DNA: The Genetic Material

Chapter 14

Genetic Material

Frederick Griffith, 1928

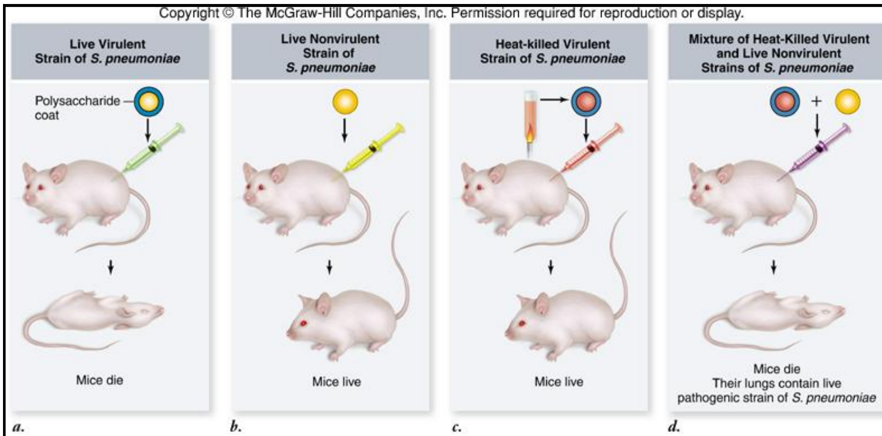
Streptococcus pneumoniae, a pathogenic bacterium causing pneumonia

2 strains of *Streptococcus*:

- S strain virulent
- R strain nonvirulent

Griffith infected mice with these strains

2



Griffith's results:
- live S strain cells killed mice
- live R strain cells did not kill mice
- heat-killed S strain cells did not kill mice
- heat-killed S strain + live R strain cells killed mice

Genetic Material

Griffith's conclusion:

- information specifying virulence passed from dead S strain cells into live R strain cells
- Griffith: transfer of information **transformation**

Genetic Material

Avery, MacLeod, & McCarty, 1944

repeated Griffith's experiment using purified cell extracts & discovered:

- removal of all protein from transforming material did not destroy its ability to transform R strain cells
- DNA-digesting enzymes destroyed all transforming ability
- transforming material → DNA

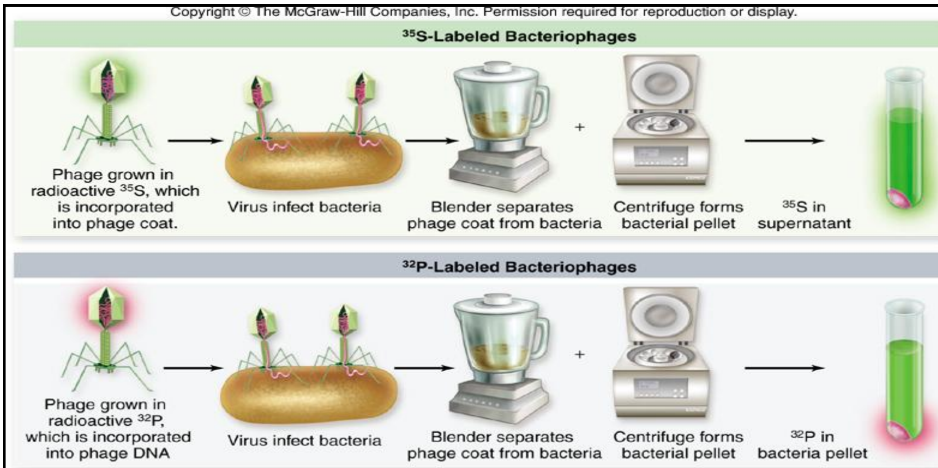
5

Genetic Material

Hershey & Chase, 1952

- investigated **bacteriophages**: viruses that infect bacteria
- bacteriophage composed of only DNA & protein
- to determine which of these molecules is genetic material injected into bacteria

