

## CHAPTER 2

### MORGAN: GENES ARE LOCATED ON CHROMOSOMES

*In 1910, Thomas H. Morgan explored the application of Mendel's theories to animals, using *Drosophila melanogaster*, the fruit fly. His work showed conclusively that specific genes were located on specific chromosomes.*

#### VARIATION IN INDEPENDENT ASSORTMENT

With the rediscovery of Mendel's theories in 1900, gene segregation patterns were rapidly demonstrated in a wide variety of organisms. In many cases, they conformed closely to Mendel's predictions; in others, aberrant ratios were obtained, which were later shown to result from gene interaction. Always, however, regular patterns of segregation were observed. It is no surprise that Mendel's theory became the focus of intense experimental interest.

The chromosomal theory of inheritance did not have such an easy birth. Although it was enunciated clearly by Walter S. Sutton in 1902, many investigators found it difficult to accept: if genes segregate independently of one another because they are on separate chromosomes, then why can one observe more independently assorting genes than there are chromosomes? Within-chromosome recombination was not yet suspected and would not be understood for many years.

#### ENTER DROSOPHILA MELANOGASTER

Thomas H. Morgan correctly perceived that the success of genetic investigators depended critically upon the choice of the organism to be investigated. Much of the work in the early years had centered upon agricultural animals and plants: we knew how to grow successive generations of them, and the information had direct practical bearing. Morgan abandoned agricultural utility in favor of experimental utility—plants just took too long between generations, and they took up too much space. Morgan wanted an organism with which one could carry out many crosses, with many progeny, easily and quickly. With this in mind, he began to investigate the genetics of *Drosophila*. No genetic varieties were available in *Drosophila*, so Morgan set out to find them. He obtained his first mutant in 1910, from normal red eyes to white. At last he could set out to examine Mendelian segregation.

#### MORGAN'S HISTORIC FRUIT FLY CROSSES

First, Morgan crossed the white-eyed male he had found to a normal female, and he looked to see which trait was dominant in the  $F_1$  generation: all the progeny had red eyes. Now, would the white-eye trait reappear, segregating in the  $F_2$  progeny as Mendel had predicted? In the  $F_2$ , there were 3470 red-eyed flies and 782 white-eyed flies, roughly a 3:1 ratio. Allowing for some deficiency in recessives, this was not unlike what Mendel's theory predicted. But in this first experiment, there was a result that was *not* predicted by Mendel's theory: *all the white-eyed flies were male!*

At this point, Morgan had never seen a white-eyed fly that was female. The simplest hypothesis was that such flies were inviable (this might also explain the deficiency of recessives in the 3:1 ratio above). Perhaps the white-eyed trait somehow killed female flies preferentially? Morgan preferred a straightforward test: if any of the  $F_2$  females carried the white-eye trait but did not show it, then it should be revealed by a test cross to the recessive parent. It was. Crossing red-eyed  $F_2$  females back to the original

white-eyed male, he obtained 129 red-eyed females, 132 red-eyed males, and 88 white-eyed females, 86 white-eyed males.

Again, this was a rather poor fit to the expected 1:1:1:1 ratio due to a deficiency in recessives. The important thing, however, was that there were fully 88 white-eyed female flies. Clearly, it was not impossible to be female and white-eyed. Why, then, were there no white-eyed females in the original cross?

