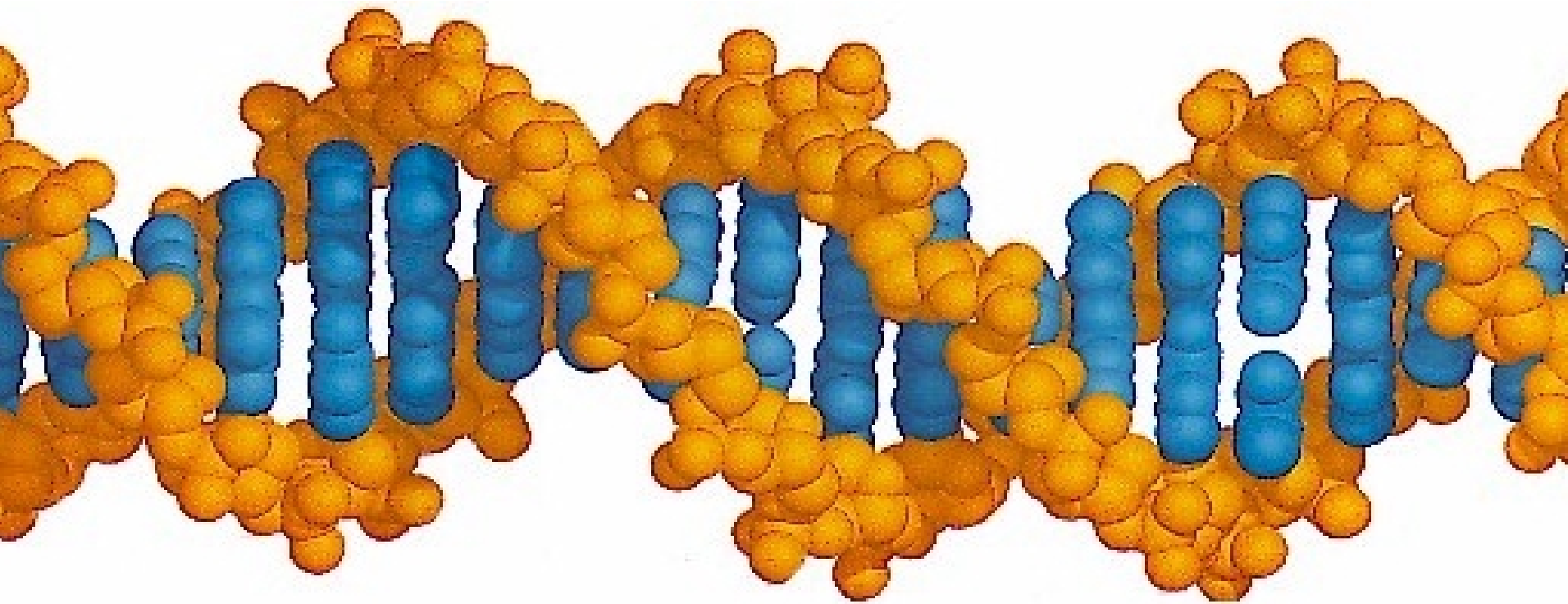
A Short History of DNA Technology



STARS SOUTHWESTERN

1865 - Gregor Mendel

The Father of Genetics

The Augustinian monastery in old Brno, Moravia

STARS SOUTHWESTERN

1865 - Gregor Mendel

- Law of Segregation
- Law of Independent Assortment
- Law of Dominance

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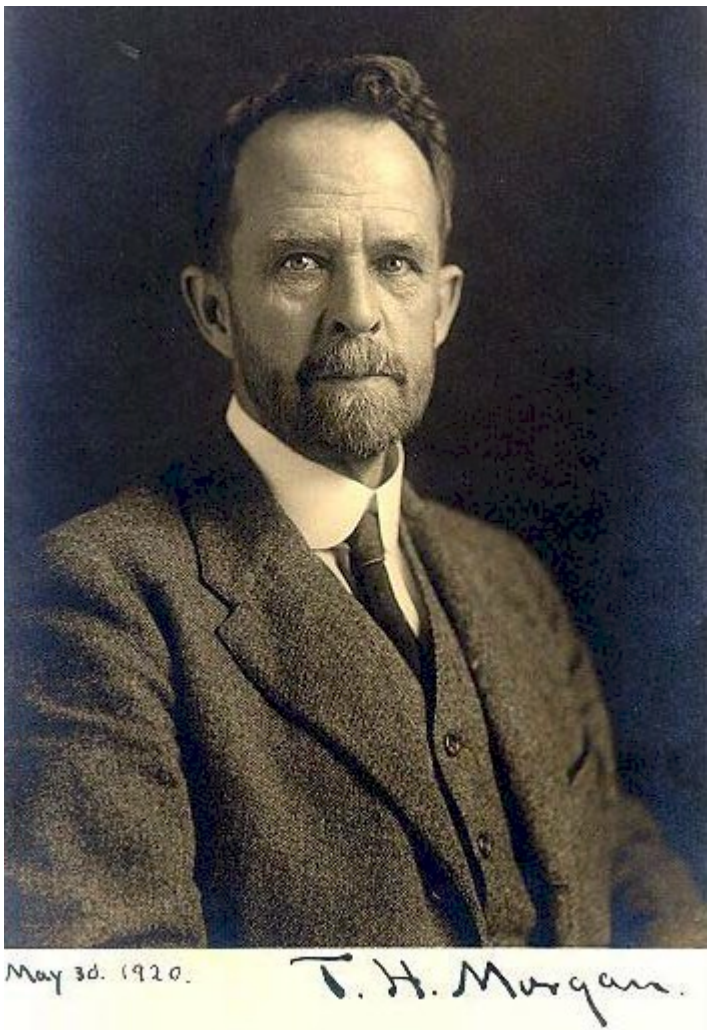
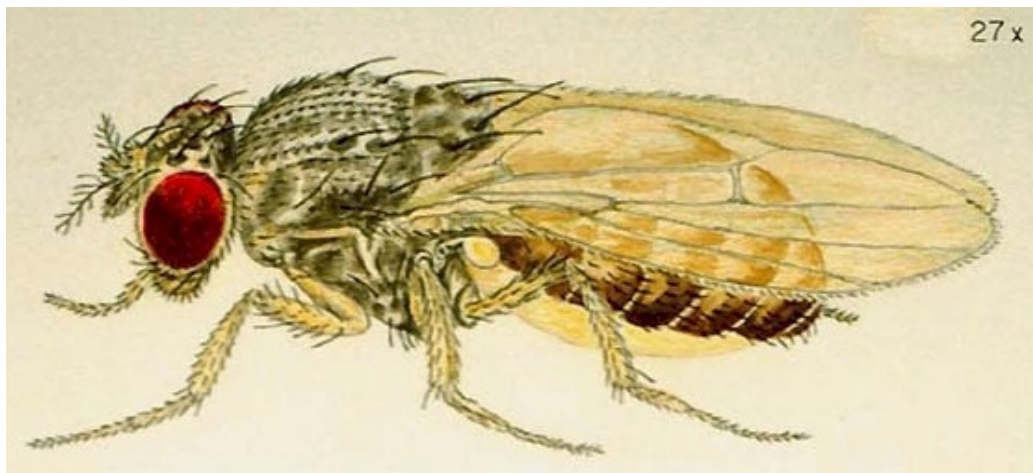
1915 - T.H. Morgan