6



- Bacteriophage DNA labeled phosphorus (^{32}P)
- Bacteriophage protein labeled sulfur (^{35}S)
- radioactive molecules tracked
-only bacteriophage DNA (^{32}P) entered bacteria & used to produce more bacteriophage
- conclusion: DNA → genetic material

7

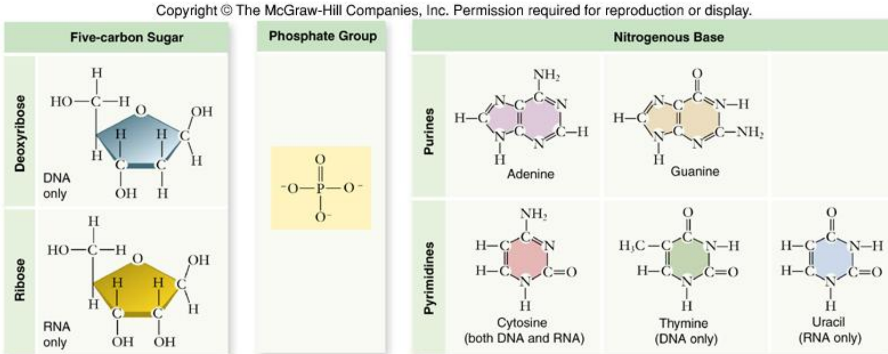
DNA Structure

DNA: **nucleic acid**.

Building blocks of DNA: **nucleotides**, each composed of:

- 5-carbon sugar called **deoxyribose**
- phosphate group (PO_4)
- nitrogenous base
  - adenine, thymine, cytosine, guanine

8

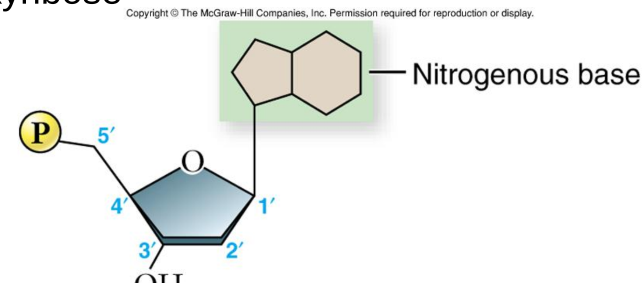


9

DNA Structure

Nucleotide structure consists of

- nitrogenous base attached to the 1' carbon of deoxyribose
- phosphate group attached to the 5' carbon of deoxyribose
- free hydroxyl group (-OH) at the 3' carbon of deoxyribose



10

DNA Structure

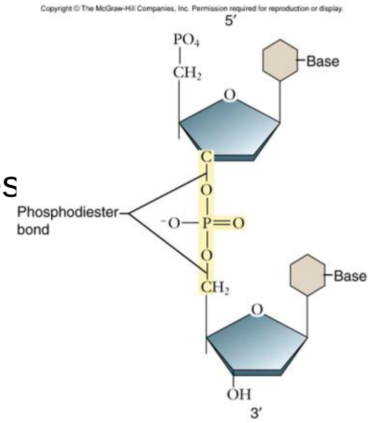
Nucleotides connected to
each other to form long chain

phosphodiester bond:

bond between adjacent nucleotides

- formed between phosphate group
  of 1 nucleotide
  & 3' –OH of next nucleotide

Chain of nucleotides
5' to 3' orientation



11

DNA Structure

Determining the 3-dimmensional structure of DNA involved the work of a few scientists:

- Erwin Chargaff determined that
  - amount of adenine = amount of thymine
  - amount of cytosine = amount of guanine

This is known as Chargaff's Rules

12

DNA Structure

Rosalind Franklin & Maurice Wilkins

- Franklin performed X-ray diffraction studies to identify 3-D structure
- discovered DNA is helical
- discovered molecule has a diameter of 2 nm & makes a complete turn of helix every 3.4 nm

13

DNA Structure

James Watson & Francis Crick, 1953

- deduced structure of DNA using evidence from Chargaff, Franklin & others
- proposed a **double helix** structure

