The chromosomal basis

of inheritance

Thomas Hunt Morgan' s experiments. The fruit fly (Drosophila melanogaster) as a model system.

Key points:

Boveri and Sutton's chromosome theory of inheritance states that genes are found at specific locations on chromosomes, and that the behaviour of chromosomes during meiosis can explain Mendel's laws of inheritance.

Thomas Hunt Morgan, who studied fruit flies, provided the first strong confirmation of the chromosome theory .

Morgan discovered a mutation that affected fly eye colour. He observed that the mutation was inherited differently by male and female flies.

Based on the inheritance pattern, Morgan concluded that the eye colour gene must be located on the X chromosome.

Introduction

The chromosomal basis of inheritance

Where are genes found in a cell? Odds are, you've already heard the punch-line: genes lie on chromosomes. You may have even have heard the second punch line, the one that ushered in the modern genetic era: genes are stretches of DNA that specify proteins.

However, these were not always things that you could look up on Khan Academy! When Gregor Mendel began studying heredity in 1843, chromosomes had not yet been observed under a microscope. Only with better microscopes and techniques during the late 1800s could cell biologists begin to stain and observe subcellular structures, seeing what they did during cell divisions (mitosis and meiosis).

Eventually, some scientists began to study Mendel's long-ignored work and re-evaluate his model in terms of the behaviour of chromosomes. Around the turn of the 20th century, the biology community started to make the first tentative connections between chromosomes, meiosis, and the inheritance of genes.

The chromosome theory of inheritance

Walter Sutton and Theodor Boveri generally get credit for this insight. Sutton, an American, studied chromosomes and meiosis in grasshoppers. Boveri, a German, studied the same things in sea urchins. In 1902 and 1903, Sutton and Boveri published independent papers proposing what we now call the chromosome theory of inheritance. This theory states that individual genes are found at specific locations on particular chromosomes, and that the behaviour of chromosomes during meiosis can explain why genes are inherited according to Mendel's laws.

Modified from "Chromosomal theory of inheritance: Figure 1," by OpenStax College, Biology (CC BY 3.0) and from "Thomas Hunt Morgan," (public domain).

Observations that support the chromosome theory of inheritance include:

Chromosomes, like Mendel's genes, come in matched (homologous) pairs in an organism. For both genes and chromosomes, one member of the pair comes from the mother and one from the father.

The members of a homologous pair separate in meiosis, so each sperm or egg receives just one member. This process mirrors segregation of alleles into gametes in Mendel's law of segregation.

The members of different chromosome pairs are sorted into gametes independently of one another in meiosis, just like the alleles of different genes in Mendel's law of independent assortment.

The chromosome theory of inheritance was proposed before there was any direct evidence that traits were carried on chromosomes, and it was controversial at first. In the end, it was confirmed through the work of geneticist Thomas Hunt Morgan and his students, who studied the genetics of fruit flies.

T. H. Morgan: Fun with fruit flies

Morgan chose the fruit fly, Drosophila melanogaster, for his genetic studies. What fruit flies may lack in charisma (depending on your taste in insects), they make up for in practicality: they're cheap, easy, and fast to grow. You can raise hundreds of them in a little bottle with sugar sludge at the bottom, and many geneticists still do this today!

Image credit: "Drosophila melanogaster - top," by André Karwath (CC BY-SA 2.5).

Morgan's crucial, chromosome theory-verifying experiments began when he found a mutation in a gene affecting fly eye colour . This mutation made a fly's eyes white, rather than their normal red.

Unexpectedly, Morgan found that the eye colour gene was inherited in different patterns by male and female flies. Male flies have an X and a Y chromosome (XY), while female flies have two X chromosomes (XX). It didn't take Morgan long to realize that the eye colour gene was being inherited in the same pattern as the X chromosome.

This may have come as a surprise to Morgan, who had been a critic of the chromosome theory!

A "sex limited" inheritance pattern

What made Morgan think that the eye colour gene was on the X chromosome? Let's look at some of his data.

The first white-eyed fly he found was male, and when this fly was cross with normal, red-eyed female flies, the F_1 offspring were all red-eyed —telling Morgan that the white allele was recessive. So far, so good, no surprises there.

