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Hybrid dysgenesis-induced response to selection in *Drosophila melanogaster*

PATRICIA M. PIGNATELLI AND TRUDY F. C. MACKAY*
Institute of Animal Genetics, West Mains Road, Edinburgh EH9 3JN, Scotland

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Summary

In *Drosophila melanogaster*, the *P–M* and *I–R* systems of hybrid dysgenesis are associated with high rates of transposition of *P* and *I* elements, respectively, in the germlines of dysgenic hybrids formed by crossing females of strains without active elements to males of strains containing them. Transposition rates are not markedly accelerated in the reciprocal, nondysgenic hybrids. Previous attempts to evaluate the extent to which hybrid dysgenesis-mediated *P* transposition contributes to mutational variance for quantitative characters by comparing the responses to selection of *P–M* dysgenic and nondysgenic hybrids have given variable results. This experimental design has been extended to include an additional quantitative trait and the *I–R* hybrid dysgenesis system. The selection responses of lines founded from both dysgenic and nondysgenic crosses showed features that would be expected from the increase in frequency of initially rare genes with major effects on the selected traits. These results differ from those of previous experiments which showed additional selection response only in lines started from dysgenic crosses, and can be explained by the occasional occurrence of large effect transposable element-induced polygenic mutations in both dysgenic and nondysgenic selection lines. High rates of transposition in populations founded from nondysgenic crosses may account for the apparently contradictory results of the earlier selection experiments, and an explanation is proposed for its occurrence.

1. Introduction

Nearly 20% of the *Drosophila melanogaster* genome is composed of dispersed, moderately repeated, transposable element (TE) sequences (Rubin, 1983; Finnegan & Fawcett, 1986). These sequences can be grouped into structural categories (*copia*-like, *foldback* (*FB*), *F*, *P*, and *I*) which have structural homology to retrovirus and other TE sequences in taxa ranging from prokaryotes to mammals (Shapiro & Cordell 1982; Finnegan, 1985). In *D. melanogaster*, most 'spontaneous' visible mutations are caused by insertions of transposable elements (Rubin 1983). Genetic and molecular analyses of a number of such TE-induced mutations and their revertants has revealed an astonishing array of phenotypic effects. Insertions into coding regions or imprecise excisions extending into coding regions may both result in a null phenotype. Gene expression can be affected by an insertion in a non-coding region causing quantitative or qualitative changes in the gene products, or the developmental timing or tissue specificity of expression (Chia *et al.* 1986; Tsubota & Schedl, 1986). The phenotypic effect of an insertion depends on the exact site of insertion and the sequence of the inserted element (Rubin, 1983; Tsubota & Schedl, 1986), can be modified by the insertion of a second element at or beside the originally inserted sequence (Rubin, 1983; Engels, 1988; Mount, Green & Rubin, 1988), and regulated by unlinked loci which enhance or suppress the mutant phenotype associated with the insertion (Modolell, Bender & Meselson, 1983; Rubin, 1983; Mount, Green & Rubin, 1988).

Because TE's are so common and cause such a diverse array of phenotypes, it is reasonable to ask what their effect, if any, is on variation for quantitative traits. This can be assessed by generating new TE-induced mutations and observing their effects on metric traits. Not all TE's transpose sufficiently frequently to make experimental investigation of their effects on quantitative variation feasible, although transposition is frequent enough to cause differentiation between strains and between individuals within strains in the sites they occupy (Montgomery & Langley, 1983; Ronsseray & Anxolabéhère, 1986;

* Corresponding author. Department of Genetics, Box 7614, North Carolina State University, Raleigh, North Carolina 27695-7614, USA.

Leigh Brown & Moss, 1987; Montgomery, Charlesworth & Langley, 1987). However, some families of TE do transpose at high rates when individuals of strains containing them are crossed to strains without them – the *P* (Kidwell, Kidwell & Sved, 1977; Bingham, Kidwell & Rubin, 1982). *I* (Bucheton & Picard, 1978; Bucheton *et al.* 1984), and possibly *hobo* (Blackman *et al.* 1987; Yannopoulos *et al.* 1987) elements of Drosophila.

