

Erratum

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Genes that Escape X-Inactivation in Humans Have High Intraspecific Variability in Expression, Are Associated with Mental Impairment but Are Not Slow Evolving

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We wish to bring to the readers' attention that, owing to a scripting error, column 3 of [supplementary table S3](#) was incorrectly specified. This column described the X-inactivation status of the genes in our sample. We now issue a replacement and augmented [supplementary table S3](#). We are grateful to Mr Kerem Wainer Katsir for bringing this issue to our attention.

Previously, we merged our data with that of Park et al. to test for differences between classes in Ka/Ks. Owing to the error in specification of column 3, these merged data are also incorrect. The data presented in Park et al. (2010) are therein said to be derived from Carrel and Willard (2005). It has, however, also come to our attention that the data in Park et al and Carrel and Willard, while similar, are not identical. We now therefore present both of these data sets and a consensus merge of all three.

In the newly [supplementary table S3](#), only two genes show evidence of escaping X-inactivation in all informative samples in our RNA-seq data and accordingly, in the newly merged data, very few genes ($N = 7$) show evidence of escaping X-inactivation across the three data sets. Despite this, our prior conclusion (in contrast to those of Park et al.) that genes that escape X-inactivation do not evolve especially slowly remains. The new merged data set comprises 461 genes, which we again apportion into always escape, never escape, and sometimes escape. We find no evidence for heterogeneity between the three classes in Ka/Ks (Kruskal–Wallis test: $P = 0.575$). Eliminating any genes for which $Ka/Ks > 1$ does not affect this conclusion (Kruskal–Wallis test, $P = 0.732$). Comparing the “always escape” genes with the other two classes, we see no evidence that they evolve at a significantly different rate (P for comparison of always escape to inactive = 0.853, comparing always escape to heterogenous = 0.637). Thus, as we previously found, we cannot replicate the result of Park et al. that those genes that always escape have significantly low Ka/Ks.

Similarly, and as we previously reported, considering genes that ever escape X-inactivation as a single class (the union of sometimes and always), we again find no evidence that these evolve any slower than those that never escape (Mann–Whitney U test, $P = 0.344$) with those escaping having a marginally higher median rate ($Ka/Ks = 0.1906$ for genes that never escape and 0.1913 for those that always or sometimes escape).

While as before, and commonly reported, median expression rate is a predictor of Ka/Ks (Spearman correlation, $\rho = -0.23$, $P = 8.25e-05$), control for covariance with expression level does not affect conclusions. After control for expression level (by considering the residuals from the loess regression of Ka/Ks against $\log[\text{expression level}]$), the Kuskall–Wallis test is still nonsignificant ($P = 0.36$). The P value is 0.39 when excluding genes with $Ka/Ks > 1$.

We apologize for any inconvenience caused.

Supplementary table S3

In this table, we present for 461 X-linked genes their names, Ensembl ID, specification as to whether, when we find evidence of escape, this evidence is replicated or not, our status (including the number of samples showing evidence of escape and the number of potentially informative samples). In addition, we now present the status as described in Carrel and Willard (2005) and in Park et al. (2010). Finally we present the merged status, the Ka/Ks ratio, and Log of the expression level. “Inactive or Inactivated” indicates no evidence that the gene escapes X-inactivation and informative samples are available, “escape” implies X-inactivation escape in all relevant samples, whereas “Heterogeneous” implies evidence for escape in some but not all informative samples.

References

- Carrel L, Willard H. 2005. X-inactivation profile reveals extensive variability in X-linked gene expression in females. *Nature* 434:400–404.
 Park C, Carrel L, Makova KD. 2010. Strong purifying selection at genes escaping X chromosome inactivation. *Mol Biol Evol.* 27:2446–2450.

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