BIO-373

Genetics & Genomics

Introduction to genetics

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What is the human genome?

It's a history book - a narrative of the journey of our species through time.

It's a shop manual, with an incredibly detailed blueprint for building every human cell.

And it's a transformative textbook of medicine, with insights that will give health care providers immense new powers to treat, prevent and cure disease.

Francis Collins

A brief history of genetics

1600–1850: **The Dawn of Modern Biology**

- Invention of new technologies (seeing is believing)

William Harvey: **Theory of epigenesis** (1651)

- New structures such as organs are not present in the early embryo but are formed later
- Sequential development of embryos via growth and differentiation
- Precursor to our understanding that genes control developmental processes

Schleiden and Schwann: **The cell theory** (1838-1839)

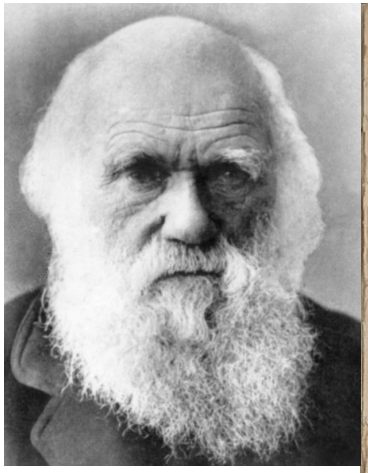
- All living organisms are composed of cells and the cell is the fundamental unit of structure and function
- Cells become biology's “atoms”

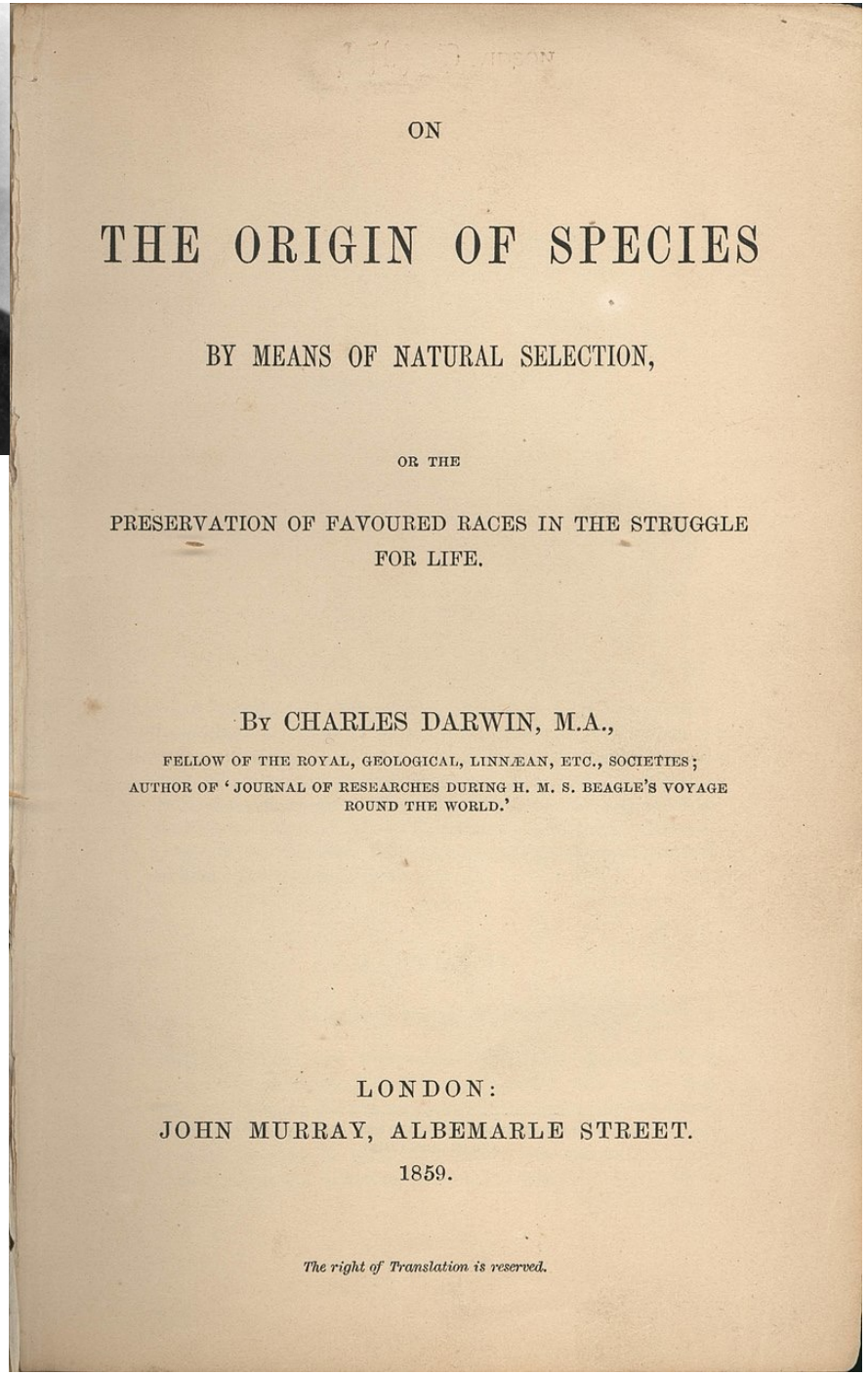
Remark and Virchow: **Omnis cellula e cellula** (1852-1855)