Movement of *P* and *I* elements is associated with the *P–M* and *I–R* systems of hybrid dysgenesis, respectively. The term 'hybrid dysgenesis' (Kidwell, Kidwell & Sved, 1977) refers to the aberrant phenotypic and genetic properties displayed by the F_1 hybrids of such interstrain crosses, which include high frequencies of lethal, visible and chromosomal mutations and characteristic temperature-sensitive sterility. In the *P–M* and *I–R* systems, hybrid dysgenesis occurs in the progeny of $M♀♀ \times P♂♂$ and $R♀♀ \times I♂♂$ crosses, but not in the F_1 of the reciprocal, nondysgenic $P♀♀ \times M♂♂$ and $I♀♀ \times R♂♂$ crosses (for reviews see Bregliano & Kidwell, 1983 and Engels, 1988). The *P* and *I* elements are families of intact elements and their various deletion derivatives (O'Hare & Rubin, 1983; Bucheton *et al.* 1984). The relationship between a strain's ability to induce or repress dysgenesis and its molecular complement of *P* and *I* elements in terms of their copy numbers, ratios of defective to intact elements, sequences and genomic locations has not been fully determined. Although all of the above factors are likely to be important, it would be fair to generalize that high rates of transposition and accompanying hybrid dysgenesis occurs in each system when strains bearing complete *P* or *I* elements are crossed to strains containing no such elements or only defective elements with no repressor activity.

P–M dysgenic crosses have been utilized successfully to induce mutations at many known loci (for a review see Kidwell, 1986). Mackay (1984, 1985) reasoned that mutations at quantitative trait loci could be induced in the same manner, and proposed that a comparison of the responses to selection for a quantitative trait from dysgenic ($M♀♀ \times P♂♂$) and nondysgenic ($P♀♀ \times M♂♂$) hybrids would give an indication of the magnitude of *P*-element-induced mutational variance for the selected trait. Replicate dysgenic and nondysgenic populations were selected for 16 generations for high and low abdominal bristle score. The dysgenic selection lines exhibited increased responses to selection, heritabilities, and phenotypic variances compared to the lines initiated from nondysgenic crosses. This was interpreted as evidence of *P*-element-induced mutational variance affecting abdominal bristle score. The *P*-induced mutational variance ($V_m = 1{\cdot}8$) and mutational heritability ($h_m^2 = 0{\cdot}35$) for abdominal bristle score were estimated from the average difference in additive genetic variance between the dysgenic and nondysgenic selection lines. It would take an accumulated dose of 750000 r X-rays to generate this level of genetic variation, which is of the same order as that found in natural populations for this trait. Similar levels of mutational variation for abdominal and sternopleural bristle score, and for female productivity, were found when variation for these traits among homozygous second chromosomes which had accumulated *P* elements was compared to variation among control, *P*-free, second chromosomes (Mackay, 1987). In addition, *P* element mutagenesis has been shown to have deleterious effects on homozygous fitness (Fitzpatrick & Sved, 1986; Mackay, 1986) and viability (Yukuhiro, Harada & Mukai, 1985; Mackay, 1986) of second chromosomes passed through dysgenic crosses.

However, other experiments designed to estimate *P*-induced mutational variance for malathion resistance (Morton & Hall, 1985) and abdominal bristle score (Torkamanzehi, Moran & Nicholas, 1988) from *P–M* dysgenic and nondysgenic crosses have yielded less clear-cut resuls. In these experiments the selection lines founded from the nondysgenic crosses showed greater average responses to selection. Mackay (1986, 1987) also found that second chromosomes passed through nondysgenic crosses accumulated nearly equal amounts of mutational variance to those passed through an initial dysgenic cross. An interpretation which accounts for these contradictory results is that *P*-element transposition occurs equally frequently in populations descending from both reciprocal crosses. It this interpretation is correct, *P*-induced mutations affecting the selected trait would occur regardless of the direction of the initial interstrain cross, and only those which have major effects on the selected trait would be detectable from responses to selection. Consequently there would be great variation in response of replicate populations to selection.