## **X AND Y CHROMOSOMES**

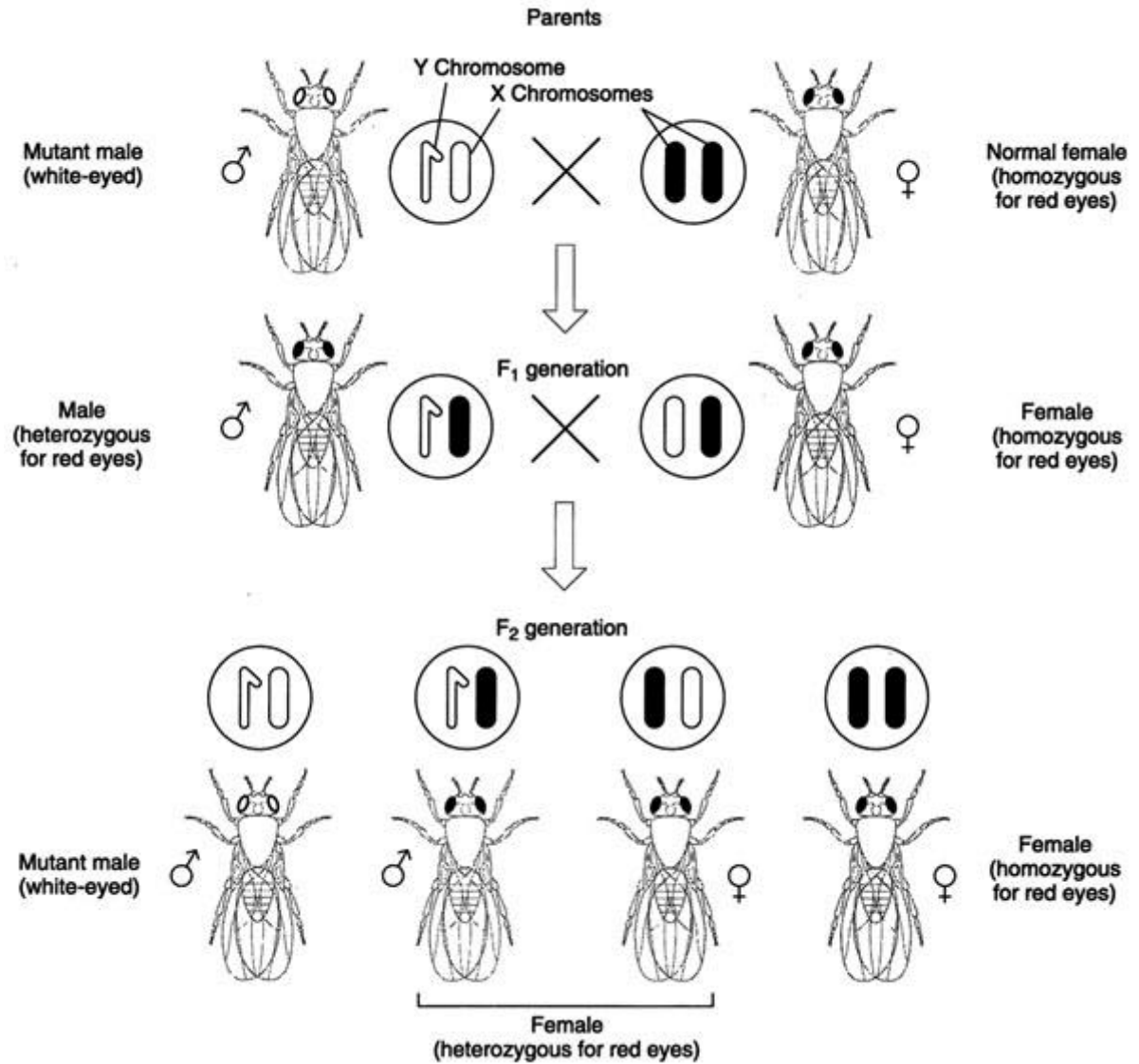
Not seeing how Sutton's chromosomal theory could explain this curious result, Morgan suggested that perhaps it reflected uneven gamete production. Recall that Mendel assumed equal proportions of gametes in his model of factor segregation. Alterations in these proportions could, with some tortuous further assumptions, perhaps explain the peculiar behavior of white-eye.

Facts leading to a far simpler, more beautiful, explanation were already in existence, however, in the work of the early chromosome cytologists. In 1891, H. Henking, studying meiosis in haploid male wasps, saw a deeply staining chromosomelike element that passed to one pole of the cell at anaphase, so that half the sperm received it and half did not. He labeled it "X," because he was not sure whether it was a chromosome or not. In 1905, Nettie Stevens and Edward Wilson again encountered these peculiar X chromosomes when studying grasshoppers, meal worms and *Drosophila*. Grasshopper males, like wasps, possessed an X chromosome with no pair, while meal worm male X chromosomes are paired to a very small partner chromosome, and *Drosophila* male X chromosomes are paired to a large but quite dissimilar partner chromosome. These unusual partners to the X chromosome were called, naturally, "Y" chromosomes. Stevens and Wilson went on to show that the female had two counterparts to the X and no Y. This led simply to a powerful, and essentially correct, theory of sex determination. What if the genes for sex reside on the X or Y chromosomes, along the lines of Sutton's 1902 theory? In this model, females are XX and males are XY, just as observed cytologically. Thus, sperm may contain either an X or a Y chromosome, while all the female gametes will contain a copy of the X chromosome. In forming a zygote, sperm that carry an X chromosome will produce an XX zygote (female), while sperm that carry a Y chromosome will produce an XY zygote (male). This simple model explained the 1:1 proportions of males to females usually observed, as well as the correspondence of sex with chromosome cytology.

## **SEX LINKAGE**

This theory provided a really simple explanation of Morgan's result, and he was quick to see it: what if the white-eye was like Wilson's sex trait and it resided on the X chromosome? Morgan had only to assume that the Y chromosome did *not* have this gene (it was later shown to carry almost no functional genes). Knowing from his previous crosses that white-eye is a recessive trait, the results he obtained could be seen to be a natural consequence of Mendelian segregation!

Thus, a typically Mendelian trait, white-eye, is associated with an unambiguously chromosomal trait, "sex." *This result provided the first firm experimental confirmation of the chromosomal theory of inheritance.* This association of a visible trait that exhibited Mendelian segregation with the sex chromosome (*sex linkage*) was the first case in which a specific Mendelian gene could be said to reside on a specific chromosome (figure 2.1). It firmly established the fusion of the Mendelian and chromosomal theories, marking the beginning of modern genetics.



**Figure 2.1**  
**Morgan's experiment demonstrating the chromosomal basis of sex linkage in *Drosophila*.** The white-eyed mutant male fly was crossed to a normal female. The F<sub>1</sub> generation flies all exhibited red eyes, as expected for flies heterozygous for a recessive white-eye allele. In the F<sub>2</sub> generation, all the white-eyed F<sub>2</sub>-generation flies were male.