Matthew Stanley Meselson (1930–) [1]

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Matthew Stanley Meselson conducted DNA and RNA research in the US during the twentieth and twenty-first centuries. He also influenced US policy regarding the use of chemical and biological weapons. Meselson and his colleague Franklin Stahl demonstrated that DNA replication is semi-conservative. Semi-conservative replication means that every newly replicated DNA double helix, which consists of two individual DNA strands wound together, contains one strand that was conserved from a parent double helix and that served as a template for the other strand. Meselson's work enabled researchers to better explain and control cellular development by showing how DNA are copied when a cell divides and interpreted when a cell makes proteins.

Meselson was born in Denver, Colorado, to Ann and Hyman Meselson on 24 May 1930. At the age of two, Meselson and his family moved to Los Angeles, California, where he grew up as an only child. According to Meselson, even as a boy he wanted to be a scientist. Meselson built his own chemistry lab in the garage of his home using a chemistry set given to him by his uncle Morris. According to Frederic Lawrence Holmes, a historian of science, Meselson said that his interest in chemistry continued to develop in high school because his chemistry teacher, Elizabeth Butcher, challenged him. Meselson also claimed that he was fascinated by the question of how life originated. He said that he wondered whether electricity was the source of life, and he imagined himself as an electrochemist discovering the means to create life.

By taking classes over the summers, Meselson earned enough high school credits to graduate a year and a half early. However, because he did not complete three years of physical education, Meselson did not formally graduate from high school. In 1946, Meselson enrolled at the University of Chicago [3] in Chicago, Illinois, which did not require a high school diploma. The University of Chicago [3] did not offer a specialized chemistry degree program, so Meselson enrolled in the general program and graduated with a Bachelor of Philosophy degree in 1949. After he graduated, Meselson traveled throughout Europe for a year. According to Meselson, seeing the post-WWII destruction made him interested in learning how to prevent future wars.

In September 1950, Meselson attended the California Institute of Technology [4], also called Caltech, in Pasadena, California, to earn a degree that qualified him for graduate work in science. Linus Pauling, a two time Nobel Laureate, taught Meselson's first year chemistry course. Meselson stated that Pauling was his favorite teacher because unlike his other teachers at Caltech, Pauling explained the reasoning behind scientific phenomena. Pauling later became Meselson's academic mentor. After a year at Caltech, Meselson re-enrolled at the University of Chicago [3] where he earned a letter from the dean that was equivalent to a Bachelor of Science Degree in Chemistry.

While exploring graduate programs in the summer of 1953, Meselson attended a pool party hosted by Peter Pauling, a colleague of Meselson's from Caltech and the son of Linus Pauling. At the party, Linus Pauling asked Meselson about his graduate plans and later invited Meselson to work with him as a graduate student. Meselson accepted the offer and became Pauling's last graduate student.

In the fall of 1953, Meselson began his graduate work at Caltech. His early graduate work focused on x-ray [5] crystallography, a method that involves shooting x-ray [5] beams at a crystal of a molecule to determine the structure of that molecule. According to Meselson, during his graduate program he started thinking about the possibility of density-gradient centrifugation, a method to separate substances based on their molecular weights, which he later developed and used to determine how DNA replicates itself. Meselson attributed the inspiration to create density-gradient centrifugation to two experiences he had during his early graduate work. First, Meselson said that he learned about isotopes in one of Pauling's chemistry classes. Isotopes are atoms of the same element that contain a different number of neutrons, or uncharged particles, than the most stable form of that element, causing the isotope to have a different weight than the stable form. Second, Meselson attended a lecture given by Jacques Monod [6], Monod, who studied bacteria in France. During the lecture, Monod said that he wanted to see if bacteria produced different proteins in response to changes in their chemical environment. However, according to Meselson, the method Monod suggested to identify new protein production was flawed. Meselson stated that Monod's lecture made him hypothesize how he could apply the concepts he learned Pauling to the task of separating substances by weight.