- All cells arise from pre-existing cells (by cell division)
- Organisms are made of cells → the cell is the basic unit → cells from cells

Evolution

- **Darwin – 1859**





ON

THE ORIGIN OF SPECIES

BY MEANS OF NATURAL SELECTION,

OR THE

PRESERVATION OF FAVOURED RACES IN THE STRUGGLE FOR LIFE.

By CHARLES DARWIN, M.A.,

FELLOW OF THE ROYAL, GEOLOGICAL, LINNÆAN, ETC., SOCIETIES;
AUTHOR OF 'JOURNAL OF RESEARCHES DURING H. M. S. BEAGLE'S VOYAGE ROUND THE WORLD.'

LONDON:
JOHN MURRAY, ALBEMARLE STREET.
1859.

The right of Translation is reserved.

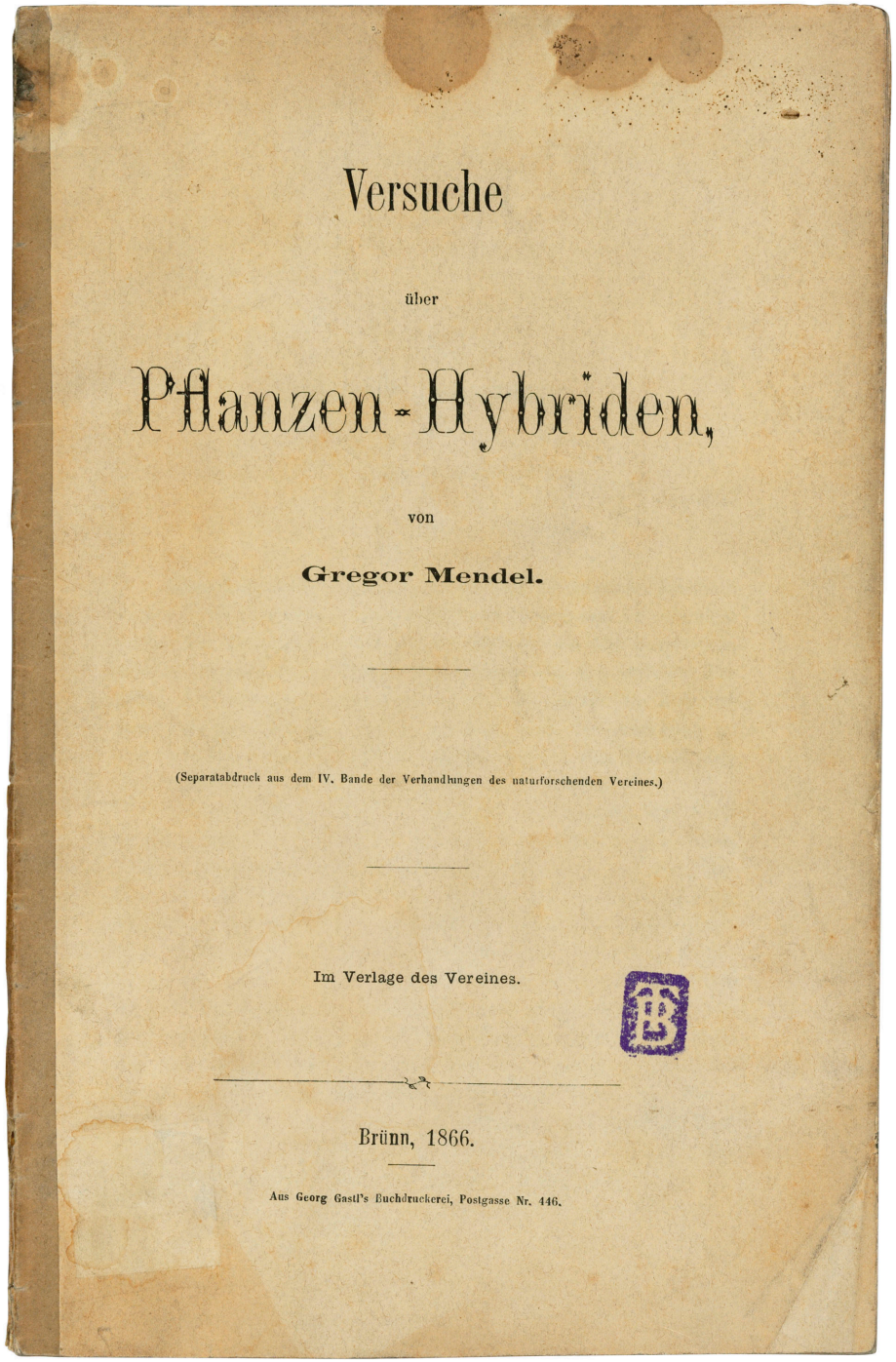
- **Theory of evolution**
  - **Descent with modification**
    - Existing species arose from other ancestral species
  - **Natural selection**
    - Mechanism for evolution

