Sage - Spring 2023

Welcome to

Session 3 of

"Genes for Very Smart but Ignorant People"

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Course Outline

1. *Gregor Mendel: How a monk came to discover the rules of inheritance*

2. *Genes and chromosomes - the fly in the ointment*

3. *Microbiologists discover that most genes are made of DNA*

4. *How two amateurs beat the A team to solve the structure of DNA*

5. *The genetic code. Again an obscure team of players beats the pros.*

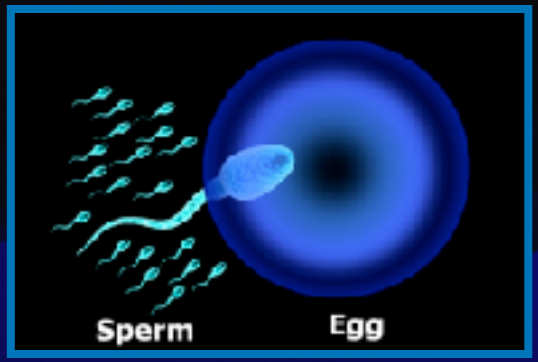
6. *How genes are controlled. The French connection.*

Mendel's discoveries
Genes come in pairs

(except sperm and eggs)

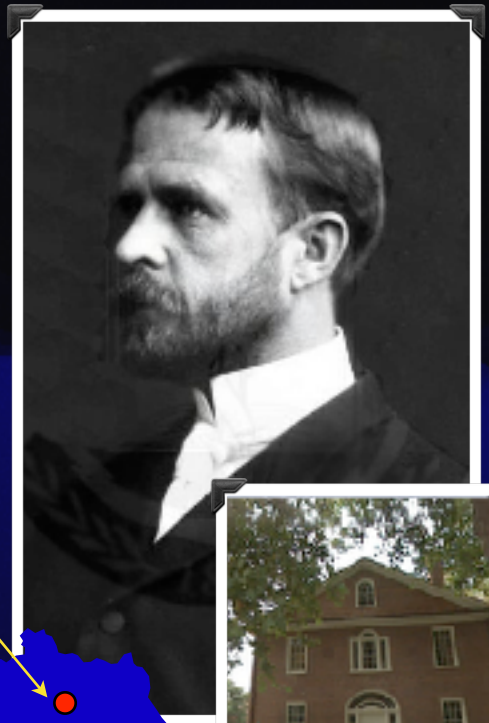
A pair of genes

2. One of each pair is *randomly* apportioned out to the next generation in sperm and eggs.



Then I talked about

Thomas Hunt Morgan



In the first years of the twentieth century, chromosomes were thought to carry genes, but the evidence was weak.

Morgan himself was a critic of the idea.

But starting in 1910, his opinion was to change dramatically when he began to work with Drosophila melanogaster, the fruit fly.

Drosophila melanogaster

In January 1910, a peculiar looking fly showed up in one of the bottles in his laboratory.

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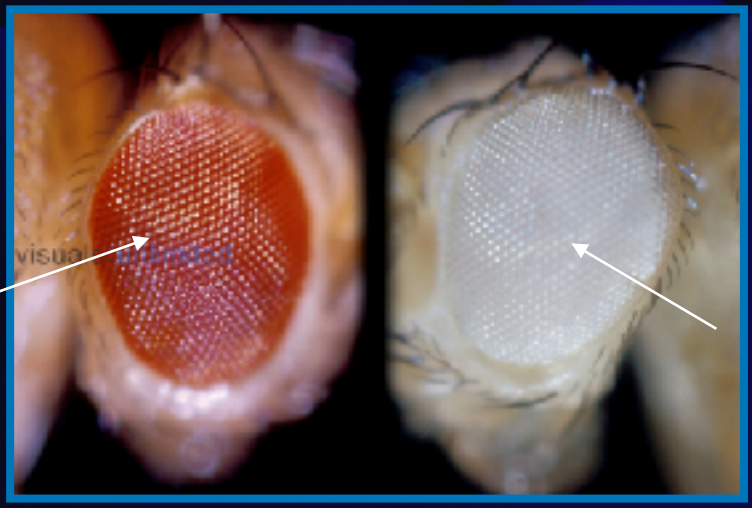
It was a male with white eyes.

