appreciated until decades later when DNA's role in heredity was established.

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Frederick Griffith

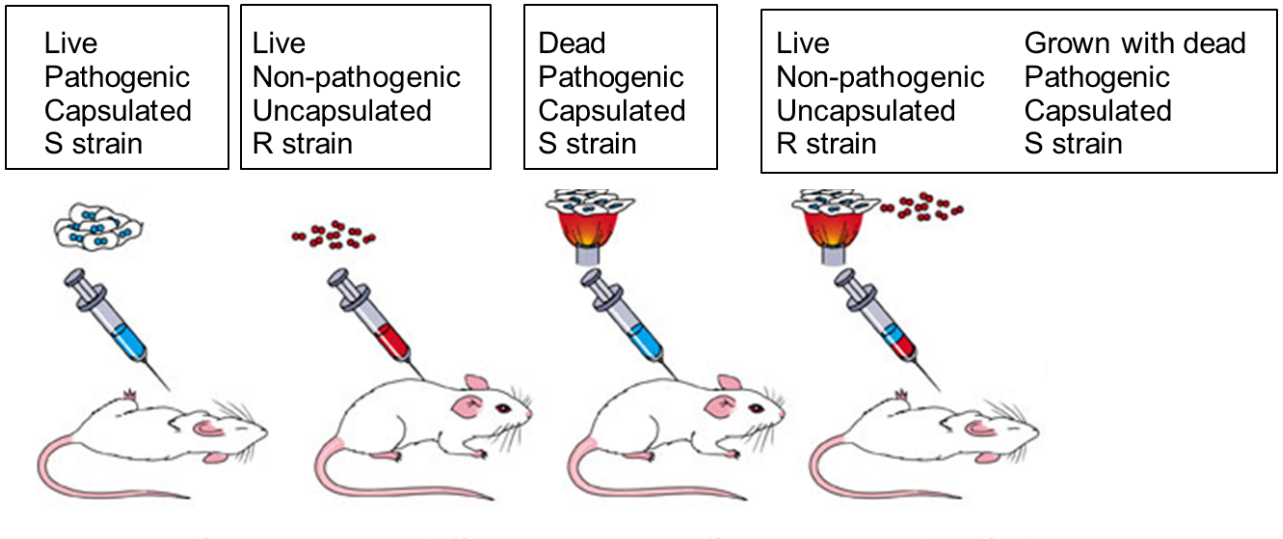
(1879 - 1941)

British bacteriologist demonstrated the process of bacterial Transformation (transforming principle) in 1928.

Aimed to develop vaccined against Streptococcus pneumoniae, responsible for pneumonia.

Studied two strains: the S (smooth) strain (virulent) and the R (rough) strain (non-virulent).

Laid the groundwork for later identification of DNA as the molecule responsible for genetic transformatior



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Avery-MacLeod-McCarty (1944)


(1877–1955)


(1909–1972)

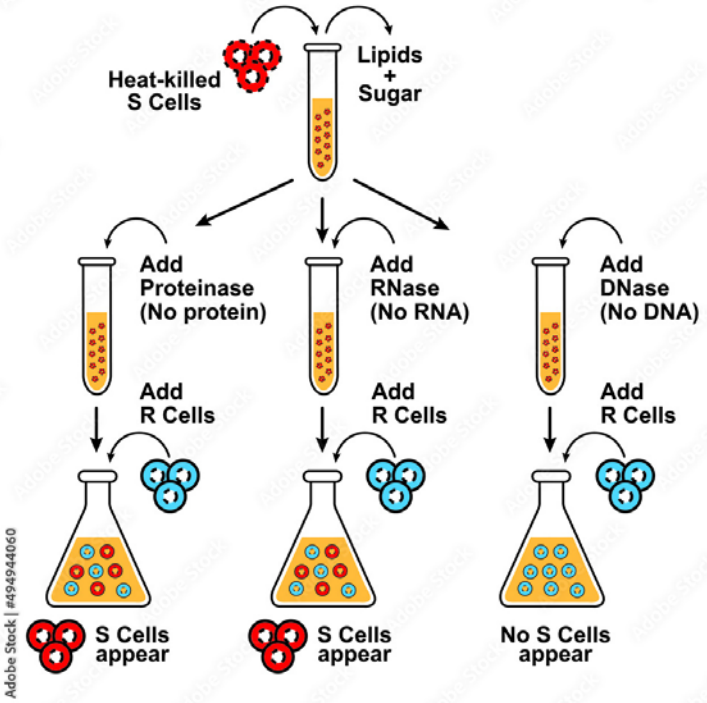

(1911–2005)

Oswald Avery, Colin MacLeod, and Maclyn McCarty

Identified Griffith's transforming principle as DNA.

Worked with heat-killed S strain cell extracts

Systematically removing proteins, lipids, carbohydrates, & RNA, leaving only DNA.



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Erwin Chargaff

(1905-2002)

Austrian-American biochemist.

Discovered that DNA composition varies between species (1940).

Disproved the idea that DNA is the same in all organisms.

Bbase-pairing nature of DNA, crucial to the discovery of DNA's double helix structure.

Formulated Chargaff's Rules,
"in any given DNA sample, amount of adenine = thymine, and cytosine = guanine".

Despite his groundbreaking work, Chargaff was critical of the reductionist approach of molecular biology that followed, particularly the use of DNA for genetic engineering.