1865



Genetics of *Drosophila*

- Short generation time
- Easy to maintain
- Only 4 pairs of chromosomes



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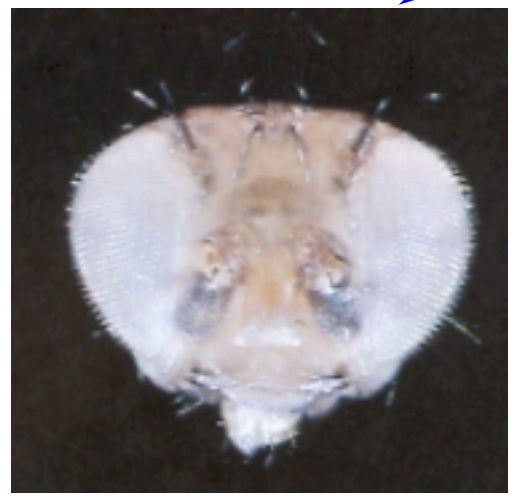
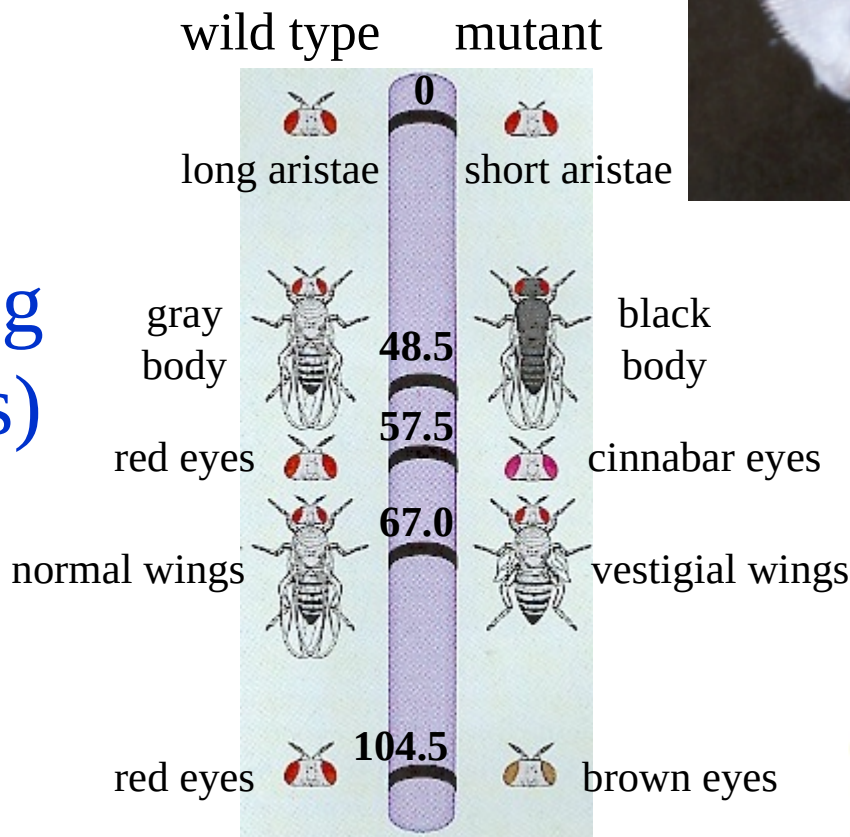
1915 - T.H. Morgan

1865



- Genes located on chromosomes
- Sex-linked inheritance
- Gene linkage
- Recombination
- Genetic mapping (cross-over maps)

