Letter to the Editor

Transposable Element Distribution in *Drosophila*

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BECAUSE of the strong influence of transposable elements (TEs) on genomic diversity, the way their copy number is contained in population is one of the main problems of population genetics. Although various mechanisms may be involved, selection appears to be more and more accepted as the primary mechanism controlling the transpositional spread of elements and their distribution throughout the genome of *Drosophila*. However, there is some debate as to what precise mechanism underlies the term of selection (CHARLESWORTH and LANGLEY 1991; BIÉMONT 1992). Selection against the deleterious effects of insertions and selection against the gross chromosomal rearrangements caused by ectopic exchange between copies (unequal recombination) appear thus as alternative or complementary processes. Although the first hypothesis was initially proposed by CHARLESWORTH and CHARLESWORTH (1983) and MONTGOMERY *et al.* (1987), because of the observation of a low proportion of some TE insertions on the X in comparison with the autosomes (because selection is more efficient on the X chromosome due to the hemizygoty of the *Drosophila* male), it was subsequently dismissed because (1) not all elements and not all populations seem to follow this rule, and (2) the selection coefficient against deleterious mutations estimated from data on natural populations is too high in comparison with the transposition rate for insertions to be maintained. The model of ectopic exchange proposed by LANGLEY *et al.* (1988) was generally accepted as an alternative hypothesis, because, according to CHARLESWORTH *et al.* (1997), it better fulfills the data obtained in *Drosophila*, and could even explain many other observations in population genetics such as evolutionary dynamics of repetitive DNA in eukaryotes (CHARLESWORTH *et al.* 1994b) and background selection (CHARLESWORTH 1996). The role of selection against insertional effects of TEs was discounted. From our experiments, we conclude that this last hypothesis is not to be rejected but remains instead a main force

acting against active TEs in natural populations. This does not mean, of course, that this is the sole force operating, as wrongly interpreted by CHARLESWORTH *et al.* (1997).

The idea that selection is too strong (1–2%) in comparison with the transposition rates (of the order of 10^{-4} in laboratory lines, but 10^{-3} in natural populations of *D. simulans* for the 412 elements: VIEIRA and BIÉMONT 1997) comes mainly from the value of selection coefficients associated with deleterious mutations in natural populations and not from those mutations associated with TE insertions. This discrimination between the two types of mutations has been used only recently in attempts to incorporate TEs into the background selection model (CHARLESWORTH 1996) and to understand their impact on viability decline in *Drosophila* (KEIGHTLEY 1996). Curiously, in the model of background selection the selection coefficient associated with mutations due solely to TE insertions was estimated to be 2×10^{-4} , a value quite low and comparable to the above transposition rate estimate. This low value was, however, considered to be in agreement with the ectopic model (CHARLESWORTH 1996). It is of course quite compatible with the selection against insertions as well, especially since such a low selection coefficient value could lead to a stable and realistic equilibrium for TE copy number under this model. CHARLESWORTH *et al.* (1997) then present the data of the effects of *P* element insertions as an argument in favor of high selection coefficient, but they contradict themselves because *P* elements are usually excluded from tests of models because their copy numbers are not at equilibrium and because of the hybrid dysgenesis phenomenon associated with these elements (CHARLESWORTH and LANGLEY 1991). Moreover, selection coefficients may vary widely between insertion sites and the distribution of this value is more interesting than its mean, as rightly proposed by KEIGHTLEY (1994). More importantly, reanalyzing the data of MUKAI *et al.* (1972) and OHNISHI (1977) on viability decline due to accumulation of spontaneous mutations in *Drosophila*, KEIGHTLEY (1996) concludes that the 1–2% rate of decline in viability could be due in part to selective improvement of the balancer chro-

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mosomes used, leading to the conclusion that the deleterious mutation load is much lower than previously thought, with TEs causing minor mutagenic effects, an idea that CHARLESWORTH *et al.* (1997) should take into consideration.

One important point not mentioned by CHARLESWORTH *et al.* (1997) is the observation of temporary high movements of some TEs, as reported in laboratory lines and natural populations (BIÉMONT 1992), and of variation in TE insertion rate between populations and species (see HOOGLAND and BIÉMONT 1996; VIEIRA and BIÉMONT 1996a,b). If transposable elements can be submitted now and then to high rates of mobilization, then the models no longer hold. Hence, in case of recent mobilization of the TEs under analysis no difference between TE distributions should be observed between the autosomes and the X chromosomes (MONTGOMERY *et al.* 1987; CHARLESWORTH and LAPID 1989; CHARLESWORTH *et al.* 1992a,b, 1994b), but this absence of effect could not be used as an argument against the insertional selection effect model (a lower proportion of insertions on the X chromosomes in comparison with the autosomes is expected under this model: MONTGOMERY *et al.* 1987; CHARLESWORTH and LAPID 1989; CHARLESWORTH *et al.* 1992a,b, 1994b).

