Alfred Day Hershey (1908–1997)

During the twentieth century in the United States, Alfred Day Hershey studied phages, or viruses that infect bacteria, and experimentally verified that genes were made of deoxyribonucleic acid, or DNA. Genes are molecular, heritable instructions for how an organism develops. When Hershey started to study phages, scientists did not know if phages contained genes, or whether genes were made of DNA or protein. In 1952, Hershey and his research assistant, Martha Chase, conducted phage experiments that convinced scientists that genes were made of DNA. For his work with phages, Hershey shared the 1969 Nobel Prize in Physiology or Medicine with Max Delbrück and Salvador Luria. Hershey conducted experiments with results that connected DNA to the function of genes, thereby changing the way scientists studied molecular biology and the development of organisms.

Hershey was born on 4 December 1908 to Alma Wilbur and Robert Hershey in Owosso, Michigan. He attended public schools in both Owosso and Lansing, Michigan, where his father worked as a stockkeeper at an automobile factory. For his higher education, Hershey attended Michigan State College, later called Michigan State University, in East Lansing, Michigan. There, he received his Bachelor's of Science in chemistry in 1930 and his PhD in bacteriology and chemistry in 1934. Hershey wrote his doctoral dissertation on the separation of chemical constituents, or components like sugars, fats, and proteins, from different strains of the Brucella bacterial group. Through that work, Hershey showed how researchers could distinguish between different bacterial types based on the ratio of different chemical components within those types.

In 1934, Hershey joined the faculty at Washington University in St. Louis in St. Louis, Missouri, as an instructor in the bacteriology and immunology department. Starting in 1936, Hershey collaborated with researcher Jacques Bronfenbrenner, the head of the department. From 1936 to 1939, Hershey and Bronfenbrenner primarily studied different conditions that affected the growth rate of bacteria grown in the laboratory. In the early and mid-1940s, the two scientists started to study phages, or viruses that infect bacteria. Specifically, Hershey and Bronfenbrenner studied how bacteria's immune systems responded to phages.

According to historians, collaboration with Bronfenbrenner shaped Hershey's early work. Biographers of the researcher Max Delbrück, a prominent phage researcher at Vanderbilt University in Nashville, Tennessee, wrote that Hershey designed his experiments during the early 1940s to support Bronfenbrenner's description of phages. Bronfenbrenner argued that phages were small protein molecules. At the time, some scientists had observed that phages appeared to be large molecules. To support Bronfenbrenner's view, Hershey attempted to explain why other scientists observed phages to be large by demonstrating that large particles absorbed smaller phage particles. Scientists later found that phages are large molecules which can contain both protein and nucleic acid, including DNA.

In addition to investigating phages in the early 1940s, Hershey helped establish the Phage Group, an association of scientists who conducted standardized research on phages and attended yearly meetings and courses to advance the field. In the early 1940s, Hershey began communicating with Delbrück. After receiving an invitation from Delbrück, Hershey presented his research on immune responses to phages at Vanderbilt in January 1943. In April 1943, Hershey invited Delbrück and Salvador Luria, Delbrück's collaborator, to St. Louis to discuss their phage research. Scientists and historians consider these meetings to be the beginning of the Phage Group.

Starting in the 1940s, Hershey began communicating with Delbrück. In a letter sent to Delbrück in October 1943, Hershey wrote about his frustrations with his phage research. Hershey's frustrations were related to his efforts to support Bronfenbrenner's small particle view of phages, a view that Delbrück did not support. According to Delbrück biographers, he eventually convinced Hershey to forsake Bronfenbrenner's theory about phages. Hershey later expressed that he appreciated Delbrück's support. In 1945, Hershey married Harriet Davidson. The two had a son named Peter in 1956.

Hershey first published his major findings about two types of phages called T2 and T4 in 1946 and 1947. Scientists knew that when phages infect bacteria, those phages replicate and eventually cause bacteria to burst. When the infected bacteria burst, they leave behind plaques, or dark spots, in the places they used to grow. Hershey made multiple observations about how phages infect bacteria by studying plaque formation, and those observations served as evidence for the idea that phages contain genes. Hershey reported changes in the ways that plaques formed and asserted that those changes were caused by a change or mutation in the phages. Hershey also found that when he infected bacteria with two different types of phages, hybrid phages of both types formed. That observation revealed that the phages somehow exchanged genetic materials. Hershey showed that, like other organisms, phages contained genes. That discovery gave scientists a new way to study genetics through phages. Hershey continued to characterize genetic recombination, or the exchange of genetic materials, between phages throughout the rest of the 1940s.