In 1954, Meselson visited Max Delbrück, the Nobel Laureate, biophysicist, and head of the biology division at Caltech, to discuss the structure of DNA. Meselson had met with Delbrück the year before to discuss the same subject, but Delbrück had sent Meselson away because Meselson did not know enough about DNA. During their second meeting, Delbrück stated that he disagreed with the semi-conservative model of DNA replication suggested by James Watson [7] and Francis Crick [8] at the

In the summer of 1954, Meselson met Franklin Stahl, a doctoral student at the University of Rochester in Rochester, New York, who studied viruses. Meselson and Stahl agreed to study DNA replication together. Meselson and Stahl began their collaboration in the fall of 1956. The researchers worked on a variety of projects, including Meselson's method of density-gradient centrifugation, which became a part of Meselson's doctoral thesis in May 1957. Meselson obtained a PhD in chemistry later that year under the supervision of Linus Pauling.

Density-gradient centrifugation, which Meselson first thought of while watching Monod's lecture, separates molecules by their weights. To perform density-gradient centrifugation, researchers place a sample in a solution that has a density within the range of the densities of the contents of the sample. Some molecules in the sample will have a higher density than the solution, and some have a lower density. The difference of densities enables the molecules to separate and suspend in solution when researchers spin them in a centrifuge. By the end of the centrifuge run, researchers can separate the molecules based on their density, which is determined by the molecule's weights.

After a year of trial and error with all of their projects, Meselson and Stahl conducted Meselson-Stahl experiment between October 1957 and January 1958. They applied density-gradient centrifugation to separate the DNA made by *Escherichia coli B*, which is a bacteria commonly used for research. To separate DNA by weight, the researchers labeled the DNA with nitrogen isotopes. Nitrogen is a component of DNA, so as bacteria grow and make DNA, the bacteria strip nitrogen from the environment. Given this process, Meselson and Stahl first grew *E. coli* in an environment rich with nitrogen-15, which is a heavy isotope of nitrogen that contains fifteen neutrons per atom. The first generation of *E. coli* used heavy nitrogen to make DNA. The researchers then shocked the environment by adding an excess amount of nitrogen-14, which is the lighter and more stable form of nitrogen that contains fourteen neutrons per atom. *E. coli* used the excess of nitrogen-14 to make DNA for subsequent generations. Meselson and Stahl lyzed, or burst, the bacteria so the DNA contents released. The researchers then centrifuged each generation and analyzed the ratios of DNA densities. Meselson and Stahl found that the ratios of heavy isotope DNA and light isotope DNA were what would be expected if DNA replicated itself semi-conservatively, thereby verifying the Watson-Crick model for DNA.

In 1958, Meselson became an assistant professor of chemistry at Caltech, but he resigned two years later to become a research fellow at Caltech instead. In the summer of 1960, Meselson worked with the biologist François Jacob and the biologist Sydney Brenner [9] to investigate messenger RNA. Messenger RNA is a short-lived molecule that carries genetic information from the DNA to a different part of the cell that makes proteins. Prevaling theories at the time attributed the role of messenger RNA to a different molecule, but Meselson and the team of researchers used Meselson's density-gradient centrifugation to provide evidence against that theory and instead for the necessity for messenger RNA. The team's results helped indicate how DNA leads to the production of proteins, which have many functions in cells.

While Meselson studied messenger RNA, he married a flutist named Katherine Kaynis whom he met during a music festival several years before in Aspen, Colorado. According to Holmes, Meselson said that he wanted to leave Los Angeles, so in February 1961, he and his wife moved to Cambridge, Massachusetts, so he could work at Harvard University [10] as an associate professor of natural sciences. In 1963, Meselson won the National Academy of Science Award in Molecular Biology for having created the method of density-gradient centrifugation. Around the same time, Meselson began to publically oppose the use of chemical and biological weapons, including herbicides like Agent Orange sprayed by the US military during the Vietnam War. He consulted for the US Arms Control and Disarmament Agency, headquartered in Washington, D.C., which aimed to establish policies for the use of different kinds of weapons. Meselson remained in the organization [11] until 1973. In 1966, while still teaching at Harvard, Meselson and John Edsall, a fellow chemistry professor from Harvard, obtained the signatures of 5000 scientists to petition the White House to end the spraying of herbicides in Vietnam.

Meanwhile, Meselson continued his research at Harvard. In 1968, he and another researcher isolated restriction enzymes. Enzymes are proteins that help with necessary chemical reactions in a cell. Restriction enzymes are enzymes found in certain bacteria that degrade DNA from foreign bacteria. Meselson's research on restriction enzymes enabled future scientists to decode and understand the specific genetic instructions in DNA.