Ordinarily, fruit flies have brilliant red eyes. The male that he found had no pigment in its eyes.



Normal

White Eyes

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About that time, his wife was in the hospital, pregnant with their third child, Lilian.

When he visited her, the first thing she asked was:
"Well, how is the white-eyed fly?"

"It's doing well," he answered.

And, only after a pause, he continued,
"Oh, yes, and how is the baby?"

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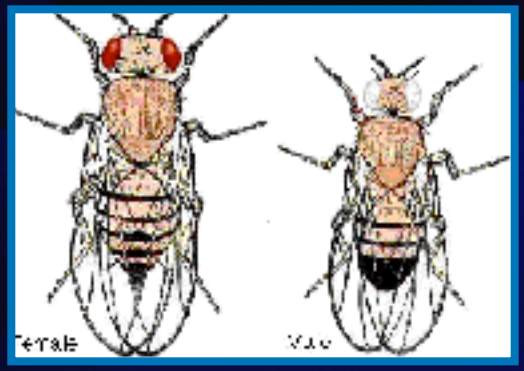
What did he do with this white eyed male?

He crossed it with some virgin females.



♀ ♂

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Warning.

We're into some heavy lifting, some hard-core genetics.

Hang on. Stay with me!

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red x *white*

♀ ♂

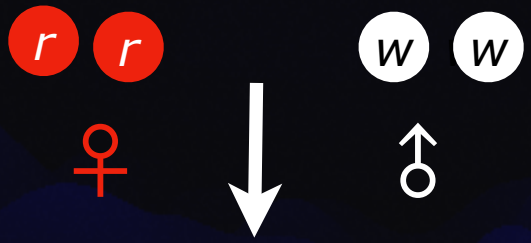
?

(Hint: red is dominant)

red ♀ x white ♂

(both males and females)

The white trait was behaving exactly like the round trait in peas.



(hybrid)

Here's the same cross, but I've shown it reflecting the fact that there are two red genes and two white ones.

Wait a second!

Now I'm going to confuse you.

I've told you that Mendel found that genes come in pairs.

But why are the white and red genes a pair?

For that matter, why are the round and wrinkled genes considered a pair?

It has to do with the fact that, in a sense, there really isn't such a thing as a white gene!

(or the wrinkled gene that I talked about last week)

Here's the key to understanding:

Genes are entities that specify the structure of proteins, not traits.

We'll talk about proteins in much more depth in a future seminar.

For now, think of proteins as miniature machines that do all the work in organisms.

The reason that the genes we'e been calling white and red are a pair is because they both specify the same protein

(a machine that is involved in transferring red pigment into the eye, the ATP-binding cassette transporter).

When that protein doesn't do its job, the fly's eyes become white.

So...

Sometimes, one or both copies in a pair are defective. This may lead to a change in the organism, a visible trait, because a defective gene results in a defective protein that in turn produces a visible change an organism - a trait.

Confusingly, geneticists often name the gene after the defect it causes even though if it were working properly, the defect would not occur!

It would be clearer if genes were named for the protein they specify.

The white gene should be called ATP-binding cassette transporter gene.

For convenience, I'll continue to call it 'white'.

Confused?

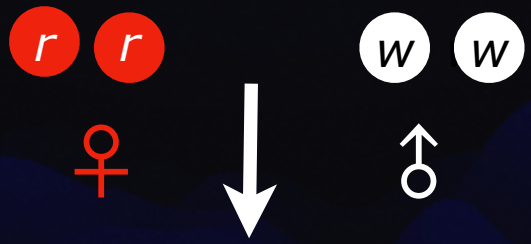
You're not alone.

Generations of students have been in the same boat.

OK?

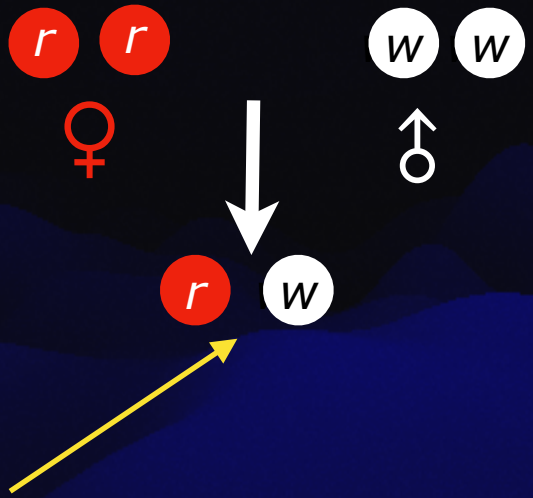
Don’t be too concerned if you don’t get it at first, matters are only going to get worse.

