Dosage Compensation and X-inactivation

Although females have twice as many X-linked genes, the amount of protein produced by these genes is the same in females as it is in males**.**

Reduced protein production (called dosage compensation) occurs as a result of **inactivating** one X chromosome by coiling and condensing it. When condensed, it cannot be transcribed, that is, it cannot be used to produce mRNA..

Condensed X chromosomes, called ***Barr bodies***, are visible using ordinary light microscope techniques.

The table below shows the number of Barr bodies in normal cells and in the cells of people with an abnormal number of X chromosomes.

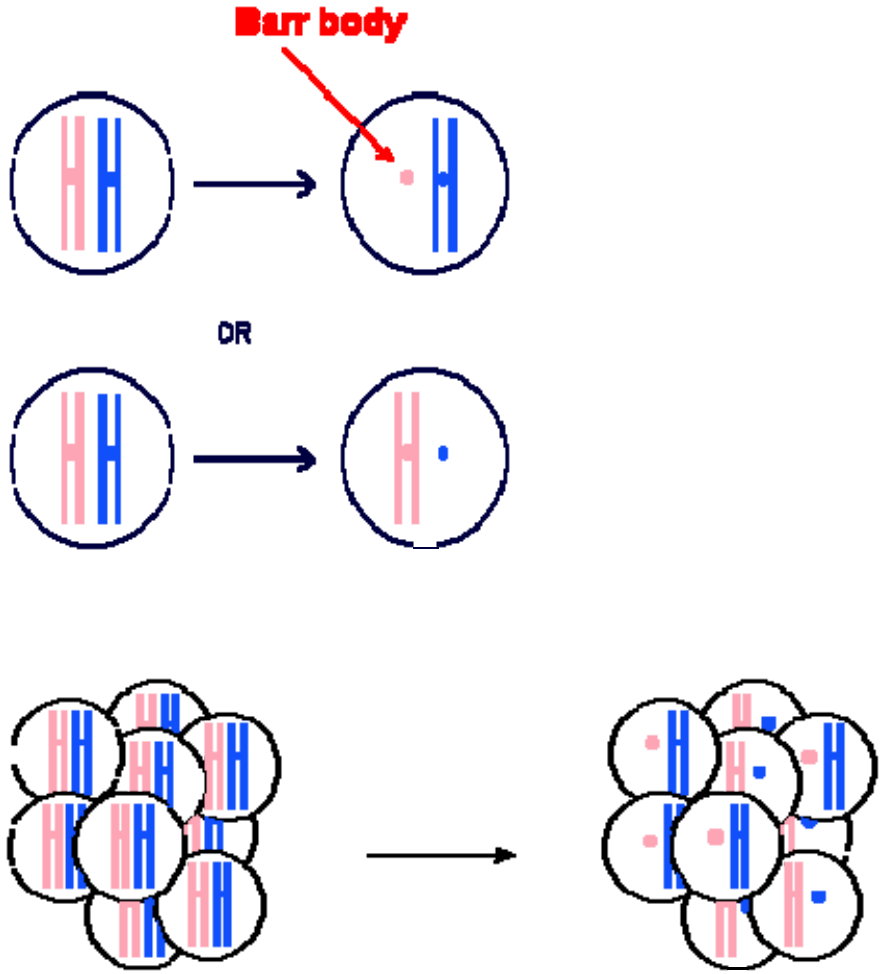
Genetic Condition	**# Barr Bodies per Cell**
normal male	0
normal female	1
XXX female	2
XXXX female	3
XXY (Klinefelter male)	1

In summary, one X chromosome remains active, the others are inactivated by forming Barr bodies.