Chargaff's DNA Database Composition in Various Species (%)

Species	A	T	G	C
Homo sapiens	31.0	31.5	19.1	18.4
Drosophila melanogaster	27.3	27.6	22.5	22.5
Zea mays	25.6	25.3	24.5	24.6
Neurospora crassa	23.0	23.3	27.1	26.6
Escherichia coli	24.6	24.3	25.5	25.6
Bacillus subtilis	28.4	29.0	21.0	21.6

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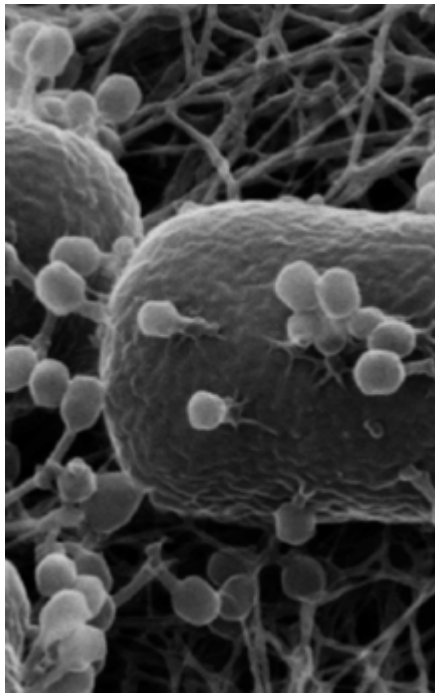
Alfred Hershey (1908–1997) & Martha Chase (1927–2003)

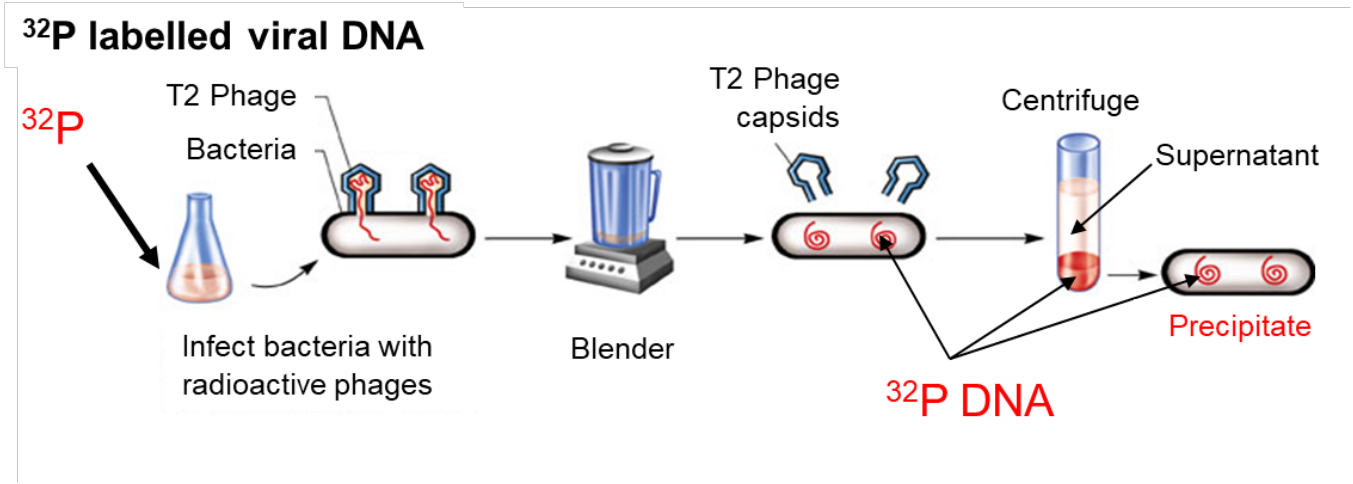
Confirmed that DNA is the genetic material, not protein.

Used T2 bacteriophage, a virus that infects bacteria, to study how genetic material is transferred.

Labeled viral DNA with radioactive phosphorus-32 and the viral coat protein with radioactive sulfur-35.

Discovered that only DNA entered the bacterial cells, the protein stayed outside.





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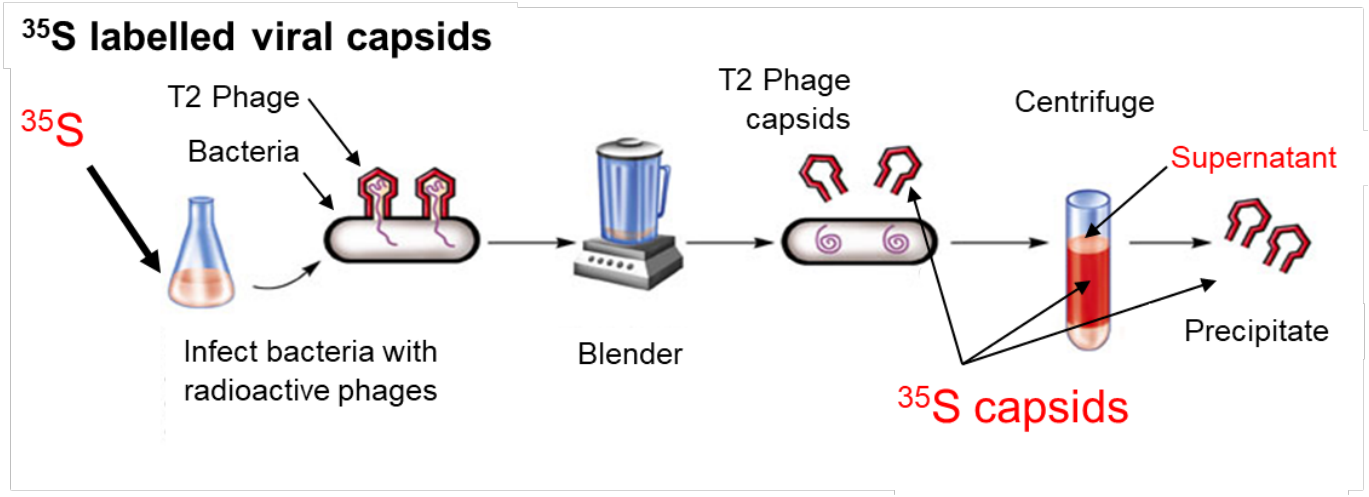

