Molecular Biology and Genetics

16-01-2024

Before we start the course, I need to know if you have the required background knowledge of nucleic acid and protein structure.

- One of the following is NOT a difference between DNA and RNA:
  - A) deoxyribose sugar
  - B) thymidine
  - C) double stranded
  - D) phosphate

  - This question tests your knowledge of facts. There will be very few questions like this one on the exams.

- You have isolated a new virus from CSJMU pond. It has the following genome composition:

%A = 35; %U = 25; %G = 10; %C = 30

What could be the genome of this virus?

A) Double stranded DNA
B) Single stranded DNA
C) Double stranded RNA
D) Single stranded RNA

- A long, long time ago, scientists were trying to label DNA and proteins to see which one was the genetic material. Based on the structures of nucleic acids and proteins, which of the following radioactive isotopes would you use to label only proteins but not DNA ?

  - A) ^{32}P
  - B) ^{35}S
  - C) ^{3}H
  - D) ^{14}C

  (Knowledge application question)

Johannes Friedrich Miescher

Johannes Friedrich Miescher (13 August 1844 – 26 August 1895) was a Swiss physician and biologist. He was the first scientist to isolate nucleic acid in **1869**. He also identified protamine and made a number of other discoveries.

Miescher had isolated various phosphate-rich chemicals, which he called **nuclein** (now nucleic acids), from the nuclei of white blood cells in Felix Hoppe-Seyler's laboratory at the University of Tübingen, Germany.

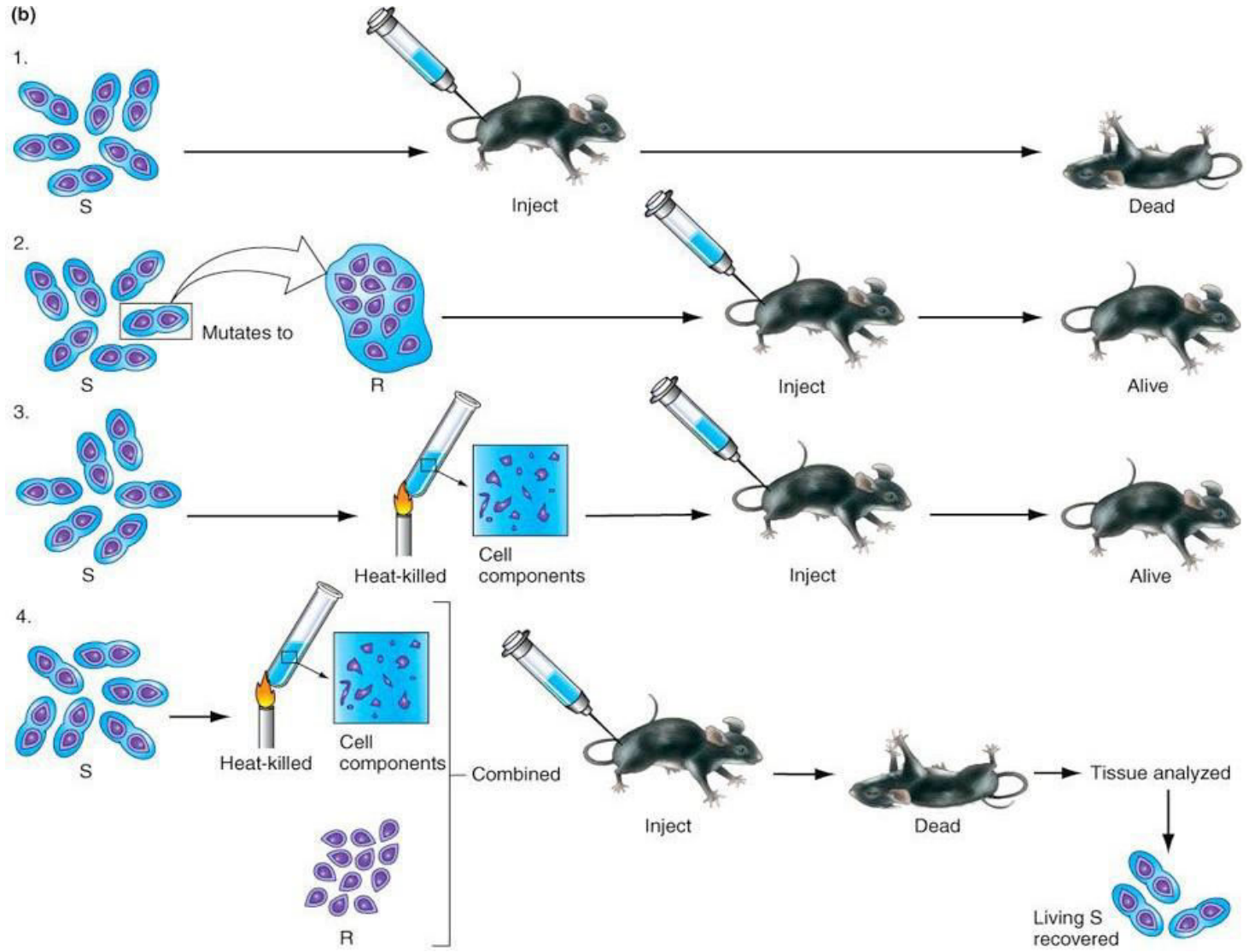
Bacterial transformation implicates DNA as the substance of genes

