Video Tutorial 7.1: X-linked genes: patterns of inheritance

In order to understand X-linkage and to become comfortable with the patterns observed in crosses and pedigrees involving this type of inheritance, it is helpful to work through problems involving X-linked genes.

Both humans and fruit flies have the sex chromosomes X and Y. In both species, females have two X chromosomes, and males have one X and one Y chromosome. As a result, genes that are on the X chromosome must be expressed in males and thus will show different patterns of inheritance than autosomal genes.

Let's consider the gene for miniature wings in the fruit fly, *Drosophila melanogaster*. In wild-type flies, the wings of the adult extend beyond the end of the abdomen, but in flies with a mutation in the gene controlling wing length, the wings are only as long as the body of the fly, a phenotype called miniature. Let's look at crosses between flies with wild-type wings and those with miniature wings and observe the resulting offspring.

X-linkage can often be revealed by observing what are known as reciprocal crosses. In one cross, the male carries the mutant trait, while in the other (cross) the female has the trait. By comparing the results of these two crosses, we can often tell if the trait is X-linked.

Let's look the offspring from the two reciprocal crosses.

What do we see when we mate a male fly with miniature wings to a wild-type female fly? This cross yields flies with only wild-type long wings. We can conclude that miniature is a recessive trait, since none of the F1 flies were miniature, but we cannot tell if the trait is X-linked or not.

Now let's look at the reciprocal cross. When we mate a miniature-winged female with a wild-type male, we see that all the female offspring have wild-type wings, while all the males have miniature wings. Therefore, the sex of the parent carrying the mutant trait affects the outcome of the cross. From a cross of a miniature female with a wild-type male, we can conclude that the mutant miniature allele is recessive and that it is located on the X chromosome. We see that the trait is passed down from the mother to her son.

Let's write out the genotypes for the flies in these crosses. We will designate the recessive gene for miniature with a lower case *m*, and the wild-type allele as *m+*. Since the gene is on the X chromosome, let's place the allele on the chromosome when we write out the genotype. Our original female parent in Cross 1 therefore had the genotype X^{m+} / X^{m+} while the male parent was X^{m} and Y.

Let's draw Punnett squares for these crosses to show the genotypes of the flies.

All the F1 flies in this cross inherited one X chromosome from the mother and therefore received the wild-type allele, *m+*. All the offspring appear wild-type in wing length, since *m+* is the dominant allele.

Now let's look at the reciprocal Cross 2.

Our female parent in this case had two X chromosomes with the miniature allele, *m*, and the male parent was X^{m+} and Y.

Here is the Punnett square for this cross:

Again, all the F1 flies in this cross received an X chromosome from the mother, which in this case carried the *m* allele for miniature wings. All the female offspring also received a wild-type allele from their fathers. Since wild type is dominant over miniature, the females display wild-type long wings. Since the males have only one X chromosome, they must express the *m* allele, so have miniature wings. This pattern of inheritance, in which the sons inherit the trait from their mothers, is an indication of X-linked genes.

Pedigrees can also reveal X-linkage. Let's look at the family tree of Queen Victoria, who was the Queen of England from 1837-1901. Many of her descendants had hemophilia, a disease in which the blood does not clot effectively. The individuals affected by hemophilia are indicated by the filled shapes. You will quickly notice that the disease is observed only in Queen Victoria's male descendants, shown as squares. This indicates that hemophilia is an X-linked condition.

From this pedigree, you can also deduce which females were carriers; they are the women who gave birth to affected sons. We can color in the circles of the carriers to indicate that these women are heterozygous for the X-linked gene. Their sons had a 50% chance of inheriting the mutant allele on the X chromosome , which would cause hemophilia.

Is it possible for a woman to have hemophilia? Which parents would produce a daughter with the disease? You have probably answered that this could happen if a woman who was a carrier married a man with hemophilia. Their daughter would receive the mutant allele on the X chromosome from her father, and there would be a 50% chance that the mother would contribute an X chromosome with the mutant allele as well, leading to the disease.

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