Inactivation

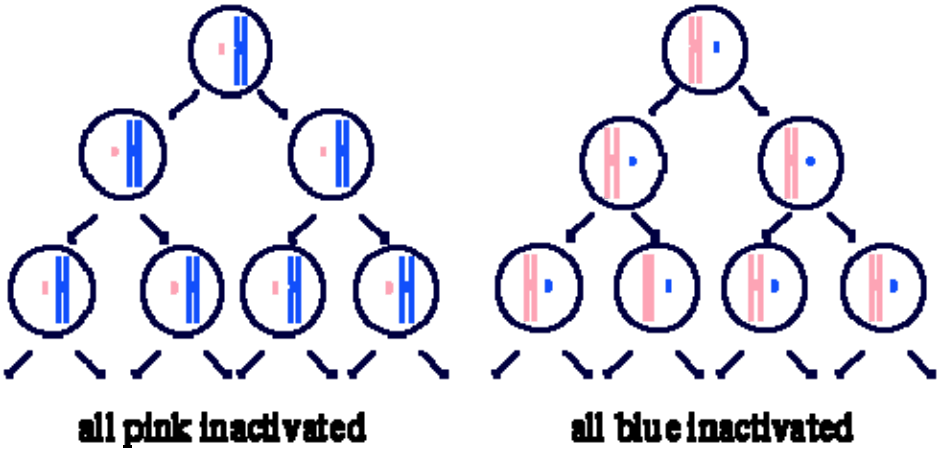
Inactivation occurs early in embryonic development (12-16 days).

In females, each cell normally contains two X chromosomes. The X chromosome that is inactivated is determined randomly.



Once inactivation occurs, all daughter cells of a particular cell have the ***same X chromosome*** inactivated.

All of the "pink" chromosomes in the drawing below (left side of diagram) have been inactivated. All future cells produced by this cell will have the pink chromosome inactivated. In the diagram on the right, all of the blue chromosomes have been inactivated. All future generations of this cell will have the blue chromosome inactivated.



Females are therefore ***mosaics*** with respect to the X chromosome. Patches of body cells will have the maternally inherited X chromosome inactivated and other patches will have the paternally inherited one inactivated.

Example of Mosaicism: Calico Cats

A calico cat has patches of orange and patches of black

X = orange
X^1 = black

MALES:

XY = orange

X^1Y = black

FEMALES:

XX = orange

X^1 X^1 = black

X X^1 = orange or black patches

All cells descended from an X^1 cell (X is inactive) are orange-yellow.

All cells descended from an X cell (X^1 is inactive) are black.

Human Example - Anhydrotic Dysplasia

Anhydrotic dysplasia is a disease that results in the absence of sweat glands.

It is inherited as an X-linked recessive disease.

Let X = normal sweat glands and X' = absence of sweat glands. Normal males are XY. Affected males are X'Y and do not have sweat glands.

Normal females are XX, heterozygous females are XX' and have patches of skin with sweat glands and patches of skin without sweat glands. Females that are X'X' do not have sweat glands.

Other Information

Should heterozygous females for colorblindness be able to see color?

Suppose: X = color vision
x = colorblind

The Retina of a heterozygous (Xx) female will have some cells with the "X" inactivated and other cells with the "x" inactivated.

A heterozygous carrier of red-green colorblindness has some colorblind cells in her retina. The non-colorblind cells enable her to see color.

Turner's syndrome is an abnormality in females where there is only one X chromosome; the other is missing. Why aren't Turners syndrome females normal? Evidence indicates that some genes in the Barr body remain active. Their DNA is uncoiled and extends from the Barr body. If the Barr bodies of a normal female were missing, she would exhibit Turners Syndrome.

A person with Klinefelter's syndrome has a Y chromosome and more than one X chromosome.

If X inactivation were complete, this shouldn't be a problem—these folks should be normal males. And yet, as the fact that they have a syndrome implies, they have health problems. Why is this?

Firstly, only one of their X chromosomes is active. Having the Y chromosome doesn't seem to affect X inactivation itself.

The problem comes from the fact that X inactivation is not complete. X inactivation starts at the middle of the chromosome and spreads towards the ends. Apparently it peters out

before it makes it all the way.

The genes at the ends will still lead on to Klinefelter's syndrome. In fact, many of the symptoms of Klinefelter's are really those of a feminized male.

But the incomplete X inactivation is OK for women—these genes are supposed to be double expressed in females. The petering out process doesn't stop at the same place for each woman. So some women have different genes turned on at different levels. Scientists are exploring what having more or less of these extra genes might mean for women.

As you can tell, the extra X chromosome in Klinefelter's is already inactivated. To "cure" Klinefelter's, scientists would need to learn completely shut off the extra X chromosomes very early on without affecting the active X. A pretty tall order that isn't likely to happen anytime soon.