Because of the potential utility of TE-induced mutagenesis for elucidating the nature of variation for quantitative traits at the genetic and molecular levels (Mackay, 1985, 1988), it is important to resolve any questions about the magnitude of their polygenic mutational effects. Therefore, we have extended observations on the responses to selection of dysgenic and nondysgenic hybrids to another quantitative trait, sternopleural bristle number, and to the *I–R* system of hybrid dysgenesis. Our results are consistent with an interpretation of the occurrence in some selection lines of TE-induced mutations of large effect on the selected trait, regardless of the direction of the initial interstrain cross. An explanation for the occurrence of transposition in populations descending from nondysgenic interstrain crosses is proposed, based on our current knowledge of the regulation of transposition of *P* elements.

2. Materials and methods

(i) *Drosophila strains*. The following strains were used as parents to found selection lines: Harwich (*IP*), Canton-S (*IM*), Luminy (*IQ*), *se* F_8 (*RM*). (The letters in brackets are the dual strain designations in the *I–R* and *P–M* systems of hybrid dysgenesis, respectively.) All strains were kindly given to us by M. G. Kidwell.

(ii) *Selection lines*. Two replicates of divergent artificial selection lines for abdominal bristle score (number of bristles on the most posterior sternite) and sternopleural bristle score (sum of scores of left and right sternopleural plates) were established from the progeny of reciprocal crosses of the following strains. (*a*) Harwich (*IP*) and Canton-S (*IM*), at 20 °C. Selection for sternopleural bristle score only was performed from these crosses, as the results of selection for abdominal bristle score from inter-Harwich and Canton-S crosses have been reported by Mackay (1984, 1985). Mainly *P*-element transposition is expected from these crosses. (*b*) Canton-S (*IM*) and *se* F_8 (*RM*), at 25 °C. Mainly *I*-element transposition is expected from these crosses. (*c*) Luminy (*IQ*) and *se* F_8 (*RM*), at 25 °C. Some transposition may occur from crosses of *Q* (weak *P*) and *M* strains, so these crosses weakly test for any interaction between the two systems. It was not possible to use progeny of crosses of Harwich (*IP*) and *se* F_8 (*RM*) for this test, because no temperature was found at which the doubly dysgenic hybrids were fertile.

Crosses of *RP* and *RM* strains were not constructed because *RP* strains had not been found in natural populations at the time the experiment was initiated (Kidwell, 1983), although strains with the *RP* cytotype have subsequently been synthesized (Kidwell & Sang 1986; Anxolabéhère *et al.* 1987).

All 40 lines were maintained with selection for 10 generations. Each generation 50 males and 50 females were scored for the appropriate bristle trait, and the 10 most extreme individuals of each sex were selected. Subsequent to Generation 10 the lines were maintained in discrete generations without selection in bottle populations. All cultures were maintained on cornmeal-agar-molsses medium.

