Genet. Res., Camb. (2007), **89**, *pp.* 433–434. © 2008 Cambridge University Press
doi:10.1017/S0016672308009646 Printed in the United Kingdom

What prevents transposable elements from taking over the genome? a commentary on 'A test for the role of natural selection in the stabilization of transposable element copy number in a population of *Drosophila melanogaster*' by Elizabeth Montgomery, Brian Charlesworth and Charles H. Langley

TRUDY F. C. MACKAY*
Department of Genetics, Campus Box 7614, North Carolina State University, Raleigh, NC 27695, USA

In addition to unique sequences, eukaryotic genomes contain a surprisingly large fraction of dispersed copies of repeated sequences – transposable elements (TEs). In *Drosophila melanogaster*, for example, there are over 50 different families of TEs with an average of 20 copies per family, which in total constitute approximately 10% of the genome (Finnegan, 1992). Since the rate of TE transposition generally exceeds the rate of excision (Nuzhdin & Mackay, 1995), one or more forces must act to counter the spread of TE copies. One obvious hypothesis is that TE insertions can cause deleterious mutations and that purifying natural selection against the mutations will contain the spread of TEs. An equilibrium copy number will be achieved when the loss of TE copies from selection balances their gain from transposition (Charlesworth & Charlesworth, 1983). However, it is also possible that the copy number of each TE family is autonomously controlled by the elements themselves. Under this model, equilibrium copy numbers would be achieved if the rate of transposition decreases or the rate of excision increases, as copy number increases (Charlesworth & Langley, 1986). Montgomery *et al.* (1987) conduct an elegant population genetic test to differentiate between selection and self-regulated transposition as mechanisms containing TE copy number, and present a new 'ectopic exchange' hypothesis to explain their results.

Montgomery *et al.* (1987) argue that these two hypotheses can be discriminated by comparing the distribution of TE copy numbers between the *X* chromosome and autosomes. Selection against recessive or partially recessive effects of TEs on fitness predicts a lower copy number on the *X* chromosome, since deleterious mutations are fully exposed to selection in hemizygous males. The self-regulation hypothesis predicts that TE copy numbers will be in proportion to the size of the chromosomes. Here, previous theory (Charlesworth & Charlesworth, 1983) on the population dynamics of TEs was extended to predict the relative abundance of TE copies on the *X* and autosomes under the two hypotheses. The predictions were that the *X* chromosome is expected to contain 11 and 17% of the total number of copies under the selection and self-regulation hypotheses, respectively. The authors determined copy numbers of *roo*, *297* and *412* TEs on homozygous *X*, second and third chromosomes from 20 lines derived from a single natural population, by *in situ* hybridization to polytene chromosomes. The chromosomal distribution of the three element families was not the same for the three element families. There was a deficiency of *412* elements on the *X* chromosome, consistent with the prediction of the selection model. However, the chromosomal copy number distribution for the *roo* and *297* elements was as predicted by the self-regulation hypothesis. This latter observation was puzzling, because available information on the distribution of insertion sites of TEs in natural populations of *Drosophila* was consistent with some control of copy number by a selective mechanism, since individual insertion sites are rare (Montgomery & Langley, 1983).

These observation led to the proposal of the 'ectopic exchange' hypothesis of unequal or non-homologous recombination between TE copies: 'Recombination between insertions at different sites would lead to chromosome rearrangements that are generally dominant lethal, or so deleterious that their probability of transmission and/or survival

* e-mail: trudy_mackay@ncsu.edu

in subsequent generations is substantially reduced when compared with that of a simple insertional mutation'. This alternative selection model is one of selection against dominant mutations, which is equally effective on the *X* chromosomes and autosomes, but will still yield a skewed site frequency distribution towards rare insertions. Stabilization of copy number under this model occurs because the rate of induction of rearrangements will increase with square of copy number. This model also makes a testable prediction of more TE copies in chromosomal regions of reduced recombination, provided the rate of non-homologous recombination is correlated with the rate of homologous recombination. Preliminary data on X-linked *roo* element insertion sites as well as increased accumulation of TE copies near the breakpoints of segregating inversions, where recombination is absent, supported the ectopic exchange hypothesis. This paper stimulated much empirical and theoretical research on the population genetics of TEs.

References

Charlesworth, B. & Charlesworth, D. (1983). The population dynamics of transposable elements. *Genetical Research* **42**, 1–27.

Charlesworth, B. & Langley, C. H. (1986). The evolution of self-regulated transposition of transposable elements. *Genetics* **112**, 359–383.

Finnegan, D. J. (1992). Transposable elements. In *The Genome of* Drosophila melanogaster (ed. D. L. Lindsley & G. Zimm), pp. 1096–1107. Academic Press, New York.

Montgomery, E. A. & Langley, C. H. (1983). Transposable elements in Mendelian populations. II. Distribution of three *copia*-like elements in a natural population of *Drosophila melanogaster*. *Genetics* **104**, 473–483.

Montgomery, E., Charlesworth, B. & Langley, C. (1987). A test for the role of natural selection in the stabilization of transposable element copy number in a population of *Drosophila melanogaster*. *Genetical Research* **49**, 31–41.

Nuzhdin, S. V. & Mackay, T. F. C. (1995). The genomic rate of transposable element movement in *Drosophila melanogaster*. *Molecular Biology and Evolution* **12**, 180–181.