Discovery of the Genetic Material

Once Mendel’s work was rediscovered in the 1900s, scientists began to search for the molecule involved in inheritance. Scientists knew that genetic information was carried on the chromosomes in eukaryotic cells, and that the two main components of chromosomes are DNA and protein. For many years, scientists tried to determine which of these macromolecules—nucleic acid (DNA) or proteins—was the source of genetic information.

Griffith

The first major experiment that led to the discovery of DNA as the genetic material was performed by Frederick Griffith in 1928. Griffith studied two strains of the bacteria *Streptococcus pneumoniae*, which causes pneumonia. He found that one strain could be transformed, or changed, into the other form.

Of the two strains he studied, one had a sugar coat and one did not. Both strains are shown in Figure 1. The coated strain causes pneumonia and is called the smooth (S) strain. The noncoated strain does not cause pneumonia and is called the rough (R) strain because, without the coat, the bacteria colonies have rough edges.

![Smooth strain — *S. pneumoniae*](image1) ![Rough strain — *S. pneumoniae*](image2)

*Figure 1* The smooth (S) strain of *S. pneumoniae* can cause pneumonia, though the rough (R) strain is not disease-causing. The strains can be identified by the appearance of the colonies.

Follow Griffith’s study described in Figure 2. Notice the live S cells killed the mouse in the study. The live R cells did not kill the mouse, and the killed S cells did not kill the mouse. However, when Griffith made a mixture of live R cells and killed S cells and injected the mixture into a mouse, the mouse died. Griffith isolated live bacteria from the dead mouse. When these isolated bacteria were cultured, the smooth trait was visible, suggesting that a disease-causing factor was passed from the killed S bacteria to the live R bacteria. Griffith concluded that there had been a transformation from live R bacteria to live S bacteria. This experiment set the stage for the search to identify the transforming substance.
Explain why Griffith concluded there had been a change from live R bacteria to live S bacteria.

Avery

In 1944, Oswald Avery and his colleagues identified the molecule that transformed the R strain of bacteria into the S strain. Avery isolated different macromolecules, such as DNA, proteins, and lipids, from killed S cells. Then he exposed live R cells to the macromolecules separately. When the live R cells were exposed to the S strain DNA, they were transformed into S cells. Avery concluded that when the S cells in Griffith's experiments were killed, DNA was released. Some of the R bacteria incorporated this DNA into their cells, and this changed the bacteria into S cells. Avery’s conclusions were not widely accepted by the scientific community, and many biologists continued to question and experiment to determine whether proteins or DNA were responsible for the transfer of genetic material.

Reading Check Explain how Avery discovered the transforming factor.

Hershey and Chase

In 1952, Alfred Hershey and Martha Chase published results of experiments that provided definitive evidence that DNA was the transforming factor. These experiments involved a bacteriophage (bakter uh fay ee), a type of virus that attacks bacteria. Two components made the experiment ideal for confirming that DNA is the genetic material. First, the bacteriophage used in the experiment was made of DNA and protein. Second, viruses cannot replicate themselves. They must inject their genetic material into a living cell to reproduce. Hershey and Chase labeled both parts of the virus to determine which part was injected into the bacteria and, thus, which part was the genetic material.

Radioactive labeling Hershey and Chase used a technique called radioactive labeling to trace the fate of the DNA and protein as the bacteriophages infected bacteria and reproduced. Follow along in Figure 3 as you continue learning about the Hershey-Chase experiment. They labeled one set of bacteriophages with radioactive phosphorus ($^{32}$P). Proteins do not contain phosphorus, so DNA and not protein in these viruses would be radioactive. Hershey and Chase labeled another set of bacteriophages with radioactive sulfur ($^{35}$S). Because proteins contain sulfur and DNA does not, proteins and not DNA would be radioactive.
Hershey and Chase infected bacteria with viruses from the two groups. When viruses infect bacteria, they attach to the outside of the bacteria and inject their genetic material. The infected bacteria then were separated from the viruses.