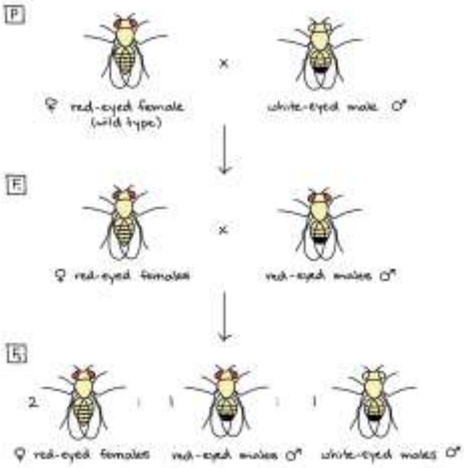

Image modified from "Drosophila melanogaster," by Madboy74 (CC0/public domain).

But when the F_1 flies were crossed to each other, something strange happened: all of the female F_2 flies were red-eyed, while about half of the male F_2 flies were white-eyed. Clearly, the male and female flies were inheriting the trait in different patterns. In fact, they were inheriting it in the same pattern as a particular chromosome, the X.

X marks the spot

Let's see how inheritance of the X chromosome can explain what Morgan saw. Earlier, we said that female flies have an XX genotype and male flies have an XY genotype. If we stick the eye colour gene on the X chromosome (writing it as a little subscript, w + for red and w for white), we can use a punnet square to show Morgan' s first cross:

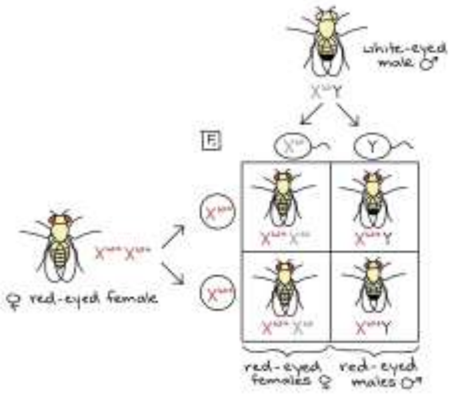

Image modified from "Drosophila melanogaster," by Madboy74 (CC0/public domain).

The predictions match the F_1 phenotypes, but this set of phenotypes could also be explained by a gene that is not on the X chromosome, since all the flies were red-eyed (regardless of sex). So the real test comes when the F_1 flies are mated to make the F_2 generation:

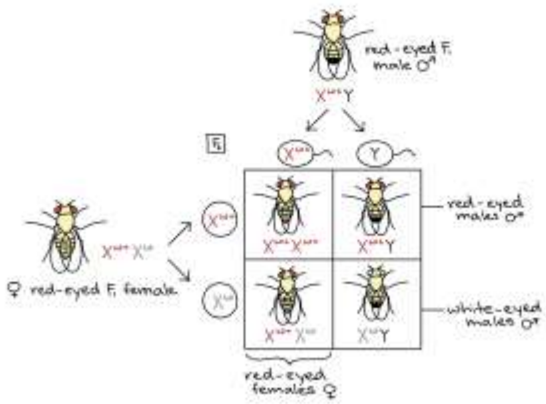

Image modified from "Drosophila melanogaster," by Madboy74 (CC0/public domain).

Here is where the X makes the difference. Our punnet square with the eye colour gene on the X Chromosomes correctly predicts that all of the female flies will have red eyes, while half of the male flies will have white eyes. The male flies get their only X chromosome from their mother, who is heterozygous (X^w+ X^w), leading to the fifty-fifty split of phenotypes.

Confirming the model

Morgan did lots of other experiments to confirm an X chromosome location for the eye colour gene. He was careful to rule out alternative possibilities (for instance, that it was simply impossible to get a white-eyed female fruit fly).

Pulling together all of his observations, Morgan concluded (correctly) that the gene must lie on, or be very tightly associated with, the X chromosome. A strong confirmation of this conclusion came later, from Morgan's student Calvin Bridges. Bridges showed that rare male or female flies with unexpected eye colours were produced through nondisjunction (failure to separate) of sex chromosomes during meiosis— basically, the exception that proved the rule.

Morgan also found mutations in other genes that were not inherited in a sex-specific pattern. We now know that genes are borne on both sex and non-sex chromosomes, in species from fruit flies to humans.