In 1969, Meselson continued his work with chemical and biological weapons as a leader of the American Association of the Advancement of Science antiwar movement. In December 1969, the American Association of the Advancement of Science appointed Meselson as head of the Herbicide Assessment Committee, which traveled to Vietnam in 1970 to witness the effects of Agent Orange. However, the committee could not draw any significant conclusions because of limited access to sprayed areas. The 2014 book *Toxic War* by Peter Sills states that Meselson helped publicize an unofficial report by the Bionetics Research Laboratories of Bethesda, Maryland, about the birth defects [12] caused by Agent Orange, an herbicide used in the Vietnam War. Meselson also worked with Henry Kissinger, US President Richard Nixon's National Security Advisor. Sills states that Meselson

As a researcher, Meselson increasingly studied animals instead of bacteria. His research first focused on the evolution of gene regulation. Genes are regulated by chemical signals that activate the gene so that proteins can be made from that gene. Starting in the early 1970s, Meselson studied the common fruit fly (Drosophila melanogaster). In 1976, Meselson became the Thomas Dudley Cabot Professor of Natural Sciences at Harvard University. Meselson worked with his graduate students to study heat-shock responses in Drosophila. When Meselson's team applied heat to certain cell tissues in Drosophila, the cells stopped producing certain proteins and quickly produced new ones as a response to the increase of temperature. In 1981, Meselson found the same heat sensitive mechanism in mice, thereby extending evidence for gene regulation to more animals. In 1982, Meselson also contributed to the finding of a transposon in Drosophila. A transposon is a mobile piece of DNA that helps regulate genes. Meselson's studies further illustrated how genes not only code for different proteins, but can also control the amount of protein produced.

While conducting research at Harvard, Meselson married one of his research technicians, Sarah Page, after divorcing his first wife. With his second wife, Meselson had two children, Zoe and Amy. In 1980, Meselson divorced his second wife. In 1986, he married his third wife, a medical sociologist and anthropologist, Jeanne Guillemin, who also spoke out against biological weapons.

Meselson attributes a paper he read in 1970 by John Turner, a professor at the University of York in York, England, as the motivation behind the research he began in the 1980s. In the paper, Turner questions the benefit of sexual reproduction by noting some drawbacks of sex. After reading the paper, Meselson learned about Bdelloid Rotifers, a class of ancient aquatic animals that reproduce only asexually, meaning without a partner. Because asexual species clone themselves to reproduce, most go extinct because rarely are new genes introduced into lineages, which as a result evolve slowly, especially in comparison to changing environments. Sexual species avoid that issue because their reproduction varies the genes inherited by offspring. The prolonged existence of Bdelloid Rotifers challenged theories about why sexual reproduction is favorable to asexual reproduction. In 1989, Meselson began researching Bdelloid Rotifers to determine if they were truly asexual throughout their entire existence.

Meselson continued his involvement with banning the use of chemical and biological weapons. In 1990, Meselson and Julian Perry Robinson of the University of Sussex in Brighton, England, co-founded the Harvard Sussex Program on Chemical and Biological Weapons. The program promoted public policy aimed at limiting the use of chemical and biological weapons internationally. In 2001, Meselson and Robinson wrote "A Draft Convention to Prohibit Biological and Chemical Weapons under International Criminal Law". The document proposes that the use of chemical and biological weapons should be an international crime.

Meselson's research on Bdelloid Rotifers continued in May 2000 when he proposed a method for identifying species that remained asexual throughout their entire lifespans. Meselson used that method, which later papers called the "Meselson Effect" to classify Bdelloid Rotifers as asexual organisms. However, many scientists opposed Meselson's conclusions, stating that the "Meselson Effect" also indicated infrequent sexual reproduction rather than no sexual reproduction.

In 2001, Frederic Lawrence Holmes, a historian and professor at Yale University in New Haven, Connecticut, published Meselson, Stahl, and the Replication of DNA: A History of "The Most Beautiful Experiment in Biology." Holmes worked for twelve years with Meselson and Stahl to write the biography of the two men and their experiment. Meselson is a member of many national and international societies, including the National Academy of Sciences. Into the second decade of the twenty-first century, he remained co-director of the Harvard Sussex Program, and he served on the Center for Arms Control and Non-Proliferation Advisory Board to the US Secretary of State. Meselson received the Macarthur Fellowship, the 2008 Mendel Medal of the UK Genetics Society, and the Thomas Hunt Morgan Medal from the US Genetics Society.

Sources


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