Calvin Bridges’ Experiments on Nondisjunction as Evidence for the Chromosome Theory of Heredity (1913-1916) [1]

By: Gleason, Kevin Keywords: Thomas Hunt Morgan [2] Drosophila [3]

From 1913 to 1916, Calvin Bridges performed experiments that indicated genes [5] are found on chromosomes. His experiments were a part of his doctoral thesis advised by Thomas Hunt Morgan [6] in New York, New York. In his experiments, Bridges studied Drosophila [7], the common fruit fly, and by doing so showed that a process called nondisjunction caused chromosomes, under some circumstances, to fail to separate when forming sperm [8] and egg [9] cells. Nondisjunction, as described by Bridges, caused sperm [8] or egg [9] cells to contain abnormal amounts of chromosomes. In some cases, that caused the offspring produced by the sperm [8] or eggs to display traits that they would typically not have. His research on nondisjunction provided evidence that chromosomes carry genetic traits, including those that determine the sex of an organism.

At the beginning of the twentieth century, other researchers were starting to establish the role that chromosomes play in heredity. In 1910, Morgan provided some evidence that genes [8], or the material factors that were thought to control heredity, are located on the chromosome. While Morgan was mating Drosophila [10], which typically had red eyes, Morgan found that one of the offspring flies had white eyes. He proceeded to mate the white-eyed fly with other flies, and he observed a generation of offspring in which only some of the male offspring, but only the male offspring, had white eyes. Later, he observed a generation of flies that contained males and females with white eyes. He theorized that the gene controlling eye color was sex-linked, meaning it was found on the X chromosome. Males have one X chromosome and one Y chromosome, XY, while females have two X chromosomes, XX. In males, only one copy of a sex-linked gene is required in order for them to express a trait, such as white eyes. Two copies are required in females, which is why Morgan observed generations in which only males contained the trait.

Like his mentor Morgan, Bridges, a researcher in Morgan’s lab at Columbia University [11], began to study Drosophila [7] offspring that did not follow normal inheritance patterns. Typically, males inherit all of their sex-linked traits from their mothers, because their mothers give them their only X chromosome. Females inherit their sex-linked traits from both their mothers and fathers, who both must pass on an X chromosome. Bridges identified instances in which the opposite had occurred. He observed males that had inherited sex-linked traits from their fathers and females that had inherited sex linked traits from only their mothers. He referred to those flies as exceptional males and exceptional females.

Bridges theorized that the unusual inheritance pattern resulted from an error in meiosis [12], the process of cell division that results in the formation of sperm [8] and eggs. Meiosis reduces the number of chromosomes in a germ cell by half, resulting in eggs that have one X chromosome or sperm [8] with one X or one Y chromosome. He hypothesized that a process called nondisjunction was occurring during meiosis [12] of female cells. According to Bridges’s hypothesis, during nondisjunction in the females, their two X chromosomes do not separate to form normal eggs with a single X chromosome each. Instead, nondisjunction creates eggs with either two X chromosomes or with none. If those abnormal eggs are fertilized with normal sperm [8], which have either an X or Y chromosome, the female offspring would be XX-Y, and the male offspring would have a single X chromosome, XO. In Drosophila [7], unlike in humans [13], the Y chromosome does not play a role in determining sex. Instead, the number of X chromosomes determines sex in flies. Consequently, no flies are born with a single Y chromosome or three X chromosomes, as flies with those numbers of X chromosomes died as fertilized eggs or as embryos. To Bridges, the theory of nondisjunction explained his observation that in exceptional cases, males inherited all of their sex-linked traits from their fathers, as they would be XO, and females from their mothers, as they would be XX-Y.

In 1913, Bridges published an article describing his nondisjunction hypothesis. He described how he had observed the unusual inheritance pattern while breeding the same species of flies that Morgan was using. Bridges mated female white-eyed flies with male red-eyed flies. Because Bridges found that exceptional flies only occurred in one out of every 1600 flies, he developed a method to increase the frequency of exceptional flies, which made his research more efficient. He found that by taking exceptional females and mating them with normal males, the offspring would have a higher frequency of exceptional females and males. He then observed the offspring of that mating, and found that five percent of the daughters had white eyes like their mothers and five percent of sons had red eyes like their fathers. Bridges later determined that the presence of a Y chromosome in the XXY exceptional females caused higher rates of nondisjunction in their offspring. He proposed that his observations were evidence that nondisjunction was occurring in the female flies.

In 1916, Bridges published an article expanding on his earlier research. To provide more evidence in support of his
nondisjunction hypothesis, Bridges mated flies carrying many other genes known to be sex-linked. Those genes showed similar but unusual inheritance patterns. Bridges also used a microscope to examine the chromosomes of the offspring. Because X and Y chromosomes look different, Bridges could see whether or not the atypical offspring had the chromosomes that he had predicted they have. He observed that the atypical females had two X chromosomes and one Y chromosome, XXY, and the atypical males had one X chromosome, XO. Those results provided further evidence to Bridges that nondisjunction had occurred during meiosis of female cells, as he had hypothesized.

Bridges concluded that his results had implications beyond supporting his hypothesis. First, it provided further evidence that genes are located on chromosomes. While Morgan and others had previously proposed the same conclusion, Bridges stated that his experiments on nondisjunction provided irrefutable evidence that genes are on chromosomes. Secondly, he concluded that sex is determined in Drosophila by the X chromosome and not the Y chromosome. He found that the presence of the Y chromosome did not determine sex, rather the number of X chromosomes did. In humans, the Y chromosome determines sex.

Following the publication of his experiments, Bridges and the researchers in Morgan's lab continued studying heredity and the chromosome, as well as nondisjunction. In 1933, Morgan won the Nobel Prize in Physiology or Medicine for his research that established the role chromosomes play in heredity. Although Bridges was not a recipient of that award, Morgan shared a portion of the prize money with him.

In 2016, the journal Genetics published an article discussing the impact of Bridges' 1916 publication. In their review, the authors acknowledged that he helped establish the chromosome theory of heredity through his research on nondisjunction. They also asserted that his article was a cornerstone in the field of genetics, and had shaped genetic research throughout the twentieth century.

Sources


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