Chapter 8
DNA Structure and Chromosomal Organization
DNA Carries the Genetic Information
Frederick Miescher (1860s)

- Isolated nuclei from pus cells
- Chemically extracted nuclein
- It contained H, C, O, N, and P
- Nuclein was found in the nucleus of many other cell types
- Later, it was shown nuclein contained DNA
Fredrick Griffith (1920s)

- *Streptococcus pneumoniae* caused pneumonia in mice
- Two strains
  - Strain S (nonvirulent) formed a capsule (smooth coat); did not kill mice
  - Strain R (virulent) did not form a capsule (no coat); caused pneumonia
Mice injected with live cells of harmless strain R.

Mice live. No live R cells in their blood.
Transformation of Bacterial Strains

• Heat-killed virulent bacteria transformed the living nonvirulent bacteria

• The transforming factor passed from the dead cell to the living cells

• This transforming factor was the genetic material
S allele controls production of smooth coat

R allele cannot produce coat

The two strains of bacteria differ only in the S/R allele.

Bacteria can take up DNA from outside.

Bacteria have circular chromosomes.

Transformation

S

R

S

R

S
Oswald Avery, Colin Macleod, and Maclyn McCarty (1944)

- Used enzymes to remove DNA, RNA, or protein

Conclusions:
- Only DNA transfers heritable information from one bacterial strain to the other
- DNA controls the synthesis of specific products
**Avery, MacLeod and McCarty, 1944**

What is the nature of the ‘transforming principle?’

Fractionated S cell components to isolate transforming principle:

<table>
<thead>
<tr>
<th>Treat with</th>
<th>Material destroyed</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protease</td>
<td>Proteins</td>
<td>Transformation</td>
</tr>
<tr>
<td>RNAaase</td>
<td>RNA</td>
<td>Transformation</td>
</tr>
<tr>
<td>DNAaase</td>
<td>DNA</td>
<td>No Transformation</td>
</tr>
<tr>
<td>Ultracentrifugation</td>
<td>Fats</td>
<td>Transformation</td>
</tr>
</tbody>
</table>
Bacteriophage are viruses that infect bacteria.

They consist of a ‘head’ made of protein that encapsulates DNA.

They infect bacteria and inject genetic material into them, causing the production of more phage.

What is the nature of this genetic material??????
Bacteriophages

Phage life cycle

Phage attaches to bacterial cell.
Phage DNA is injected into cell.
Phage DNA directs synthesis of new phages assembly.
Host cell is lysed; phages begin new cycle of infection.

Fig. 8.2

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Hypothesis is:

Genetic material could be either DNA or proteins.

Known that DNA incorporates phosphorus but not sulfur.

Known that proteins incorporate sulfur but not phosphorus.

Therefore:

Addition of $^{32}\text{P}$ will label DNA but not proteins

Addition of $^{35}\text{S}$ sulfur will label proteins but not DNA.
Hershey and Chase’s Experiments

- \(^{35}\text{S}\) labels protein
- Protein remains outside of the cells

\(^{35}\text{S}\) remains outside cells

Fig. 8.3
- $^{32}\text{P}$ labels DNA
- DNA is inserted in the cells

$^{32}\text{P}$ remains inside cells
Conclusion:

DNA is the genetic material
Review of terms

- Atoms
- Elements
- Molecules
- Bonds
  - Covalent bonds
  - Hydrogen bonds

![Diagram of Covalent and Hydrogen bonds](image)
Nucleic Acids

• Two types
  – DNA
  – RNA

• Composed of nucleotides
  Nucleotides are composed of
  – Pentose sugar (deoxyribose or ribose)
  – Phosphate group
  – Base (either a purine or pyrimidine)
Nucleotide Components

- Pentose sugar
  - (deoxyribose or ribose)
- Strongly acidic phosphate group
Nitrogen-containing Bases

Purines
Adenine (A)
Guanine (G)

Pyrimidines
Cytosine (C)
Thymine (T) in DNA
Uracil (U) in RNA

Fig. 8.5c
Nucleotide Components

- Sugar
- Base
- Phosphate
Polynucleotides Are Directional

Five prime end

Three prime end

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DNA polynucleotide chain

5’ end

O\(^-\)

O\(^-\) -P = O

O

5’

CH\(_2\)

O

Base

3’ H

H

5’

CH\(_2\)

O

Base

3’ H

H

3’ end
Structure of DNA

1950-3

DNA is a double helix

1953

Rosalind Franklin

Maurice Wilkins

Jim Watson

Francis Crick
James Watson and Francis Crick (1953)

They developed the molecular model of DNA using information from many researchers

Their model was based on:

- X-ray crystallography – gives information on physical structure
- Chemical information about nucleotide composition
Rosalind Franklin Worked with Maurice Wilkins

