Hermann Joseph Muller (1890-1967) [1]

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Hermann Joseph Muller studied the effects of x-ray [4] radiation [5] on genetic material in the US during the twentieth century. At that time, scientists had yet to determine the dangers that x-rays presented. In 1927, Muller demonstrated that x-rays, a form of high-energy radiation [5], can mutate the structure of genetic material. Muller warned others of the dangers of radiation [5], advising radiologists to protect themselves and their patients from radiation [5]. He also opposed the indiscriminate use of radiation [5] in medical and industrial fields. In 1946, he received the Nobel Prize in Physiology or Medicine [6] for his lifetime work involving radiation [5] and genetic mutation. Muller's worked enabled scientists to directly study mutations without having to rely on naturally occurring mutations. Furthermore, Muller showed that radiation [5], even in small doses, leads to genetic mutations primarily in germ cells [7], cells which give rise to sperm [8] and egg [9] cells.

Muller was born on 21 December 1890 in New York City, New York, to Frances Lyons Muller and Hermann Muller, Sr. He attended a public elementary school in the Manhattan borough of New York City, New York New York City, and began to study science. He later attended Morris High School in the Bronx borough of New York City where he and his friends founded a science club. In 1907, at the age of sixteen, Muller received the Cooper-Hewitt Fellowship, a scholarship awarded to students from New York City who excelled on their college entrance examinations. Later that year, Muller used the fellowship to enroll at Columbia University [10] in New York City.

During Muller's undergraduate years at Columbia University [10], he studied genetics after taking a course taught by Edmund Beecher Wilson [11], who studied genetics and cell biology. After he graduated in 1910, Muller remained as a graduate student at Columbia University [10]. From 1910 to 1915, he studied heredity and genetic mutations in the fruit fly (*Drosophila* *[12]*) with the guidance of Thomas Morgan, who researched the role that chromosomes play in heredity.

As a part of Morgan's research team, Muller verified earlier theories that chromosomes are the physical components by which offspring inherit traits from their parents. Morgan's studied mutations to create a map of gene locations on fruit fly chromosomes. In doing so, they discovered paired or homologous chromosomes randomly exchange genetic material with each other during egg [9] and sperm [8] cell development, a process later called crossing over. In 1915, Muller coauthored a book with Morgan called *The Mechanism of Mendelian Heredity* *[13]* that included sections on the crossing over of chromosomes. After receiving his PhD for his work on the crossing over of chromosomes in 1916, Muller left Columbia University [10] to teach at Rice Institute in Houston, Texas, where he continued to research genetic mutations.

In 1920, Muller moved to Austin, Texas, to become a professor at the University of Texas. At the University of Texas, he used x-rays in his experiments with fruit flies. At that time, a number of studies had reported the effects that x-rays had on living cells, particularly sperm [8]

cells. In 1923, Muller used x-rays to alter the rates at which chromosomes cross over. He hypothesized that exposing sperm [8] cells to x-rays would affect the rate of chromosomes crossed over. However, he found the x-ray [4]'s effects to be weak.

In 1926, Muller began investigating whether the radiation [5] from x-rays could mutate genetic material. In a series of three experiments, he exposed fruit flies to x-ray [4] radiation [5] and then mated the flies. He then tallied the total number of mutations in the offspring of the fruit flies he had exposed to x-ray [4] radiation [5] compared to offspring of fruit flies he had not exposed. Muller found that the offspring of exposed fruit flies exhibited significantly more mutations than the offspring of unexposed fruit flies. Muller found that germ cells [7], the cells that produce sperm [8] and egg [9] cells, subjected to x-rays had a 15,000 percent increase in the frequency of mutations when compared to untreated germ cells [7]. From the experiments, Muller concluded that x-rays had induced genetic mutations in the fruit flies.

While at the University of Texas, Muller published the results of his experiment in "Artificial Transmutation of the Gene" in 1927. According to one of his students, Elof Carlson, many scientists considered the article to be incomplete due its lack of a methods section and data. Soon after, Muller released a more comprehensive account of the experiments in 1927 when he presented "The Problems of Genic Modification" at the Fifth International Congress of Genetics in Berlin, Germany. Not only did Muller expose an unknown consequence of radiation [5], but he also demonstrated that scientists could use radiation [5] to induce mutations in their genetic research.

In 1932, Muller helped distribute a Communist student newspaper called *The Spark* across the University of Texas. A communist supported group published the newspaper, which featured views that many criticized for being socialist. Muller himself was an outspoken socialist with Communist sympathies, and his involvement with the publication made him the subject of a US Federal Bureau of Investigation inquiry, although he was never indicted for his participation. Following the investigation, Muller left the University of Texas for research jobs in Europe, where he spent the next eight years studying the structure of the chromosome through the use of radiation [5]. Muller spent his first year in Europe working at the Kaiser Wilhelm Institute for Brain Research, later called the Max Planck Institute for Brain Research, in Frankfurt, Germany. He worked alongside Nikolay Timofeev-Ressovsky, the director of the institute's genetic division who studied radiation [5] genetics. They studied the frequency of genetic mutations after exposure to various wavelengths of radiation [5] and the mechanism of how chromosomes break.

In 1934, Muller left Germany to direct a genetics laboratory at the Institute of Applied Botany in Leningrad, Union of Soviet Socialist Republics (USSR), later renamed Saint Petersburg, Russia. There, Muller continued his work on mutations and chromosome structure and traveled the country lecturing on genetics. From 1934 to 1937, he was the senior geneticist at the Institute of Genetics of the Academy of Sciences in Moscow, USSR. Around the late 1930's, the USSR's government-backed scientists began to reject the chromosome theory of inheritance, Mendelian genetics, which Muller studied. The USSR began to favor the works of Trofim Lysenko, a Soviet soldier and biologist who argued that organisms inherited traits through the environment. In 1937, following the USSR's shift in theories about genetics, Muller moved to the University of Edinburgh [14] in Edinburgh, Scotland. While in Edinburgh, Muller wrote a report for the Medical Research Council [15] of Great Britain stating that when germ cells [7] are exposed to radiation [5], even small amounts, they will undergo genetic mutations. He insisted that radiologists must protect themselves and their patients from those dangers.

In 1940, Muller returned to the United States to take a temporary research position at Amherst College in Amherst, Massachusetts. At Amherst, he studied the relationship between aging and spontaneous genetic mutations, mutations that occur during normal cell processes and not as a result of radiation [5]. During that time, he consulted on the Manhattan Project, the secret effort in the US to develop the atomic bomb. Muller provided advice on experiments pertaining to the mutational effects of radiation [5].

In 1945, Muller became a professor in the zoology department at Indiana University [16] in Bloomington, Indiana, where he remained until his death. Following the 1945 bombings of the Japanese cities Hiroshima and Nagasaki, Muller expressed his concerns about the dangers of radiation [5] to the public. He urged the medical community to be more scrupulous with their use of radiation [5] therapy, and he insisted that necessary precautions must be taken to protect and shield gonads exposed to radiation [5].

In 1946, Muller received a Nobel Prize in Physiology or Medicine [6] for his 1927 work on radiation [5]-induced genetic mutations. The prize committee recognized Muller for both his discovery as well as his influence prompting related studies in the following years. Muller continued to study genetic mutations, publishing the article "Our Load of Mutations" in 1950 and "The Relation of Recombination to Mutational Advance" in 1964. Both articles addressed the role mutations play in the evolution [17] of organism populations.

Muller died 5 April 1967 in Indianapolis, Indiana, at the age of seventy-six.

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