Oswald Theodore Avery (1877-1955)

Oswald Theodore Avery studied strains of pneumococcus of the genus Streptococcus in the US in the first half of the twentieth century. This bacterium causes pneumonia, a common cause of death at the turn of the twentieth century. In a 1944 paper, Avery demonstrated with colleagues Colin Munro MacLeod and Maclyn McCarty that deoxyribonucleic acid, or DNA, instead of protein, formed the material of heritable transformation in bacteria. Avery helped untangle some of the relationships between genes and developmental processes.

Avery was born in Halifax, Canada, on 21 October 1877 to Elizabeth Crowdy Avery and Joseph Francis Avery, a Baptist clergyman. Avery had an older brother, Ernest, and a younger brother, Roy. In 1887, Avery and his family moved to New York City, New York, where he spent much of the next sixty-one years of his life. In 1893, Avery received his high school diploma from the New York Male Grammar School, New York, and then he moved to the Colgate Academy, a preparatory department of Colgate University in Hamilton, New York. Avery received his Bachelor of Arts degree in Humanities at Colgate University in 1900, where he excelled in public speaking and debate. In 1904 Avery graduated with a medical degree from the College of Physicians and Surgeons of Columbia University in New York City.

After graduation from Columbia and working in clinical practice, in 1907 Avery became a researcher and lecturer in bacteriology and immunology in the Brooklyn borough of New York City at the Hoagland Laboratory, a privately funded bacteriological research laboratory. During his six years at the Hoagland Laboratory, Avery underwent practical bacteriological, immunological, and chemical training while studying the bacteriology of fermented milk products. In 1913, Avery began a career that lasted thirty-five years at the Rockefeller Institute for Medical Research in New York City, where he obtained full membership in 1923, and where he became a Member Emeritus in 1943.

From 1913 to 1930, Avery's research at the Rockefeller Institute examined pneumococcus's capacity to cause pneumonia, also known as its virulence. Avery also studied how human immune systems responded to different strains of pneumococcus. Using microscopic observation and immunochemical techniques, Avery and his colleagues made several findings. These discoveries included a correlation between virulence and the presence of a bacterial capsule, which protects the bacteria against ingestion by other microorganisms. Avery and his colleagues also discovered that differences in surface carbohydrates, called polysaccharides, characterize strains of pneumococcus and their virulences. Avery and colleagues also showed that antibodies are specific to the capsule's carbohydrates, and that those antibodies work by negating the capsule's ability to prevent ingestion by other organisms. From those findings, Avery and his colleagues concluded that to effectively make people immune to the bacteria, scientists must preserve the chemical integrity of bacteria's capsules when preparing an immunization.

These were the first studies to demonstrate the degree to which surface carbohydrates functioned in immunological processes, and they led to medicines such as a serum treatment for type I pneumococcus. Avery's studies also demonstrated the value of analyzing chemical and cellular components, in contrast to immunological methods that focused on the whole organism.

By 1930, developments in bacteriology and immunology changed the direction of Avery's research. In late 1920s, medical officer Frederick Griffith for the Ministry of Health's pathological laboratory in England reported his discoveries in pneumococci. There are two strains of type II pneumococci: virulent S strain, which has a smooth appearance, and harmless R strain, which has a rough appearance. Griffith found that with S strain pneumococci killed with heat, researchers could convert live R form into the live S strain. Griffith also claimed that this conversion, a phenomenon he called

transformation, was heritable across generations of pneumococci. Avery initially doubted the claim that laboratory manipulations could result in a heritable changes in pneumococcus's virulence and that differences between strains of pneumococci extended beyond surface carbohydrate structures. Subsequent studies duplicated Griffith's results and convinced Avery. Avery shifted his research focus to the identification of the chemical basis of transformation.

Avery researched bacterial transformation in the early 1930s. During this time, Avery suffered from the onset of the Graves' disease, an autoimmune disorder, until a thyroidectomy slowed the progression of the disease in 1934 and enabled Avery to return to his research. In 1935, Avery's research associates came to include Colin Munro MacLeod, whom Maclyn McCarty replaced in 1941. It took Avery, MacLeod, and McCarty more than a decade to isolate and identify DNA as the material of genetic inheritance. In 1944 the trio published ”Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types Induction of Transformation by a Deoxyribonucleic Acid Fraction Isolated from Pneumococcus Type III.” In the report, the three scientists identified DNA as the material in pneumococci that held the transforming properties observed by Griffith.

Avery and his colleagues began their experiment by creating liquid cultures of S strain of type III pneumococci, which they then chilled, centrifuged, collected, and heat-killed. They chemically extracted a filtered liquid, or filtrate, from which Avery and his colleagues, chemically and through the use of enzymes, removed the proteins, carbohydrates, and lipids. They extracted a small amount of the transformation-inducing material from what was initially a seventy-five liter sample of liquid culture. When analyzed, this material, which took the form of a fibrous mass, exhibited the same nitrogen/phosphorus ratio as DNA. Avery and his colleagues treated the material with more enzymes to ensure the absence of proteins and ribonucleic acid, or RNA. The resulting product, when tested on R bacteria, retained its transforming property. However, when they added DNA-digesting enzymes into it, it lost this property. Avery concluded that DNA was the material that caused Griffith's heritable transformation in pneumococcus. This discovery implied that DNA was the material of genetic inheritance.

Though Avery became a foreign member of the Royal Society of London within a year of publishing his paper, many scientists did not immediately accept DNA as the genetic material. Critics still argued that protein was the material for inheritance and they suggested other explanations for the phenomena observed by Avery and his colleagues, such as that trace amounts of protein contaminated the DNA, that transformation by DNA only happened in bacteria, or that DNA was simply an agent that caused genetic mutations. However, later work confirmed Avery, MacLeod, and McCarty's findings. In 1945, Avery received the Copley Medal from the Royal Society of London, and in 1947 he received the Lasker Award. Scientists that win the Lasker Award often receive the Nobel Prize soon after. In Avery's case, the Lasker Award prediction did not hold true. Nobel Laureate Arne Tiselius said that Avery was the most conspicuous omission from the list of Nobel Prize winners. Avery retired in 1948 to Nashville, Tennessee, where he died of liver cancer at the age of seventy-eight on 20 February 1955.

Avery's research in bacteriology and immunology enabled molecular studies in developmental genetics. The identification of DNA's role in bacterial transformation by Avery, MacLeod, and McCarty partly accelerated and intensified DNA studies in the mid-twentieth century. Their discovery influenced later work such as Erwin Chargaff's DNA base composition studies between 1949 and 1953, Alfred Day Hershey and Martha Cowles Chase's 1952 experimental results on DNA's role in virus reproduction, and James Watson and Francis Harry Compton Crick's modeling of the DNA double helix in 1953. Within the next few decades, the acceptance of DNA as the genetic material led to research on DNA structure, mechanisms of storage and expression of information in DNA, and the genetic basis of developmental processes.

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