Franklin William Stahl (1929–)

Franklin William Stahl studied DNA replication, bacteriophages, and genetic recombination in the US during the mid-twentieth and early twenty-first centuries. With his colleague Matthew Meselson, Stahl performed an experiment called the Meselson-Stahl experiment, which provided evidence for a process called semi-conservative DNA replication. Semi-conservative replication is a process in which each strand of a parental DNA double helix serves as a template for newly replicated daughter strands, so that one parental strand is conserved in every daughter double helix. Those findings supported the Watson-Crick Model for DNA replication proposed in 1953 by James Watson and Francis Crick, convincing many biologists about DNA´s structure and replication in the 1950s. Stahl´s genetics research, especially that of DNA replication, showed researchers how genetic information is distributed within a cell and is passed down from cell to cell.

Stahl was born in Boston, Massachusetts, on 8 October 1929 to Eleanor Condon Stahl and Oscar Stahl. In 1947, he enrolled as an undergraduate at Harvard University in Cambridge, Massachusetts, to major in biology. According to Frederic Lawrence Holmes, a historian of science, Stahl intended to attend medical school after he graduated. However, as Holmes stated, Stahl needed to commute and work part-time to pay for his education, which contributed to his grades not being high enough for him to attend medical school. Holmes explains that after Stahl's second year at Harvard he realized that his grades were not high enough for acceptance to medical school. He considered teaching high school biology. But his mother convinced him to pursue a graduate degree, and as genetics had interested Stahl at Harvard, he decided to study genetics. Stahl graduated with a Bachelor´s degree in biology in 1951 from Harvard.

In the fall of 1951, Stahl started at the University of Rochester in Rochester, New York, as a graduate student in biology studying with Donald R. Charles who studied classical genetics. Holmes states that Stahl applied to three schools and chose the university because it was the only school that accepted him with financial aid. In the summer of 1952, Stahl took a course about bacteriophages, viruses that specifically infect bacteria, at the Cold Spring Harbor Laboratory in Cold Spring Harbor, New York, taught by August H. (Gus) Doermann. Afterwards, Stahl focused his studies on bacteriophages. Scientists studied bacteriophages to learn about DNA because, at the time, they considered bacteriophages, which contained only protein and DNA or RNA, to be the simplest organisms. During the summer of 1953, Stahl joined Doermann´s research group in Oak Ridge, Tennessee, to study bacteriophages, in preparation for Doermann´s move to the University of Rochester.

In 1954, Stahl enrolled in summer courses at the Marine Biological Laboratory in Woods Hole, Massachusetts. There he met Matthew Meselson, a graduate student from the California Institute of Technology (Caltech) in Pasadena, California, who approached Stahl after he heard about Stahl´s laboratory skills and proposed to study DNA replication with Stahl. In 1954, scientists debated whether DNA replicated the way James Watson and Francis Crick had proposed in 1953. The model created by Watson and Crick, called the Watson-Crick Model suggested that DNA made copies of itself within cells, a process called DNA replication, when the two strands of DNA separate from each other and become templates for new daughter DNA strands. That process was later called semi-conservative replication. However, some scientists contested the model because DNA strands, which wound tightly together, were too entwined to separate. After their meeting, Meselson and Stahl aimed to determine with experiments how DNA replicated.

After his summer at the Marine Biological Laboratory, Stahl returned to the University of Rochester in the fall of 1954 to complete his graduate research on bacteriophages with Doermann. Stahl´s

work focused on the damage to the genetic material of certain bacteriophages caused by a radioactive isotope of phosphorus. Radioactive isotopes are unstable and often harm organisms, but they have properties that, when scientists attach them to molecules, help scientists trace those molecules. Stahl and Doermann´s research helped researchers incorporate radioactive phosphorus into DNA to track the subunits of DNA as the DNA replicated. Stahl´s research also examined genetic recombination, or gene mixing, in bacteriophages as they reproduce.

Stahl met Mary Morgan, a student at Antioch College in Yellow Springs, Ohio, in July 1955. Morgan was from Rochester, and they married one week after their first date and traveled to Pasadena, California, so Stahl could study at Caltech as a postdoctoral fellow. However, two months after they moved, Stahl´s wife left him and went to Chicago, Illinois, while pregnant with their first child. Stahl and his wife did not reunite until she gave birth to their first child in the spring of 1956.

At Caltech, Stahl continued to study bacteriophage genetics while Meselson completed his thesis. Holmes states that while at Caltech Stahl experienced difficulties with both his research and personal life. According to Holmes, Stahl struggled with some of his research and drank heavily. However, Stahl revived his marriage. His wife wanted to put their child up for adoption, but Stahl´s mother convinced him to serve as the child´s parent himself. When Stahl travelled to Chicago in 1956, his wife decided to keep the child, named Andrew, and they move to Pasadena with Stahl.

Stahl began his collaboration with Meselson in the summer of 1956. Stahl and Meselson initially tried to study DNA replication in bacteriophages. Using a method conceived by Meselson to separate molecules, they placed a sample containing isotopes of different densities on a medium made of different densities then spun them in a centrifuge, called density-gradient centrifugation. They studied many aspects of DNA, and throughout their collaboration, Stahl prepared bacteriophage samples, analyzed the data, and wrote the progress reports.

