

GENES ESCAPING X-INACTIVATION

In biology, things are often far more complex than we once imagined, and DeCasien's work brings this into sharp focus through the lens of genes that escape X chromosome inactivation (XCI).

While it was traditionally believed that XCI was a relatively uniform process and that genes in the pseudoautosomal regions (PAR) completely escaped inactivation to be expressed from both sex chromosomes, this research reveals a much more nuanced reality. DeCasien (1) demonstrates that XCI actually extends into these PAR areas, influencing genes like CD99 and PLCXD1 and explaining why many of them unexpectedly show higher expression in males.

The study further challenges the long-held assumption that higher expression in females is a definitive marker of a gene escaping inactivation. It turns out that many genes previously labeled as "escapers" based on sex-biased expression are actually subject to XCI, while others that do escape show no significant difference between sexes. This intricate landscape is heavily dictated by the 3D architecture of the genome; genes grouped within the same Topologically Associating Domains (TADs) tend to share similar escape patterns. Ultimately, the interplay between varying XCI intensity and sex-specific enhancer activity creates a sophisticated regulatory balance that shapes how our sex chromosomes function across different tissues.

1. [10.1186/s12864-026-12611-3](https://doi.org/10.1186/s12864-026-12611-3)