# Classifying escape genes based on escape frequency threshold

A majority of the genes on the X chromosome are subject to X chromosome inactivation and only express one allele in each cell. Yet, ~10% of the genes consistently escape XCI, and another 12-20% of the genes are “variable escape” genes, which show considerable inter-individual differences in their escape status.

Most of the existing studies classify escape genes based on a threshold of the percentage of samples where each gene escapes XCI (which we call PE). For example, in the data set below *HCC1* escapes in 3/10 of the samples, resulting in PE of 30%.

Table

Description automatically generated

The PE of a gene is used to classify its escape status. Genes which escape in nearly all samples are classified as “escape”; genes which escape in some but not all samples are “variable”; genes which escape in few or no samples are “inactive”. **Escape Frequency Thresholds** are used to delineate each classification.

For example, the GEUVADIS lymphoblast study uses 25% and 75% thresholds.

* %escape ≤ 25% → Silenced (S)
* 25% < %escape < 75%  → Variable escape (VE)
* %escape  ≥ 75% → Escape (E)

Applying these thresholds to our example data set will classify *HCFC1* as “variable”.

Table

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**CHANGING ESCAPE FREQUENCY THRESHOLDS**

Different studies use different frequency threshold to classify escape, variable escape and inactivated genes. In order to harmonize results across studies and allow users to flexibly classify escape genes, X-Viz gives users the freedom to change the escape frequency thresholds.

The left side panel contains sliders which modify the lower and upper thresholds. These sliders are available only for studies which contain sample level information of escape status.

Graphical user interface, text, application

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Changing the escape thresholds will modify the classification sensitivity for the selected study. In our example data set, modifying the thresholds to 33% and 66% will re-classify the escape status of the *HCFC1* gene.

Timeline

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Table

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Modifying the escape thresholds will also update the gene position graphic. Note, this graphic is only available for studies which include positional data (“start” column).

**Graphic of 25% and 75% thresholds for *HCFC1*:**

Timeline

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**Graphic of 33% and 66% thresholds for *HCFC1*:**

Timeline

Description automatically generated with low confidence

**Graphic of 25% and 75% thresholds for *Tukiainen et al. GTEx study*:**

Timeline

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**Graphic of 33% and 66% thresholds for *Tukiainen et al. GTEx study*:**

Timeline

Description automatically generated with medium confidence