# X Chromosome

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## Why in News?

Recent genomic studies have uncovered the significant role of the X chromosome in various biological processes and diseases, particularly **autoimmune diseases and** Alzheimer's disease.

## What is the X Chromosome?

- **About:** The X chromosome is **one of the two sex chromosomes** found in humans and many other organisms. It plays a crucial role in sex determination and carries genes essential for various bodily functions.
- **Sex Determination:** Females typically have **two X chromosomes (XX)**, while males have one **X and one Y chromosome (XY).**
    - The presence or absence of the Y chromosome determines biological sex.
- **Genes and Functions:** The X chromosome encodes approximately 800 genes that code for proteins involved in diverse biological functions.
    - Loss of function of these genes can lead to a variety of genetic diseases, which can be broadly classified into three categories:
        - X-linked genetic diseases.
        - Diseases influenced by X-chromosome inactivation (XCI) escape.
        - Diseases linked to X-chromosome aneuploidies.
- **X-Linked Genetic Diseases:** It results from **mutations in genes on the X chromosome.**
    - **Males**, having only one X chromosome**, are more likely to express the mutations and develop the disease.**
    - Females, with two X chromosomes, have a **better chance of having a healthy copy of the gene to offset a mutated one,** reducing their risk of developing the full disease.
    - **Examples: Red-green colorblindness** (affecting around 8% of males).
        - ***Duchenne muscular dystrophy*** (1 in every 3,500-5,000 boys born in India) and ***Agammaglobulinemia*** (1 in 200,000 live births).
- **X-Chromosome Aneuploidies:** Numerical aneuploidies of the X chromosome can cause certain diseases.
    - Aneuploidy is a genetic condition where an organism has an **abnormal number of chromosomes in its cells.**
        - Human cells typically have 46 chromosomes, 23 from each parent. In aneuploidy, a cell may have an extra copy of a chromosome (trisomy) or a missing copy (monosomy).
    - **Examples:**
        - **Klinefelter syndrome** (characterised by an extra X chromosome, XXY).
        - **Turner syndrome** (loss of one X chromosome in females, X instead of XX).
- **X-chromosome inactivation (XCI) Escape:** In females with two X chromosomes, one X chromosome is randomly inactivated in each cell (except for egg cells) to prevent an imbalance of X-linked genes. **This process is called X-inactivation or lyonization.**
    - Issues like incomplete inactivation (escape) or skewed inactivation can lead to abnormal gene expression, contributing to **X-linked disorders, certain cancers, and autoimmune conditions.**

    - The molecular mechanisms behind XCI were discovered in the 1990s, involving two **non-coding RNAs called Xist and Tsix.**
        - Xist coats and inactivates one of the X chromosomes, while Tsix (reverse of Xist) regulates this process.
    - Recent research has shown that up to a quarter of genes on the X chromosome can escape inactivation and be expressed, even after the XCI process.

## How is XCI Linked to Autoimmune Diseases?

- Autoimmune diseases, such as systemic *lupus erythematosus*, rheumatoid arthritis, **and Sjögren's syndrome**, are more common in females than males.
- A recent study found that **changing the activity of a gene Xist reactivated other inactive genes on the X chromosome.**
    - This **caused immune system changes** that led to lupus-like symptoms, such as increased autoantibodies and inflammation.
- The findings suggest a link between these gene changes and autoimmune diseases, offering hope for new treatments.

## Note

Autoimmune diseases occur when the **body's immune system mistakenly attacks healthy cells** as if they were foreign organisms.

## How is the X Chromosome Linked to Alzheimer's Disease?

- Alzheimer's disease exhibits a sex bias, with **women having a higher risk compared to men.**
    - A study suggests that the **gene USP11,** involved in protein modification, escapes X inactivation and is expressed more in females.
    - Increased expression of USP11 encourages the accumulation of tau protein in the brain, contributing to the **development of Alzheimer's disease.**
- This opens new avenues for developing targeted treatments for Alzheimer's disease.

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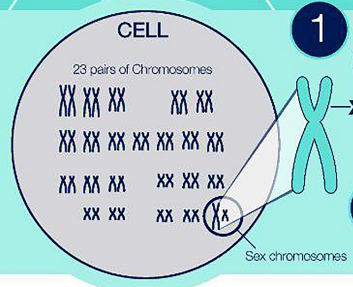
# X Chromosome



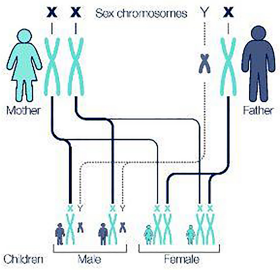

1 In the nucleus of each cell, DNA is packaged in thread-like structures called **chromosomes**.

**X Chromosome**

2 Most human cells contain 23 pairs of chromosomes. One set of chromosomes comes from the mother, while the other comes from the father. The twenty-third pair is the **sex chromosomes**, while the rest of the 22 pairs are called **autosomes**.

3 Typically, biologically female individuals have two X chromosomes (**XX**) while those who are biologically male have one X and one Y chromosome (**XY**). However, there are exceptions to this rule.

4 Biologically female people inherit an X chromosome from their father, and the other X chromosome from their mother. Biologically male people always inherit their X chromosome from their mother.



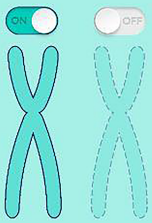

5 The X chromosome is about three times larger than the Y chromosome, containing about 900 genes, while the Y chromosome has about 55 genes.

X Chromosome

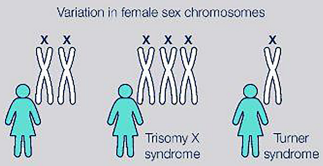
Y Chromosome

6 Female mammals have two X chromosomes in every cell. However, one of the X chromosomes is **inactivated**. Such inactivation stops transcription from occurring, hence making sure a potentially toxic double dose of X-linked genes does not occur.

7 An inactivated X chromosome gets condensed into a small, dense structure in the nucleus, and is called a Barr body. Barr bodies are commonly used to determine sex.




8 Changes in the structure or number of X chromosomes can lead to a number of diseases. For example, **trisomy X syndrome** is caused by the presence of three X chromosomes instead of two. **Turner syndrome** occurs when women inherit only one copy of the X chromosome.




9 Some women have a rare super color vision trait called **tetrachromacy**, which is linked to the X chromosome. These women can see up to **100 million shades of color** because they have four types of cone cells in their eye instead of the usual three.

10 Contrary to popular belief, **calico** is not a breed of cats, but rather a **distinctive coat color pattern** linked to the X chromosome. Over 95% of calico cats are female. The patches of fur on a calico cat are orange and black, and the color depends on which X chromosome is inactivated within each patch of color.