(Independently proposed by Alfred Wallace)

Heredity

- **Mendel – 1866**

- Observations showing that “genetic factors” allow the transmission of traits between generations



Versuche

über

Pflanzen-Hybriden,

von

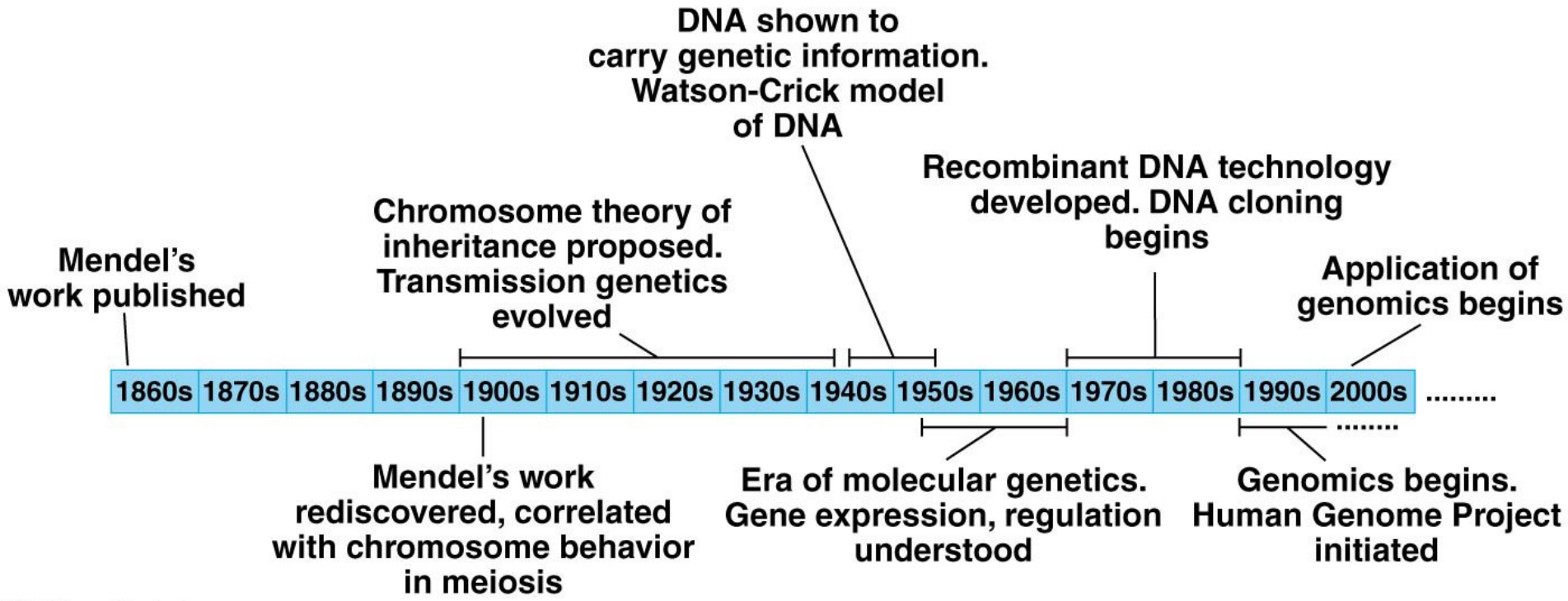
Gregor Mendel.

(Separatabdruck aus dem IV. Bande der Verhandlungen des naturforschenden Vereines.)

Im Verlage des Vereines.