- 1928 – Frederick Griffith – experiments with smooth (S), virulent strain ***Streptococcus pneumoniae***, and rough (R), nonvirulent strain
  – Bacterial transformation demonstrates transfer of genetic material

- 1944 – Oswald Avery, Colin MacLeod, and MacIyn McCarty –
  – determined that DNA is the transformation material

Griffith experiment

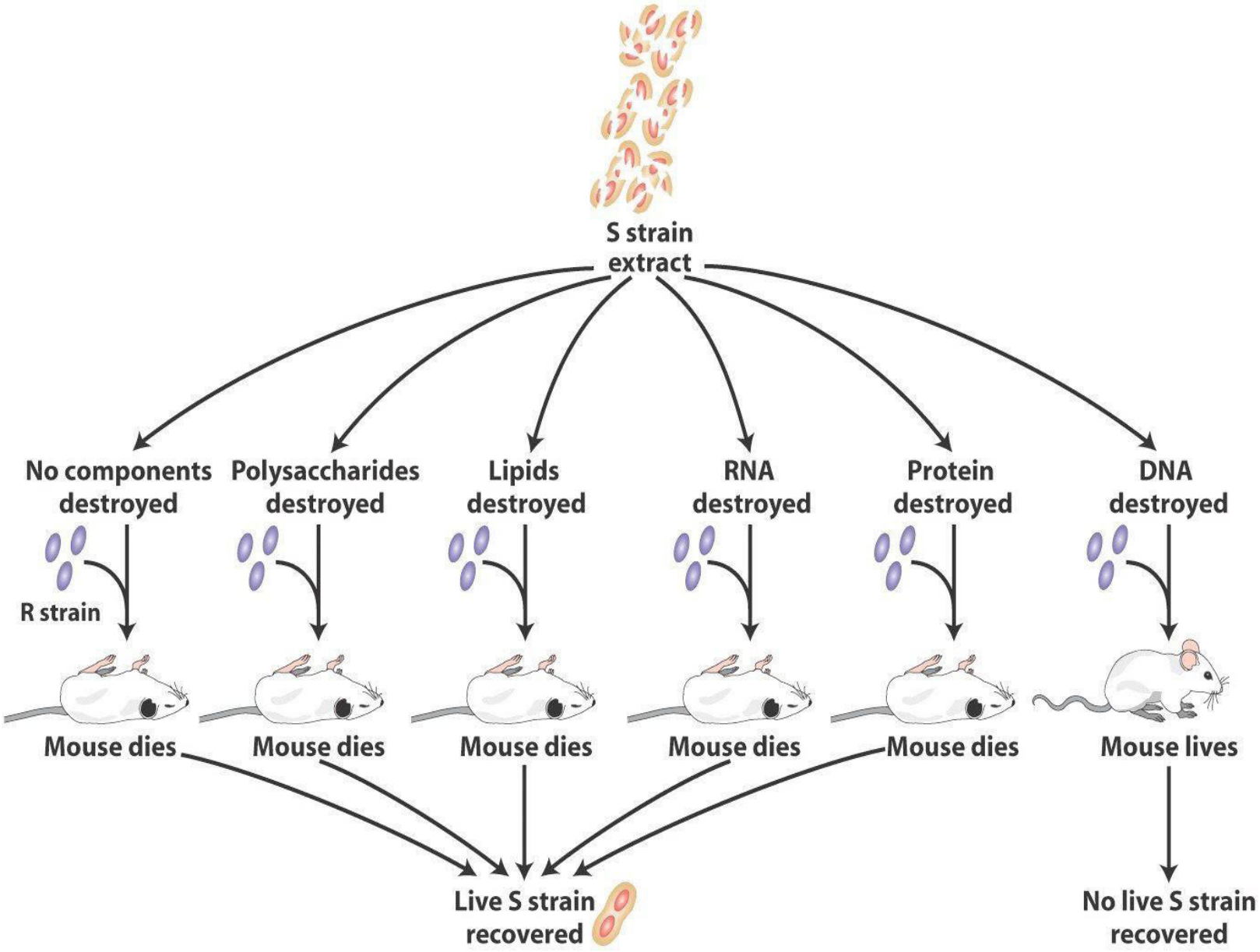
Streptococcus pneumoniae



Griffith's Experiment

- Griffith observed that live S bacteria could kill mice injected with them.
- When he heat killed the S variants and mixed them with live R variants, and then injected the mixture in the mice, they died.
- Griffith was able to isolate the bacteria from the dead mice, and found them to be of the S variety.
- Thus the bacteria had been *Transformed* from the rough to the smooth version.
- *The ability of a substance to change the genetic characteristics of an organism is known as transformation.*
- Scientists set out to isolate this 'transforming principle' since they were convinced it was the carrier of the genetic information.