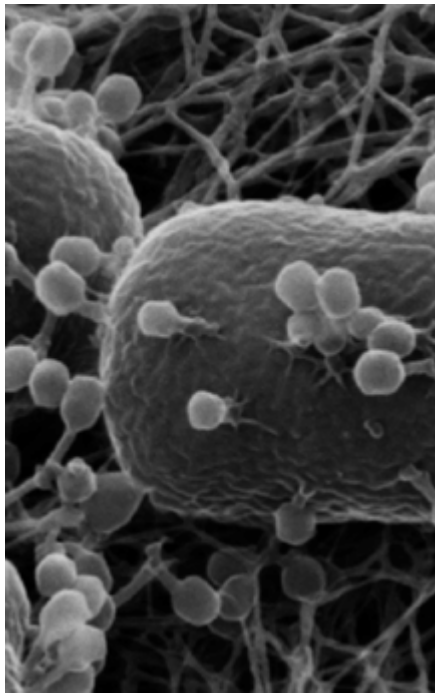

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Rosalind Franklin & Maurice Wilkins

(1920-1958)

(1916-2004)

Rosalind was a British biophysicist & X-ray crystallographer.

Franklin's X-ray diffraction images of DNA (Photo 51) provided key evidence of the helical structure of DNA.

Also conducted important research on the molecular structures of viruses, coal, and graphite.

Did not receive the recognition she deserved because her data was shared by Maurice with Watson and Crick without her knowledge.

Died at 37 of ovarian cancer before the Nobel Prize was given to Watson, Crick, & Wilkins in 1962.

Maurice was a Kiwi British physicist & molecular biologist.

Significant contributions to biophysics, and X-ray diffraction studies of viruses and other biological molecules.

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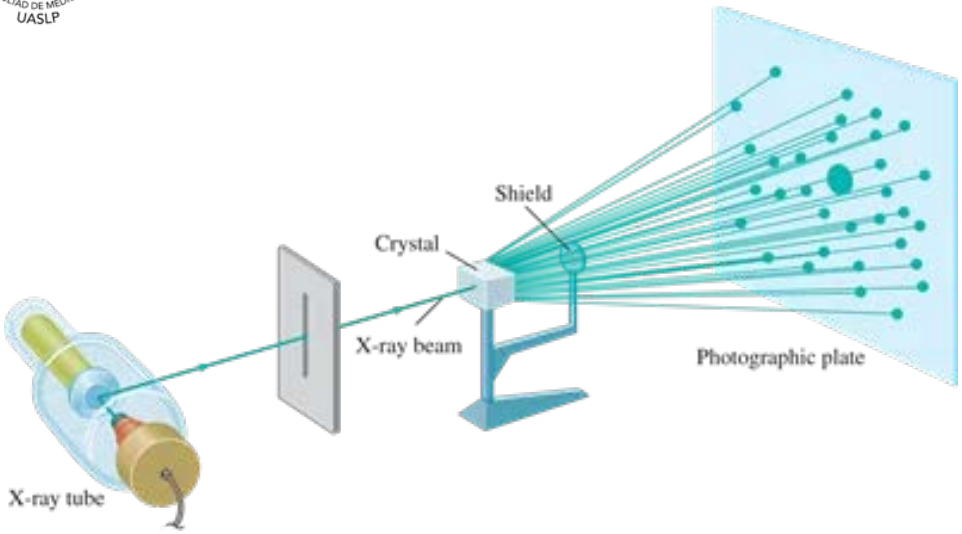
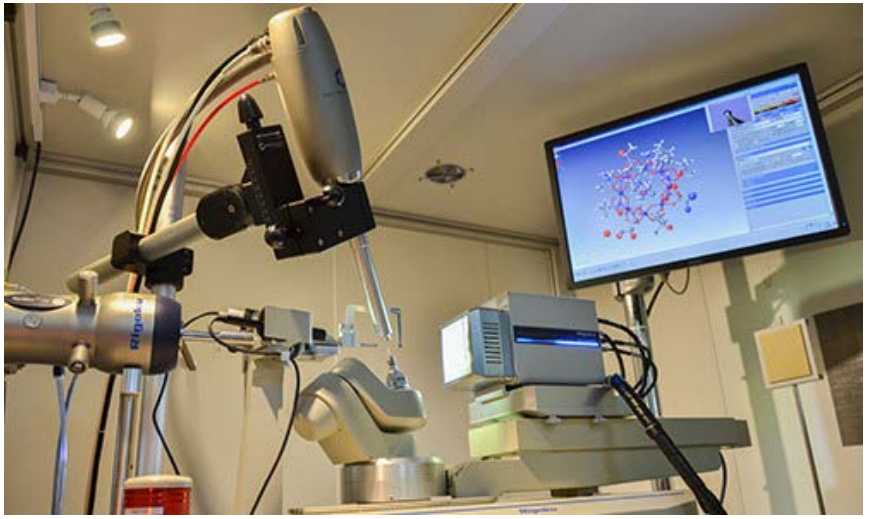
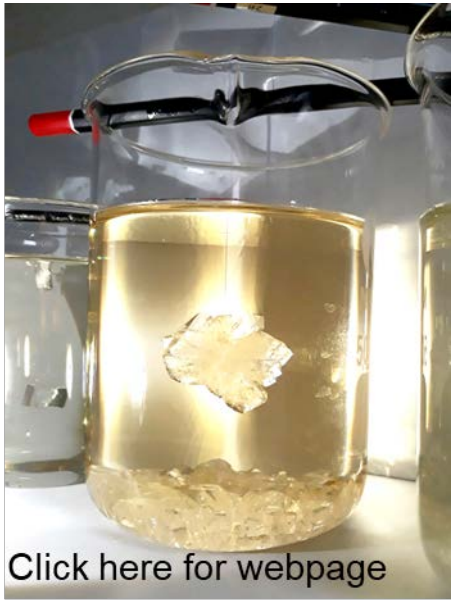
Biomolecule crystallography