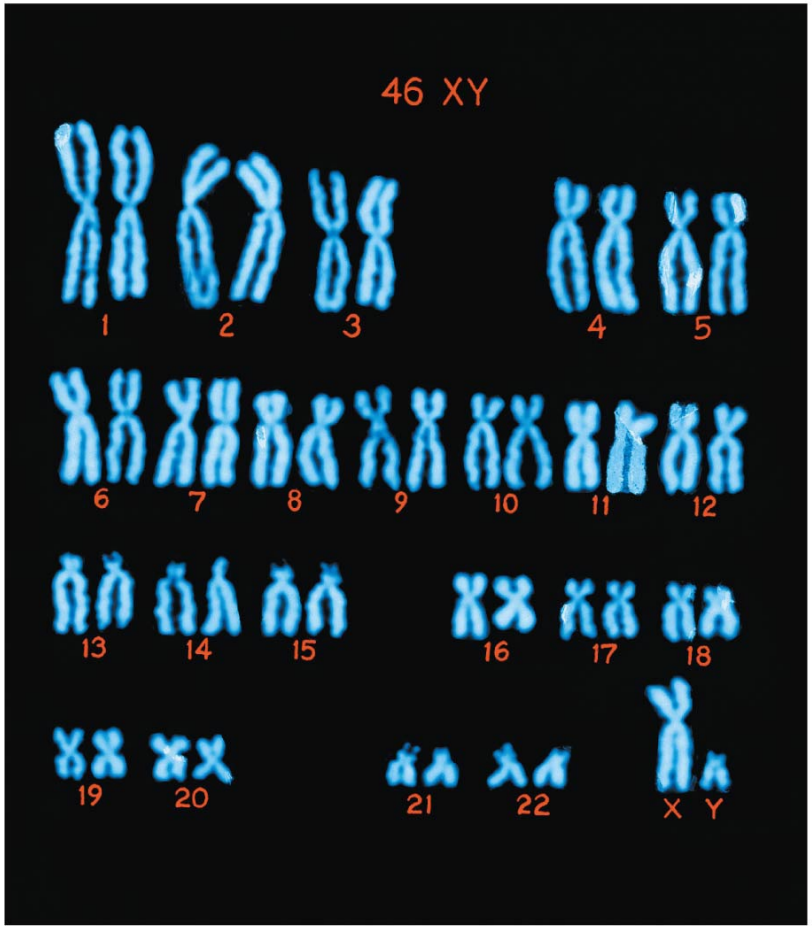
Brünn, 1866.

Aus Georg Gastl's Buchdruckerei, Postgasse Nr. 446.


DNA shown to carry genetic information. Watson-Crick model of DNA
Recombinant DNA technology developed. DNA cloning begins
Chromosome theory of inheritance proposed. Transmission genetics evolved
Application of genomics begins
Mendel's work published
1860s
1870s
1880s
1890s
1900s
1910s
1920s
1930s
1940s
1950s
1960s
1970s
1980s
1990s
2000s
.....
.....
Mendel's work rediscovered, correlated with chromosome behavior in meiosis
Era of molecular genetics. Gene expression, regulation understood
Genomics begins. Human Genome Project initiated

Chromosomal theory of inheritance

- **Boveri & Sutton – 1902/03**
- Genes are carried on chromosomes, which undergo segregation and independent assortment during meiosis
- Chromosomes are the physical basis (object) of Mendel's law



DNA is the carrier of genetic information (not proteins)

- **Avery, MacLeod & McCarty – 1944**

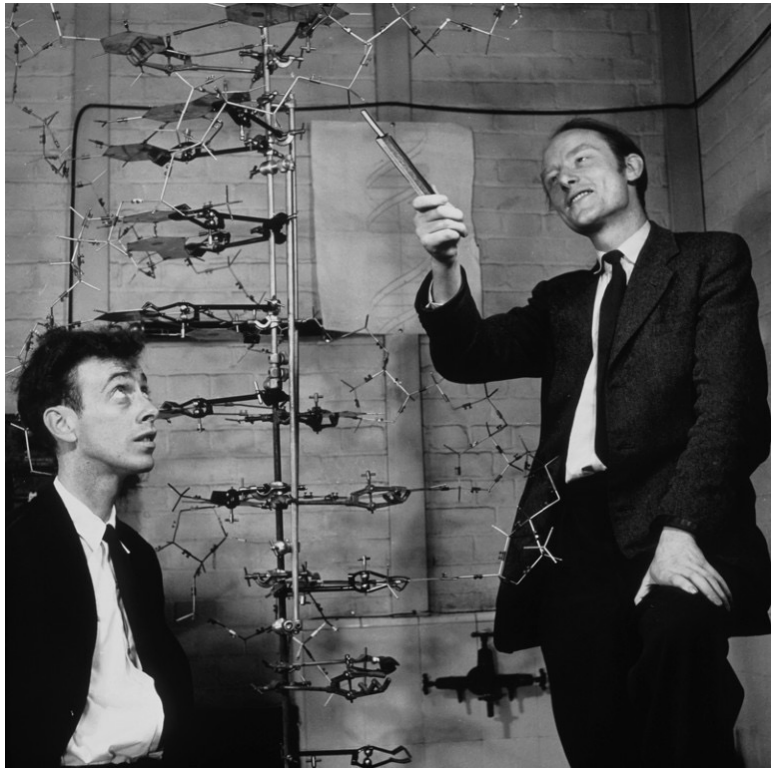
- Used mouse infection with *S. pneumococcus* bacteria to demonstrate that DNA alone is the substance that causes bacterial “transformation” with virulent strains