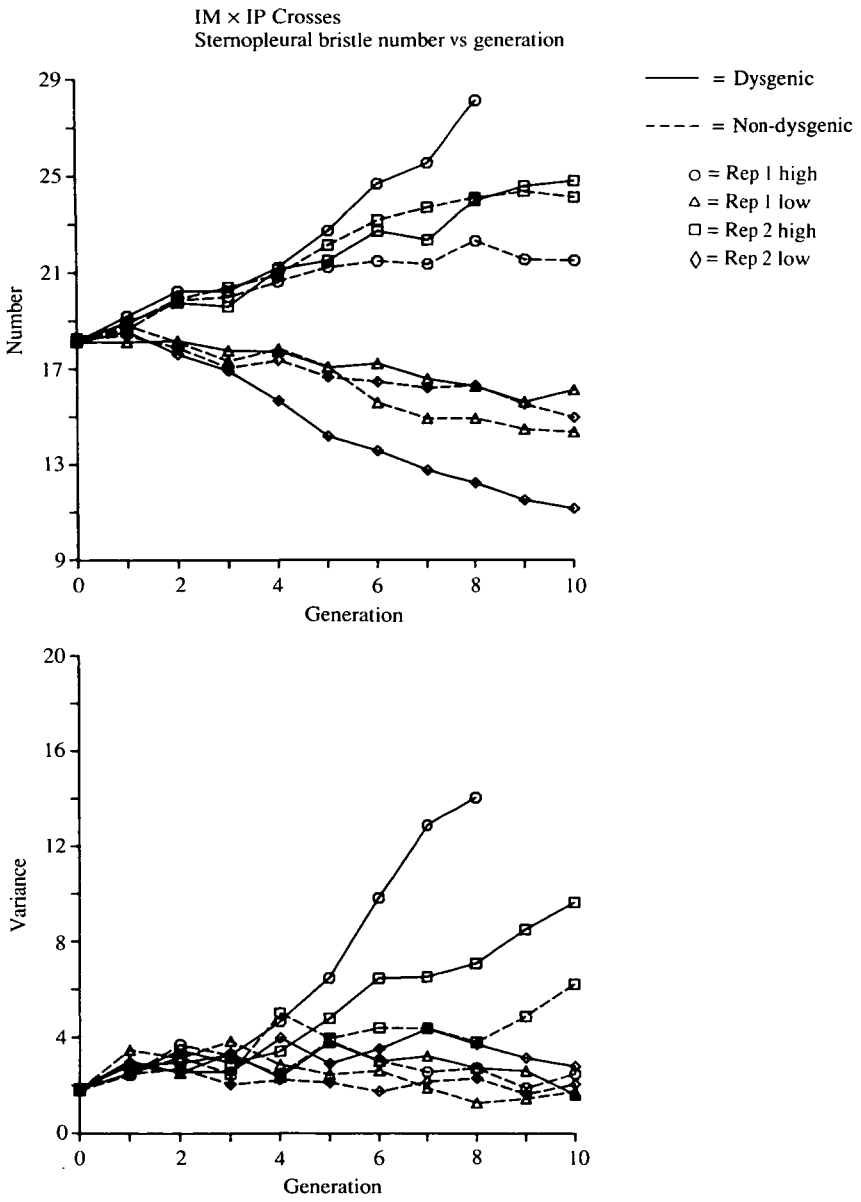
3. Results

Generation means and variances of the forty selection lines are presented in Figures 1–5. Because of the potential contribution to response by transposable element-induced mutations affecting bristle score, note that new mutations with a large effect on a quantitative trait arising during the course of selection will be expected to cause the following modifications to the usual pattern of response to selection. (1) There will be sudden 'jumps' in response. (2) Accelerated response will be accompanied by a corresponding increase in genetic (and consequently phenotypic) variance in the line which harbors the mutant allele. Variance may subsequently decline if the mutant allele becomes fixed in the selected line, or may remain elevated if it continues to segregate (if, for example, the mutant homozygote has a deleterious effect on fitness). (3) Asymmetries in response to divergent selection may be observed. (4) There will be increased variance in response of replicate lines to selection, compared to that expected from drift and sampling given the additive variance segregating in the base population.

Are any of these atypical features apparent from the selection responses detailed in Figures 1–5? Note that there are several clear examples of accelerated resonse: one high and one low $IM \times IP$ dysgenic sternopleural bristle line; one high $RM \times IM$ nondysgenic sternopleural bristle line; and one high $RM \times IQ$ dysgenic and one low $RM \times IQ$ nondysgenic abdominal bristle line. For several of these lines the large responses were accompanied by increases in phenotypic variance and heritability (see Tables 2–4 for details).