**Tracking DNA** Hershey and Chase examined Group 1 labeled with $^{32}$P and found that the labeled viral DNA had been injected into the bacteria. Viruses later released from the infected bacteria contained $^{32}$P, further indicating that DNA was the carrier of genetic information.

When examining Group 2 labeled with $^{35}$S, Hershey and Chase observed that the labeled proteins were found outside of the bacterial cells. Viral replication had occurred in the bacterial cells, indicating that the viruses’ genetic material had entered the bacteria, but no label ($^{35}$S) was found. **Table 1** summarizes the results of the Hershey-Chase experiment.

<table>
<thead>
<tr>
<th>Summary of Hershey-Chase Results</th>
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<tbody>
<tr>
<td><strong>Group 1 (Viruses labeled with $^{32}$P)</strong></td>
</tr>
<tr>
<td>Infected Bacteria</td>
</tr>
<tr>
<td>• Labeled viral DNA ($^{32}$P) found in the bacteria</td>
</tr>
<tr>
<td>• Viral replication occurred</td>
</tr>
<tr>
<td>• New viruses contained $^{32}$P</td>
</tr>
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</table>

Based on their results, Hershey and Chase concluded that the viral DNA was injected into the cell and provided the genetic information needed to produce new viruses. This experiment provided powerful evidence that DNA, not protein, was the genetic material that could be passed from generation to generation in viruses.

**Reading Check** Explain why it is important that new viruses were produced in the bacteria.

<table>
<thead>
<tr>
<th><strong>VOCABULARY</strong></th>
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<tbody>
<tr>
<td><strong>ACADEMIC VOCABULARY</strong></td>
</tr>
<tr>
<td><strong>Transform</strong></td>
</tr>
<tr>
<td>to cause a change in type or kind</td>
</tr>
<tr>
<td>Avery used DNA to transform bacteria.</td>
</tr>
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</table>
DNA Structure

After the Hershey-Chase experiment, scientists were more confident that DNA was the genetic material. The clues had led to the identification of the genetic material, but the questions of how nucleotides came together to form DNA and how DNA could communicate information remained.

Nucleotides

In the 1920s, the biochemist P. A. Levene determined the basic structure of nucleotides that make up DNA. Nucleotides are the subunits of nucleic acids and consist of a five-carbon sugar, a phosphate group, and a nitrogenous base. The two nucleic acids found in living cells are DNA and RNA. DNA nucleotides contain the sugar deoxyribose (dee ahk sih RI bos), a phosphate, and one of four nitrogenous bases: adenine (A duh neen), guanine (GWAH neen), cytosine (Si tuh seen), or thymine (THI meen). RNA nucleotides contain the sugar ribose, a phosphate, and one of four nitrogenous bases: adenine, guanine, cytosine, or uracil (YOO ruh sihl). Notice in Figure 4 that guanine (G) and adenine (A) are double-ringed bases. This type of base is called a purine base. Thymine (T), cytosine (C), and uracil (U) are single-ringed bases called pyrimidine bases.

![Figure 4](image)

Figure 4: Nucleotides are made of a phosphate, sugar, and a base. There are five different bases found in nucleotide subunits that make up DNA and RNA.

Identify the structural difference between purine and pyrimidine bases.

Chargaff

Erwin Chargaff analyzed the amount of adenine, guanine, thymine, and cytosine in the DNA of various species. A portion of Chargaff’s data, published in 1950, is shown in Figure 5. Chargaff found that the amount of guanine nearly equals the amount of cytosine, and the amount of adenine nearly equals the amount of thymine within a species. This finding is known as Chargaff’s rule: \( C = G \) and \( T = A \).

![Figure 5](image)

Figure 5: Chargaff’s data showed that though base composition varies from species to species, within a species \( C = G \) and \( A = T \).
The structure question

When four scientists joined the search for the DNA structure, the meaning and importance of Chargaff’s data became clear. Rosalind Franklin, a British chemist; Maurice Wilkins, a British physicist; Francis Crick, a British physicist; and James Watson, an American biologist, provided information that was pivotal in answering the DNA structure question.