Back to Morgan and his cross with the white eyed fly.



This is the hybrid

The r's represent the normal (non-defective) version of the white gene. The w's represent a damaged version of the same gene.

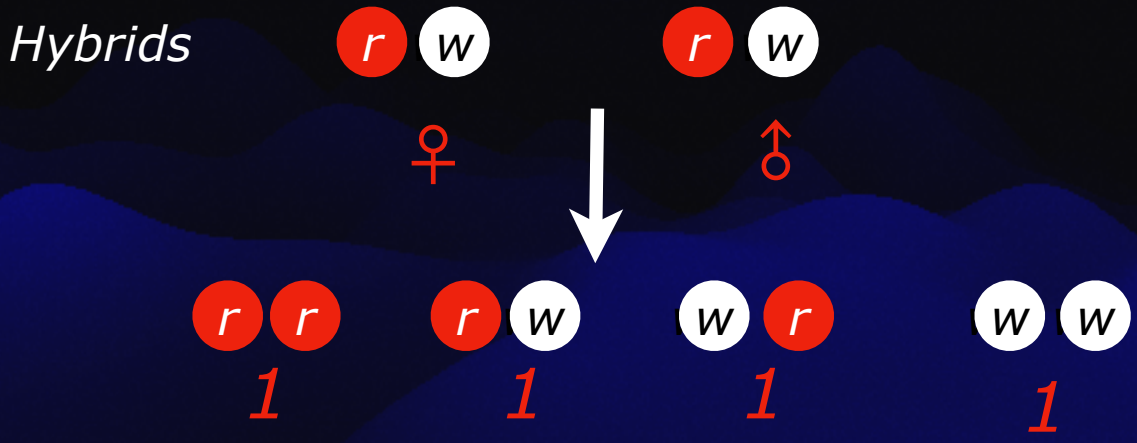


The hybrid has one defective and one normal version of the white gene.

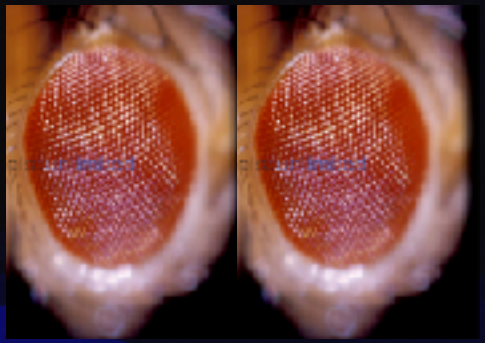
The next step, of course, that Morgan took was to cross the hybrids to one another.

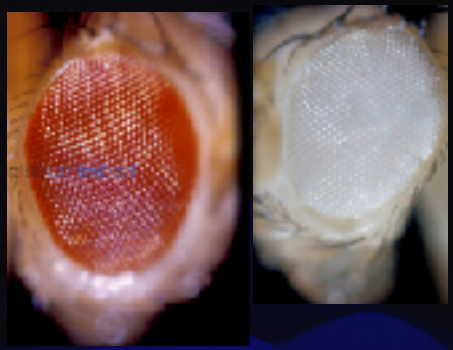
Again, the results came out just as Mendel would have predicted.

Red:White (3:1)



But Morgan noticed something unexpected.





♀ 2

♂ 1

♂ 1

All the female flies had red eyes. Half the male flies had white eyes. From that you get a 3:1 ratio, but a peculiar one.

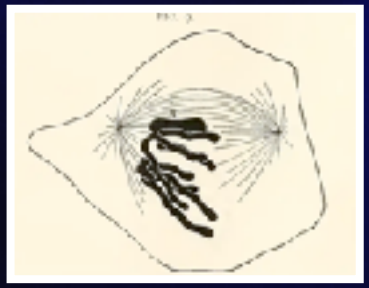
What's going on?