- Before, it was widely believed that proteins carried genetic information

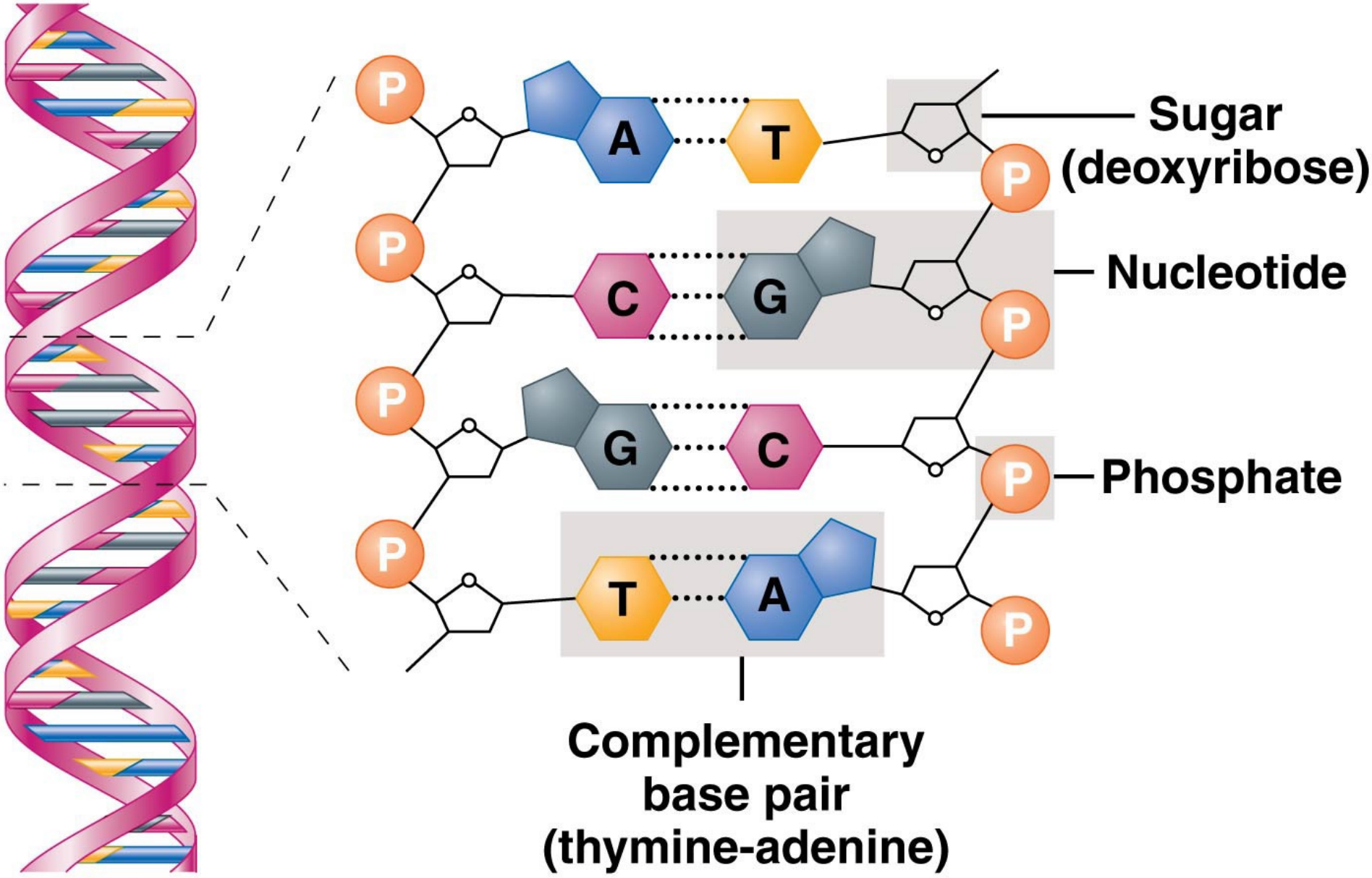
- Elegant controls with proteases, RNases, and DNases came two years later

Structure of DNA

- **Watson and Crick – 1953**
- DNA is a double-stranded helix made of nucleotides
- Complementary base pairing across the helix: A–T and G–C