In 1950, Hershey moved his research to the Carnegie Institution of Washington Department of Genetics in Cold Spring Harbor, New York. In 1951, he ended his investigation into genetic recombination in phages. That same year, Chase, a geneticist, joined Hershey's lab as a research assistant. Hershey and Chase began to research the chemistry of the genetic properties of phages.

Despite Hershey and others' extensive study of genetic phenomena in phages, scientists in 1951 did not agree about which substances governed the genetic properties of phages. At the time, scientists debated whether genes were made of protein or DNA. In 1944, Oswald Avery and his research group at the Rockefeller Institute in New York City, New York, published experimental findings that supported the theory that genes were made of DNA. However, the experiments failed to convince all scientists. Even in the 1950s, some scientists continued to assert that genes must be made of protein and not DNA.

From 1951 to 1952, Hershey and Chase conducted a series of experiments, later called the Hershey-Chase experiments, that convinced scientists that genes were composed of DNA instead of protein. By the time Hershey and Chase began those experiments, scientists had evidence that phages contained both DNA and protein. To distinguish between the DNA and protein in phages, Hershey and Chase used a technique called radioactive isotope labeling. During radioactive isotope labeling, researchers label phages with alternate forms of chemical elements, called isotopes, that emit unique radioactive signals. Hershey and Chase used a phosphorus label to identify DNA because DNA contains phosphorus but no sulfur, and a sulfur label to identify protein because the amino acids of proteins can contain sulfur but no phosphorus.

In the early 1950s at the Carnegie Institution, Hershey and Chase conducted experiments that demonstrated that the protein and DNA parts of phages separated when phages infected bacteria. Hershey and Chase demonstrated that when phages infected bacteria, the phages adhered to the outer membranes of the bacteria and injected their DNA into the host bacteria. The infection process resulted in empty phage protein shells that remained stuck to the outer bacterial membranes. In 1952, Hershey and Chase conducted the Waring blender experiment. They used a kitchen blender called the Waring Blender because the slow stir speed could remove phage protein coats stuck to the bacterial membranes without damaging the bacteria. That allowed Hershey and Chase to isolate the phage material that entered the cell. Hershey and Chase showed that phages injected only their DNA into bacteria during infection, and that DNA served as the genetic replicating element of phages whose replication eventually resulted in bacterial cells bursting.

According to historians, Hershey and Chase largely succeeded in convincing scientists that genes were made of DNA. Prior to the publication of his and Chase's results, Hershey sent letters to his colleagues describing his experimental findings. In 1952, James Watson, a scientist who would later propose a structure for DNA, presented Hershey's findings at a symposium in Oxford, United Kingdom. Many scientists, including Delbrück, praised Hershey for his and Chase's experiments.

Throughout the rest of the 1950s and into the early 1960s, Hershey focused on developing experimental methods to study DNA. Chase left Hershey's lab in 1953 and their collaboration ended. In 1955, Hershey addressed some issues with the Waring Blender experiment, acknowledging that small amount of protein was injected with DNA during phage infection and that he could not identify the function of that protein. However, according to Hershey, that finding did not dissuade scientists from supporting the view that genes were made of DNA. From 1953 to the early 1960s, Hershey worked to develop experimental methods to analyze chromosomes, or the extended, thread-like structure of DNA, in T2 and T4 phages. In 1958, Hershey was elected to the National Academy of Sciences headquartered in Washington DC.

Beginning in the early 1960s and continuing into the 1970s, Hershey studied the DNA chromosome structure for a type of phage called phage λ, or lambda phage. In the mid-1960s, Hershey found that the shape of DNA in phage λ was a single, circular molecule, rather than a linear strand-like in other phages and microorganisms. Later, Hershey wrote multiple essays on phage λ. In 1969, he, Delbrück, and Luria shared the Nobel Prize in Physiology or Medicine for their research about the replication mechanisms and the genetic structure of viruses. Hershey won the award specifically for his phage research and for the Hershey-Chase experiments. In 1971, he edited The Bacteriophage λ, a book detailing research about phage λ. Hershey continued to conduct research until his retirement in 1974.