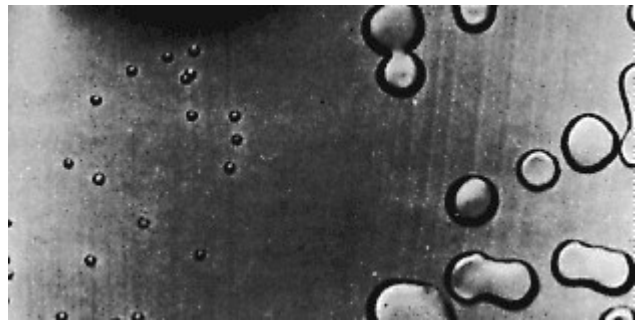


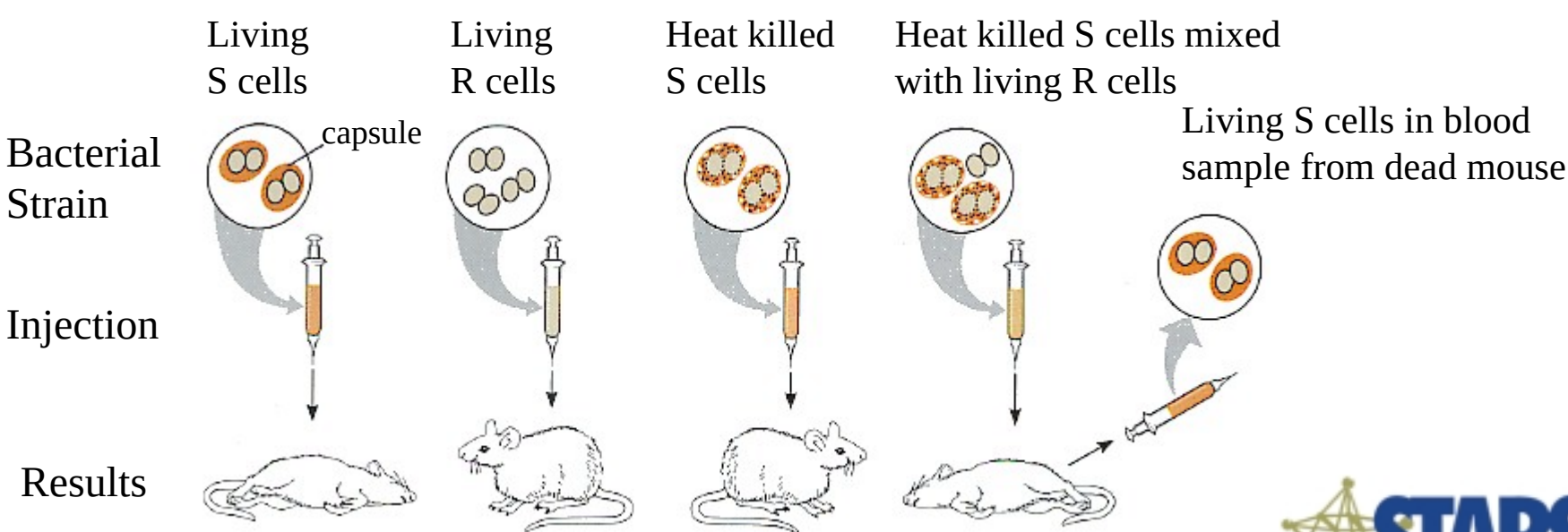
1928 - Frederick Griffith

1865

Transformation of *Streptococcus pneumoniae*

"Rough" colonies "Smooth" colonies





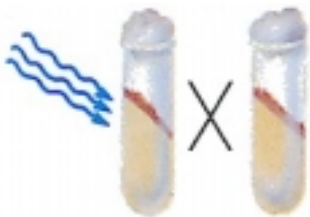
Beadle & Tatum - 1941

1865

One Gene - One Enzyme Hypothesis

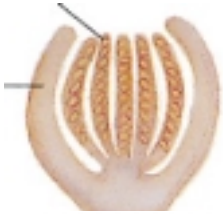
Neurospora crassa

X-rays

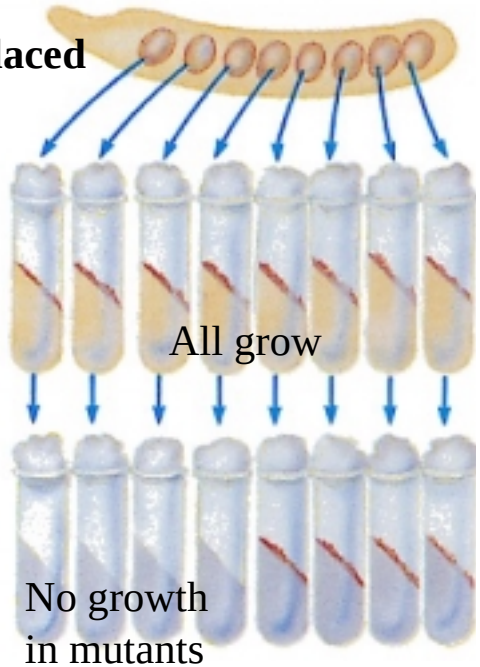


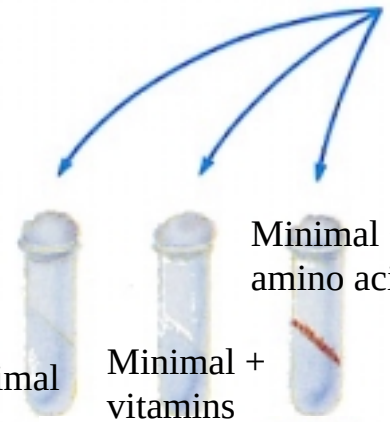
Ascus

Fruiting body

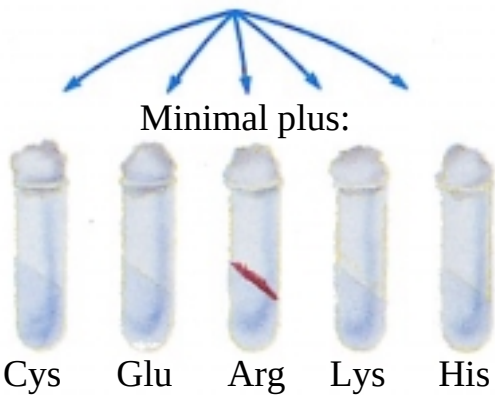


Ascospores placed on complete medium





Fragments placed on minimal medium



Mutant deficient in enzyme that synthesizes arginine

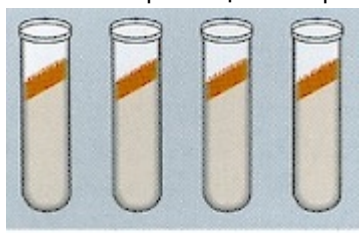
Beadle & Tatum - 1941

1865

Minimal Medium | + Ornithine | + Citruline | + Arginine

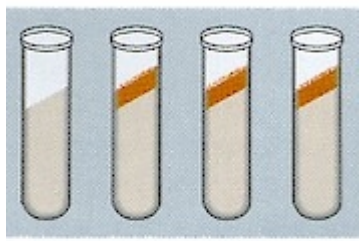
Gene A | Gene B | Gene C

Wild type



Precursor → Enz A → Ornithine → Enz B → Citruline → Enz C → Arginine

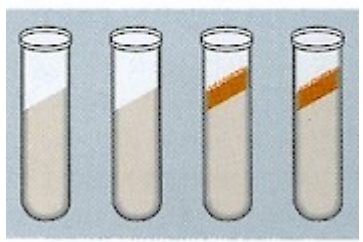
Class I Mutants



Metabolic block

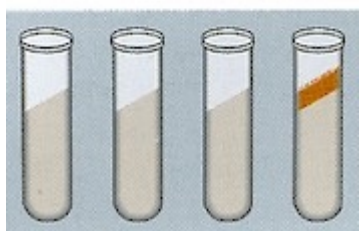
Precursor ✕ Ornithine → Enz B → Citruline → Enz C → Arginine

Class II Mutants



Precursor → Enz A → Ornithine ✕ Citruline → Enz C → Arginine

Class III Mutants

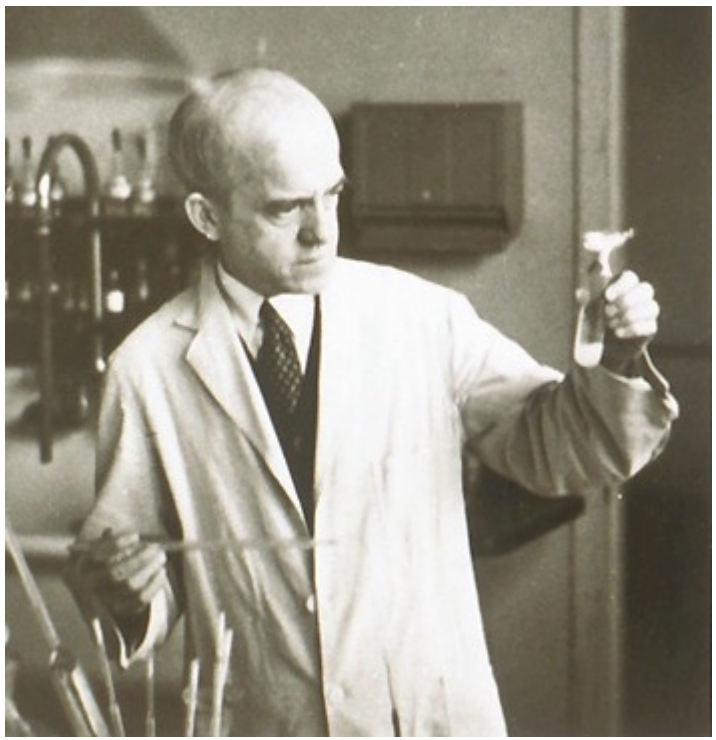


Precursor → Enz A → Ornithine → Enz B → Citruline ✕ Arginine

1865

1944 - Avery, MacLeod & McCarty

Purified DNA as transforming factor



Oswald Avery

- Work not well-received
- Protein more complex & better able to store information

Colin MacLeod

Maclyn McCarty

1947 - Erwin Chargoff

1865

DNA bases follow certain "rules"

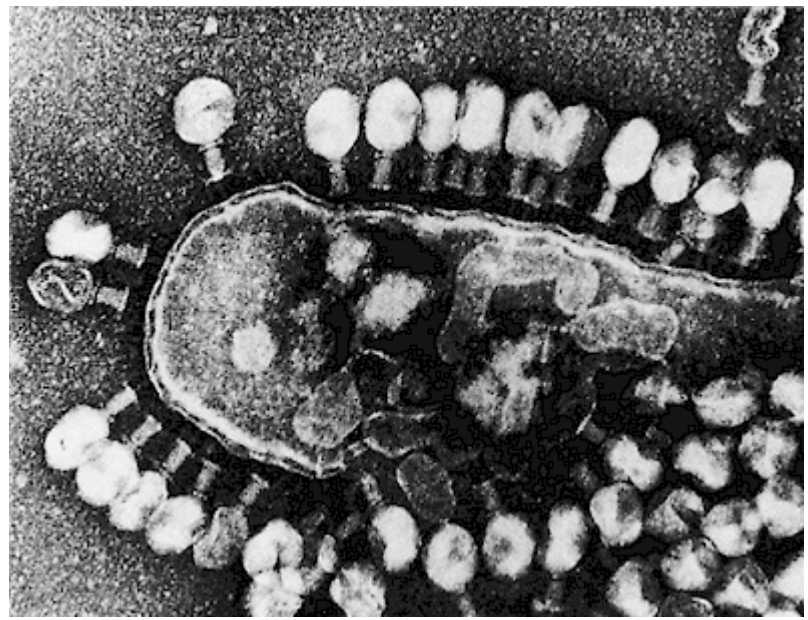
- Base composition is species specific
- A = T, C = G for all species