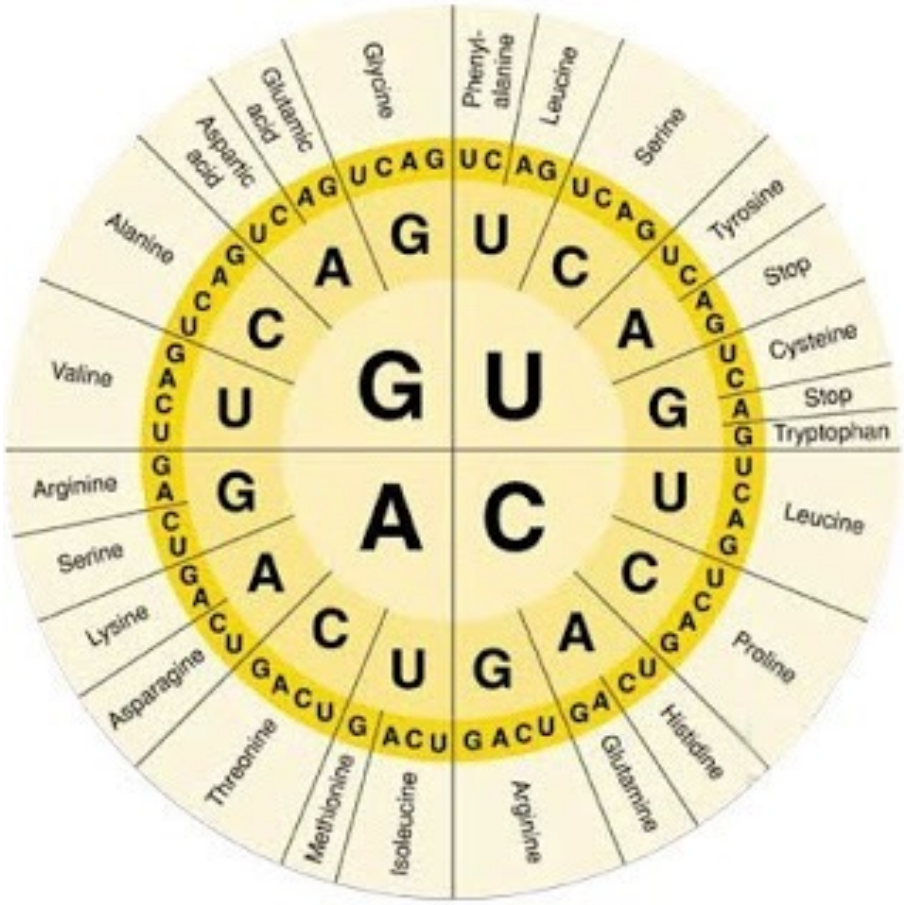


What Rosalind Franklin truly contributed to the discovery of DNA's structure
https://www.nature.com/articles/d41586-023-01313-5


P
A
T
C
G
G
C
T
A
Sugar
(deoxyribose)
Nucleotide
Phosphate
Complementary
base pair
(thymine-adenine)