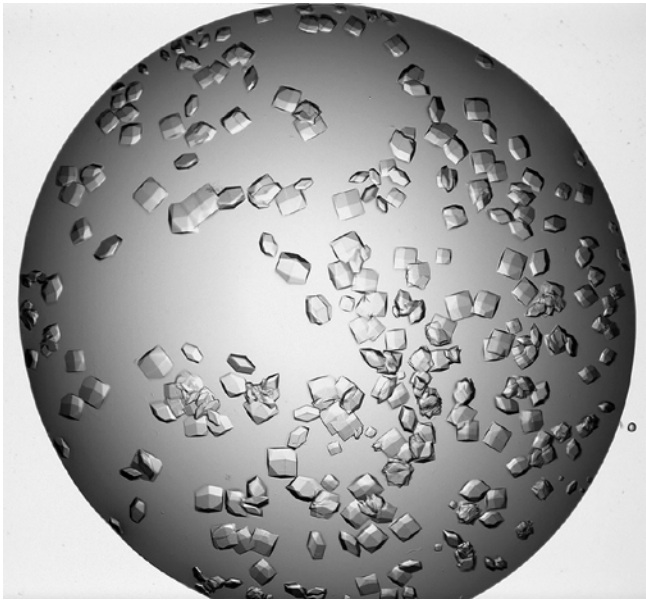


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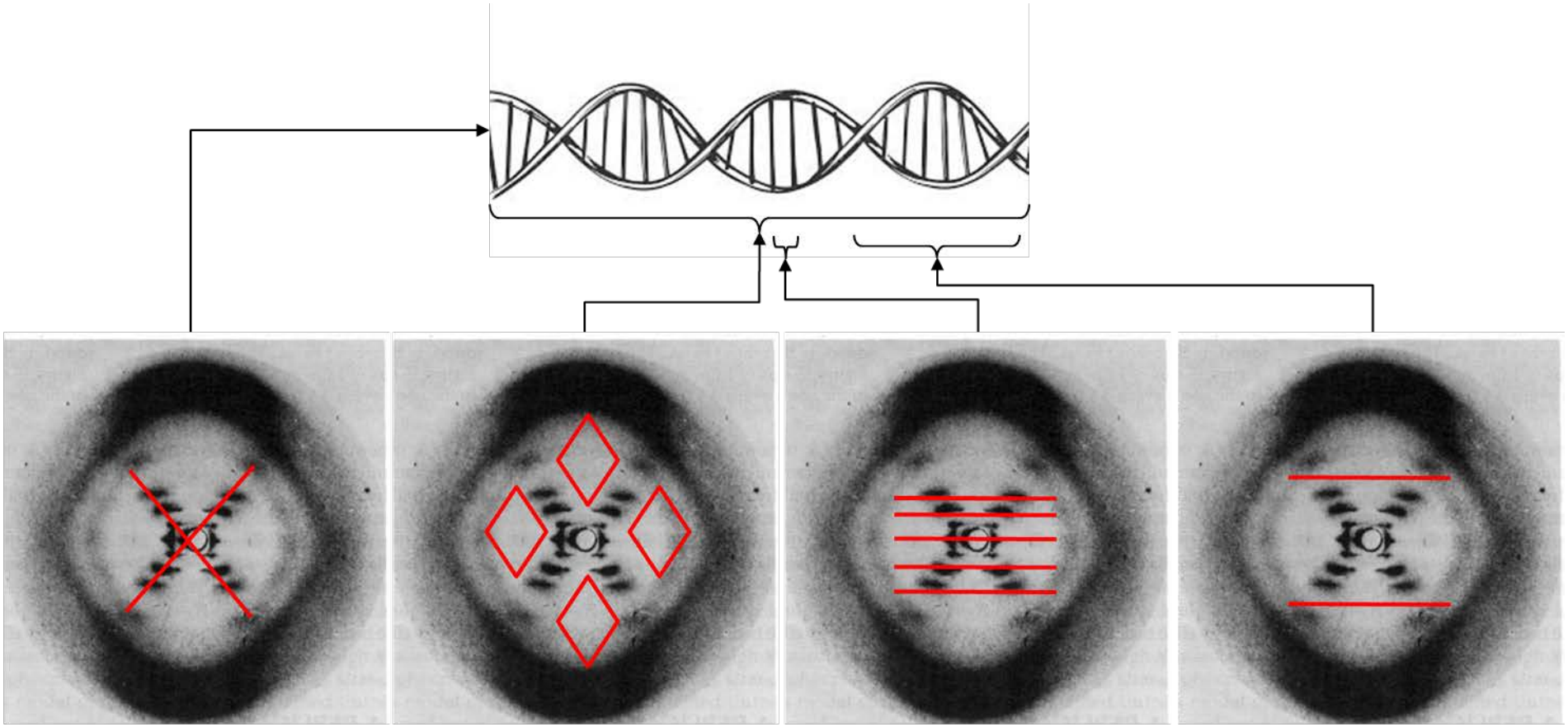
Photo 51