1952 - Hershey & Chase

1865

Viral DNA (not protein) programs cells

Martha Chase & Alfred Hershey



Bacteriophages

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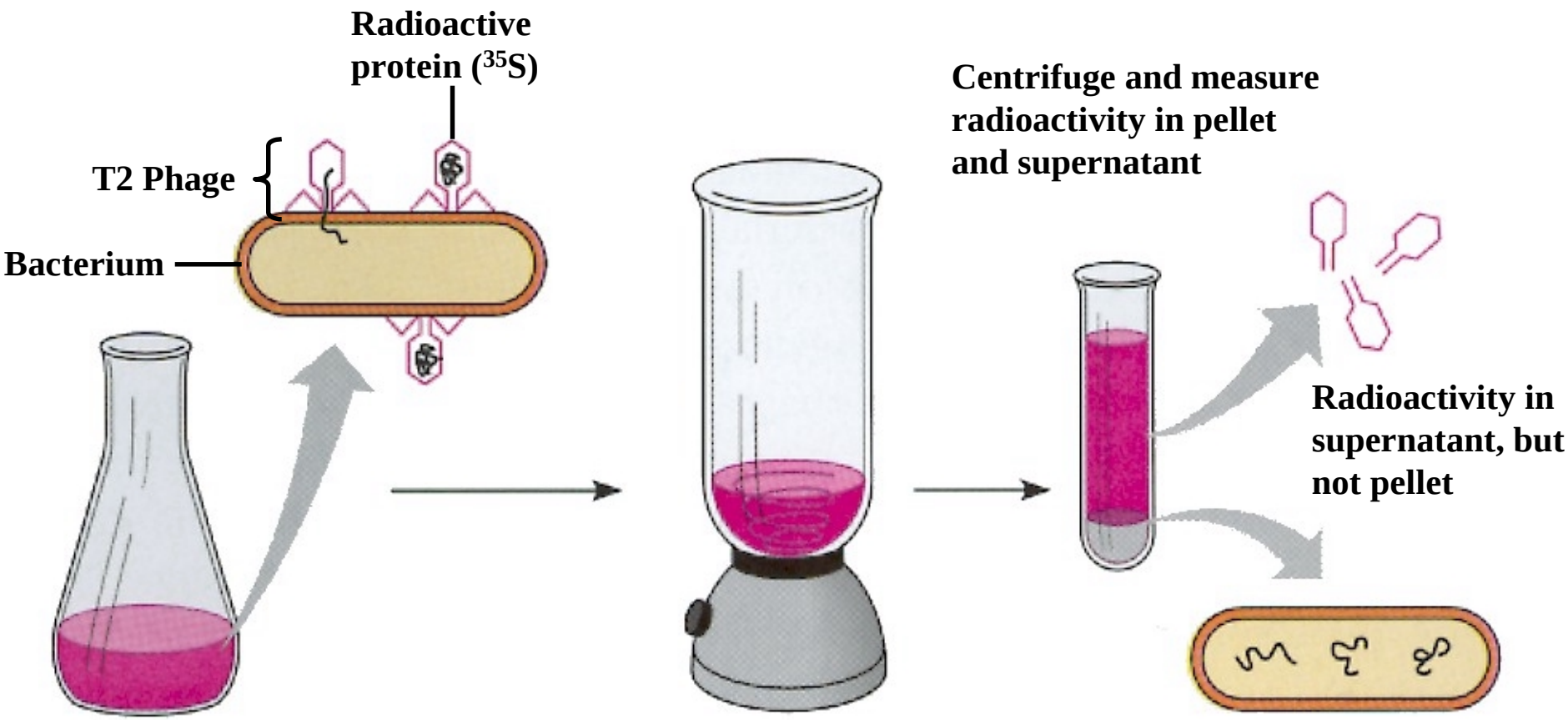
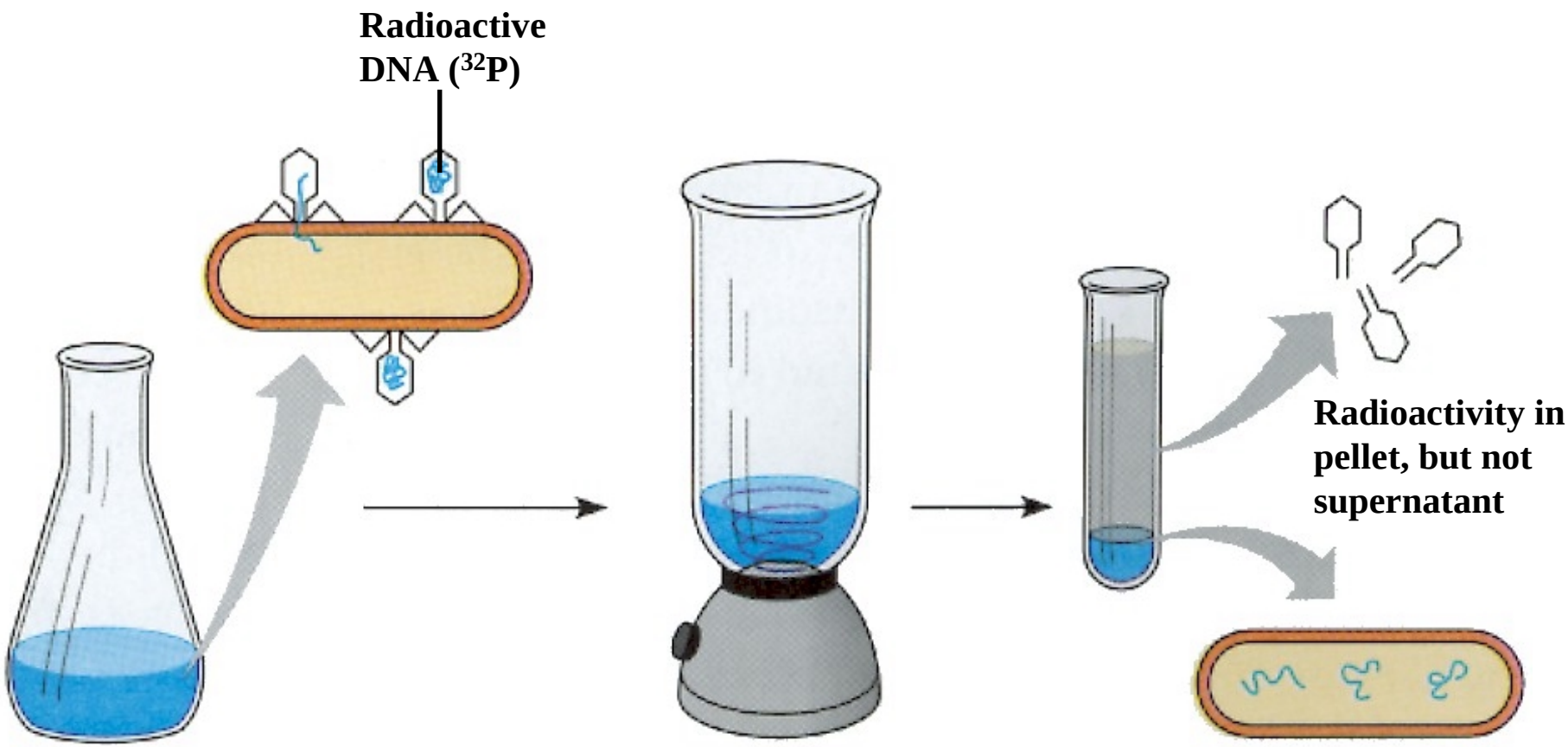
1952 - Hershey & Chase

1865



1952 - Hershey & Chase

1865



Therefore, it is the viral DNA, and not protein, that programs cells to make copies of the virus.