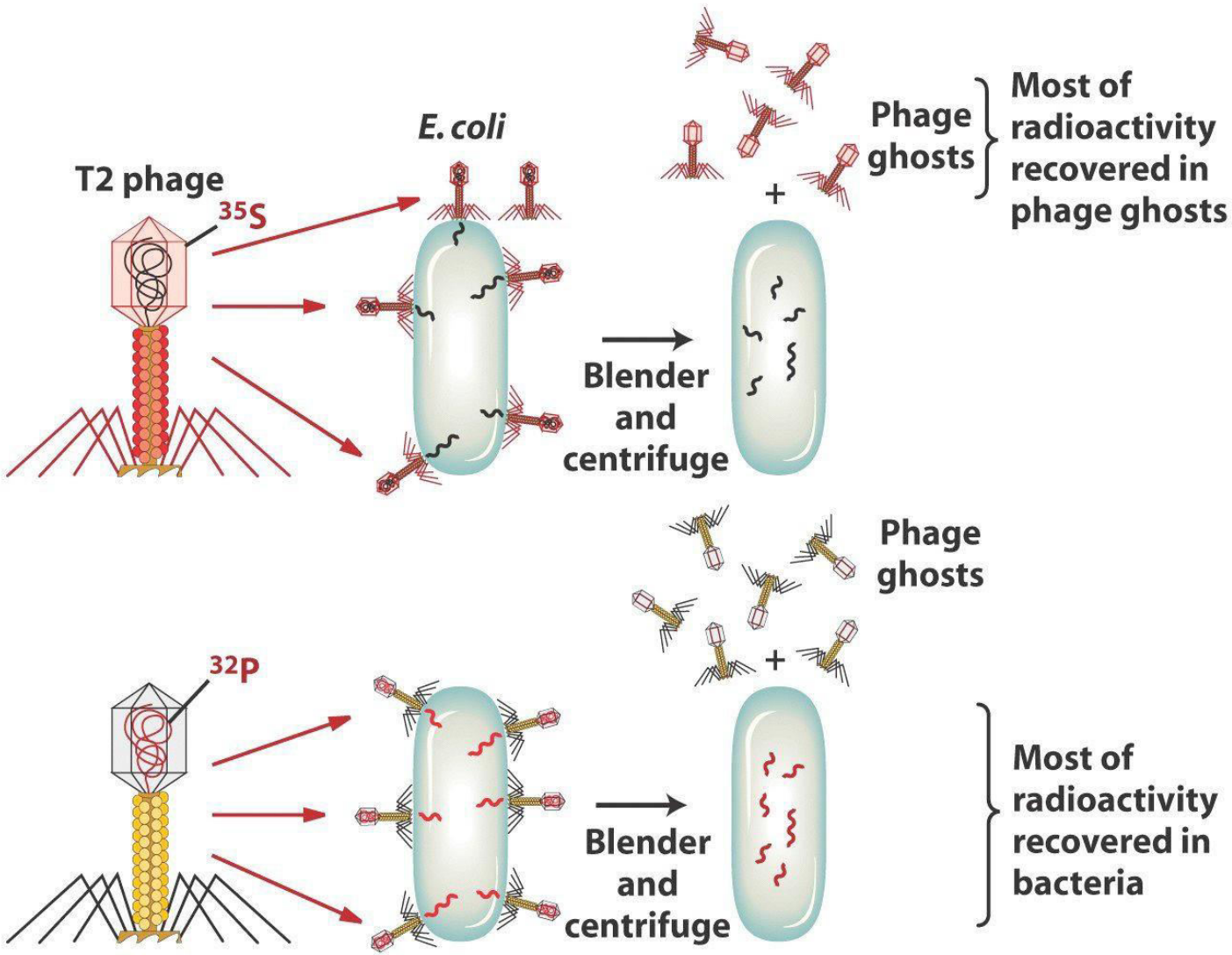
Avery, MacLeod, McCarty Experiment: Identity of the Transforming Principle



Hershey and Chase experiment

- 1952 – Alfred Hershey and Martha Chase provide convincing evidence that DNA is genetic material
- Waring blender experiment using T2 bacteriophage and bacteria
- Radioactive labels ^{32}P for DNA and ^{35}S for protein