Helical molecule

Filamentous molecule

0.34 nm minor repeating units

3.4 nm major repeating units

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James Watson & Sir Francis Crick

(1928–)

(1916–2004)

Watson is an American molecular biologist and geneticist.

Director and president of Cold Spring Harbor Laboratory

Watson's reputation has been marred in later years by controversial statements regarding race and intelligence.

Crick was a British molecular biologist, physicist, and neuroscientist.

Used Rsoalind Frankiln's X-ray diffraction data to propose the double-helix model of DNA.

Crick described the central dogma of molecular biology (flow of genetic information from DNA through RNA to protein).

Shifted focus to neuroscience, studying consciousness and brain function.

Crick was known for his interdisciplinary approach, combining physics, biology, and chemistry to solve complex biological problems.

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James Watson

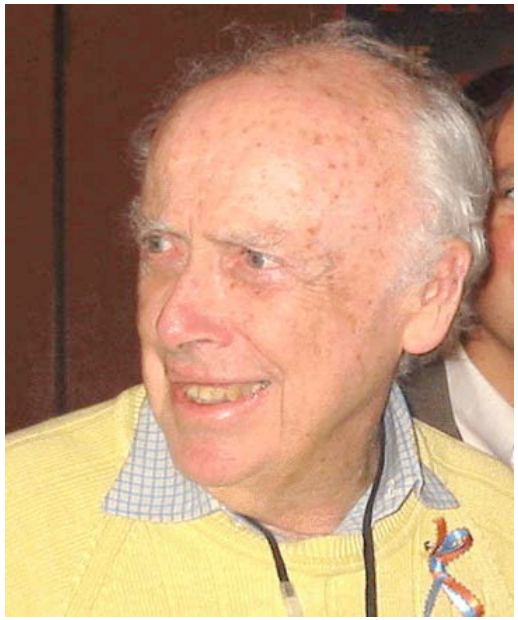
Genetic screening and genetic engineering to cure “stupidity” and “make all girls pretty”.

“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”.



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Francis Crick

Important theoretical molecular biologist .

The genetic code.

Central dogma.

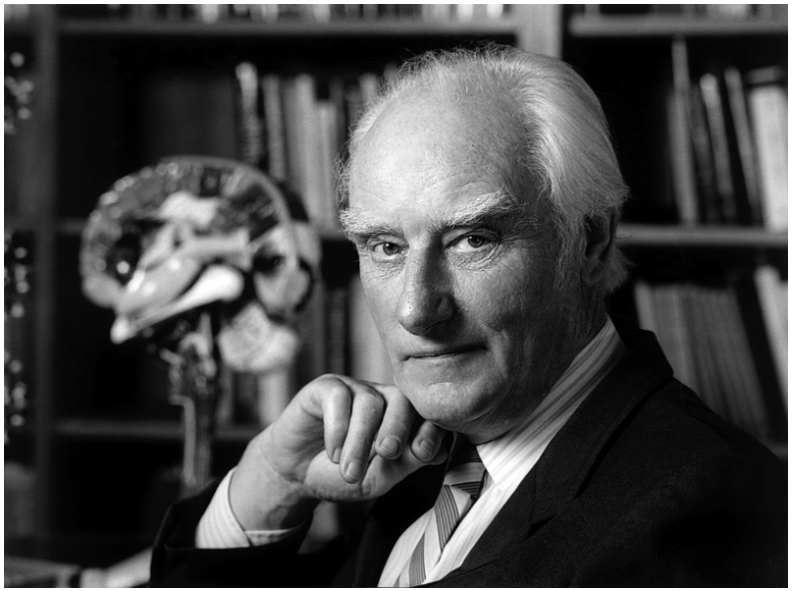
Important contributions to theoretical neurobiology

Advance the scientific study of human consciousness.

Icosahedral symetry of viruses.

Protein translation.

mRNA, tRNA



"Christianity may be OK between consenting adults in private but should not be taught to young children."