A clue came from an unlikely source.

lubber grasshopper

The lubber grasshopper has very large cells in its testes. Under a microscope, you can see

chromosomes



when cells are dividing

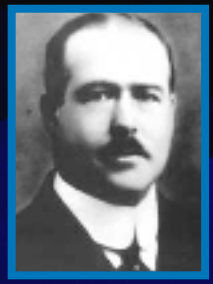
Walter Sutton

In 1902, Walter Sutton, a young graduate student in Edmund Wilson's laboratory at Columbia had shown that grasshopper ***chromosomes come in pairs, and that one of each pair is randomly passed to each sperm cell.***

Walter Sutton

Amazing. Where have you heard that before?

Both genes and chromosomes occur in pairs, and one of each pair is randomly passed on to the next generation in sex cells.

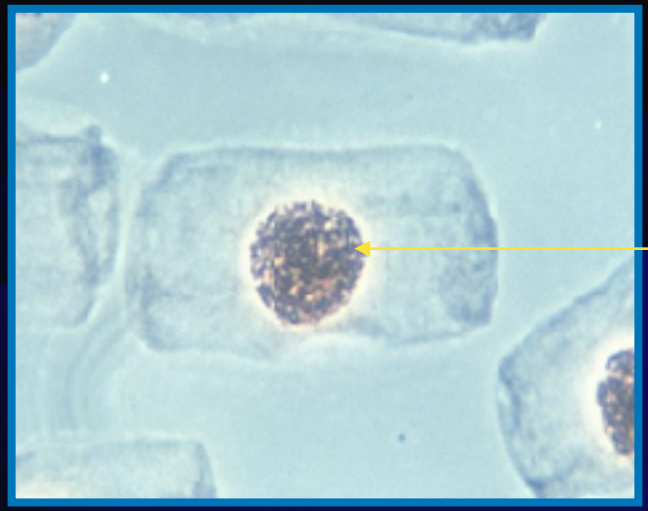


Walter Sutton

Chromosomes behave exactly like Mendel's determinants!

Here's a picture of some chromosomes

Human chromosomes (46)



Chromosomes in a plant cell

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Sutton published his observations in two short papers.

He later quit graduate school to became a physician.

He died of a burst appendix at the age of 39.

Morgan knew that chromosomes couldn't be equivalent to genes - there were too many genes and too few chromosomes.

But he began to suspect that chromosomes might be carriers of multiple genes.

This was Morgan's first clue - that chromosomes might carry genes, including the gene for white eyes.


Nettie Stevens

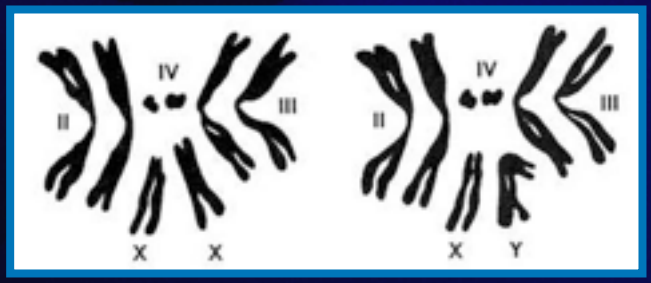
Another clue also came from a colleague, Morgan's former student, Nettie Stevens who was doing research at Bryn Mawr.

She had shown that one pair of chromosomes was different from the others in many organisms.

It existed in two forms in male cells, but not in females.

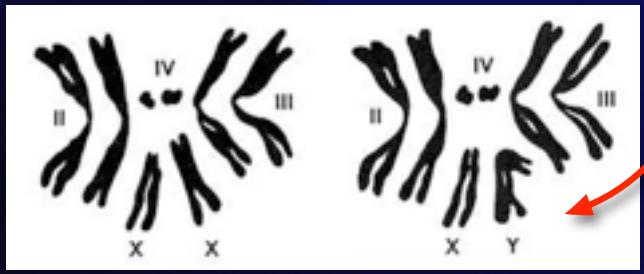
Males produced sperm in which this special chromosome was present either in one form or the other.

For example, here's the situation in fruit fly cells



♀ ♂

There are four pairs of chromosomes in females.In males there are three pairs and + one peculiar "pair".



Today, we call the unpaired chromosome in males the "Y" chromosome. The other chromosome, of which there are two in females and one in males, is called the "X" chromosome.

Stevens discovered that the X and Y chromosomes play a role in determining the sex of an individual.

They're called 'sex chromosomes' for that reason.

