"Sex Limited Inheritance in Drosophila" (1910) by Thomas Hunt Morgan

In 1910, Thomas Hunt Morgan performed an experiment at Columbia University, in New York City, New York, that helped identify the role chromosomes play in heredity. That year, Morgan was breeding Drosophila, or fruit flies. After observing thousands of fruit fly offspring with red eyes, he obtained one that had white eyes. Morgan began breeding the white-eyed mutant fly and found that in one generation of flies, the trait was only present in males. Through more breeding analysis, Morgan found that the genetic factor controlling eye color in the flies was on the same chromosome that determined sex. That result indicated that eye color and sex were both tied to chromosomes and helped Morgan and colleagues establish that chromosomes carry the genes that allow offspring to inherit traits from their parents.

Prior to Morgan's fly experiments, other researchers were studying heredity. In 1865, scientist Gregor Mendel in eastern Europe published an article describing heredity experiments he had performed using pea plants. By mating pea plants, Mendel observed that the resulting offspring inherited characteristics, such as seed color and seed shape, in predictable patterns. Mendel hypothesized that there were heritable factors, later called genes, controlling the development of those characteristics.

By the early 1900s, other scientists aiming to explain heredity began to reapply Mendel's theory. In the late nineteenth century, researchers discovered structures inside the nuclei of cells. Researchers called those structures chromosomes because of the way staining materials colored them. Staining chromosomes enabled researchers to observe chromosomes throughout development. In 1902, Walter Sutton, a researcher at Columbia University, and Theodor Boveri, a researcher at the University of Würzburg in Würzburg, Germany, each observed that chromosomes behaved in a manner that was consistent with Mendel's theories. Boveri and Sutton hypothesized that chromosomes carried heritable factors, or genetic material. Researchers called Boveri and Suttons' theory the Boveri-Sutton chromosome theory.

By 1904, Morgan had begun to study the processes that affect heredity and development at Columbia University. However, Morgan, like other scientists at that time, was reluctant to accept the Boveri-Sutton chromosome theory. Morgan argued that scientists had a bias towards associating phenomena, like the inheritance of traits, with known structures, like the chromosome. Similarly, he argued that if one gene didn't explain a phenomenon, scientists could argue that any number of genes might. In 1910, Morgan published an article explaining why he was reluctant to accept the Bover-Sutton chromosome theory.

Later that year, Morgan made an observation that eventually provided evidence in support of the chromosome theory. In 1910, Morgan was studying Drosophila at Columbia University to find what he called mutants, or individual flies that had atypical, heritable characteristics, such as white eyes instead of the normal red eyes. In May of 1910, after breeding thousands of flies, he observed a single male fly with white eyes, which he called a white mutant. Typically, both male and female flies have red eyes. To explain the white eye mutation, Morgan bred the mutant fly and observed how the mutation was inherited throughout successive generations.

In 1910, Morgan published details of his research in an article titled "Sex Limited Inheritance in Drosophila." First, Morgan took the white mutant and bred it with pure red-eyed female flies. All of the females that resulted from that breeding had red eyes. Morgan then took those red-eyed females and mated them with the original white-eyed mutant male to determine whether or not

the inheritance of eye color followed Mendel's inheritance patterns. If Mendel's patterns applied to Morgan's flies, there would be one white-eyed fly to every three red-eyed flies in the resulting generation of flies, regardless of sex. Although Morgan did observe one white-eyed fly to every three red flies, that inheritance pattern was not shared equally across males and females. Most of the white-eyed flies were male. That result indicated that the flies did not follow Mendel's ratio in a traditional sense.

After observing the white-eye inheritance pattern, Morgan hypothesized that a factor, or gene, controlling eye color was located on the X chromosome. Female flies have two X chromosomes, and males have one X chromosome and one Y chromosome. If a trait, like eye color, correlated with a specific factor on the X chromosome, then the trait was called X-linked. Because males only have one X chromosome, they display all X-linked traits. Females, on the other hand, often need an Xlinked trait to exist on both X chromosomes to display that trait. Morgan hypothesized that, in his breeding experiment, the first generation of flies contained males only with white eyes because the gene controlling eye color was on the X chromosome. Males displayed the white eye trait because the trait was present on their only X chromosome. Females did not display the white eye trait because the trait was only present on one of their X chromosomes.

To test his hypothesis that the white-eyed trait was on the X chromosome, Morgan mated other specific groups of flies together and observed the offspring. Prior to doing so, Morgan predicted what the sex and eye color ratios of the offspring would be if his hypothesis were true. By comparing the observed results with the predicted results, Morgan determined that his hypothesis was supported. In one mating, Morgan took a red-eyed male and mated it with a white-eyed female. He predicted and observed that half of the flies would be red-eyed females and the other half would be white-eyed males. That mating showed that the occurrence of the white-eyed trait is limited to the X chromosome, as only male offspring were capable of displaying the white-eyed trait with a single copy of the trait. Morgan showed that inheritance of a trait could differ between sexes.

In the following years, Morgan and a group of scientists at Columbia University established the chromosome theory of inheritance, which described the role that chromosomes play in heredity. In 1911, Morgan published more details of his experiments with the white-eyed mutant, an account in which Morgan explicitly stated that chromosomes carry heritable factors, or genes. In 1915, Morgan, and his colleagues, Alfred Henry Sturtevant, Calvin Bridges, and Herman Joseph Muller published the book Mechanism of Mendelian Heredity. That book contained contemporary scientific information about heredity and included the results of Morgan's white-eyed mutant experiments.

In 1933, Morgan won the Nobel Prize in Physiology or Medicine for his work establishing the chromosome's involvement in heredity.

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