Many scientists wrote memoirs about Hershey describing his character and effect on the scientific community. Watson detailed Hershey's post-retirement interests in sailing, gardening, and computers. Franklin Stahl, a scientist who researched phages and DNA replication, wrote about Hershey's originality, manner of scientific writing, and his thoroughness as an editor.

Hershey died from congestive heart failure on 22 May 1997 at his home in Syosset, New York.

Sources

1. Altman, Lawrence K. "Alfred D. Hershey, Nobel Laureate for DNA Work, Dies at 88." New York Times, May 24, 1997. https://www.nytimes.com/1997/05/24/us/alfred-d-hershey-nobel-laureate-for-dna-work-dies-at-88.html (Accessed July 25, 2018).
2. Avery, Oswald, Colin MacLeod, and Maclyn McCarty. "Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types: Induction of Transformation by a Desoxyribonucleic Acid Fraction Isolated from Pneumococcus Type III." The Journal of Experimental Medicine 79 (1944): 137–58. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2135445/pdf/137.pdf (Accessed July 18, 2018).
3. Cairns, John. "Alfred Hershey (1908-97)." Nature 388 (1997): 130.
4. Campbell, Allan, and Franklin W. Stahl. "Alfred D. Hershey." Annual Review of Genetics 32 (1998): 1–6.
5. Fischer, Ernst Peter, and Carol Lipson. Thinking About Science: Max Delbrück and the Origins of Molecular Biology. New York: W. W. Norton & Company, 1988.
6. Fry, Michael. "Chapter 4 – Hershey and Chase Clinched the role of DNA as Genetic Material: Phage Studies Probelled the Birth of Molecular Biology." In Landmark Experiments in Molecular Biology, 111–42. Academic Press, 2016.
7. Hershey, Alfred Day, and Jacques Bronfenbrenner. "On Factors Limiting Bacterial Growth. I." Proceedings of the Society for Experimental Biology and Medicine 36 (1937): 556–61.
8. Hershey, Alfred Day, Kalmanson, George M., and Jacques Bronfenbrenner. "Quantitative Methods in the Study of the Phage-Antiphage Reaction." Journal of Immunology 46 (1943): 267–79.
9. Hershey, Alfred D., and Martha Chase. "Independent Functions of Viral Protein and Nucleic Acid in Growth of Bacteriophage" The Journal of General Physiology 36 (1952): 39–56.
10. Huston, Ralph C., Huddleson, Irvin, F., and Alfred Day Hershey. "The Chemical Separation of Some Cellular Constituents of the Brucella Group of Micro-Organisms." PhD diss., Michigan State College, 1934.
11. Holmes, Frederic L. Meselson, Stahl, and the Replication of DNA: A History of "The Most Beautiful Experiment in Biology." New Haven: Yale University Press, 2001.

12. Hopson, Janet L., and Norman K. Wessells. Essentials of Biology. New York: McGraw-Hill, 1990.
13. Judson, Horace Freeland. The Eighth Day of Creation. Cold Spring Harbor: Cold Spring Harbor Laboratory Press, 1996.
14. Kalmanson, George, and Jacques Bronfenbrenner. “Studies on the Purification of Bacteriophage.” The Journal of General Physiology 23 (1939): 203–28. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2237916/pdf/203.pdf (Accessed July 25, 2018).
15. Luria, Salvador, and Max Delbrück. “Mutations of Bacteria from Virus Sensitivity to Virus Resistance.” Genetics 28 (1943): 491–511. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1209226/pdf/491.pdf (Accessed July 25, 2018).
16. Morange, Michel. A History of Molecular Biology. Cambridge: Harvard University Press, 1998.
17. Olby, Robert Cecil. The Path to the Double Helix: The Discovery of DNA. Seattle: University of Washington Press, 1974.
18. Shampo, Marc A., and Robert A. Kyle. ”Alfred Hershey—Nobel Prize for Work in Virology.” Mayo Clinic Proceedings 79 (2004): 590.
19. Stahl, Franklin W., and Hershey, Alfred D. We Can Sleep Later: Alfred D. Hershey and the Origins of Molecular Biology. Woodbury: Cold Spring Harbor Laboratory Press, 2000.
20. Watson, James, and Francis Crick. “Molecular Structure of Nucleic Acids.” Nature 171 (1953): 737–738. https://profiles.nlm.nih.gov/ps/access/SCBBYW.pdf (Accessed July 25, 2018).