Discovery of DNA and DNA Structure
Mendel’s laws of inheritance

• The law of independent assortment
  – Traits are inherited independently of one another

• The law of independent segregation
  – An organism inherits one allele for each trait from each parent

• The law of dominance
  – For each trait, one allele is dominant and one is recessive, resulting in a 3:1 ratio of the dominant phenotype over the recessive phenotype
One gene – one enzyme hypothesis

• Garrod – alkaptonuria results from a recessive gene which causes a deficiency in the enzyme that converts homogentisic acid into a colorless product

• Beadle and Tatum – *Neurospora crassa* auxotrophs are blocked at a specific step in the metabolic pathway and accumulate large quantities of the substance formed just prior to the blocked step
Griffith’s bacterial transformation

• Mouse injections
  – Virulent S strain = death
  – Nonvirulent R strain = healthy
  – Heat-killed S strain = healthy
  – Nonvirulent R strain + heat-killed S strain = death
Avery, MacLeod, and McCarty showed the transforming principle is DNA.

**Preparation of transforming principle from S strain**
- Encapsulated S strain
- 1. Disrupt cells
  2. Centrifuge
- Cell-free extract
  1. Precipitate with ethanol
  2. Redissolve in water
- Transforming principle from S strain

**Addition of transforming principle to R strain**
- Transforming principle from S strain
- R strain
- Mix and spread on agar plates
- Culture containing both S and R cells

Figure 1.13
Chargaff's rules

• G + C content can vary widely among DNA from different organisms
• [A] = [T] in all DNAs
• [G] = [C] in all DNAs
The Hershey-Chase experiment

Figure 1.14

Part B courtesy of Robert Duda, University of Pittsburgh.
Franklin and Wilkins: X-ray diffraction of DNA

Figure 1.16

The Watson-Crick model: DNA is a double helix

Figure 1.17
Each DNA strand is the template for synthesis of a new strand.

Figure 1.19
Nucleic acids differ in their pentose sugar.
Pyrimidine and purine bases of DNA and RNA

Figure 1.04a:

(a) Pyrimidine

Pyrimidine bases

Thymine (T)
Cytosine (C)

Figure 1.04b:

(b) Purine

Purine bases

Adenine (A)
Guanine (G)

Figure 1.05:

Uracil (U)

Thymine - DNA only
Uracil - RNA only
Deoxyribonucleosides have a base attached to deoxyribose

Figure 1.06
Ribonucleosides have a base attached to ribose

Figure 1.07
Nucleotides have a phosphate group attached to the sugar

(a) 5′-nucleoside monophosphates

Uridine-5′-monophosphate (5′-UMP) or 5′-uridylate

Thymidine-5′-monophosphate (5′-dTMP) or 5′-thymidylylate

Figure 1.08a
# Bases, nucleosides, and nucleotides

## TABLE 1.1 Comparison of Major Features in A-, B-, and Z-Forms of DNA

<table>
<thead>
<tr>
<th>Base</th>
<th>Sugar</th>
<th>Nucleoside</th>
<th>5’-Mononucleotide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uracil (U)</td>
<td>ribose</td>
<td>uridine</td>
<td>Uridine-5’-monophosphate or 5’-uridylate (5’-UMP)</td>
</tr>
<tr>
<td>Cytosine (C)</td>
<td>ribose</td>
<td>cytidine</td>
<td>Cytidine-5’-monophosphate or 5’-cytidylate (5’-CMP)</td>
</tr>
<tr>
<td>Adenine (A)</td>
<td>ribose</td>
<td>adenosine</td>
<td>Adenosine-5’-monophosphate or 5’-adenylate (5’-AMP)</td>
</tr>
<tr>
<td>Guanine (G)</td>
<td>ribose</td>
<td>guanosine</td>
<td>Guanosine-5’-monophosphate or 5’-guanylate (5’-GMP)</td>
</tr>
<tr>
<td>Thymine (T)</td>
<td>deoxyribose</td>
<td>deoxythymidine</td>
<td>Deoxythymidine-5’-monophosphate or 5’-deoxythymidylate (5’-dTMP)</td>
</tr>
<tr>
<td>Cytosine (C)</td>
<td>deoxyribose</td>
<td>deoxycytidine</td>
<td>Deoxycytidine-5’-monophosphate or 5’-deoxycytidylate (5’-dCMP)</td>
</tr>
<tr>
<td>Adenine (A)</td>
<td>deoxyribose</td>
<td>deoxyadenosine</td>
<td>Deoxyadenosine-5’-monophosphate or 5’-deoxyadenylate (5’-dAMP)</td>
</tr>
<tr>
<td>Guanine (G)</td>
<td>deoxyribose</td>
<td>deoxyguanosine</td>
<td>Deoxyguanosine-5’-monophosphate or 5’-deoxyguanylate (5’-dGMP)</td>
</tr>
</tbody>
</table>

1Deoxythymidine and deoxythymidine-5’-monophosphate are also called thymidine and thymidine-5’-monophosphate, respectively. When thymine is attached to ribose, the nucleoside is called ribothymidine and the nucleotide is called ribothymidylate. This nomenclature convention follows from the fact that thymine is most frequently attached to deoxyribose.
Nucleotides are joined 5’→3’ in both DNA and RNA

Figure 1.10
A:T and G:C base pairs in DNA

Figure 1.18
The central dogma:
DNA → RNA → Protein

Figure 1.20
Figure 01: Major and minor grooves in B-DNA

Figure 27_MID: B) B-DNA (Middle)Structures in spacefilling display viewed from the side

Figure 32: A space-filling model of triplex DNA

Figure 04: DNA melting curve.
Figure 05: Effect of G-C content on DNA melting temperature.
Figure 06: Several effects of cooperativity of base-stacking.
Figure 07: The effect of lowering the temperature to 25°C after strand separation has taken place.
Southern blot analysis: an experiental method for identifying a specific DNA fragment in a gel.
Figure 23: Southern blot of genomic DNA from normal tissue (N) and from a tumor (T) from a patient with breast cancer

Figure 17A: Closed covalent circle
Figure 17B: Singly-nicked circle
Figure 18A: Linear double-stranded DNA

Figure 18D: Unwound circle

Figure 19B: Negative superhelix

Figure 31A: Inverted repeats

Figure 31B: Cruciform structure

## Table T01: Sizes of Various DNA Molecules

<table>
<thead>
<tr>
<th>Source of DNA</th>
<th>Size in Base Pairs (bp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmid pBR322*</td>
<td>4,361</td>
</tr>
<tr>
<td>Simian virus 40 (SV40)</td>
<td>5,200</td>
</tr>
<tr>
<td>Phage T7*</td>
<td>39,937</td>
</tr>
<tr>
<td>Phage λ*</td>
<td>48,502</td>
</tr>
<tr>
<td>F plasmid*</td>
<td>99,159</td>
</tr>
<tr>
<td>Vaccinia virus strain WR</td>
<td>194,711</td>
</tr>
<tr>
<td>Fowlpox virus</td>
<td>266,145</td>
</tr>
<tr>
<td><em>Mycoplasma genitalium</em></td>
<td>580,073</td>
</tr>
<tr>
<td>Yeast chromosome IV</td>
<td>1,531,929</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>4,639,221</td>
</tr>
<tr>
<td>Human chromosome 1</td>
<td>245,522,847</td>
</tr>
</tbody>
</table>

Note: Phages (viruses that infect bacteria) and plasmids marked with an asterisk have *E. coli* as a host. *Mycoplasma genitalium* is the smallest known free-living bacterium. For yeast and humans the molecular mass of the largest DNA molecule in the organism is given.