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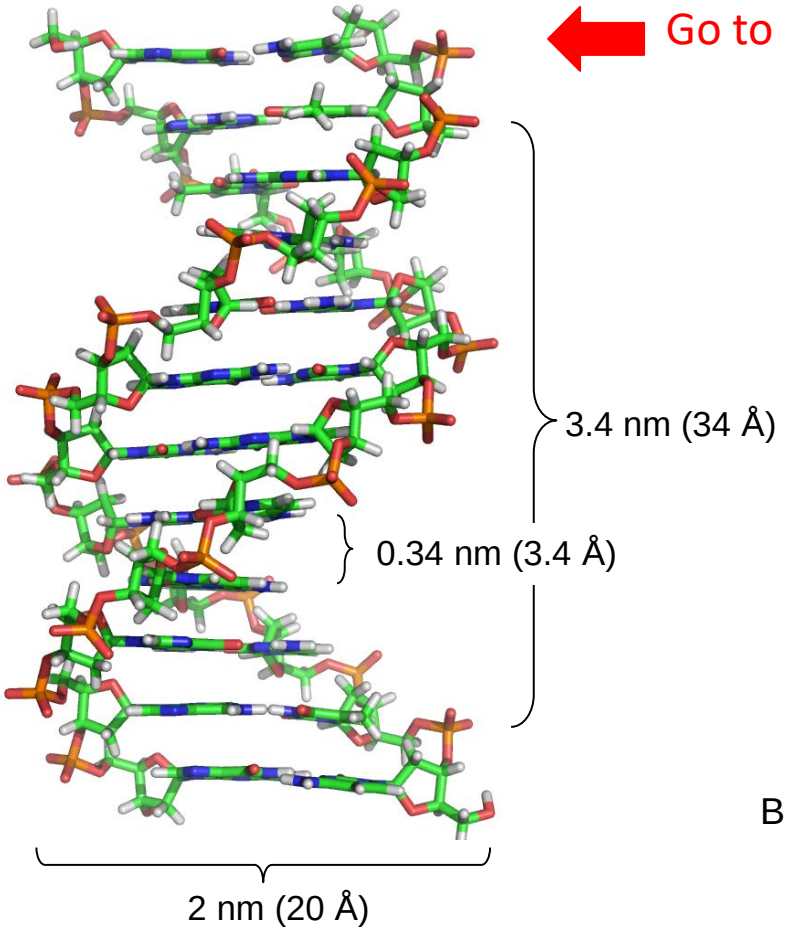
DNA structure



Go to PyMol

- Estructura helicoidal
- Forma filamentosa (molécula larga)
- Unidades menores cada 0.34 nm (3.4 Å)
- Unidad mayor cada 3.4 nm (34 Å)

Breviario cultural: 1 Ångström = 0.1 nanómetros

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Fred Sanger

(1918-2013)

One of four researchers to have received two Nobel Prizes

Marie Curie
- 1903 Nobel Prize in Physics, radioactivity.
- 1911 Nobel Prize in Chemistry, discovery of radium and polonium.

Linus Pauling
- 1954 Nobel Prize in Chemistry, chemical bonds.
- 1962 Nobel Peace Prize, Anti-nuclear weapons testing activism.

John Bardeen
- 1956 Nobel Prize in Physics, invention of the transistor.
- 1972 Nobel Prize in Physics, theory of superconductivity.

Frederick Sanger
- 1958 Nobel Prize in Chemistry, structure of insulin.
- 1980 Nobel Prize in Chemistry, DNA sequencing techniques.

International Committee of the Red Cross:
- 1917 and 1944 Nobel Peace Prizes for humanitarian efforts
- 1963 Nobel Peace Prize for promoting international humanitarian law.

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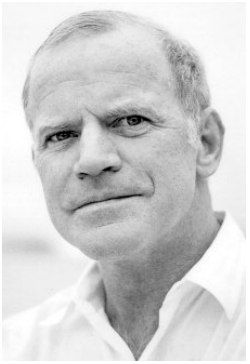
Kary Mullis



(1944–2019)

American biochemist, invented the Polymerase Chain Reaction in 1983.

A technique that revolutionized molecular biology.

Awarded the 1993 Nobel Prize in Chemistry (shared with Michael Smith) for contributions to DNA chemistry.

PCR became a foundational tool in genetic research, forensic science, medical diagnostics, and numerous fields of biological science.

Mullis' discovery greatly advanced DNA fingerprinting, gene cloning, and the study of infectious diseases, including HIV.

Known for his eccentric personality and skepticism about HIV causing AIDS and climate change.

Outspoken advocate for psychedelic drugs and credited his creative insights in part to his use of LSD during the 1960s.

Amateur surfer.

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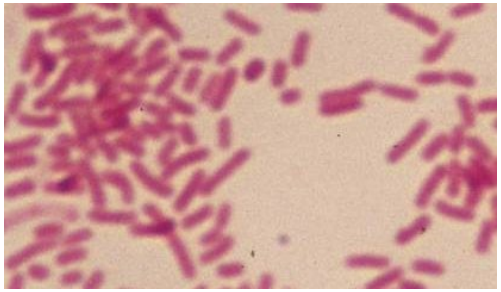
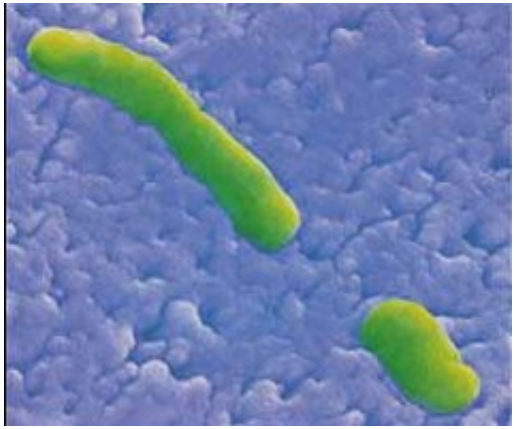
Haemophilus influenza genome (1995)





First bacteria sequenced.

Non-motile Coccobacillus G-Neg.