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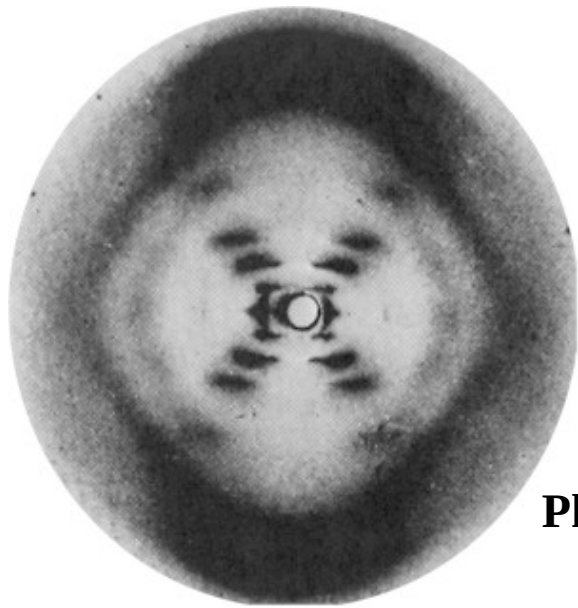
1953 - Franklin & Wilkins

Elucidation of the helical nature of DNA

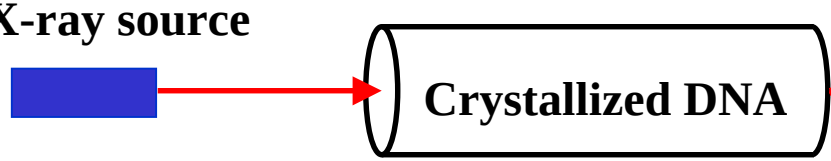
Rosalind Franklin

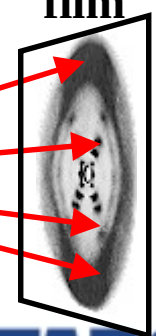


Photographic film

Maurice Wilkins

X-ray source





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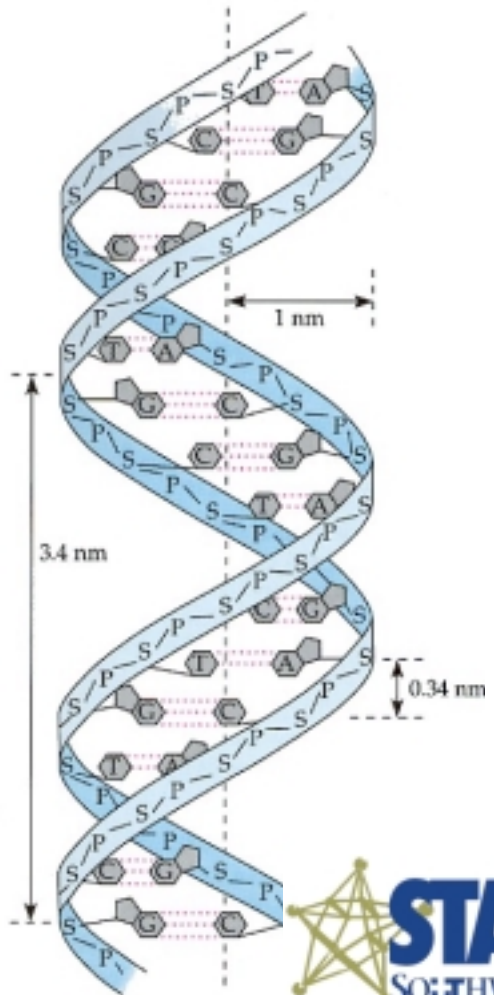
1953 - Watson & Crick

Description of the 3-D structure of DNA

Francis Crick & James Watson



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1953 - Watson & Crick

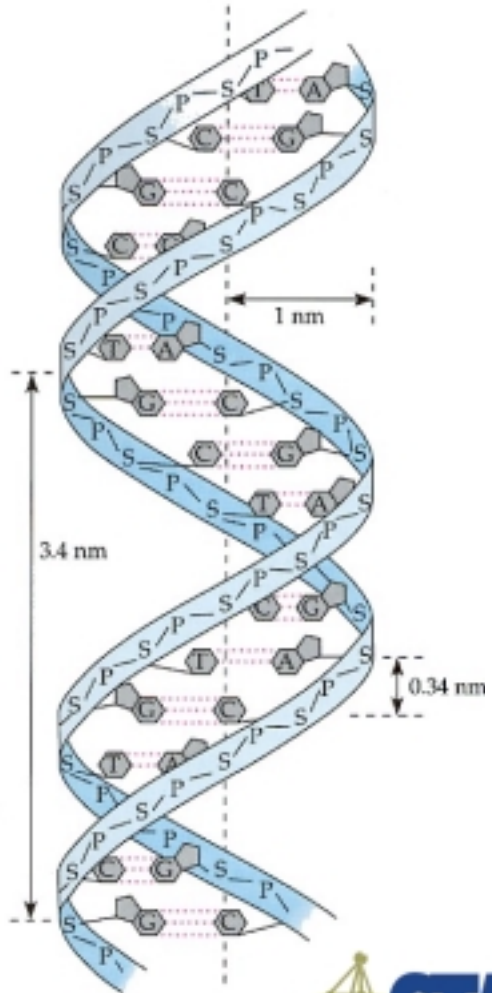
What they deduced from:

Franklin's X-ray data

- Double helix
- Uniform width of 2 nm
- Bases stacked 0.34 nm apart

Chargoff's "rules"

- Adenine pairs with thymine
- Cytosine pairs with guanine



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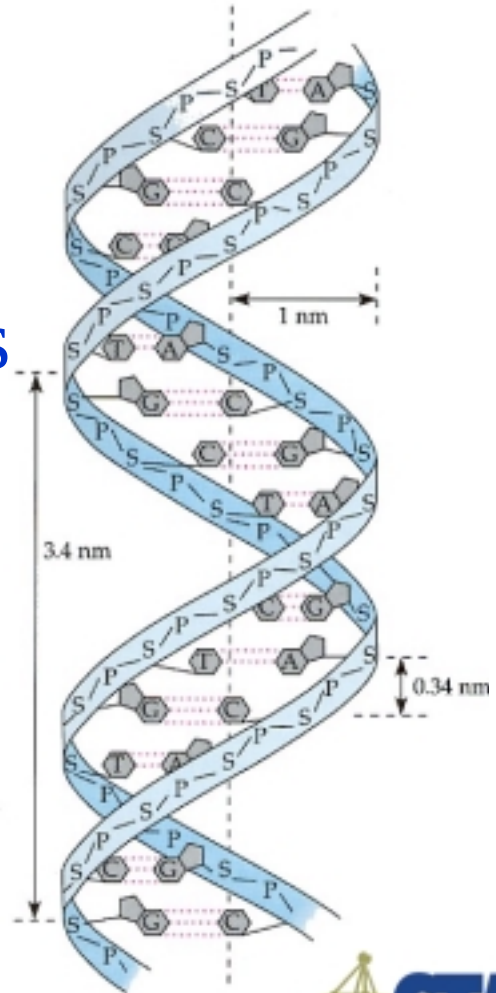
1953 - Watson & Crick

What they came up with on their own:

- Bases face inward, phosphates and sugars outward
- Hydrogen bonding
- Hinted at semi-conservative model for replication



