Identifying DNA as the Genetic Material

**KEY CONCEPT** DNA was identified as the genetic material through a series of experiments.

**MAIN IDEAS**
- Griffith finds a “transforming principle.”
- Avery identifies DNA as the transforming principle.
- Hershey and Chase confirm that DNA is the genetic material.

**Connect to Your World**
Some people think that a complicated answer is better than a simple one. In the early 1900's, for example, most scientists thought that DNA’s chemical composition was too repetitive for it to be the genetic material. Proteins, which are more variable in structure, appeared to be a better candidate. Starting in the 1920s, experiments provided data that did not support this idea. By the 1950s, sufficient evidence showed that DNA—the same molecule that codes for GFP in the glowing mouse—carries genetic information.

**MAIN IDEA**
Griffith finds a “transforming principle.”

In 1928 the British microbiologist Frederick Griffith was investigating two forms of the bacterium that causes pneumonia. One form is surrounded by a coating made of carbohydrates. This form is called the S form because its colonies look smooth. The second form of bacteria does not have a smooth coating and is called the R, or rough, form. As you can see in **FIGURE 1.1**, when Griffith injected the two types of bacteria into mice, only the S type killed the mice. When the S bacteria were killed with heat before injection, the mice were unaffected. Therefore, only live S bacteria would cause the mice to die.

**FIGURE 1.1 Griffith’s Experiments**

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Griffith’s mice</td>
<td>A transferable material changed harmless bacteria into disease-causing bacteria.</td>
</tr>
</tbody>
</table>

The S form of the bacterium is deadly; the R form is not.

- Live S bacteria: Dead mouse
- Live R bacteria: Live mouse
- Heat-killed S bacteria: Live mouse
- Heat-killed S bacteria + live R bacteria: Dead mouse
Griffith next injected mice with a combination of heat-killed S bacteria and live R bacteria. To his surprise, the mice died. Even more surprising, he found live S bacteria in blood samples from the dead mice. Griffith concluded that some material must have been transferred from the heat-killed S bacteria to the live R bacteria. Whatever that material was, it contained information that changed harmless R bacteria into disease-causing S bacteria. Griffith called this mystery material the “transforming principle.”

**Infer** What evidence suggested that there was a transforming principle?

**MAIN IDEA**

**Avery identifies DNA as the transforming principle.**

What exactly is the transforming principle that Griffith discovered? That question puzzled Oswald Avery and his fellow biologists. They worked for more than ten years to find the answer. Avery’s team began by combining living R bacteria with an extract made from S bacteria. This procedure allowed them to directly observe the transformation of R bacteria into S bacteria in a petri dish.

Avery’s group next developed a process to purify their extract. They then performed a series of tests to find out if the transforming principle was DNA or protein.

- **Qualitative tests** Standard chemical tests showed that no protein was present. In contrast, tests revealed that DNA was present.
  - **Chemical analysis** As you can see in **FIGURE 1.2**, the proportions of elements in the extract closely matched those found in DNA. Proteins contain almost no phosphorus.
- **Enzyme tests** When the team added to the extract enzymes known to break down proteins, the extract still transformed the R bacteria to the S form. Also, transformation occurred when researchers added an enzyme that breaks down RNA (another nucleic acid). Transformation failed to occur only when they added an enzyme that specifically destroys DNA.

In 1944 Avery and his group presented this and other evidence to support their conclusion that DNA must be the transforming principle, or genetic material. The results created great interest. However, some scientists questioned whether the genetic material in bacteria was the same as that in other organisms. Despite Avery’s evidence, some scientists insisted that his extract must have contained protein.

**Summarize** List the key steps in the process that Avery’s team used to identify the transforming principle.

**FIGURE 1.2 Avery’s Discoveries**

**CHEMICAL ANALYSIS OF TRANSFORMING PRINCIPLE**

<table>
<thead>
<tr>
<th></th>
<th>% Nitrogen (N)</th>
<th>% Phosphorus (P)</th>
<th>Ratio of N to P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample A</td>
<td>14.21</td>
<td>8.57</td>
<td>1.66</td>
</tr>
<tr>
<td>Sample B</td>
<td>15.93</td>
<td>9.09</td>
<td>1.75</td>
</tr>
<tr>
<td>Sample C</td>
<td>15.36</td>
<td>9.04</td>
<td>1.69</td>
</tr>
<tr>
<td>Sample D</td>
<td>13.40</td>
<td>8.45</td>
<td>1.58</td>
</tr>
<tr>
<td>Known value for DNA</td>
<td>15.32</td>
<td>9.05</td>
<td>1.69</td>
</tr>
</tbody>
</table>


**Analyze** How do the data support the hypothesis that DNA, not protein, is the transforming principle?
Hershey and Chase confirm that DNA is the genetic material.

Conclusive evidence for DNA as the genetic material came in 1952 from two American biologists, Alfred Hershey and Martha Chase. Hershey and Chase were studying viruses that infect bacteria. This type of virus, called a bacteriophage (bak-TIR-ee-uh-fayj), or “phage” for short, takes over a bacterium’s genetic machinery and directs it to make more viruses.

Phages like the ones Hershey and Chase studied are relatively simple—little more than a DNA molecule surrounded by a protein coat. This two-part structure of phages offered a perfect opportunity to answer the question, Is the genetic material made of DNA or protein? By discovering which part of a phage (DNA or protein) actually entered a bacterium, as shown in FIGURE 1.3, they could answer this question once and for all.

Hershey and Chase thought up a clever procedure that made use of the chemical elements found in protein and DNA. Protein contains sulfur but very little phosphorus, while DNA contains phosphorus but no sulfur. The researchers grew phages in cultures that contained radioactive isotopes of sulfur or phosphorus. Hershey and Chase then used these radioactively tagged phages in two experiments.

- **Experiment 1** In the first experiment, bacteria were infected with phages that had radioactive sulfur atoms in their protein molecules. Hershey and Chase then used an ordinary kitchen blender to separate the bacteria from the parts of the phages that remained outside the bacteria. When they examined the bacteria, they found no significant radioactivity.

- **Experiment 2** Next, Hershey and Chase repeated the procedure with phages that had DNA tagged with radioactive phosphorus. This time, radioactivity was clearly present inside the bacteria.

From their results, Hershey and Chase concluded that the phages’ DNA had entered the bacteria, but the protein had not. Their findings finally convinced scientists that the genetic material is DNA and not protein.

**Apply** How did Hershey and Chase build upon Avery’s chemical analysis results?

**FIGURE 1.3** This micrograph shows the protein coat of a bacteriophage (orange) after it has injected its DNA into an *E. coli* bacterium (blue). (colored TEM; magnification 115,000×)