X-ray crystallographic pictures of DNA

Suggested:

• DNA is a helix

• Phosphates on the outside

• Information about the distances between bases
Chargaff Rule of Base Composition of DNA

Amount of A = Amount of T
Amount of G = Amount of C

- A forms hydrogen bonds with T
- G forms hydrogen bonds with C
<table>
<thead>
<tr>
<th></th>
<th>% of base in DNA</th>
<th>Ratios</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>A</td>
<td>T</td>
</tr>
<tr>
<td><strong>Human</strong></td>
<td>31.0</td>
<td>31.5</td>
</tr>
<tr>
<td><strong>Drosophila</strong></td>
<td>27.3</td>
<td>27.6</td>
</tr>
<tr>
<td><strong>E. coli</strong></td>
<td>26.1</td>
<td>23.9</td>
</tr>
<tr>
<td><strong>C. elegans</strong></td>
<td>31.2</td>
<td>29.1</td>
</tr>
</tbody>
</table>
DNA Is a Double-Stranded Helix

Key to the bases:
- A = Adenine
- T = Thymine
- C = Cytosine
- G = Guanine
- U = Uracil (RNA)

Fig. 8.7
Important Properties of the Model

• Genetic information is stored in the sequence of bases in the DNA

• The model offers a molecular explanation for mutations

• Complementary strands of DNA can be used to explain how DNA copies itself
Molecular Model of DNA
1962 Nobel Prize

• Awarded to Watson, Crick, and Wilkins for their work on the molecular structure of DNA

• Franklin had died in 1958
RNA Is Single Stranded

- Transfers genetic information from the nucleus to the cytoplasm
- Participates in protein synthesis
- It is a component of ribosomes
- Contains ribose sugar and A, U, G, and C

Fig. 8.11
<table>
<thead>
<tr>
<th></th>
<th>DNA</th>
<th>RNA</th>
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</thead>
<tbody>
<tr>
<td>Sugar</td>
<td>Deoxyribose</td>
<td>Ribose</td>
</tr>
<tr>
<td>Bases</td>
<td>Adenine</td>
<td>Adenine</td>
</tr>
<tr>
<td></td>
<td>Cytosine</td>
<td>Cytosine</td>
</tr>
<tr>
<td></td>
<td>Guanine</td>
<td>Guanine</td>
</tr>
<tr>
<td>Thymine</td>
<td></td>
<td>Uracil</td>
</tr>
</tbody>
</table>
Nuclear Chromosomes

- DNA is packed into chromosomes by several levels of coiling and compaction
Nuclear Chromosomes

- **Chromatin** makes up chromosomes; it is a complex of DNA and protein
- **Histones** are DNA-binding proteins
  - They assist in compacting and folding DNA into a chromosome
  - Shorten the DNA length by a factor of 6 or 7
- **Nucleosomes** are bead-like structures composed of histones wrapped with DNA
(b) At times when a chromosome is most condensed, the chromosomal proteins interact, which packages loops of already coiled DNA into a “supercoiled” array.

(c) At a deeper level of structural organization, the chromosomal proteins and DNA are organized as a cylindrical fiber.

(d) Immerse a chromosome in saltwater and it loosens up to a beads-on-a-string organization. The “string” is one DNA molecule. Each “bead” is a nucleosome.

(e) A nucleosome consists of part of a DNA molecule looped twice around a core of histones.

Fig. 8.13
Three models for DNA replication:

1. Conservative

2. Semi-conservative

3. Dispersive
Conservative model of replication
Semi-conservative model of replication
Dispersive model of replication
Meselson and Stahl 1958

Showed that DNA replicates semi-conservatively
DNA in 6M CsCl

Centrifugation for 50-60 h at 100,000 × g results in generation of gradient of CsCl and banding of DNA

Increasing density

\(^{14}\text{N}-\text{DNA}\)

\(^{15}\text{N}-\text{DNA}\)
After 1 round of replication:

If replication is conservative:
Would predict that would see heavy DNA band and light DNA band, but no intermediate DNA band.

If replication is semi-conservative:
Would predict that would see intermediate band only.

If replication is dispersive:
Would predict that would see intermediate band only.
After 2 rounds of replication:

If replication is semi-conservative:
Would see light band and intermediate band.

If replication is dispersive:
Would see one band lighter than the previous intermediate band.
Semi-Conservative Replication of DNA

DNA Polymerase catalyzes the synthesis of DNA using a template of DNA and nucleotides

Fig. 8.15
DNA Replication

• Strands are unwound and separate

• New bases pair
  G with C
  T with A

• New DNA composed of one “old” strand and one “new” strand

Fig. 8.15
Complementary base pairing preserves information

5’ ATGCTGGGCTCATGCGCTA 3’ template
3’ TACGACCCGAGTACGCGAT 5’ New strand