

X Chromosome Inactivation (XCI): The epigenetic process which silences one X chromosome in females to achieve gene dosage balance between males and females. [1]

Xa: the active X chromosome

Xi: the inactive X chromosome

Xm: maternally inherited X chromosome

Xp: paternally inherited X chromosome

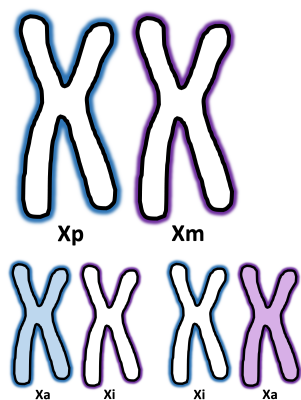


Figure 1: The paternally inherited (X_p) chromosome in and the maternally inherited chromosome (X_m). The active chromosome X_a is represented with color filled in, while the inactive chromosome X_i is represented with no color fill.

Escape: The status of genes which are expressed on X_i . These genes “escape” inactivation.

Inactive: The status of genes which are suppressed on X_i .

Variable: The status of genes which are expressed on X_i in some tissues/individuals, but not in all tissues/individuals. [2]

Mosaicism: X_a and X_i are typically randomly assigned to either X_p or X_m in each cell. *Mosaicism* refers to the heterogeneity of X_a/X_i assignment among a set of cells.

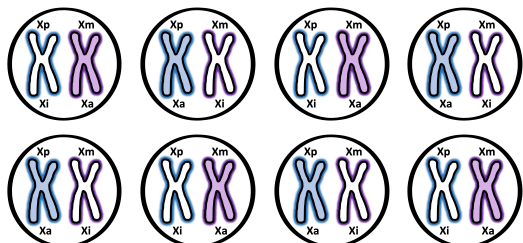


Figure 2: Mosaicism. A sample of six cells with differences in X_a/X_i assignments.

Skew: A ratio which represents the mosaicism of X_a/X_i assignment in a set of cells.

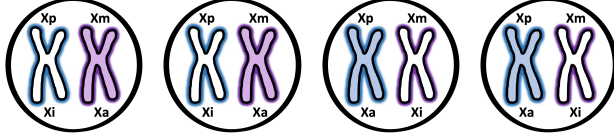


Figure 3a: Skew Ratio 1. Two samples have X_i assignment on X_m , while two samples have X_i assignment on X_p . The resulting skew ratio is 50:50.

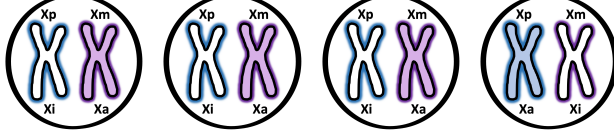


Figure 3b: Skew Ratio 2. Three samples have X_i assignment on X_m , while one sample has X_i assignment on X_p . The resulting skew ratio is 25:75.

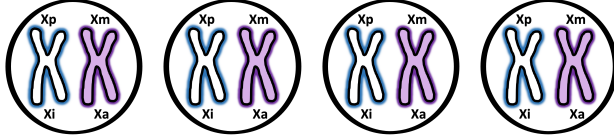


Figure 3c: Skew Ratio 3. All four samples have X_i assignment on X_m . The resulting skew ratio is 0:100. This is a rare occurrence in nature, and is often referred to as non-random assignment or fully skewed [3]

%Xi or tau (τ): The ratio of a gene's expression on X_i over its total expression across both X_a and X_i , referred to as %Xi [4] or τ [5]. In allele specific expression (ASE) based methods for escape inference, τ is compared to the skew ratio. Significant deviation of τ from the skew ratio reflects biallelic expression and classifies a gene as escape.

N = expression level

j = gene

i = inactive x chromosome

a = active x chromosome

$$\tau = \frac{N_{ij}}{N_{aj} + N_{ij}}$$

A note about skew: For ASE based methods, data sets with a higher skew ratio (such as 25:75) are strengthened for estimating escape expression due to the lower X_i expression levels required to infer significance.

Tau+ ($\tau+$): The τ (or %Xi) values from the subset of XCI calls which were inferred from samples which were sufficiently skewed ($>25:75$). This subset is a more robust estimate of ASE and is strengthened for escape calling. [4]