Chapter 8
The Structure, Replication, and Chromosomal Organization of DNA
## History of DNA Discoveries

<table>
<thead>
<tr>
<th>Name</th>
<th>Discovery</th>
<th>Year</th>
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<tbody>
<tr>
<td>Friedrich Miescher</td>
<td>Isolated nuclein from white blood cells</td>
<td>1869</td>
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<td>Walter Flemming</td>
<td>Named chromosomes for colored body</td>
<td>1882</td>
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<tr>
<td>Frederick Griffith</td>
<td>Discovered transforming principle</td>
<td>1928</td>
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<tr>
<td>O.Avery, C.MacCleod, M.McCarty</td>
<td>DNA is the transforming agent</td>
<td>1944</td>
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<td>P.Levene, E.Chargaff, M.Wilkins, R.Franklin</td>
<td>Discoveries of DNA components, proportions, and positions</td>
<td>1909-1950’s</td>
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<td>J.Watson &amp; F.Crick</td>
<td>3-D structure of DNA</td>
<td>1953</td>
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<td>J. Watson</td>
<td>Had his DNA sequenced</td>
<td>2008</td>
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<td>Various organizations</td>
<td>Human genome projects</td>
<td>present</td>
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Discovery of a “transforming principle”

Frederick Griffiths, 1928
- English microbiologist

- Worked with *Diplococcus pneumoniae*, which exists in two types
  - Type S (Smooth) = Produces capsule
  - Type R (Rough) = No capsule

- Capsule associated with virulence (Type S cause death and Type R does not)
Frederick Griffith’s Experiments demonstrated the transfer of genetic information (transforming principle)

DNA is that “genetic information”

Work completed by Avery, Macleod, & MacCarty, 1944

Summary of Early DNA Experiments

- **Transformation**
  - The process of transferring genetic information (DNA) between cells

- **Transforming factor**
  - The molecular agent of transformation; DNA
Elucidating the structure of DNA

Rosalind Franklin reasoned that the DNA is a helix with symmetrically organized subunits.
Elucidating the structure of DNA

James Watson and Francis Crick
- Did not perform any experiments
- Rather, they used the earlier research and inferences from model building with cardboard cutouts to solve the structure of DNA
- proposed that DNA has two polynucleotide chains oriented in opposite directions, held together by hydrogen bonding to complementary bases in the opposite strand
A single building block is a **nucleotide**

Each nucleotide is composed of:
- A deoxyribose sugar
- A phosphate group
- A nitrogenous base; one of four types
  - Adenine (A), Guanine (G)
  - Cytosine (C), Thymine (T)
Basic Chemistry: Nucleotides

(a) Adenine (A)
(b) Thymine (T) (in DNA)
(c) Guanine (G)
(d) Cytosine (C)
DNA strands are antiparallel

- The two polynucleotide chains in DNA run in opposite directions
Three Important Properties of the DNA Model

“A genetic material must carry out two jobs: duplicate itself and control the development of the rest of the cell in a specific way.”

- Francis Crick, 1953

Complementary strands provide a mechanism for DNA replication—each strand serves as a template for a new double helix
Semi-conservative DNA Replication

- The two polynucleotide strands uncoil and each is a template for synthesis of a new strand
Proteins of DNA Replication

Helicase – unwinds the DNA strands

Primase – adds a short primer to each DNA strand

DNA polymerase – adds nucleotides to form new strands

Ligase – seals the fragments of the lagging strand

*Pause and view DNA replication animation at:* http://www.dnalc.org/resources/3d/03-mechanism-of-replication-basic.html
(b) Because DNA synthesis proceeds only in the 5’ to 3’ direction, only one of the DNA strands can be assembled in a single piece.

The other new DNA strand forms in short segments, which are called Okazaki fragments after the two scientists who discovered them. DNA ligase joins the fragments into a continuous strand of DNA.

The parent DNA double helix unwinds in this direction.

The lagging DNA strand is assembled in many pieces.

Only the leading DNA strand is assembled continuously.
Each human chromosome is a single DNA molecule... does it ever get tangled?
# Variation in Genome Sizes

## Table 8.1  Genome Sizes of Some Organisms

<table>
<thead>
<tr>
<th>Organism</th>
<th>Species</th>
<th>Genome Size in Nucleotides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterium</td>
<td><em>E. coli</em></td>
<td>$4.6 \times 10^6$</td>
</tr>
<tr>
<td>Yeast</td>
<td><em>S. cerevisiae</em></td>
<td>$1.2 \times 10^7$</td>
</tr>
<tr>
<td>Fruit fly</td>
<td><em>D. melanogaster</em></td>
<td>$1.7 \times 10^8$</td>
</tr>
<tr>
<td>Tobacco plant</td>
<td><em>N. tabacum</em></td>
<td>$4.8 \times 10^9$</td>
</tr>
<tr>
<td>Mouse</td>
<td><em>M. musculus</em></td>
<td>$2.7 \times 10^9$</td>
</tr>
<tr>
<td>Human</td>
<td><em>H. sapiens</em></td>
<td>$3.2 \times 10^9$</td>
</tr>
</tbody>
</table>
Each DNA Molecule is Extensively Coiled to Allow it to Fit into the Nucleus
Structure of Nuclear Chromosomes

- **Chromatin**
  - The complex of DNA and proteins that makes up a chromosome

- **Histones**
  - DNA-binding proteins that help compact and fold DNA into chromosomes
When a chromosome is at its most condensed, the DNA is packed into tightly coiled coils.

When the coiled coils unwind, a molecule of chromosomal DNA and its associated proteins are organized as a cylindrical fiber.

A loosened fiber shows a “beads-on-a-string” organization. The “string” is the DNA molecule; each “bead” is the nucleosome.

A nucleosome consists of part of a DNA molecule looped twice around a core of histone proteins.
Centromeres and Telomeres are Specialized Chromosomal Regions

- Centromeres attach to spindle fibers during mitosis
- are chromosome tips composed of many repeats of TTAGGG that shorten with each cell division (whether this is a cause or an effect of aging is debated)
DNA marketing is being used to sell an ever-increasing number of products from jewelry containing DNA of celebrities to souvenir shirts printed with ink containing DNA of Olympic athletes.