If flies have two X's, they become females.

If they have only one X, or one X and a Y, they become males.

In other words, in flies the number of X chromosomes determine sex.

Sex differentiation in humans is a little different.

In humans the Y chromosome carries a gene, SRY, that determines the sex of offspring.

Therefore individuals with one X appear female.

Morgan therefore had four clues:

1. Chromosomes occur in pairs and probably are the carriers of multiple genes

2. One chromosome, the X, is present in one copy in males and two copies in females

3. This peculiar chromosome and its partner (Y) have something to do with determining sex

4. If the X is present in one copy, the organism becomes a male.

One other piece of information…

The Y chromosome in humans carries few genes (less than 60).

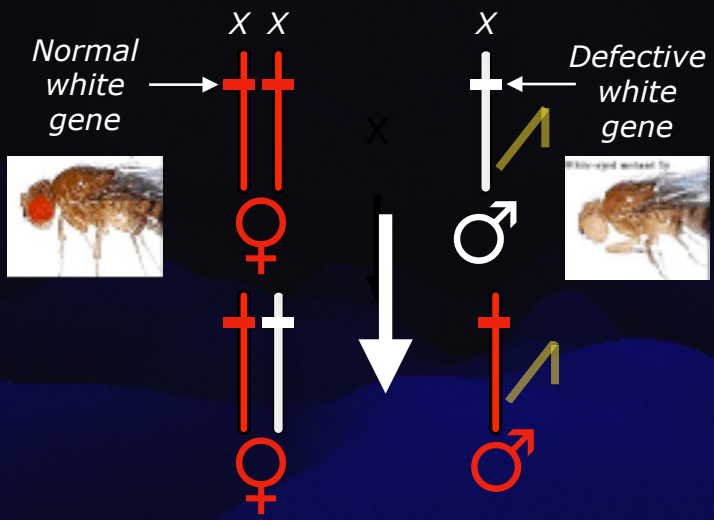
The X which is three times larger, and bears 900+ genes.

Flies are similar.

And, in particular, there's no red gene on the Y chromosome in flies.

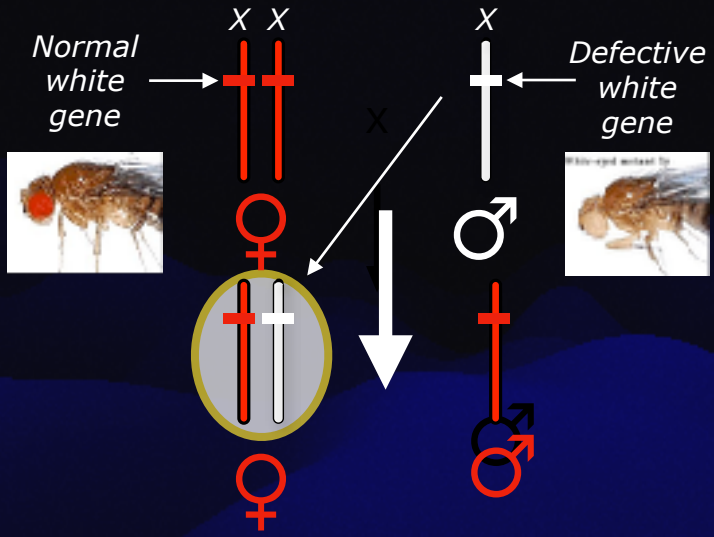
Morgan asked: What if the white-eyed male carried a defective gene on its single X chromosome?

If so, the first cross would look like this…

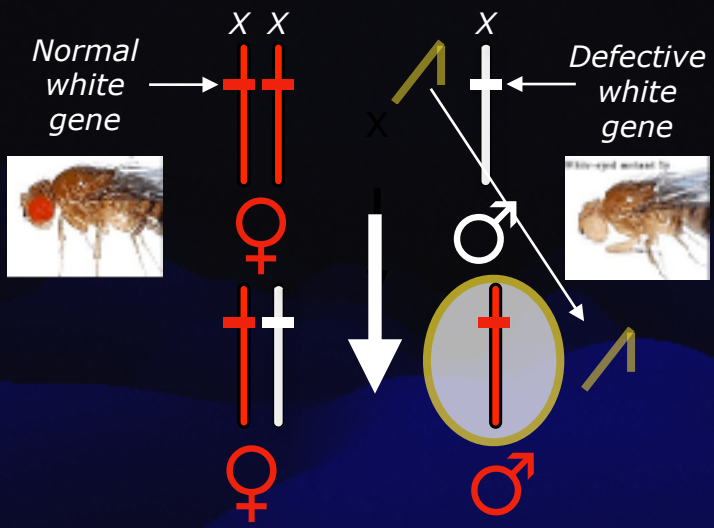


Therefore the first cross could be diagrammed like this.