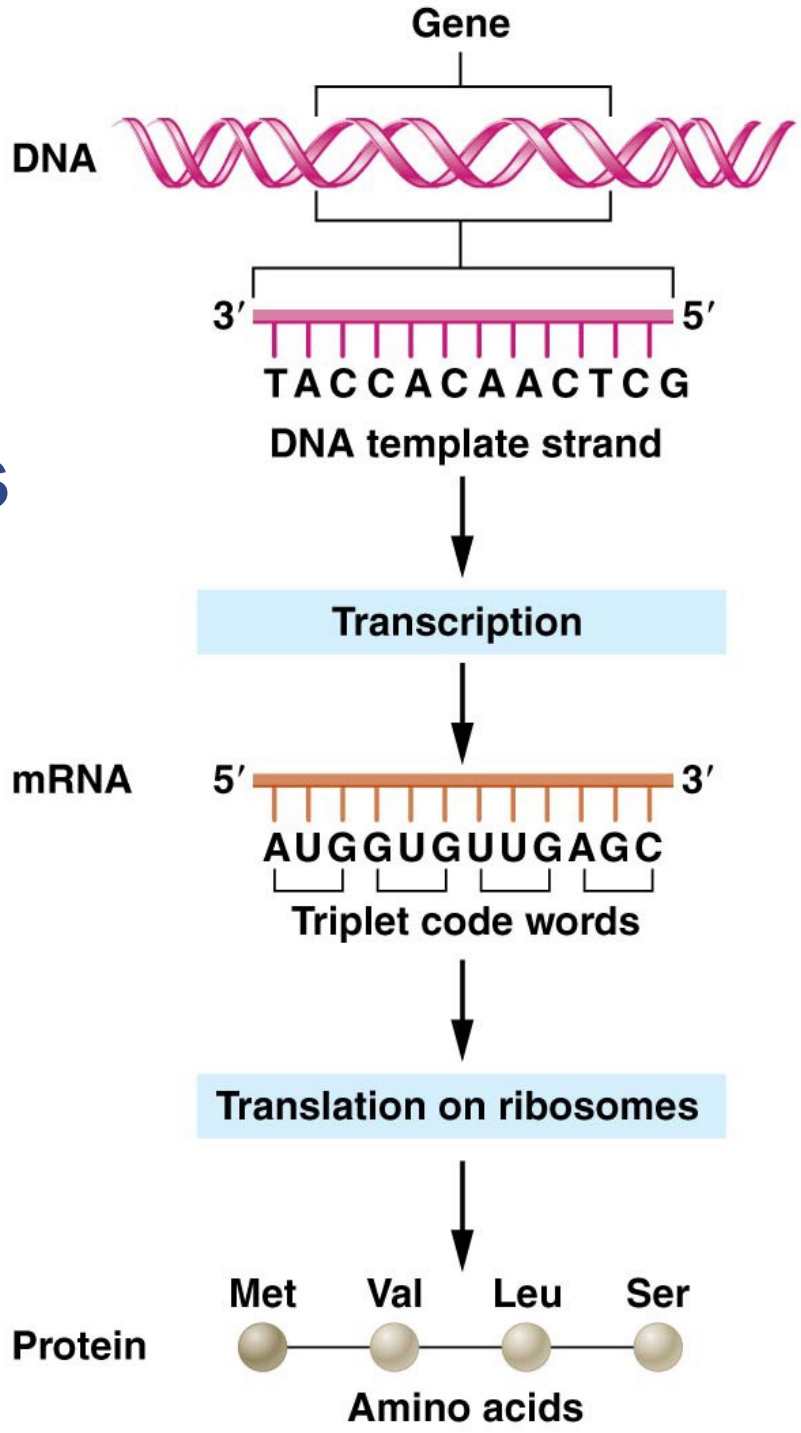
The genetic code

- **Deciphered over the following 15 years**
- Codons = triplet nucleotides present in mRNA
- Each codon encodes for insertion of a specific amino acid into a growing protein chain



