Response to 'About the X-to-Y gene conversion rate', by Cruciani *et al.*

Zoë H. Rosser, Patricia Balaresque and Mark A. Jobling

Department of Genetics, University of Leicester, University Road, Leicester, UK

Correspondence and requests for reprints should be addressed to:

Prof Mark A. Jobling, Department of Genetics, University of Leicester, University Road, Leicester LE1 7RH, UK

Tel.: +44 (0)116 252 3427

Fax: +44 (0)116 252 3378

Email: maj4@le.ac.uk

Keywords: X chromosome; Y chromosome; gene conversion; gametolog; *PRKX*; *PRKY*

Running head: Gene conversion between sex chromosomes

In July 2009 we published in this journal a report containing evidence for gene conversion between the X chromosome and the male-specific region of the Y chromosome[1] at a translocation hotspot (hotspot A; *HSA*) between the *PRKX* (MIM 300083) and *PRKY* (MIM 400008) genes. In this issue, Cruciani and colleagues[2] revisit our data and conclude that we overestimated the per-base-per-generation rate due to a failure to divide the number of conversion events within the sequence under study by the length of the sequence in base-pairs. We agree with Cruciani and colleagues[2] that we made this error, thank them for pointing it out, and apologise to the readers of the *Journal*.

We observed two X-to-Y conversion events, but calculation of an average per-base-per-generation rate for the two events is complicated by the fact that the region sequenced was shorter for one of the events (in hgQ*: 698bp) than the other (in hgA2c: 1839bp – excluding primers). In recalculating the conversion rate per base per generation we therefore consider only the twelve Y chromosomes which were sequenced for the entire 1839-bp region, which, following the approach we used previously[1], encompass between 39,757 and 56,640 generations. Given the spacing of gametologous sequence variants the single event observed here has a tract length between 4 and 125bp. Using the equation of Cruciani *et al.*[2] our corrected rate range for X-to-Y gene conversion is between 3.8×10^{-8} and 1.7×10^{-6} per base per generation – comparable to the rate found by Cruciani *et al.*[2] in their own data. The lower bound of the recalculated range is similar to the average base mutation rate (2.3×10^{-8} per base per generation[3]), while the upper bound of the range is two orders of magnitude slower than the Y-Y conversion rate within palindromes (2.2×10^{-4} per base per generation[4]).

The other conclusions of our report remain unchanged, including the similarity of the events-per-generation rates of crossover (translocation) (~1×10^{-5}; ref. 1; 5) and conversion (~6.6×10^{-6} - ~2.1×10^{-5}; ref. 1) at *HSA*. We are gratified to observe that, in their independent resequencing of *HSA*, Cruciani and colleagues[2] also discovered variants indicating conversion from the X chromosome.

References

1. Rosser ZH, Balaresque P, Jobling MA (2009) Gene conversion between the X chromosome and the male-specific region of the Y chromosome at a translocation hotspot. Am. J. Hum. Genet. 85:130-134

2. Cruciani F, Trombetta B, Macaulay V, Scozzari R (2010) About the X-to-Y gene conversion rate. Am. J. Hum. Genet. in press

3. Repping S, van Daalen SK, Brown LG, Korver CM, Lange J, Marszalek JD, Pyntikova T, van der Veen F, Skaletsky H, Page DC, et al. (2006) High mutation rates have driven extensive structural polymorphism among human Y chromosomes. Nat. Genet. 38:463-467

4. Rozen S, Skaletsky H, Marszalek JD, Minx PJ, Cordum HS, Waterston RH, Wilson RK, Page DC (2003) Abundant gene conversion between arms of massive palindromes in human and ape Y chromosomes. Nature 423:873-876

5. Schiebel K, Winkelmann M, Mertz A, Xu X, Page DC, Weil D, Petit C, Rappold GA (1997) Abnormal XY interchange between a novel isolated protein kinase gene, *PRKY*, and its homologue, *PRKX*, accounts for one third of all (Y+)XX males and (Y-)XY females. Hum. Mol. Genet. 6:1985-1989