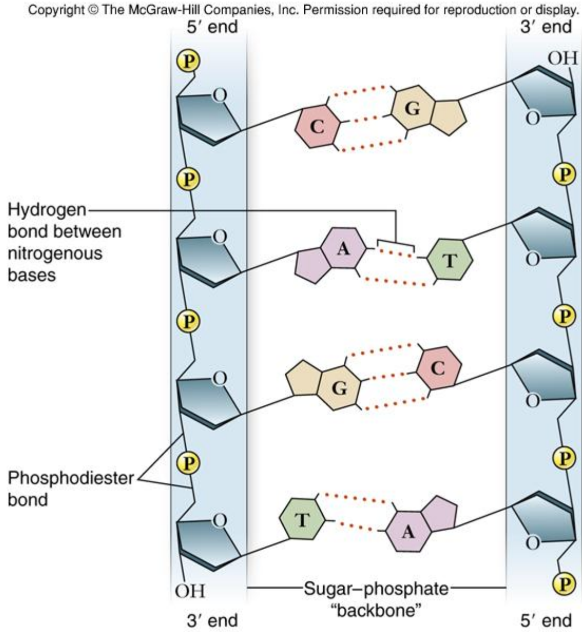
14

DNA Structure

Double helix consists of:

- 2 sugar-phosphate backbones
- nitrogenous bases toward interior of molecule
- bases form hydrogen bonds with **complementary bases** on opposite sugar-phosphate backbone

15



16

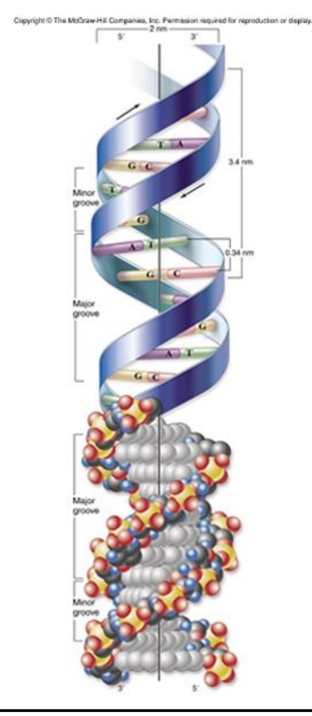
DNA Structure

Two strands of nucleotides **antiparallel** to each other

– one oriented 5’ to 3’, other 3’ to 5’

Two strands wrap around each other to create the helical shape of molecule

17



18

DNA Replication

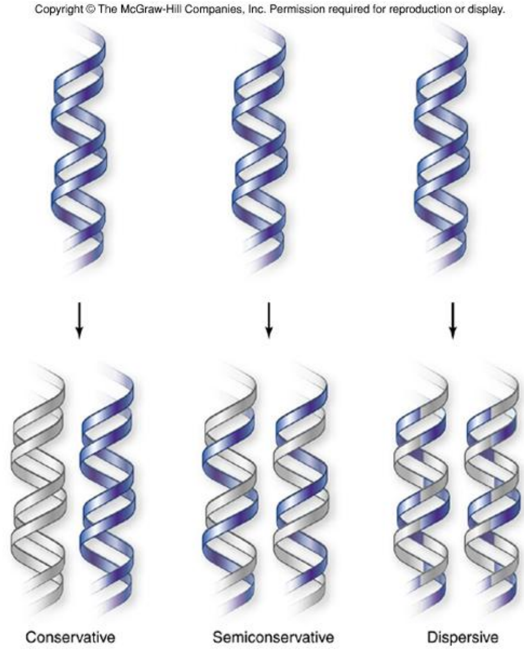
Matthew Meselson & Franklin Stahl, 1958

investigated process of DNA replication

considered 3 possible mechanisms:

- **conservative model**
- **semiconservative model**
- **dispersive model**

19



20

DNA Replication

Bacterial cells were grown in a heavy isotope of nitrogen, ^{15}N

all the DNA incorporated ^{15}N

cells were switched to media containing lighter ^{14}N

DNA was extracted from the cells at various time intervals

21

DNA Replication

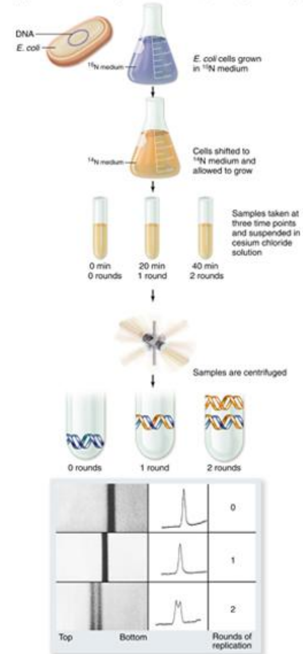
DNA from different time points analyzed for ratio of ^{15}N to ^{14}N it contained

After 1 round of DNA replication, DNA consisted of a ^{14}N-^{15}N hybrid molecule

After 2 rounds of replication, DNA contained 2 types of molecules:

- half DNA was ^{14}N-^{15}N hybrid
- half DNA was composed of ^{14}N

22



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23

DNA Replication

Meselson & Stahl concluded mechanism of DNA replication: **semiconservative model**

Each DNA strand acts as a template for synthesis of a new strand

24

The Nature of Genes

Central dogma of molecular biology states that information flows in one direction:

DNA ⟶ RNA ⟶ protein

Replication: DNA →DNA

Transcription: DNA → RNA

Translation: RNA → protein

25

DNA Replication

DNA replication includes:

- **initiation** – replication begins at an **origin of replication**
- **elongation** – new strands of DNA are synthesized by **DNA polymerase**
- **termination** – replication terminated differently in prokaryotes & eukaryotes

26

Eukaryotic DNA Replication

Larger size & complex packaging of eukaryotic chromosomes means they must be replicated from multiple origins of replication

Enzymes of eukaryotic DNA replication more complex than those of prokaryotic cells