A general test of (4) is to consider together all four replicates of divergent selection from the reciprocal crosses of a particular pair of lines, and ask whether the mean and variance of response of later gnerations are predicted adquately from parameters estimated from the early generations of selection. Input of mutational variance affecting the selected trait will cause the observed mean and variance of response to deviate from that expected given the parameters estimated from the base population. This analysis is given in Table 1. For each pair of divergent selection lines, heritability (h^2) was estimated from the regression of cumulated response on cumulated selection differential from Generations 1 (the F_2 of the cross) to 3, inclusive. The mean of the four h^2 estimates from the two replicates of both reciprocal crosses is the value given in the table. The estimate of phenotypic variance (V_p) used is that from Generation 1, pooled over all eight lines. The observed response (R) to selection was calculated for each line as the difference in mean performance between Generation 10 and Generation 1 ($-(R_{10}-R_1)$ for the low lines), and the observed mean and variance of response determined from the individual line values. (Responses were calculated from the mean score at Generation 8 for two lines that were lost at Generation 9.)

The expected response to selection per generation is the standard $R_e = ih^2(V_p)^{\frac{1}{2}}$ (Falconer 1981), where i is 1·372 for 10 selected from 50 scored of each sex, and h^2 and V_p are calculated as explained above. The predicted cumulated response at Generation 10 is then $9R_e$, assuming h^2 and V_p are constant. The predicted cumulated response to Generation 8 is $7R_e$ for the two lines that were subsequently lost. The expected variance of response from drift and sampling is approximately $2F_tV_a + (V_{p_t} - \frac{1}{2}V_{a_t})/M$ (Hill 1977), where F_t is the inbreeding coefficient at time t, V_a is the additive genetic variance segregating in the base population, V_{p_t} and V_{a_t} are the phenotypic and additive genetic variances, respectively, of a particular selection



Figures 1–5. Generation means and phenotypic variances of selection lines established from dysgenic (—) and nondysgenic (– – –) crosses. High (○) and low (△) selection lines, respectively, of the first replicate; (□) and (◇) high and low selection lines, respectively, of the second replicate.

Figure 1. *IM* × *IP* crosses, selection for sternopleural bristle number.

line at time t, and M is the number of individuals scored per line each generation. For lines maintained with 10 pairs of parents per generation, F_{10} is 0·22, assuming that the effective size is equal to the actual number of parents. V_a was estimated from h^2V_p, and V_p and V_a were assumed to remain roughly constant over 10 generations, in the absence of mutation.

Observed and expected mean responses agree moderately well (with the exception of the sternopleural bristle selection lines from progeny of Canton-S (*IM*) and *se* F_8 (*RM*) crosses). However, the observed variance in response consistently exceeds that expected from drift and sampling by more than a factor of 20. Even if the effective population size is half the actual population size, the expected variances of response exceed those observed by a factor of 12. (It is not possible to compare this magnitude of excess of observed over expected variance of selection response to cases when dysgenic crosses are not involved, as no such analyses have been published.)

A test of whether the response of a particular line is significantly greater than the mean response of all lines derived from a given cross is provided by the statistic $(R_i - R)/(E(V(R))(1 - 1/n))^{\frac{1}{2}}$, which is approximately a standard normal deviate. R_i is the observed response to Generation t of replicate i, R the observed average response to Generation t of all n replicates, and $E(V(R))$ the expected variance of response among replicate lines at Generation t. (We thank W. G. Hill for the derivation of this test).