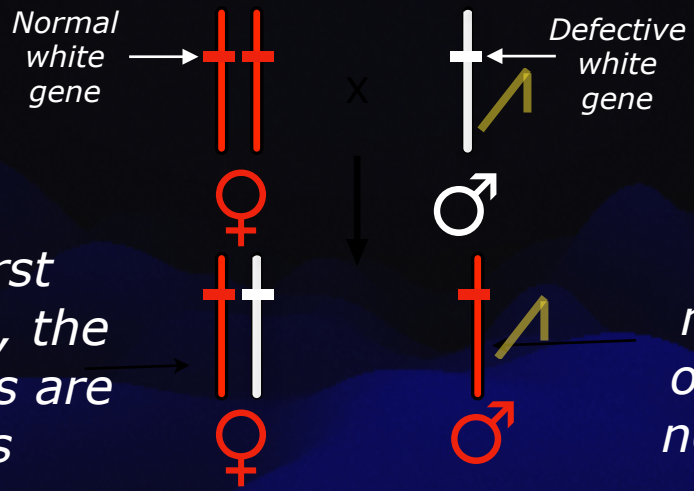
Notice that the rules change because of the single X chromosome of the male



The father has two choices. He can pass on an X chromosome to an offspring. If so, she becomes a daughter.



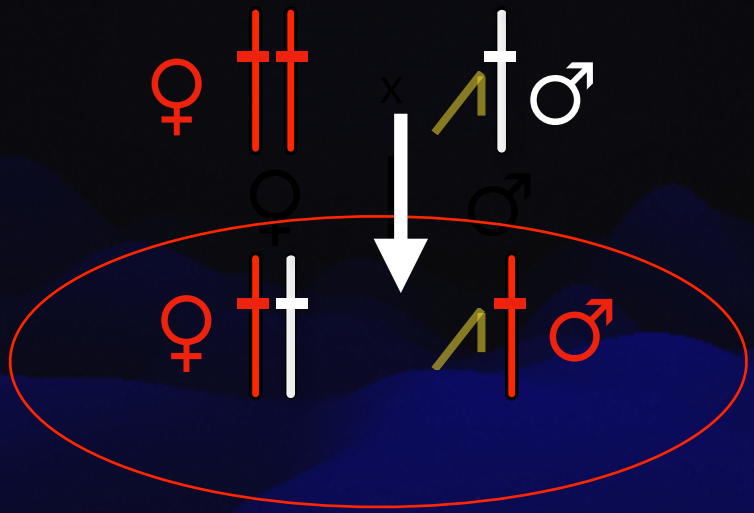
If he doesn't pass on an X, he begets a son.



In the first generation, the red females are hybrids

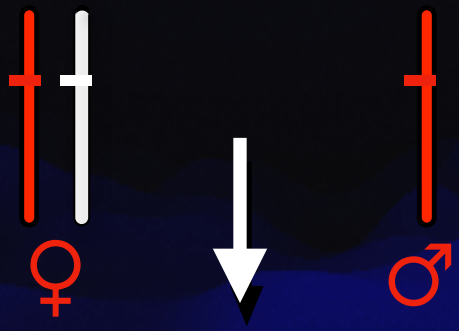
The red males carry only a single normal gene.

Both sexes have the same eye color, but are different genetically.



Now let's cross these flies to one another.

What do we get?



Can you figure it out?

How many kinds of flies will result, and what will their eyes look like?