Discovered in 1892 Pfeiffer.

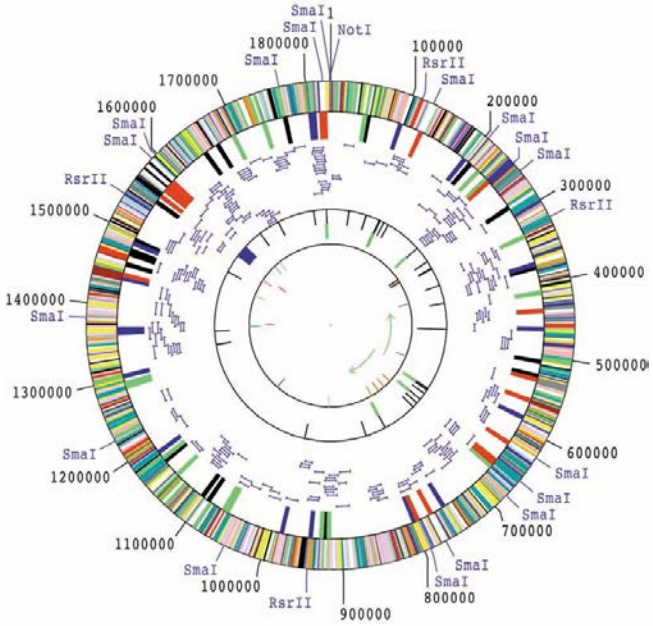
Thought to be responsible for influenza.

Causes bacteremia, meningitis, cellulitis, osteomyelitis, epiglottitis.

First free-living organism to be sequenced.

Small genome: 1’830,140 bases
1740 genes

Completed in 1995 by a Craig Venter team and Hamilton Smith at The Institute for Genomic Research (TIGR).



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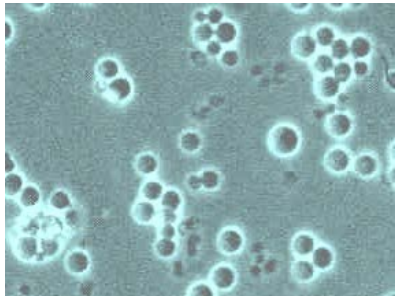
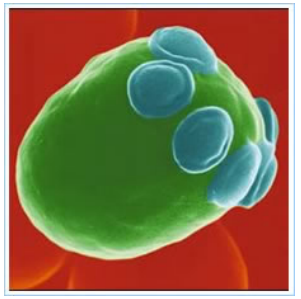
Saccharomyces cerevisiae genome (1996)

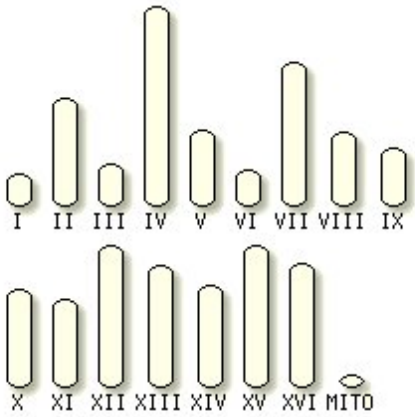




First eukaryote to be sequenced (1996).

Collaborative international sequencing effort involving 100 laboratories worldwide, coordinated by the Yeast Genome Sequencing Project (YGSP).

Genome: 12’100,000 bases
16 chromosomes
6000 genes



Sequencing accelerated research in genetics, molecular biology, biotechnology, and drug development.

Important industrially for its role in brewing, baking, and bioethanol production

23% Genomic homology to HoSa.

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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

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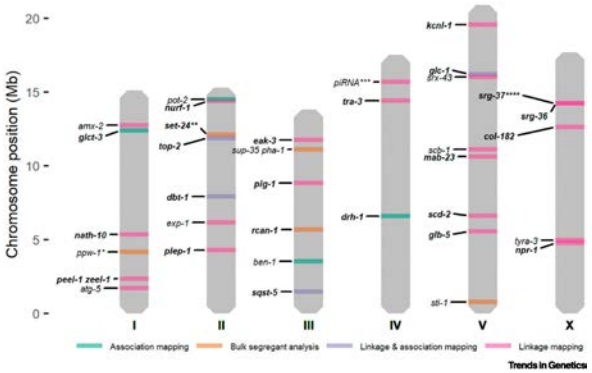
Caenorhabditis elegans genome (1998)

First multicellular organism to have its entire genome sequenced (1998).

Sequenced by the C. elegans Sequencing Consortium, led by the Wellcome Sanger Institute.

Genome: 100’000,000 bases
6 chromosomes
19,000 genes



40% of its genes have human othologs

Whole-genome shotgun sequencing.

C. elegans genome has provided deep insights into developmental biology, neurobiology, and aging.

Model organism due to its simplicity, short life cycle, and fully mapped cell lineage, with every cell in its body precisely identified and traced during development.