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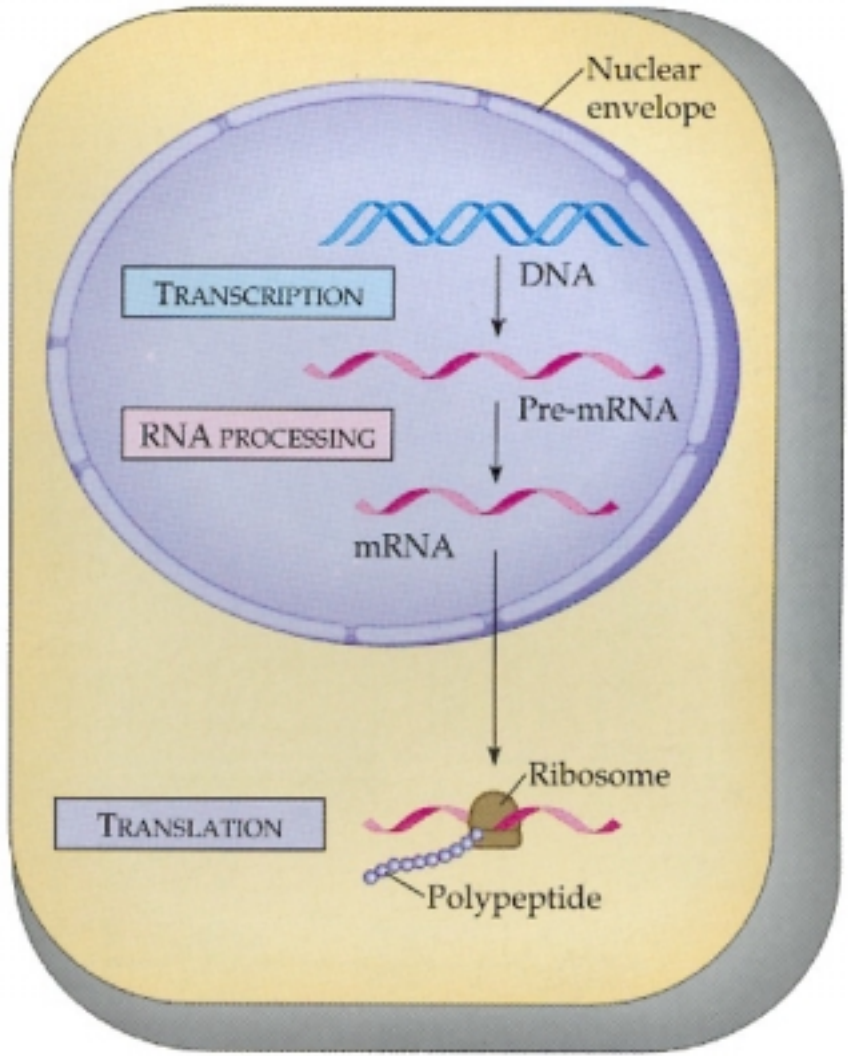
1957 - Francis Crick

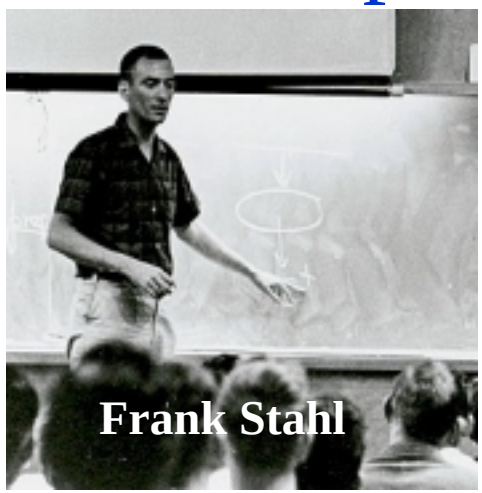
Proposal of the Central Dogma

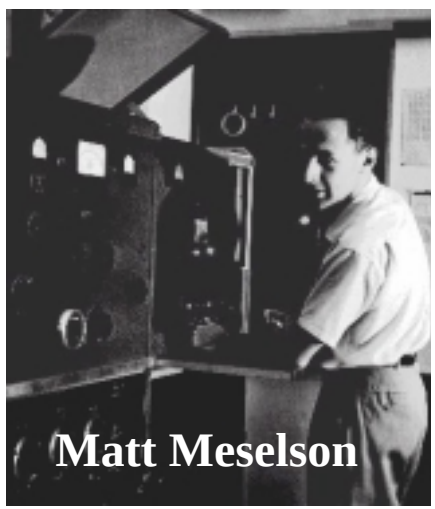


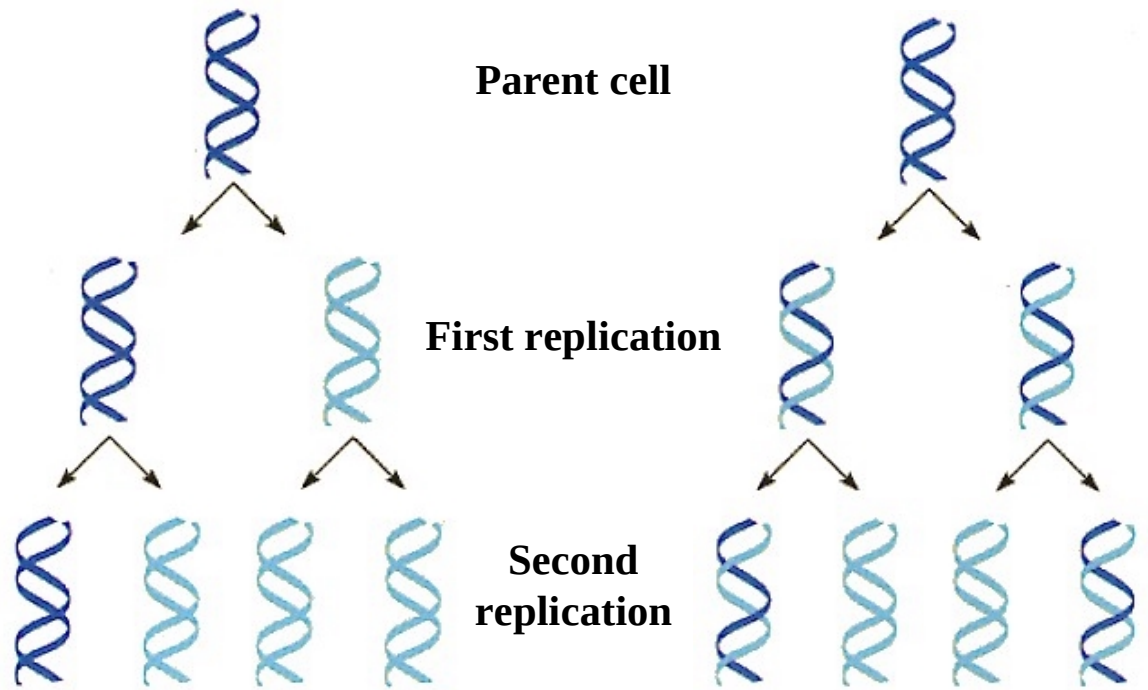
1865

1958 - Meselson & Stahl

DNA replication is semi-conservative





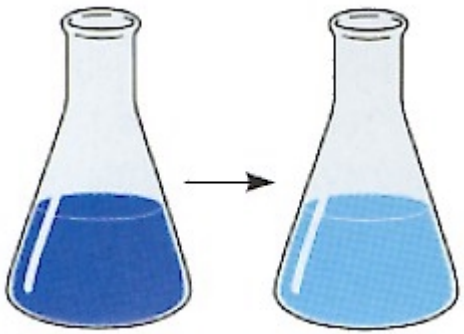


1958 - Meselson & Stahl

1865

Bacteria grown on heavy nitrogen (^{15}N) medium

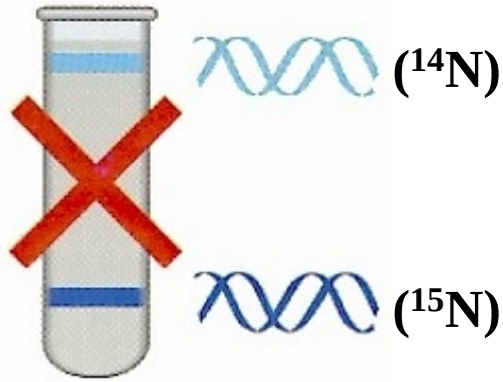
Bacteria transferred to light nitrogen (^{14}N) medium