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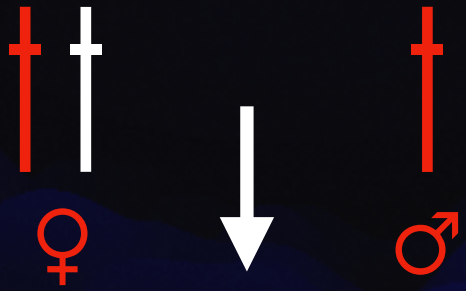
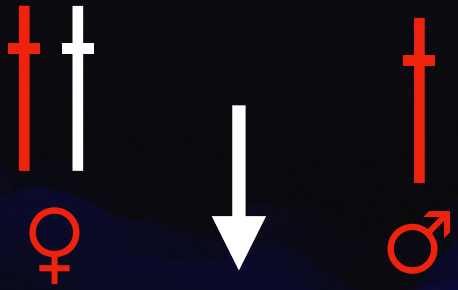


Congratulations!
You've got a daughter with beautiful red eyes

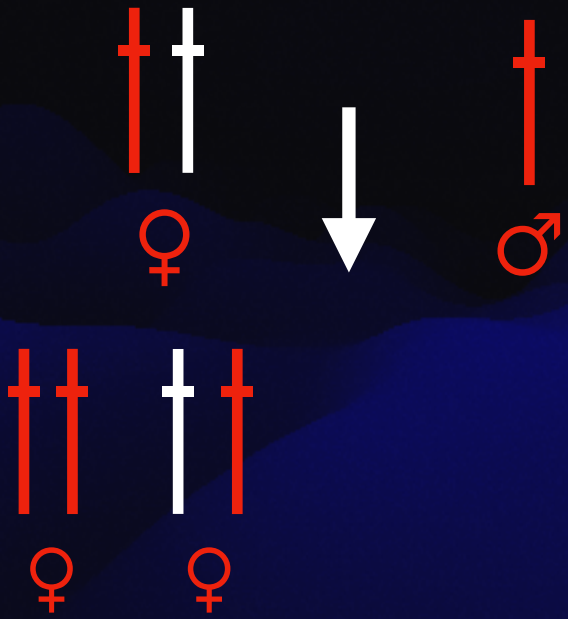
♀

The mother and father can each contribute a normal white gene.

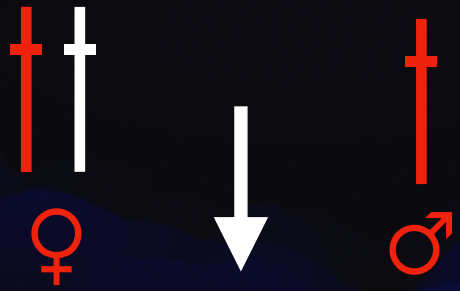


Congratulations!
Another
red-eyed girl

Or the mother can contribute a mutant white gene, while the father adds a normal one.



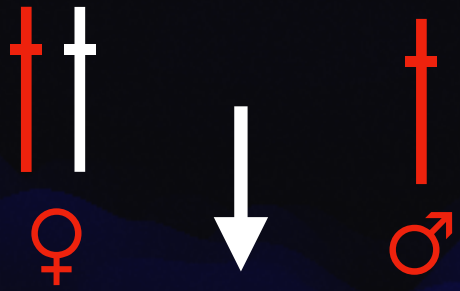
In both cases you get red eyed daughters



Congratulations! You've got a red eyed son. The father doesn't pass on X's to his sons.

♂

Half the sons will have red eyes



Congratulations!
You've got a white eyed son.
The father doesn't pass on X's to his sons.

♂

Half the sons will have white eyes

Because the genes behaved exactly as the chromosomes, Morgan had demonstrated that genes are carried by chromosomes.

They are located on chromosomes.

More evidence:

Other predictions based on the theory that genes are carried on chromosomes

One would expect that other genes must be carried on the X chromosome and that they should behave genetically exactly like the white gene.

One would expect that there would be genes on the other chromosomes. They should behave like Mendelian determinants.

One would expect that there should be more genes on the larger chromosomes than the smaller ones.

One would expect that genes on the same chromosome would move together, after all they are physically linked.

This is "an exception that proves the rule".

That is, it's an apparent exception that can be explained by the same rule and confirms that rule.

It turns out that when chromosomes pair in eggs and sperm, they break up and exchange pieces.

We'll come back to this important point next week.

Grand Summary

Summary

Genes specify the structure of proteins.

They are carried on chromosomes which occur in pairs.

Grand Summary

Summary

At fertilization one of each pair is randomly apportioned out to sperm and eggs.

One pair of chromosomes, the X and Y, are determinants of sex.