X-ray diffraction

Wilkins was working at King’s College in London, England, with a technique called X-ray diffraction, a technique that involved aiming X-rays at the DNA molecule. In 1951, Franklin joined the staff at King’s College. There she took the now famous Photo 51 and collected data eventually used by Watson and Crick. Photo 51, shown in Figure 6, indicated that DNA was a double helix, or twisted ladder shape, formed by two strands of nucleotides twisted around each other. The specific structure of the DNA double helix was determined later by Watson and Crick when they used Franklin’s data and other mathematical data. DNA is the genetic material of all organisms, composed of two complementary, precisely paired strands of nucleotides wound in a double helix.

Figure 6  Rosalind Franklin’s Photo 51 and X-ray diffraction data helped Watson and Crick solve the structure of DNA. When analyzed and measured carefully, the pattern shows the characteristics of helix structure.

Watson and Crick

Watson and Crick were working at Cambridge University in Cambridge, England, when they saw Franklin’s X-ray diffraction picture. Using Chargaff’s data and Franklin’s data, Watson and Crick measured the width of the helix and the spacing of the bases. Together, they built a model of the double helix that conformed to the others’ research. The model that they built is shown in Figure 7. Some important features of their proposed molecule include the following:

1. Two outside strands consist of alternating deoxy ribose and phosphate.

2. Cytosine and guanine bases pair to each other by three hydrogen bonds.

3. Thymine and adenine bases pair to each other by two hydrogen bonds.
DNA structure

DNA often is compared to a twisted ladder, with the rails of the ladder represented by the alternating deoxyribose and phosphate. The pairs of bases (cytosine–guanine or thymine–adenine) form the steps, or rungs, of the ladder. A purine base always binds to a pyrimidine base, ensuring a consistent distance between the two rails of the ladder. This proposed bonding of the bases also explains Chargaff’s data, which suggested that the number of purine bases equaled the number of pyrimidine bases in a sample of DNA. Remember, cytosine and thymine are pyrimidine bases, adenine and guanine are purines, and $C = G$ and $A = T$. Therefore, $C + T = G + A$, or purine bases equal pyrimidine bases. Complementary base pairing is used to describe the precise pairing of purine and pyrimidine bases between strands of nucleic acids. It is the characteristic of DNA replication through which the parent strand can determine the sequence of a new strand.

Reading Check: Explain why Chargaff’s data was an important clue for putting together the structure of DNA.

Orientation

Another unique feature of the DNA molecule is the direction, or orientation, of the two strands. Carbon molecules can be numbered in organic molecules. Figure 8 shows the orientation of the numbered carbons in the sugar molecules on each strand of DNA. On the top rail, the orientation of the sugar has the 5’ (read ‘five-prime’) carbon on the left, and on the end of that rail, the 3’ (read ‘three-prime’) carbon is on the right of the sugar-phosphate chain. The strand is said to be oriented 5’ to 3’. The strand on the bottom runs in the opposite direction and is oriented 3’ to 5’. This orientation of the two strands is called antiparallel.

Another way to visualize antiparallel orientation is to take two pencils and position them so that the point of one pencil is next to the eraser of the other and vice versa.
**Figure 8** Two strands of DNA running antiparallel make up the DNA helix.

**Explain why the ends of the DNA strands are labeled 3' and 5'**.

**The announcement**

In 1953, Watson and Crick surprised the scientific community by publishing a one-page letter in the journal *Nature* that suggested a structure for DNA and hypothesized a method of replication for the molecule deduced from the structure. In articles individually published in the same issue, Wilkins and Franklin presented evidence that supported the structure proposed by Watson and Crick. Still, the mysteries of how to prove DNA’s replication and how it worked as a genetic code remained.