An accumulation of TEs in regions with low or nearly no recombination such as the chromocenter, some low-frequency inversions, and the fourth chromosome is taken by CHARLESWORTH *et al.* (1997) as strong evidence in favor of the ectopic exchange model, which predicts such an accumulation. We consider that this argument is weak because it is known that natural selection is reduced in regions of low recombination (the HILL-ROBERTSON effect; KLIMAN and HEY 1993), thus removing TE insertions only slowly. The observation of an effect on inversions is far from clear and not seen in all inversions (SNIĘGOWSKI and CHARLESWORTH 1994). *Ad hoc* hypotheses are thus proposed to explain the absence of effect on a chromosome as well as the absence of accumulation of TEs at the tip of chromosome X, or the lower TE accumulation than expected in the centric heterochromatin if only selective effects of ectopic exchange were considered (SNIĘGOWSKI and CHARLESWORTH 1994; CHARLESWORTH *et al.* 1994a). Moreover, although a high accumulation of TEs in β -heterochromatin is well documented (VAURY *et al.* 1989; MIKLOS and COTSELL 1990), this concerns mainly some particular TEs (CHARLESWORTH *et al.* 1994a). It is surprising to see a correlation between copy number of different TEs among the lines analyzed by CHARLESWORTH *et al.* (1994a), as if some lines were more capable of accumulating many TEs than others, an important point unnoticed by the authors. We also have to take into account the idea that centromeric regions may be the birthplace, not the graveyard, of TEs as proposed by PARDUE *et al.* (1996) and that these TEs may participate in the organization and function of heterochroma-

tin (ZUCKERKANDL and HENNIG 1995), such as meiotic chromosome segregation (DERNBURG *et al.* 1996).

In their comments on the HOOGLAND and BIÉMONT (1996) article, CHARLESWORTH *et al.* dispute the methods of data analysis. First they consider that insertion site number is an unsatisfactory measure of element abundance. They failed to recognize that we work on a sample of data collected from the literature and that some lines or populations may have been submitted to drastic reductions in effective size whose effect is an increase in element frequency per occupied site. Working on insertion site number avoids this problem. No negative correlation was found between this measure and recombination rate, and no significant correlation was found either with frequency of elements per occupied site, although CHARLESWORTH *et al.* (1997) point out one significant correlation value observed on the 3L arm. That such a correlation may be only the result of the numerous tests done is not even proposed. The same analysis done on the mean number of elements per region gives the identical result with only the 3L chromosomal arm showing a significant correlation (C. HOOGLAND, unpublished results). We cannot use this significant correlation as a strong argument in favor of the ectopic exchange model, and the low power of the Spearman's rank correlation coefficient will not change the conclusion. Indeed, what is important in Figure 2 of the HOOGLAND and BIÉMONT (1996) article is the distribution of the correlation coefficient values which, for all elements except *hobo*, are centered around zero. A change in the threshold value will thus have no effect on the general conclusion.

We are perfectly aware that we know nothing about the relationship between regular meiotic exchange and ectopic exchange in *Drosophila*. If this relationship is weak on the euchromatic part of the chromosomes, we can thus question the validity of the ectopic model, which is only capable of explaining the accumulation of TEs in specific regions of the genomes, such as the centric heterochromatin, and cannot consider the entire euchromatin which usually bears active TE copies at polymorphic sites.

We thus agree entirely with the conclusion of CHARLESWORTH *et al.* (1997) that further work is necessary to settle the exact role of ectopic exchange. The same conclusion holds true for the model of selection acting against the mutational effects of TE insertions. Both models may be reconciled with selection against insertions acting mainly on the actively moving part of the TE population and ectopic exchange acting in the long run to gradually shelter these insertions in regions of low recombination. Both of these models may of course have a weaker impact than we imagine if, for example, a deleterious side-effect of the transposition process itself (NUZHIDIN *et al.* 1996) and the potential evolutionary significance of TE mediated genomic

changes through regulatory pathways (McDONALD 1995) are considered.

