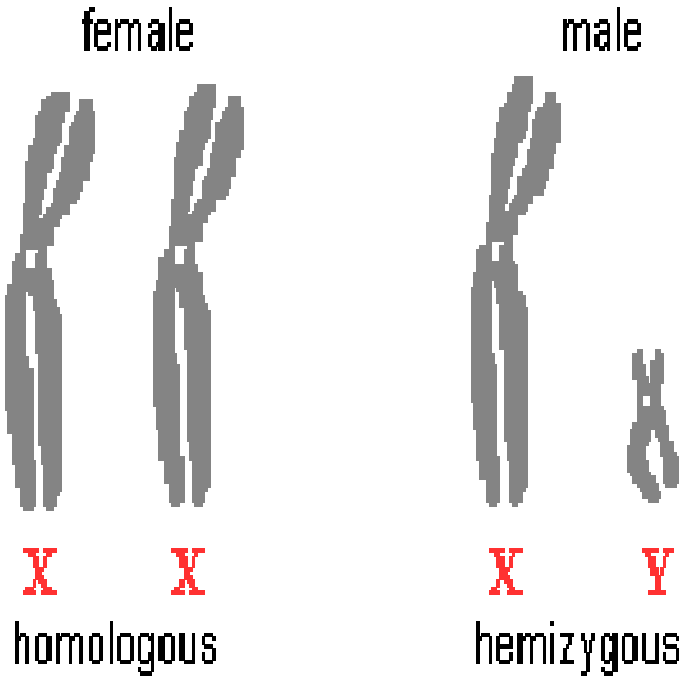
Dosage Compensation

Prof Vandana Rai
Department of Biotechnology
VBS Purvanchal University,
Jaunpur

Dosage Compensation

Sex Chromosomes:

- In humans, gender is determined by the sex chromosomes (X and Y chromosome):
- Females have two X chromosomes, males have one X and one Y chromosome
- **Females –XX (Homogametic sex)**
- **Males XY (Heterogametic sex)**



- In cells with more than two X chromosomes, only one X remains genetically active and all the others become inactivated.
- In some cells the paternal allele is expressed
- In other cells the maternal allele is expressed
- In XXX and XXXX females and XXY males only 1 X is activated in any given cell the rest are inactivated

X chromosome inactivation

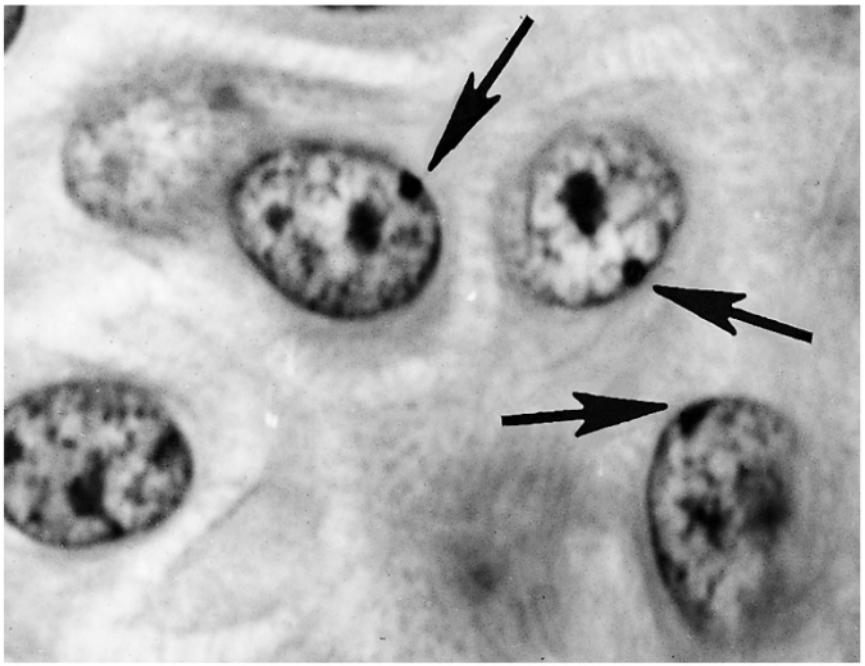
- Which chromosome is inactive is a matter of chance, but once an X has become inactivated , all cells arising from that cell will keep the same inactive X chromosome.