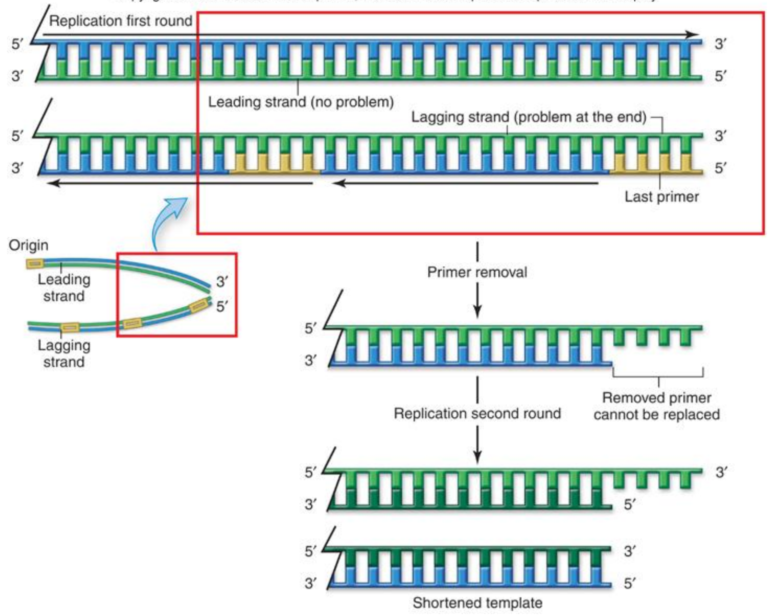
27

Eukaryotic DNA Replication

Synthesizing ends of chromosomes difficult because of lack of a primer

With each round of DNA replication, linear eukaryotic chromosome becomes shorter

28



29

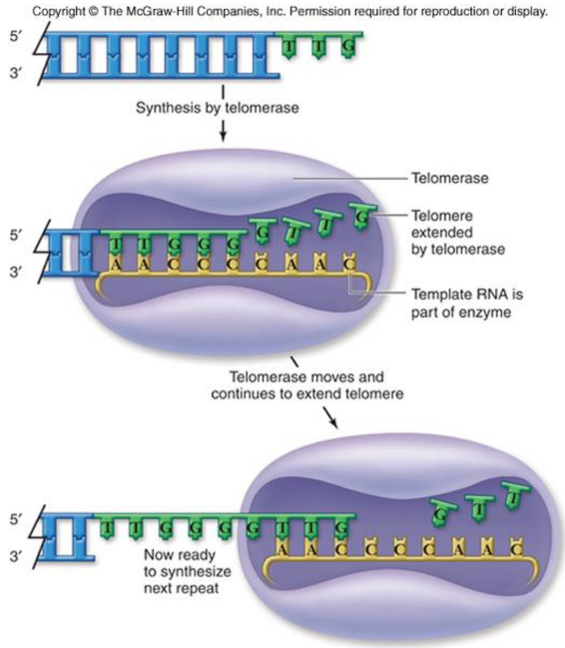
Eukaryotic DNA Replication

telomeres – repeated DNA sequence on ends of eukaryotic chromosomes

– produced by **telomerase**

telomerase contains an RNA region that is used as a template so a DNA primer can be produced

30



31

DNA Repair

- DNA-damaging agents
- repair mechanisms
- specific vs nonspecific mechanisms

32

DNA Repair

Mistakes during DNA replication can lead to changes in DNA sequence & DNA damage

DNA can also be damaged by chemical or physical agents called **mutagens**

Repair mechanisms: correct these problems

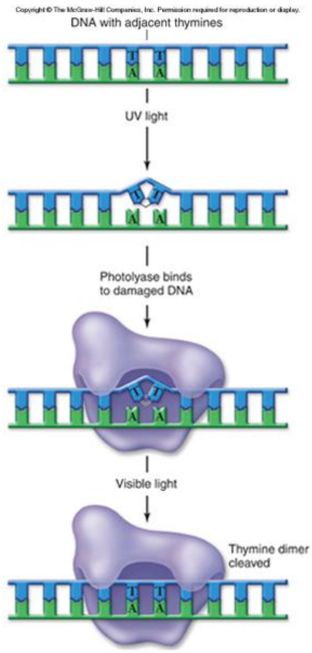
33

DNA Repair

DNA repair mechanisms can be:

- specific – targeting a particular type of DNA damage
  - photorepair of **thymine dimers**
- non-specific – able to repair many different kinds of DNA damage
  - **excision repair** to correct damaged or mismatched nitrogenous bases

34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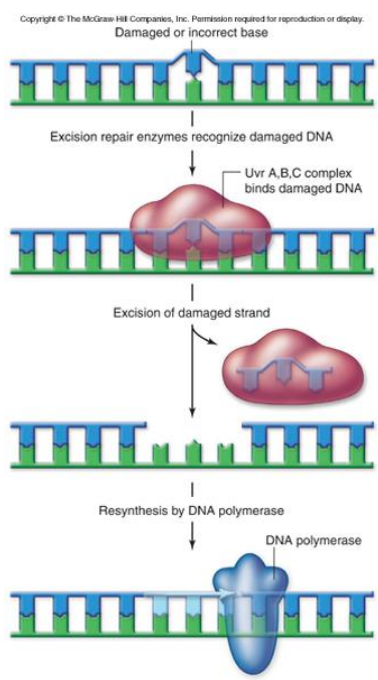
DNA with adjacent thymines
UV light
Photolyase binds
to damaged DNA
Visible light
Thymine dimer
cleaved

35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Damaged or incorrect base
Excision repair enzymes recognize damaged DNA
Uvr A,B,C complex
binds damaged DNA
Excision of damaged strand
Resynthesis by DNA polymerase
DNA polymerase

36