Centrifuge samples in a density gradient

After 20 minutes (1 replication)

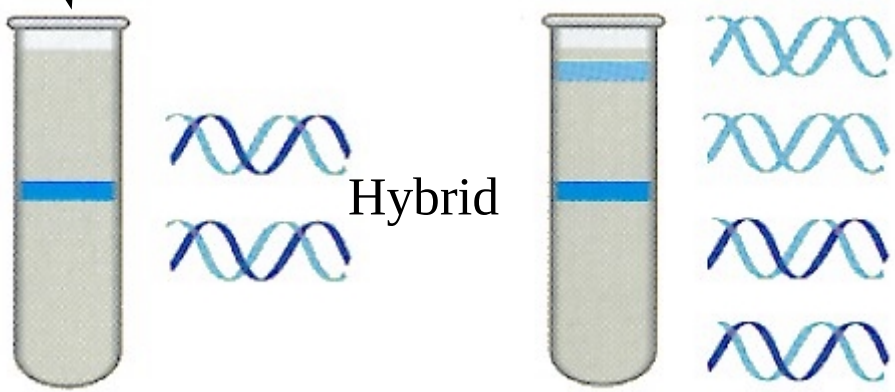
Predicted outcome based on the conservative model



After 20 minutes (1 replication)

After 40 minutes (2 replications)

Predicted outcome based on the semiconservative model



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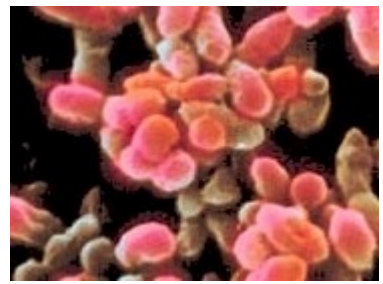
1970 - Smith & Nathans