Hersey-Chase Experiment



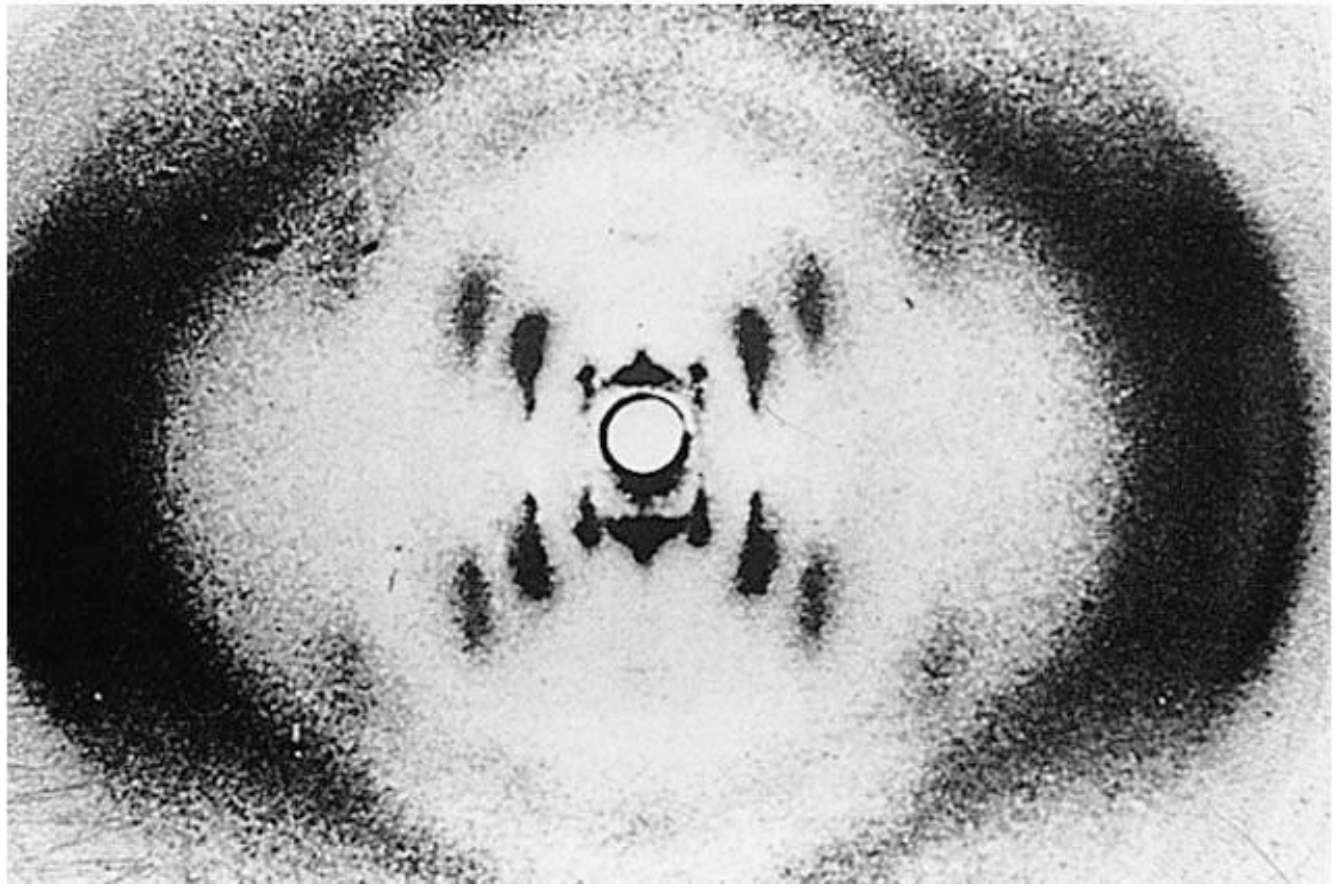
Hershey and Chase experiment

- Performed in 1952, using bacteriophage, a type of virus that have a very simple structure:
  - an outer core and an inner component.
- The phage are made up of equal parts of protein and DNA.
- It was known that the phage infect by anchoring the outer shell to the cell surface and then deposit the inner components to the cell, infecting it.
- Scientists were interested in finding out whether it was the protein component or the DNA component that got deposited inside the infected cell.
- By incorporating radiolabel either in the protein or the DNA of the infecting phage,
  - they determined that the DNA was indeed introduced into the infected bacteria, causing proliferation of new phage.