LITERATURE CITED

- BIÉMONT, C., 1992 Population genetics of transposable DNA elements. A *Drosophila* point of view. *Genetica* **86**: 67–84.
- CHARLESWORTH, B., 1996 Background selection and patterns of genetic diversity in *Drosophila melanogaster*. *Genet. Res.* **68**: 131–149.
- CHARLESWORTH, B., and D. CHARLESWORTH, 1983 The population dynamics of transposable elements. *Genet. Res.* **42**: 1–27.
- CHARLESWORTH, B., and C. H. LANGLEY, 1991 Population genetics of transposable elements in *Drosophila*, pp. 150–176 in *Evolution at the Molecular Level*, edited by R. K. SELANDER, A. G. CLARK and T. S. WHITTAM. Sinauer Associates, Sunderland, MA.
- CHARLESWORTH, B., and A. LAPID, 1989 A study of 10 transposable elements on X chromosomes from a population of *Drosophila melanogaster*. *Genet. Res.* **54**: 113–125.
- CHARLESWORTH, B., A. LAPID and D. CANADA, 1992a The distribution of transposable elements within and between chromosomes in a population of *Drosophila melanogaster*. I. Element frequencies and distribution. *Genet. Res.* **60**: 103–114.
- CHARLESWORTH, B., A. LAPID and D. CANADA, 1992b The distribution of transposable elements within and between chromosomes in a population of *Drosophila melanogaster*. II. Inferences on the nature of selection against elements. *Genet. Res.* **60**: 115–130.
- CHARLESWORTH, B., P. JARNE and S. ASSIMACOPOULOS, 1994a The distribution of transposable elements within and between chromosomes in a population of *Drosophila melanogaster*. III. Element abundances in heterochromatin. *Genet. Res.* **64**: 183–197.
- CHARLESWORTH, B., P. SNIEGOWSKI and W. STEPHAN, 1994b The evolutionary dynamics of repetitive DNA in eukaryotes. *Nature* **371**: 215–220.
- CHARLESWORTH, B., C. H. LANGLEY and P. D. SNIEGOWSKI, 1997 Transposable element distribution in *Drosophila*. *Genetics* **147**: 1993–1995.
- DERNBURG, A. F., J. W. SEDAT and R. S. HAWLEY, 1996 Direct evidence of a role for heterochromatin in meiotic chromosome segregation. *Cell* **86**: 135–146.
- HOOGLAND, C., and C. BIÉMONT, 1996 Distribution of transposable elements along the polytene chromosomes of *Drosophila melanogaster*. Test of the ectopic recombination model for maintenance of insertion site number. *Genetics* **144**: 197–204.
- KEIGHTLEY, P. D., 1994 The distribution of mutation effects on viability in *Drosophila melanogaster*. *Genetics* **138**: 1315–1322.
- KEIGHTLEY, P. D., 1996 Nature of deleterious mutation load in *Drosophila*. *Genetics* **144**: 1993–1999.
- KLIMAN, R. M., and J. HEY, 1993 Reduced natural selection associated with low recombination in *Drosophila melanogaster*. *Mol. Biol. Evol.* **10**: 1239–1258.
- LANGLEY, C. H., E. A. MONTGOMERY, R. HUDSON, N. KAPLAN and B. CHARLESWORTH, 1988 On the role of unequal exchange in the containment of transposable element copy number. *Genet. Res.* **52**: 223–235.
- McDONALD J. F., 1995 Transposable elements: possible catalysts of organismic evolution. *Trends Ecol. Evol.* **10**: 123–126.
- MIKLOS, G. L. G., and J. N. COTSELL, 1990 Chromosome structure at interfaces between major chromatin types: alpha- and beta-heterochromatin. *BioEssays* **12**: 1–6.
- MONTGOMERY, E. A., B. CHARLESWORTH and C. H. LANGLEY, 1987 A test for the role of natural selection in the stabilization of transposable element copy number in a population of *Drosophila melanogaster*. *Genet. Res.* **49**: 31–41.
- MUKAI T., S. I. CHIGUSA, L. E. METTLER and J. F. CROW, 1972 Mutation rate and dominance of genes affecting viability in *Drosophila melanogaster*. *Genetics* **72**: 333–355.
- NUZHIDIN, S. V., E. G. PASYUKOVA and T. F. C. MACKAY, 1996 Positive association between copia transposition rate and copy number in *Drosophila melanogaster*. *Proc. R. Soc. Lond. B* **263**: 823–831.
- OHNISHI, O., 1977 Spontaneous and ethyl methanesulfonate-induced mutations controlling viability in *Drosophila melanogaster*. II. Homozygous effect of polygenic mutations. *Genetics* **87**: 529–545.
- PARDUE, M. L., O. N. DANILEVSKAYA, K. LOWENHAUPT, F. SLOT and K. L. TRAVERSE, 1996 *Drosophila* telomeres: new views on chromosome evolution. *Trends Genet.* **12**: 48–52.
- SNIEGOWSKI, P., and B. CHARLESWORTH, 1994 Transposable element numbers in cosmopolitan inversions from a natural population of *Drosophila melanogaster*. *Genetics* **137**: 815–827.
- VAURY, C., A. BUCHETON and A. PÉLISSON, 1989 The β -heterochromatic sequences flanking the I elements are themselves defective transposable elements. *Chromosoma* **98**: 215–224.
- VIEIRA, C., and C. BIÉMONT, 1996a Geographical variation in insertion site number of retrotransposon 412 in *Drosophila simulans*. *J. Mol. Evol.* **42**: 443–451.
- VIEIRA, C., and C. BIÉMONT, 1996b Selection against transposable element in *Drosophila simulans* and *Drosophila melanogaster*. *Genet. Res.* **68**: 9–15.
- VIEIRA, C., and C. BIÉMONT, 1997 412 transposition rate independent of copy number in natural populations of *Drosophila simulans*. *Mol. Biol. Evol.* **14**: 185–188.
- ZUCKERKANDL, E., and W. HENNIG, 1995 Tracking heterochromatin. *Chromosoma* **104**: 75–83.

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