Discovery of restriction endonucleases

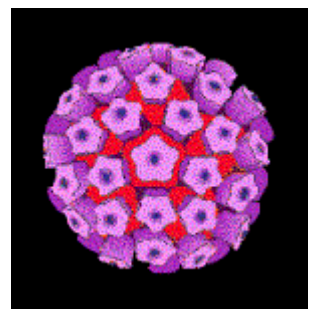
Hamilton Smith

- Discovered *Hin*dII in *Haemophilus influenzae*



Daniel Nathans

- Used *Hin*dII to make first restriction map of SV40

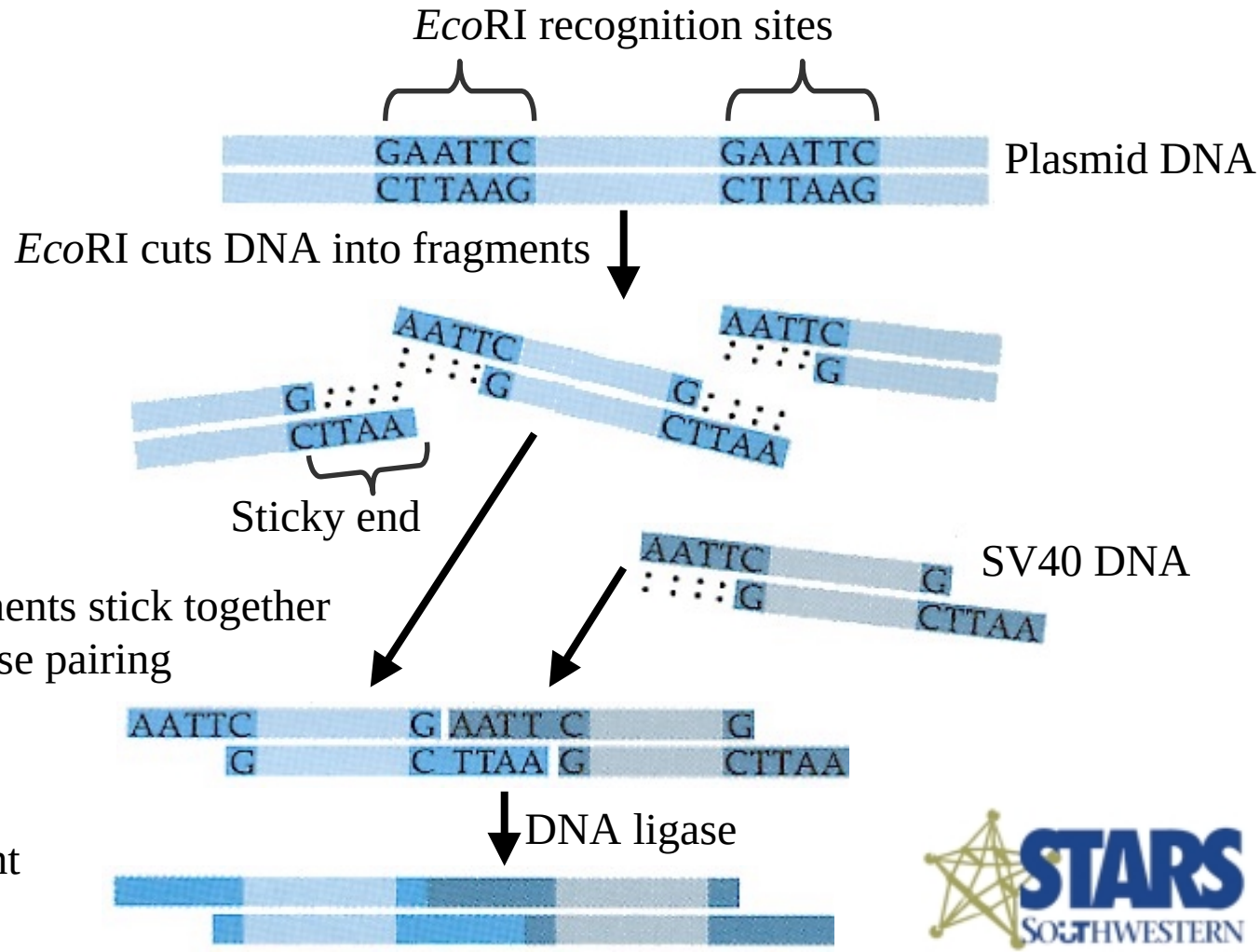


STARS Southwestern

1865

1972 - Paul Berg

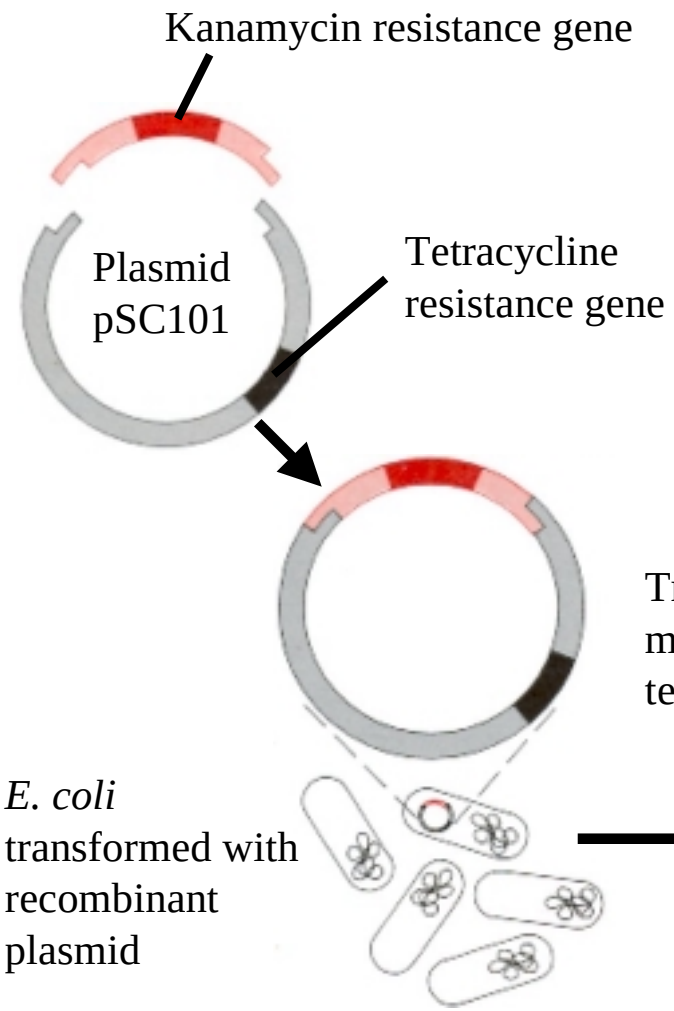
Produces first recombinant DNA using *Eco*RI



1865

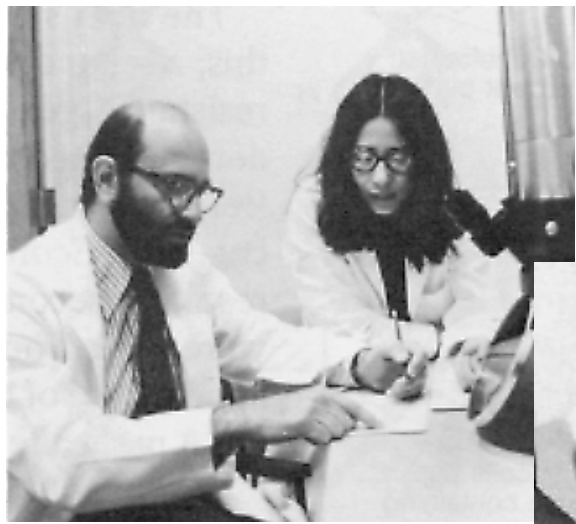
1973 - Boyer, Cohen & Chang

Transform *E. coli* with recombinant plasmid



Transformed cells plated onto medium with kanamycin and tetracycline

Only cells with recombinant plasmid survive to produce colonies



Stanley Cohen & Annie Chan

Herbert Boyer

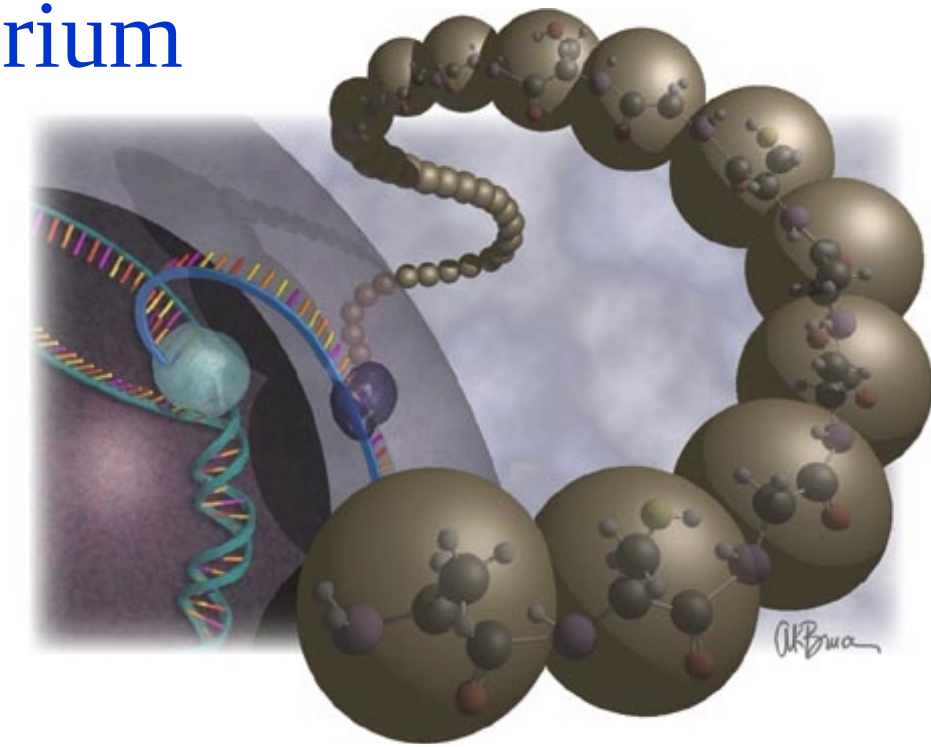
STARS SOUTHWESTERN

1977 - Genentech, Inc.

1865

First human protein (somatostatin) produced from a transgenic bacterium

- Company founded by Herbert Boyer and Robert Swanson in 1976
- Considered the advent of the Age of Biotechnology



Genentech, Inc.

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1977 - 2000 The Floodgates Open

1865

1977

- Walter Gilbert and Allan Maxam devise a method for sequencing DNA.

1978

- David Botstein discovers RFLP analysis

1980

- U.S. Supreme Court rules that life forms can be patented
- Kary Mullis develops PCR. Sells patent for $300M in 1991

1981

- First transgenic mice produced

1982

- The USFDA approves sale of genetically engineered human insulin

STARS SOUTHWESTERN

1977 - 2000 The Floodgates Open

1865

1983

- An automated DNA sequencer is developed
- A screening test for Huntington's disease is developed using restriction fragment length markers.

1984

- Alec Jeffreys introduces technique for DNA fingerprinting to identify individuals

1985

- Genetically engineered plants resistant to insects, viruses, and bacteria are field tested for the first time
- The NIH approves guidelines for performing experiments in gene therapy on humans

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1977 - 2000 The Floodgates Open

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1987

• invention of YACs (yeast artificial chromosomes) as expression vectors for large proteins

1989

• National Center for Human Genome Research created to map and sequence all human DNA by 2005.

1990

• UCSF and Stanford issued their 100th recombinant DNA patent and earning $40 million from the licenses by 1991.

• BRCA-1 discovered

• First gene therapy attempted on girl with immune deficiency

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1977 - 2000 The Floodgates Open

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1992

- U.S. Army begins "genetic dog tag" program

1994

- The Flavr Savr tomato gains FDA approval
- The first linkage map of the human genome appears

1995

- The first full gene sequence of a living organism is completed for *Hemophilus influenzae*.
- O.J. Simpson found not guilty despite DNA evidence

1996

- Genome of *Saccharomyces cerevisiae* is sequenced

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1977 - 2000 The Floodgates Open

1865

1997

- Dolly cloned from the cell of an adult ewe
- DNA microarray technology developed

1998

- The first animal genome (*C. elegans*) is sequenced

1999

- 1,274 biotechnology companies in the United States
- At least 300 biotechnology drug products and vaccines currently in human clinical trials
- Human Genome Project is on time and under budget, the complete human genome map expected in five years or less

2000?

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