The Watson-Crick Model: DNA is a double helix

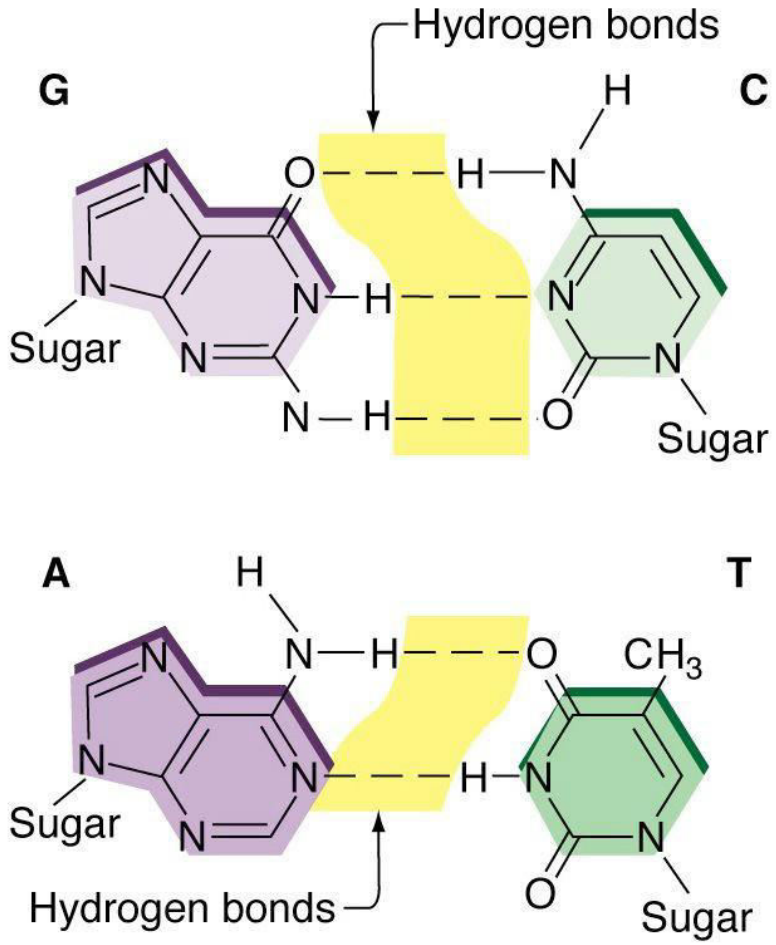
- 1951 – James Watson learns about x-ray diffraction pattern projected by DNA
- Knowledge of the chemical structure of nucleotides
  - deoxyribose sugar, phosphate, and nitrogenous base
- Erwin Chargaff's experiments demonstrate that
  - ratio of A and T are 1:1
  - ratio of G and C are 1:1
- 1953 – James Watson and Francis crick propose their double helix model of DNA structure

X-ray diffraction patterns produced by DNA fibers – Rosalind Franklin and Maurice Wilkins



Watson-Crick Model

- Double helical structure.
- The two strands are antiparallel
- It is a right handed helix, this structure is called the B DNA.
- Complementary base pairing:
  - three hydrogen bonds between C and G;
  - two hydrogen bonds between A and T.
- The arrangement of the nitrogen bases determines the genetic message.
- At each position, there are 4 possibilities,
  - therefore for a 100 base pair long molecule of DNA,
  - there are 4^{100} variations possible.



- Complementary base pairing:

– three hydrogen bonds between C and G;

–two hydrogen bonds between A and T.

