X –inactivation

How XX human females (and other female mammals) shut down one of their X chromosomes in each cell. Disorders of sex chromosome number: Klinefelter, triple X, and Turner syndromes.

Introduction

Having extra or missing chromosomes is not usually a good thing. In fact, for most chromosomes, having an extra or missing copy is lethal to humans (causing an embryo to die early in development).

Yet, human females have two X chromosomes (XX), while human males have just one (XY). Why doesn't it cause problems for men to have just one copy of the X chromosome, while women have two?

X –inactivation

As it turns out, the level of gene activity produced by a single X chromosome is the normal "dosage" for a human. Men have this dosage because, well, they only have one X chromosome! Women have the same dosage for a different reason: they shut down one of their two X chromosomes in a process called X -inactivation.

In X-inactivation, an X chromosome is compacted (or, as my intro bio professor liked to say, "crumpled up into a ball"), to make a small, dense structure called a Barr body. Most of the genes on the Barr body are inactive, meaning that they are not transcribed. The process of X -inactivation was discovered by the British geneticist Mary F. L yon and is sometimes called lyonization in her honour.

A woman has two X chromosomes, one from each parent. Which one will she inactivate? X-inactivation is a random process that happens separately in individual cells during embryonic development. One cell might shut down the paternal X, while its next door neighbour might shut down the maternal X instead. All the cells descended from each of these original cells will maintain the same pattern of X -inactivation.

Interesting note: if you were a kangaroo, what I just said would not be true! In kangaroos and other marsupials, it is always the paternal X chromosome that undergoes X -inactivation .

X -inactivation example: Calico cat

A classic example of X-inactivation is seen in cats. If a female cat is heterozygous for black and tan alleles of a coat colour gene found on the X, she will inactivate her two X's (and thus, the two alleles of the coat colour gene) at random in different cells during development.

The result of is a tortoiseshell coat pattern, made up of alternating patches of black and tan fur. The black patches come from groups of cells in which the X with the black allele is active, while the tan patches come from cells in which the X with the tan allele is active.

Although it's rarely as easy to see as in the case of the tortoiseshell cat, human females are also "mosaic" for any genes that are present in different alleles on their two X chromosomes.

Sex chromosome aneuploidies

When an organism has an extra or missing copy of a chromosome, it is said to be aneuploidy. Aneuploidies involving autosomes (non-sex chromosomes), especially large ones, are usually so harmful to development that an aneuploidy embryo can't survive to birth.

Aneuploidies of X chromosomes, however, tend to be much less harmful, despite the fact that the X is a large chromosome. This is mostly thanks to X inactivation. Although the purpose of the X inactivation system is to shut down the second X of an XX female, it can also do a pretty good job of shutting down more X chromosomes if they are present.

Examples of X chromosome aneuploidies include:

Triple X syndrome, in which a woman has an XXX genotype, which occurs in about 1out of every 1,000 female new born. Women with an XXX genotype have female sex characteristics and are fertile (able to have children). In some cases, triple X syndrome may be associated with learning difficulties, late development of motor skills in infants, and problems with muscle tone .

Klinefelter syndrome, in which males have an extra X chromosome, leading to a genotype of XXY. (In rarer cases, Klinefelter syndrome can involve several extra X's, leading to an XXXY or XXXXY genotype.) Affected men may be infertile or develop less dense body and facial hair than other men. Klinefelter syndrome is thought to affect 1out of every 500 to 1,000 male new born .

Like females, XXY males with Klinefelter syndrome will convert one X to a Barr body in each cell. Triple X females (as well as Klinefelter males with more than two X chromosomes) neutralize their extra X's by forming additional Barr bodies. For example, there would be two Barr bodies in a cell from an XXX female or XXXY male.

In Turner syndrome, a woman lacks part or all of one of her X chromosomes (leaving her with just one functional X). People with this disorder develop as females, but often have short stature and may exhibit symptoms like infertility and learning difficulties.

Turner syndrome is thought to occur in about 1out of every 2,500 female births. It has relatively mild effects because humans normally have only one X active in the cells of their body anyway.