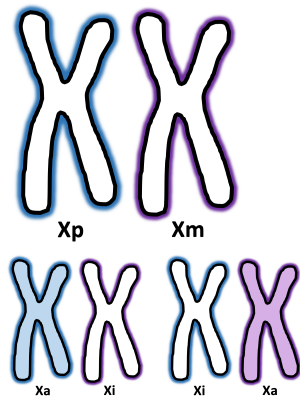**X Chromosome Inactivation (XCI)**: The epigenetic process which silences one X chromosome in females to achieve gene dosage balance between males and females. [1]

Xa: the active X chromosome

Xi: the inactive X chromosome

Xm: maternally inheritted X chromosome

Xp: paternally inheritted X chromosome

Figure 1: The paternally inherited (Xp) chromosome in and the maternally inherited chromosome (Xm). *The active chromosome Xa is represented with color filled in, while the inactive chromosome Xi is represented with no color fill.*

Escape: The status of genes which are expressed on Xi. These genes "escape" inactivation.

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

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

Mosaicism: Xa and Xi are typically randomly assigned to either Xp or Xm in each cell. *Mosaicism* refers to the heterogeneity of Xa/Xi assignment among a set of cells.
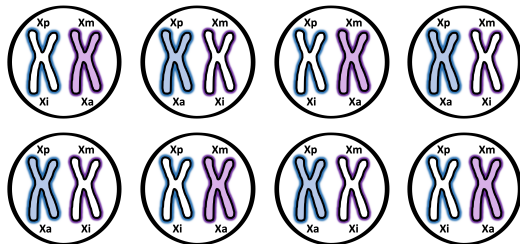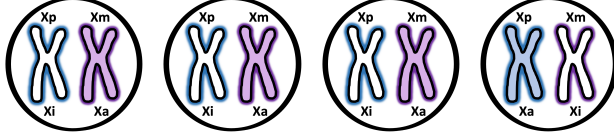

Figure 2: Mosaicism. *A sample of six cells with differences in Xa/Xi assignments.*
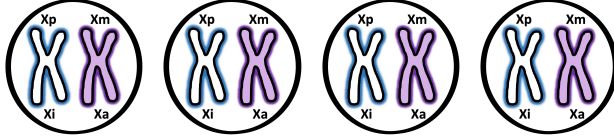
Skew: A ratio which represents the mosaicism of Xa/Xi assignment in a set of cells.
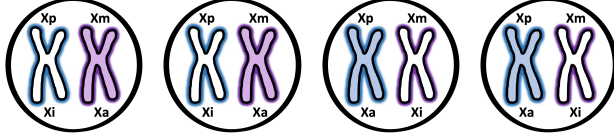
Figure 3a: Skew Ratio 1. *Two samples have Xi assignment on Xm, while two samples have Xi assignment on Xp. The resulting skew ratio is 50:50.*

Figure 3b: Skew Ratio 2. *Three samples have Xi assignment on Xm, while one sample has Xi assignment on Xp. The resulting skew ratio is 25:75.*

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

%Xi or tau (τ): The ratio of a gene's expression on Xi over its total expression across both Xa and Xi, 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 Xi expression levels required to infer significance.

Tau+ (τ+): 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]

[1] LYON MF. Gene action in the X-chromosome of the mouse (Mus musculus L.). *Nature.* 1961;190:372-373. doi:10.1038/190372a0

[2] Carrel L, Brown CJ. When the Lyon(ized chromosome) roars: ongoing expression from an inactive X chromosome. *Philos Trans R Soc Lond B Biol Sci.* 2017;372(1733):20160355. doi:10.1098/rstb.2016.0355

[3] Tukiainen T, Villani AC, Yen A, et al. Landscape of X chromosome inactivation across human tissues [published correction appears in *Nature.* 2018 Mar 7;555(7695):274]. *Nature.* 2017;550(7675):244-248. doi:10.1038/nature24265

[4] Cotton, A.M., Ge, B., Light, N. et al. Analysis of expressed SNPs identifies variable extents of expression from the human inactive X chromosome. *Genome Biol* 14, R122 (2013). doi:10.1186/gb-2013-14-11-r122

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