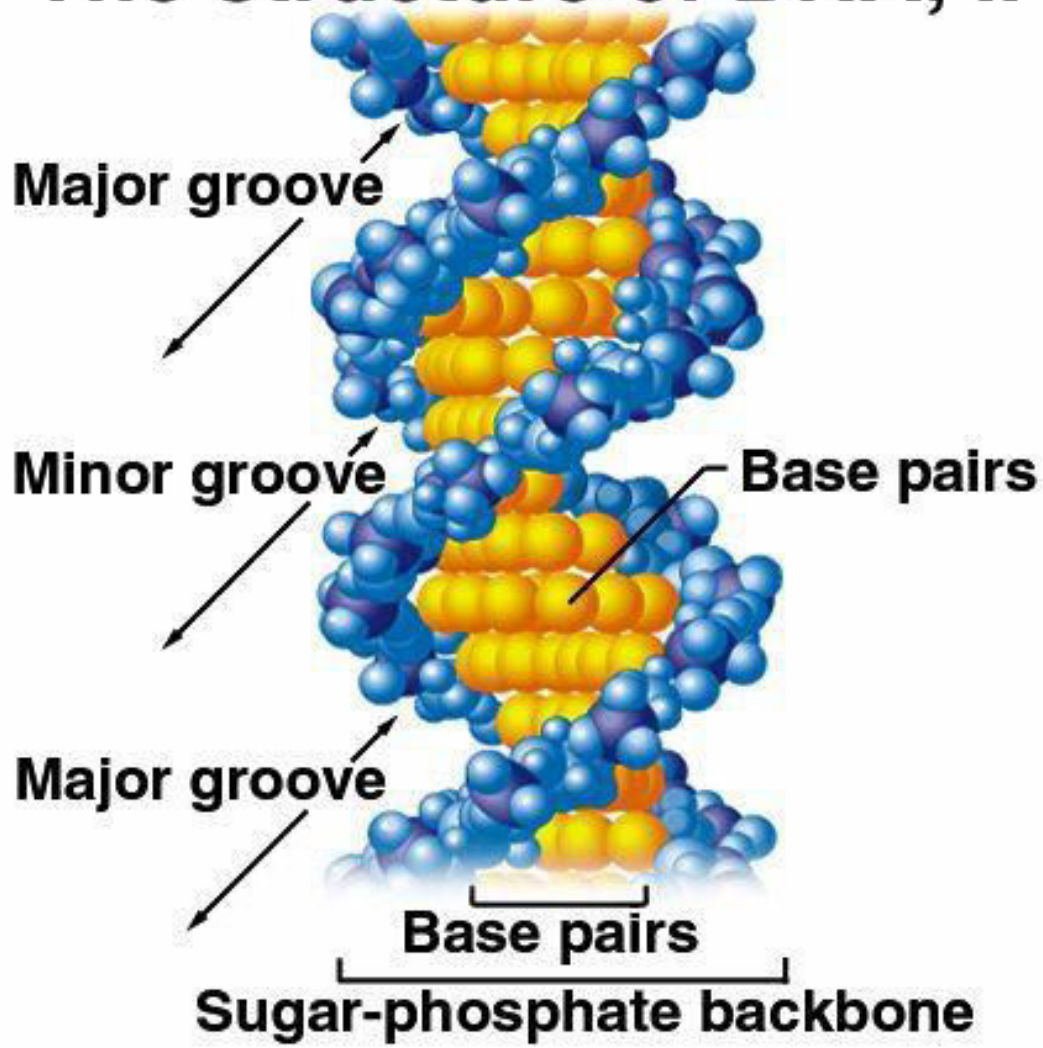
Chargaff's Rules

- Ratios of nucleotides
- A=T and G=C
- A+T does not have to equal G+C

TABLE 6.1 Chargaff's Data on Nucleotide Base Composition in the DNA of Various Organisms

	Percentage of Base in DNA				Ratios	
Organism	*A*	*T*	*G*	*C*	*A:T*	*G:C*
Staphylococcus afermentams	12.8	12.9	36.9	37.5	0.99	0.99
Escherichia coli	26.0	23.9	24.9	25.2	1.09	0.99
Yeast	31.3	32.9	18.7	17.1	0.95	1.09
*Caenorhabditis elegans**	31.2	29.1	19.3	20.5	1.07	0.96
*Arabadopsis thaliana**	29.1	29.7	20.5	20.7	0.98	0.99
Drosophila melanogaster	27.3	27.6	22.5	22.5	0.99	1.00
Honeybee	34.4	33.0	16.2	16.4	1.04	0.99
Mus musculus (mouse)	29.2	29.4	21.7	19.7	0.99	1.10
Human (liver)	30.7	31.2	19.3	18.8	0.98	1.03

The structure of DNA, II



Question

- **DNA was extracted from cells of *Staphylococcus* and found to have 37% cytosine. What percent of guanine does this species have?**

1) **37%**
2) **13%**
3) **74%**
4) **26%**

Question

What percent of thymine does this species have?

1) 37%
2) 13%
3) 74%
4) 26%