The Hershey-Chase Experiments (1952), by Alfred Hershey and Martha Chase [1]

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In 1951 and 1952, Alfred Hershey and Martha Chase conducted a series of experiments at the Carnegie Institute of Washington in Cold Spring Harbor, New York, that verified genes [4] were made of deoxyribonucleic acid, or DNA. Hershey and Chase performed their experiments, later named the Hershey-Chase experiments, on viruses that infect bacteria, also called bacteriophages. The experiments followed decades of scientists’ skepticism about whether genetic material was composed of protein or DNA. The most well-known Hershey-Chase experiment, called the Waring Blender experiment, provided concrete evidence that genes [4] were made of DNA. The Hershey-Chase experiments settled the long-standing debate about the composition of genes [4], thereby allowing scientists to investigate the molecular mechanisms by which genes [4] function in organisms.

In the early twentieth century, scientists debated whether genes [4] were made of DNA or protein. Genes control how organisms grow and develop and are the material basis for organisms’ ability to inherit traits like eye color or fur color from their parents. By 1900, scientists had identified the complete chemical composition, or building blocks, of DNA. They had also verified that all cells contained DNA, though DNA’s function remained ambiguous. Up until the 1940s, some scientists accepted the idea that genes [4] were not made of DNA. Instead, those scientists supported the idea that DNA was a molecule that maintained cell structure. Scientists supported that idea in part because of a hypothesis called the tetranucleotide hypothesis. Phoebus Levene, a researcher at the Rockefeller Institute [5] for Medical Research in New York City, New York, proposed the tetranucleotide hypothesis for DNA in 1933. According to Levene and other proponents of the hypothesis, DNA consisted of repeating sets of four different building blocks, called nucleotides. Some scientists concluded that a repeating sequence of nucleotides in DNA limited potential for variability. Those scientists considered variability necessary for DNA to function as genetic material. In other words, genes [4] needed to have the capacity for enough variation to account for the different traits scientists observe in organisms. Conversely, scientists found that proteins had many more building blocks and therefore more possible arrangements than DNA. From that, some scientists claimed that genes [4] must have been made of protein, not DNA.

The Hershey-Chase experiments were not the first studies to oppose the prevailing theory in the early 1900s that genetic material was composed of proteins. In 1944, nearly a decade before Hershey and Chase’s work, scientists published sound evidence that genes [4] were made of DNA rather than protein. Starting in 1935, Oswald Avery, another researcher at the Rockefeller Institute [5], with his research associates Colin MacLeod and Maclyn McCarty, performed experiments that showed that DNA facilitated a genetic phenomenon in bacteria called bacterial transformation. Bacterial transformation is the process by which a bacterium can get and use new genetic material from its surroundings. During bacterial transformation, a non-disease-causing bacterium can transform into disease-causing bacteria if the non-disease-causing bacteria is exposed to a disease-causing bacteria. Transformation can occur even if the disease-causing-strain is dead, implying that bacterial transformation happens when the non-disease-causing bacteria inherits genetic material from the disease-causing bacteria. Avery and his colleagues found that the inherited factor that caused bacterial transformation contained DNA. However, Avery’s group did not discount the possibility that some non-DNA component in their sample caused bacterial transformation, rather than the DNA itself. Because of that, many scientists maintained the idea that proteins must govern the genetic phenomenon of bacterial transformation.

Starting in 1951, Alfred Hershey and Martha Chase conducted a series of experiments, later called the Hershey-Chase experiments, that verified the findings of Avery and his colleagues. Hershey was a researcher who studied viruses at the Carnegie Institution of Washington [6] in Cold Spring Harbor, New York. He studied viruses that infect bacteria, also called bacteriophages, or phages. Chase became Hershey’s research technician in 1950.

In their experiments, Hershey and Chase analyzed what happened when phages infect bacteria. By the 1950s, scientists had evidence for how phages infected bacteria. They found that when phages infect a host bacterium, the phages first attach themselves to the outside of the bacterium. Then, a piece of the phage enters the bacterium and subsequently replicates itself inside the cell. After many replications, the phage causes the bacterium to lyse, or burst, thereby killing the host bacteria. Scientists classified the replicating piece as genetic material. Scientists also found that phages contained two classes of biological molecules: DNA and protein. Hershey and Chase sought to determine if the replicating piece of phages that entered bacteria during infection, the genetic parts, were solely DNA.

To perform their experiments, Hershey and Chase utilized a technique called radioactive isotope labeling. Chemical elements can exist in different structural forms called isotopes. Isotopes of the same element are nearly identical, but scientists can distinguish between them by experimental means. One way to differentiate between chemical elements with different isotopes is
protein, implying that some protein entered the cells during infection. Furthermore, the amount of contaminating protein in the
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Unlike Avery’s experiments on bacterial transformations, the Hershey-Chase experiments were more widely and immediately
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Waring Blender experiments, some protein and DNA material remained unaccounted for. Even in the final experiment, when
Hershey and Chase allowed the bacterial cells to lyse after stirring in the blender, the scientists still recovered a small amount of
protein, implying that some protein entered the cells during infection. Furthermore, the amount of contaminating protein in the
Hershey-Chase Experiments exceeded the amount of contaminating protein that Avery’s group found in their experiments.

Historians of science have studied why scientists more readily accepted the Hershey-Chase experiments than Avery’s experiments. Science historian Frederic Lawrence Holmes writes that scientists more readily accepted the results of the Hershey-Chase experiments because Hershey communicated directly with skeptical scientists. Hershey sent letters to his colleagues in which he detailed the experimental findings of the Hershey-Chase experiments. Another historian of science, Michel Morange, writes that the Hershey-Chase experiments were performed at a time when scientists were ready to accept that genetic material could be DNA. Avery’s group conducted their experiments when the tetr nucleotide hypothesis was popular and few scientists held that genes contained DNA. According to Morange, because Hershey and Chase conducted their experiments years later, scientists had gathered more experimental evidence and were willing to seriously consider that genes contained DNA.

In 1953, James Watson and Francis Crick, two scientists at the University of Cambridge in Cambridge, England, modeled the three-dimensional structure of DNA and demonstrated how DNA might function as genetic material. In 1969, Hershey shared the Nobel Prize in Physiology or Medicine with two other scientists, Max Delbrück and Salvador Luria, partly for his work on the Hershey-Chase experiments.

Sources


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