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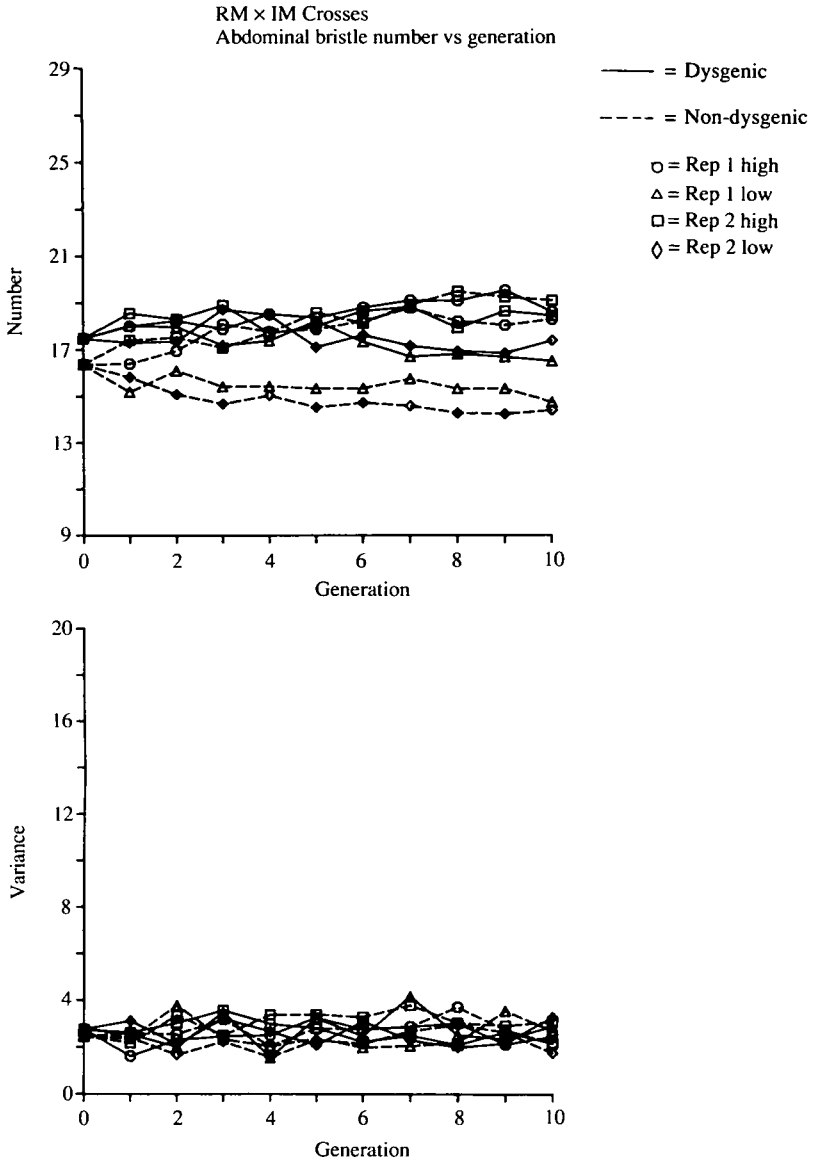

Figure 2. *RM* × *IM* crosses, selection for abdominal bristle number.

Table 1. *Comparison of observed (O) and expected (E) mean and variance of response (R) to Generation 10 to selection for abdominal (A) or sternopleural (S) bristle score from replicated reciprocal interstrain crosses. Heritability (h^2), phenotypic variance (V_p), and observed and expected mean and variance of response are calculated as described in the text.*

Cross	Bristle trait	h^2 (G1–3)	V_p (G1)	Mean *R* (G10)		Variance of *R* (G10)	
				O	*E*	*O*	*E*
IP, IM	A[a]	0·262	4·31	6·50	6·73	10·13	0·535
	S	0·195	2·75	5·04	3·98	5·49	0·260
IM, RM	A	0·023	2·37	0·92	0·45	0·66	0·048
	S	0·327	2·84	3·65	6·81	4·69	0·433
IQ, RM	A	0·169	3·46	3·67	3·89	11·56	0·289
	S	0·156	1·67	2·35	2·48	1·84	0·126

[a] Calculated from data of Mackay (1985).