**VOCABULARY**

**Science usage v. Common usage**

<table>
<thead>
<tr>
<th>Prime</th>
<th>Science usage: a mark located above and to the right of a character, used to identify a number or variable. Carbon molecules in organic molecules are numbered and labeled with a prime.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Common usage: first in value, excellence, or quality. The student found the prime seats in the stadium for watching the game.</td>
</tr>
</tbody>
</table>

**MiniLab: Model DNA Structure**

What is the structure of the DNA molecule? Construct a model to better understand the structure of the DNA molecule.

**Procedure**

1. Read and complete the lab safety form.

2. Construct a model of a short segment of DNA using the materials provided by your teacher.

3. Identify which parts of the model correspond to the different parts of a DNA molecule.

**Analysis**

1. Describe the structure of your DNA molecule.

2. Identify the characteristics of DNA that you focused on when constructing your model.

3. Infer in what way your model is different from your classmates’ models. How does this relate to differences in DNA among organisms?

**Chromosome Structure**

In prokaryotes, the DNA molecule is contained in the cytoplasm and consists mainly of a ring of DNA and associated proteins. Eukaryotic DNA is organized into individual chromosomes. The length of a human chromosome ranges from 51 million to 245 million base pairs. If a DNA strand 140 million nucleotides long was laid out in a straight line, it would be about five centimeters long. How does all of this DNA fit into a microscopic cell? In order to fit into the nucleus of an eukaryotic cell, the DNA tightly coils around a group of beadlike proteins called histones, as shown in Figure 9. The phosphate groups in DNA create a negative charge, which attracts the DNA to the positively charged histone proteins and forms a nucleosome. The nucleosomes then group together into chromatin fibers, which supercoil to make up the DNA structure recognized as a chromosome.
Review

Lesson Summary

- Griffith's bacterial experiment and Avery's explanation first indicated that DNA is the genetic material.
- The Hershey-Chase experiment provided evidence that DNA is the genetic material of viruses.
- Chargaff's rule states that in DNA the amount of cytosine equals the amount of guanine and the amount of thymine equals the amount of adenine.
- The work of Watson, Crick, Franklin, and Wilkins provided evidence of the double-helix structure of DNA.

Vocabulary Review

Each of the following sentences is false. Make the sentence true by replacing the underlined word with the correct vocabulary term.

1. The twisted ladder shape of DNA is called a [nucleotide].


Understand Main Ideas

3. **Main Idea** Summarize the experiments of Griffith and Avery that indicated that DNA is the genetic material.

4. Describe the data used by Watson and Crick to determine the structure of DNA.

5. Draw and label a segment of DNA showing its helix and complementary base pairing.

6. Describe the structure of eukaryotic chromosomes.

7. What are the basic building blocks of DNA and RNA?

   A. ribose
   B. purines
   C. nucleotides
   D. phosphorus

8. If a section of DNA has 27 percent thymine, how much cytosine will it have?

   A. 23 percent
   B. 27 percent
   C. 46 percent
   D. 54 percent

9. Which was a conclusion of Griffith's work with *Streptococcus pneumoniae*?

   A. DNA is the genetic material in viruses.
B. The structure of DNA is a double helix.
C. Bacteria exposed to DNA can incorporate the DNA and change phenotype.
D. The amount of thymine equals the amount of adenine in DNA.

Refer to the figure below to answer questions 10 and 11.

10. What is the entire labeled structure called?
A. nucleotide
B. RNA
C. base
D. phosphate

11. Which label represents the coding part of DNA?
A. A
B. B
C. C
D. D

**Constructed Response**

12. **Short Answer** Explain how DNA forms chromosomes in eukaryotic cells.

*Use the figure below to answer question 13.*

13. Summarize the experiments and data shown in the photo that led to the discovery of
Think Critically

14. Describe two characteristics that DNA needs to fulfill its role as a genetic material.

15. Evaluate Hershey and Chase's decision to use radioactive phosphorus and sulfur for their experiments. Could they have used carbon or oxygen instead? Why or why not?

16. Design How might you use radioactive phosphorus to demonstrate that the transforming compound of bacteria in Griffith's experiment was DNA?

17. Main Idea How would the results of the Hershey-Chase experiment have been different if protein were the genetic material?