STS-107 Feb 2003 (Columbia)

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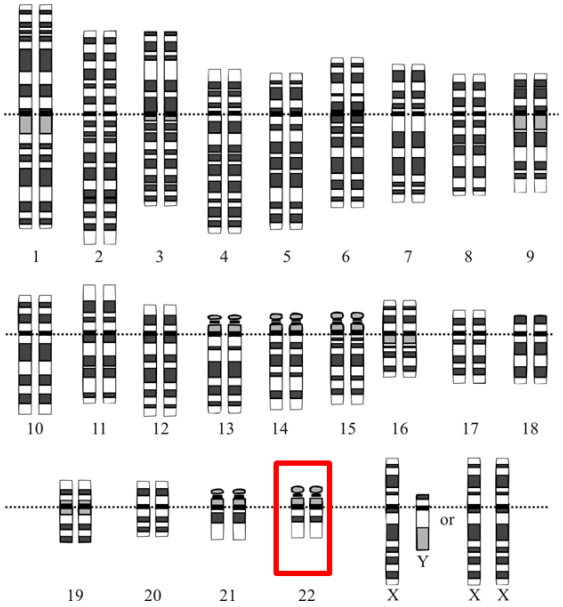
Homo sapiens chromosome 22 sequencing (1999)

First human chromosome to be sequenced.

Wellcome Trust Sanger Institute.

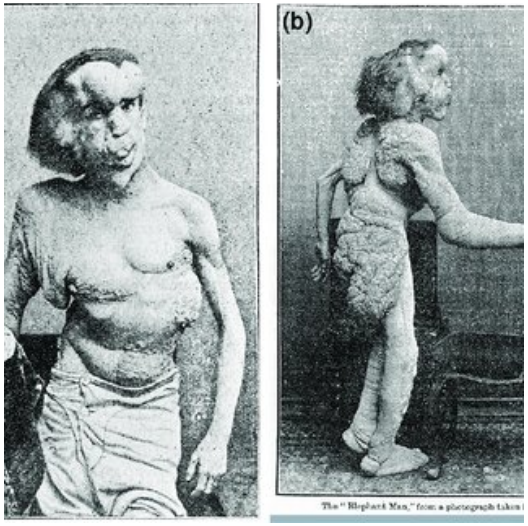
Second smallest chromosome (see 21)

51’000,000 bases
1.5 – 2.0 % total human DNA
500 and 700 genes



Mutations cause:

- Philadelphia+ Chronic myeloid leukemia t(9;22)(q34;q11).
- Amyotrophic Lateral Sclerosis
- Breast Cancer
- Type 2 Neurofibromatosis
- DiGeorge syndrome (Δ 22q11.2)
- and possibly autism



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Drosophila melanogaster genome (2000)

Most studied model organisms in genetics and developmental biology

Drosophila Genome Project

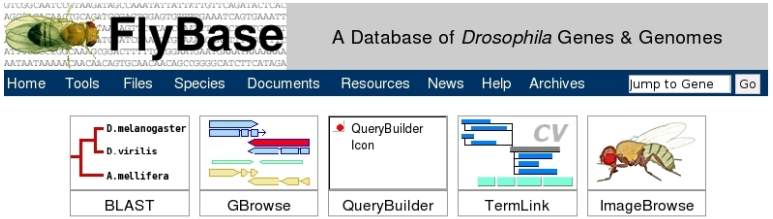
180’000,000 bases
14,000 genes
4 chromosomes (X, Y, 2, 3, and the tiny 4)

Instrumental in studying genetic inheritance, development, and gene function.

Genome provided deep insights into genomic organization, evolution, and gene regulation, and continues to serve as a reference for research in developmental biology, neurobiology, and disease models

Has contributed to several Nobel Prizes

Polytene Chromosomes, large and visible under a microscope, allow visualizing Genetic processes (transcription).



http://www.flybase.org

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Human genome project

The Human Genome Project (HGP), international initiative aimed at mapping and sequencing the entire human genome.

Began in 1990, by the US Department of Energy and National Institutes of Health.

20 institutions from six countries (USA, UK, Japan, France, Germany, and China).

First draft completed in 2001, covering about 90% of the human genome with gaps.

Declared complete in April 2003, two years ahead of schedule and under budget.

Revolutionized biomedical science, providing a foundation for understanding the genetic basis of diseases, human evolution, and biological processes.

Click on these journal covers for free access to the original HGP results and publication.

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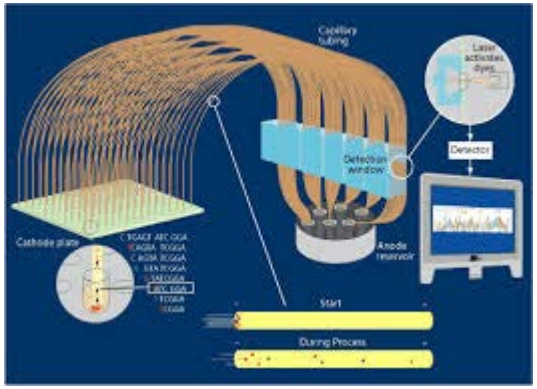
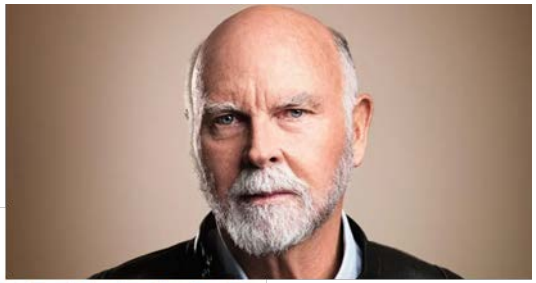
Human genome project

Led to new DNA sequencing techniques, bioinformatics, and data analysis.



Paved the way for personalized medicine, identifying genes involved in diseases, and advancing pharmacogenomics.

Private effort by Celera Genomics (Craig Venter) published own version by 2001.



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Laboratorio de Genómica Viral y Humana

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

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