- In the mouse, the inactivation apparently occurs in early in development

- In human embryos, sex chromatin bodies have been observed **by the 16th day of gestation.**

Barr Bodies

- 1940's two Canadian scientists noticed a dark staining mass in the nuclei of cat brain cells.
- Found these dark staining spots in female but not males.
- They thought the spot was a tightly condensed X chromosome .
- Number of Barr bodies= No of chromosome - 1



From N. Ason/DeHaan, Figure 9.8, *Biological World*, 1973

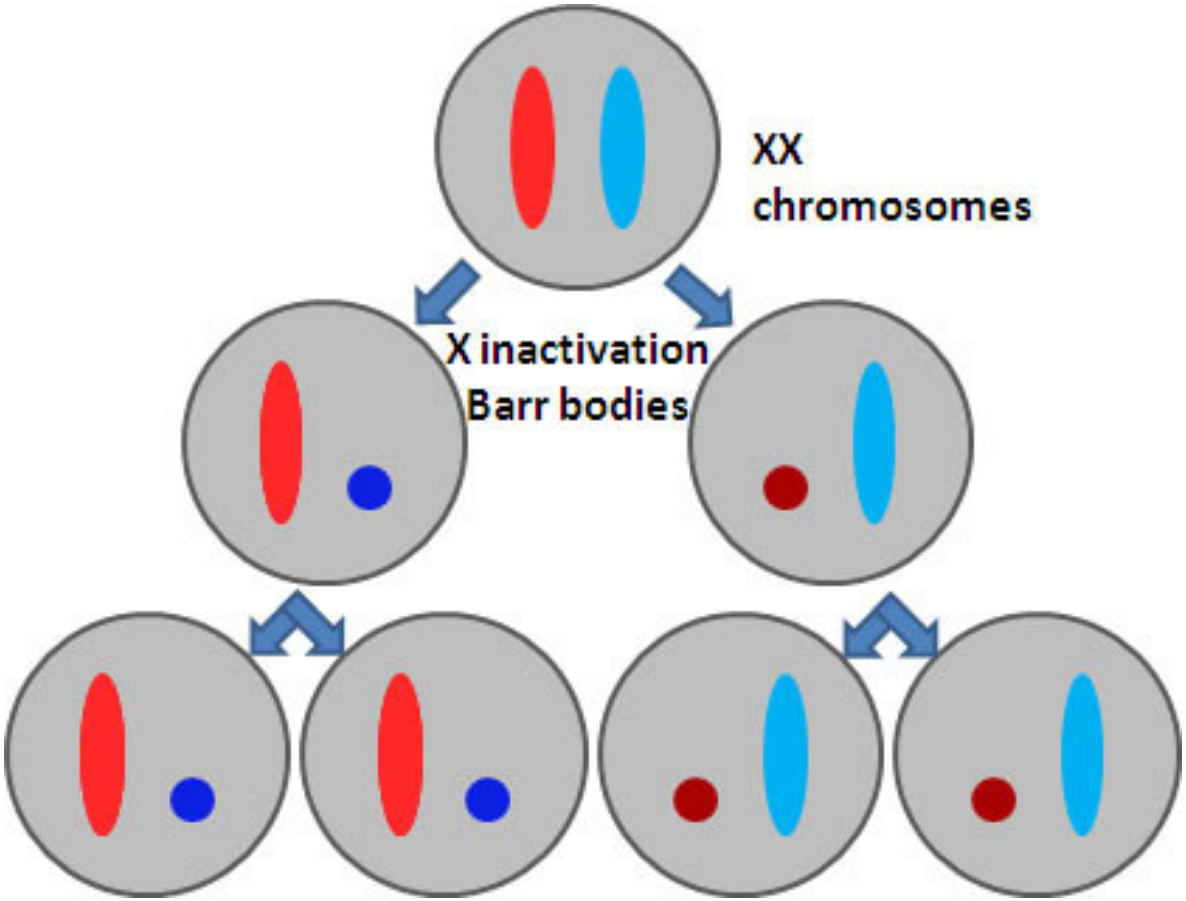
Barr bodies represent the inactive X chromosome and are normally found only in female somatic cells.