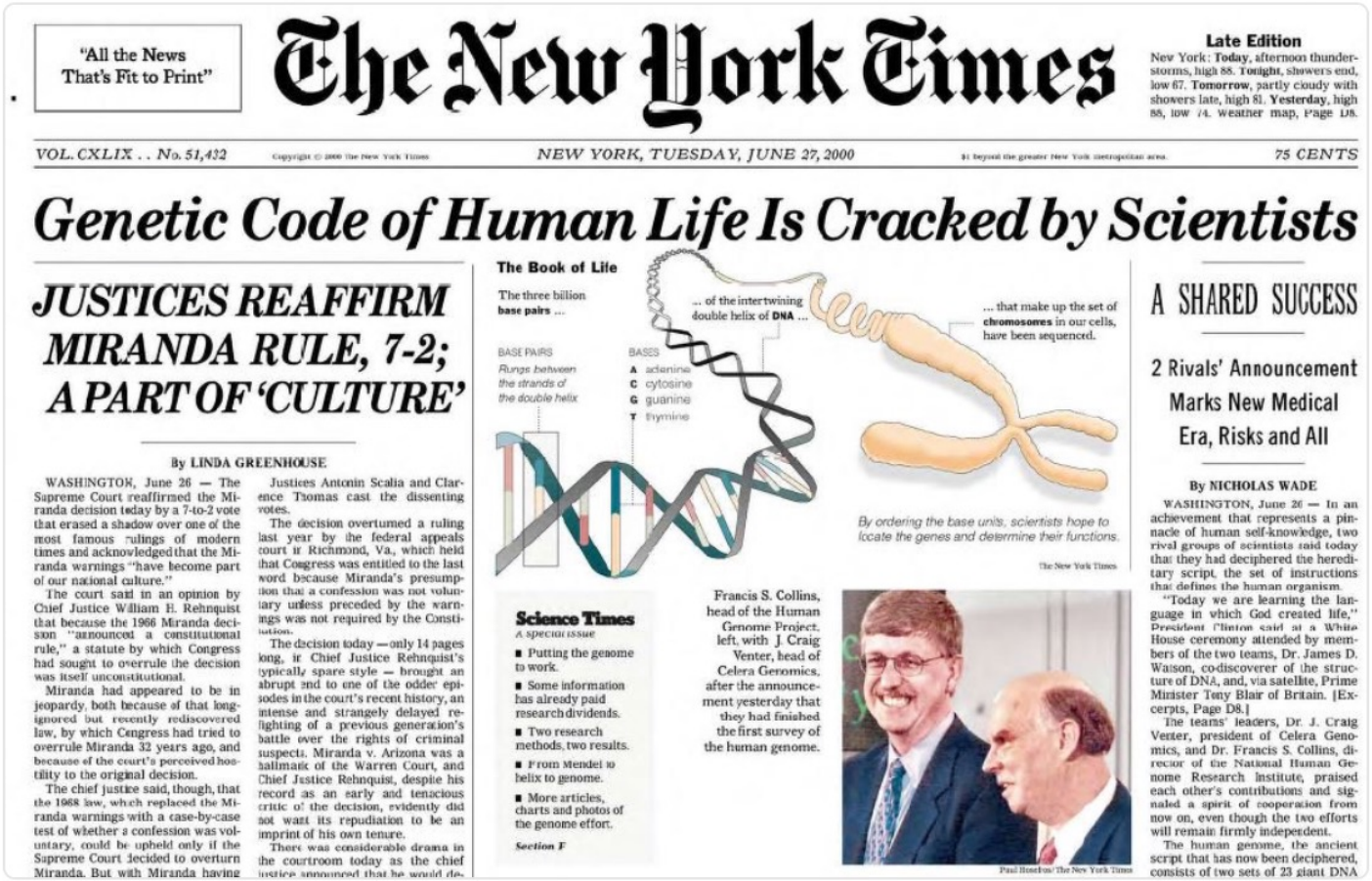
The central dogma

➔ **Molecular genetics**



The genomic era

- 2003 : End of the Human Genome Project



"All the News That's Fit to Print"

The New York Times

Late Edition
New York: **Today**, afternoon thunderstorms, high 88. **Tonight**, showers end, low 67. **Tomorrow**, partly cloudy with showers late, high 81. **Yesterday**, high 88, low 74. Weather map, Page D8.

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Genetic Code of Human Life Is Cracked by Scientists

JUSTICES REAFFIRM MIRANDA RULE, 7-2; A PART OF 'CULTURE'

By LINDA GREENHOUSE

WASHINGTON, June 26 — The Supreme Court reaffirmed the Miranda decision today by a 7-to-2 vote that erased a shadow over one of the most famous rulings of modern times and acknowledged that the Miranda warnings "have become part of our national culture."

The court said in an opinion by Chief Justice William H. Rehnquist that because the 1966 Miranda decision "announced a constitutional rule," a statute by which Congress had sought to overrule the decision was itself unconstitutional.

Miranda had appeared to be in jeopardy, both because of that long-ignored but recently rediscovered law, by which Congress had tried to overrule Miranda 32 years ago, and because of the court's perceived hostility to the original decision.

The chief justice said, though, that the 1968 law, which replaced the Miranda warnings with a case-by-case test of whether a confession was voluntary, could be upheld only if the Supreme Court decided to overturn Miranda. But with Miranda having

Justices Antonin Scalia and Clarence Thomas cast the dissenting votes.

The decision overturned a ruling last year by the federal appeals court in Richmond, Va., which held that Congress was entitled to the last word because Miranda's presumption that a confession was not voluntary unless preceded by the warnings was not required by the Constitution.

The decision today — only 14 pages long, in Chief Justice Rehnquist's typically spare style — brought an abrupt end to one of the odder episodes in the court's recent history, an intense and strangely delayed relighting of a previous generation's battle over the rights of criminal suspects. Miranda v. Arizona was a hallmark of the Warren Court, and Chief Justice Rehnquist, despite his record as an early and tenacious critic of the decision, evidently did not want its repudiation to be an imprint of his own tenure.

There was considerable drama in the courtroom today as the chief justice announced that he would de-

Science Times
A special issue
- Putting the genome to work.
- Some information has already paid research dividends.
- Two research methods, two results.
- From Mendel to helix to genome.
- More articles, charts and photos of the genome effort.

Section F

Francis S. Collins, head of the Human Genome Project, left, with J. Craig Venter, head of Celera Genomics, after the announcement yesterday that they had finished the first survey of the human genome.

Paul Hosefros/The New York Times

A SHARED SUCCESS

2 Rivals' Announcement Marks New Medical Era, Risks and All

By NICHOLAS WADE

WASHINGTON, June 26 — In an achievement that represents a pinnacle of human self-knowledge, two rival groups of scientists said today that they had deciphered the hereditary script, the set of instructions that defines the human organism.

"Today we are learning the language in which God created life," President Clinton said at a White House ceremony attended by members of the two teams, Dr. James D. Watson, co-discoverer of the structure of DNA, and, via satellite, Prime Minister Tony Blair of Britain. [Excerpts, Page D8.]

The teams' leaders, Dr. J. Craig Venter, president of Celera Genomics, and Dr. Francis S. Collins, director of the National Human Genome Research Institute, praised each other's contributions and signaled a spirit of cooperation from now on, even though the two efforts will remain firmly independent.

The human genome, the ancient script that has now been deciphered, consists of two sets of 23 giant DNA

The genomic era

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The future of genetics and genomics

- Society is faced with a host of sensitive genetics-related issues:
  - Potential discriminations
  - Privacy protection
  - Prenatal testing
  - Access to/safety of gene therapy
  - Ethical issues surrounding biotechnology