Stahl and Meselson performed what became the Meselson-Stahl experiment from October 1957 to January 1958. They switched from working with bacteriophages to working with Escherichia coli (E. coli), a type of bacteria found in the guts of mammals, to study DNA replication because bacterial DNA produced clearer results. To differentiate between parental and daughter DNA, Stahl and Meselson grew E. coli in media that contained a heavy nitrogen (^{15}N) isotopes, meaning that the nitrogen atoms in a medium contained more neutrons, or uncharged particles, than regular nitrogen (^{14}N) atoms. DNA bases contain nitrogen, so when the parental DNA replicated, it incorporated ^{15}N, giving the parental DNA molecules a higher density.

Stahl and Meselson then grew the bacteria with ^{15}N in a medium with light nitrogen^{14}N and examined the densities of the new DNA formed. As the bacteria replicated, and as the parental DNA replicated, the daughter DNA incorporated the light nitrogen. After each replication cycle for several cycles, Stahl and Meselson used density-gradient centrifugation to separate the sampled bacterial DNA by different densities. After analyzing the distribution of DNA molecules, Stahl and Meselson found that daughter DNA molecules contained parental DNA subunits and daughter DNA subunits, later determined to be single DNA strands, in a ratio that aligned with the semi-conservative DNA replication proposed by Watson and Crick. Stahl and Meselson's findings helped solidify the semi-conservative model for DNA. Stahl and Meselson published their results in 1958.

After Stahl and Meselson confirmed the Watson-Crick Model for DNA replication, Stahl remained unhappy at Caltech. Holmes reports that Meselson´s enthusiasm and fast-paced work ethic overshadowed Stahl´s research interests and input. Stahl ultimately left Caltech in May 1958 to work at the University of Missouri in Columbia, Missouri.

Stahl left the University of Missouri in 1959 after one year of teaching and researching. According to Holmes, Stahl felt that the environment of the University of Missouri was not conductive to his desire to teach molecular genetics and did not provide the necessary equipment for his research. Stahl moved to Eugene, Oregon, in the fall of 1959 to teach at the University of Oregon.

At the University of Oregon, Stahl readdressed some of the research questions he and Meselson originally worked on in 1957 surrounding mutations in bacteriophages. In 1961, using Meselson´s density-gradient centrifugation technique, Stahl and George Streisinger studied substitution mutations. Substitutions occur when specific DNA components, called nucleotide bases, are switched

for other nucleotide bases in daughter DNA during DNA replication. Stahl and Streisinger found that in a strain of T4 bacteriophages, substitutions occurred because DNA mistakenly incorporated the wrong types of bases when replicating. Stahl and Meselson had predicted that result years prior.

Stahl continued to study the genetics of T4 bacteriophages throughout the rest of the 1960s. In 1964, he determined that the DNA in T4 bacteriophages is circular rather than linear. That same year, Stahl published his first textbook titled The Mechanics of Inheritance, which surveyed new information from genetics, including his research about DNA mutations. That information included studies about the way in which genetic information from DNA was transcribed into mRNA, the molecule that relays some genetic information from DNA to proteins.

Into the 1970s, Stahl expanded his research on genetics, specifically on genetic recombination or rearrangement of genes, to study a strain of bacteriophages called λ (lambda). Genetic recombination is one cause by which offspring genetically vary from their parents, and in many cases, it´s essential for the offspring´s survival, especially for organisms that do not reproduce sexually. Stahl conducted much of his research with his wife who worked as his research technician and co-author on many of his papers. Starting in 1971 and into 1973, Stahl and his wife studied the relation between DNA replication and genetic recombination. They found that some sections of the genetic material in λ bacteriophages underwent more DNA replication during genetic recombination than other sections, thereby suggesting a more complex mechanism for genetic recombination.

Stahl and his wife´s findings about bacteriophage λ in the early 1970s led to more research about genetic recombination throughout the 1970s, 1980s, and 2000s. As described in his 1974 paper, Stahl, his wife, and other collaborators noticed a spike in the amount of genetic recombination associated with a particular mutation in the DNA of the λ bacteriophage. The number of genes recombining plummeted when the researchers removed the mutated DNA from individual bacteriophages. Stahl and his associates later linked the mutation to a particular DNA sequence. The researchers named the sequence Chi. Scientists later found that Chi was also involved in the genetic recombination of E. coli, and Stahl and his colleagues studied the interactions between Chi and proteins in the DNA of E. coli. By 1995, Stahl and his collaborators showed that Chi promoted recombination in E. coli by reducing the activity of that protein. In an article about his Chi research, Stahl reflected that his wife played a major role in his research throughout the late 1990s. Stahl continued to publish on Chi into the 2000s.

Aside from studying, the effects of Chi on genetic recombination, in the 1980s and 1900s Stahl also worked with other scientists to develop the double-strand-break repair model for DNA. The model described a mechanism by which DNA repairs itself when damaged, which introduces more genetic recombination in offspring. Stahl, Jack Szostak, a scientist from Harvard Medical School in Boston, Massachusetts, and other scientists studied yeast to discover the mechanism by which parts of DNA strands are broken and replaced by parts from different DNA molecules.

In 1985, Stahl received the American Cancer Society Research Professorship and two research grants, the MacArthur fellowship and Guggenheim Fellowship, the latter of which he had also received in 1975. In 1996, Stahl received the Thomas Hunt Morgan Medal, an award that is given to researchers who have made major contributions to the field of genetics throughout their careers. In addition to his first textbook, Stahl authored and published a second textbook in 1979 titled Genetic Recombination: Thinking About It in Phage and Fungi.

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