Lyons hypothesis

- In 1962, English geneticist Mary Lyon proposed a hypothesis for X chromosome inactivation.
- consists of-

  (i)Condensed chromosome is genetically inactive

  (ii) X inactivation in humans occurs in the early in development when embryo consists of about 32 cells, one or two days of fertilization.



https://www.scoop.it/topic/molcyt

Lyons hypothesis

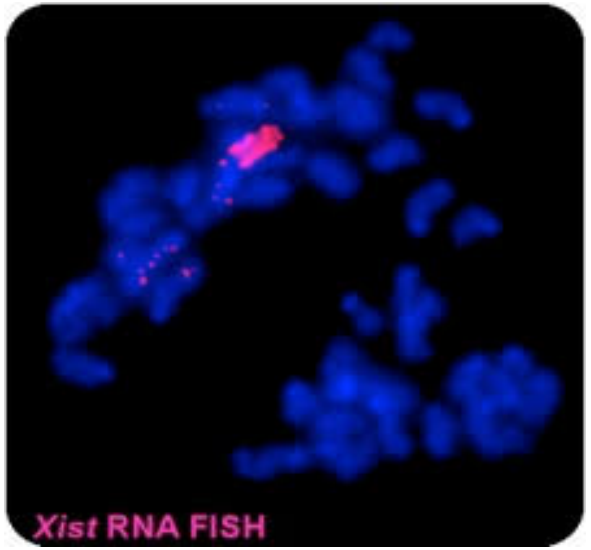
(iii)At this stage in each of the 32 cells one of the X chromosome is randomly inactivated

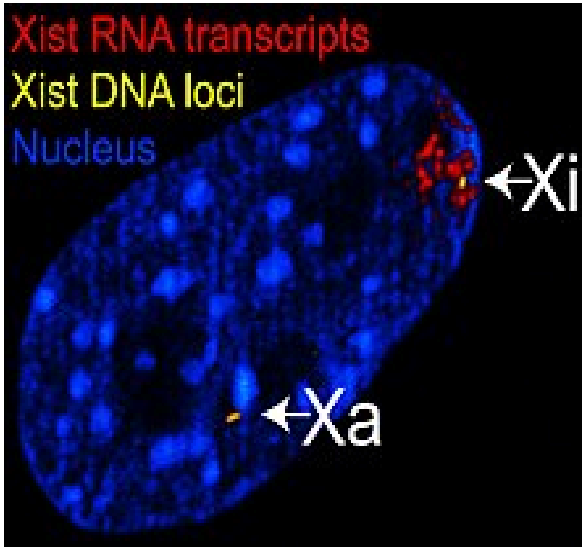
(iv)Inactivation is mitotically stable

(v)Net effect of this is to equalize the phenotypes of males and females for genes that are carried on the X chromosome.

Mechanism of X-chromosome Inactivation

- A region of the p arm of the X chromosome near the centromere called the **X-inactivation center (XIC)** is the control unit.
- This region contains the gene for **X-inactive specific transcript (*XIST*)**.
- This RNA presumably coats the X chromosome that expresses it and then **DNA methylation** locks the chromosome in the inactive state.





X-chromosome inactivation

• In humans, gender is determined by the sex chromosomes (X and Y chromosome):
• Females have two X chromosomes, males have one X and one Y chromosome
.
• The X and Y chromosomes look very different:
genes on the X have no counterpart on the Y .
•To ensure that males and females have equal levels of gene expression, one X chromosome is inactivated.

•the choice of which X is inactivated the X chromosome, one X in every female cell is inactivated random.

Random X inactivation

- Random inactivation of X chromosome results in mosaic patterns of gene expression

- **Calico cats:** always female (except in rare XXY males)
  - X chromosome has gene for coat colour
  - The gene can encode either a black pigment or orange
  - Since males have only one X, they can be either black or orange, but not both
- the X chromosome inactivation in females is random, so different patches of epidermal cells can have different colour genes
- (the gene for white coat is on another chromosome)

Suggested Reading

1. Human Molecular Genetics – Tom Stratchen & Andrew P. Read. Pub: John Wiley & Sons.
2. An introduction to Genetic Analysis – Griffith, Miller, Suzuki, Lewontin, Gelbard. Pub: W.H. Freeman & Co.
3. Genomes 2 – T.A. Brown, Pub: Wiley-Liss. John W. & Sons.
4. Emery's Elements of Medical Genetics – R.F. Mueller, I.D. Young, Pub: Churchill
5. An Introduction to Human Molecular Genetics – J.J. Pasternak, Pub: Fitzgerald Science