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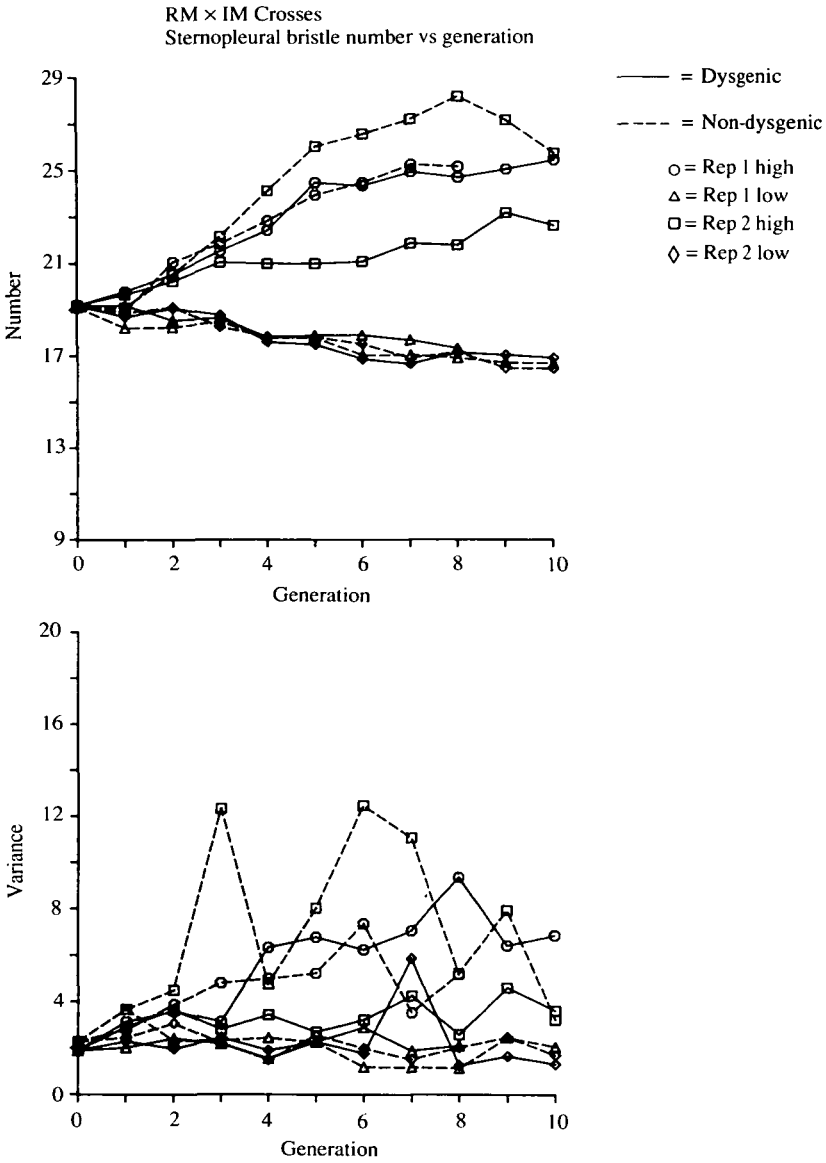

Figure 3. *RM* × *IM* crosses, selection for sternopleural bristle number.

Values of R and $E(V(R))$ are given in Table 1. The results of this test applied to all forty selection lines, as well as the selection lines of Mackay (1985), are presented in Tables 2–4. Individual line responses were judged conservatively to be significantly outside the range expected from drift and sampling if the test statistic was greater than 2 (a one-tailed test). Tables 2–4 also document heritabilities and phenotypic variances for each line separately. Heritabilities were calculated from regression of cumulated response on cumulated selection differential over the entire period of selection, and phenotypic variances were averaged from G1 to G10. Note that the lines originaly pinpointed as being deviant from a cursory examination of the selection responses of Figures 1–5 are all significant on the basis of this test; in addition, several other lines were found to have greater than expected responses.

If the data of Mackay (1985) for abdominal bristle selection from *IP* and *IM* crosses are included, there are a total of 19 lines for which significant increased responses to selection are observed. In each case the increase in response is associated with either increased phenotypic variance or heritability, compared to the base population estimates, and often both h^2 and V_p are elevated. An additional three lines from the *IP* and *IM* crosses showed substantial increases in phenotypic variance of the selected trait, but did not exhibit significant increased response to selection. Given the transpositionally unstable nature of the parental strains, a reasonable interpretation of these data is that transposable element-induced mutations with a large effect on the selected trait have occurred in some lines, and have contributed to the responses to selection.

The overall frequency of selection lines founded from the interstrain crosses performed here which show increased responses to selection (14/40 = 35%)

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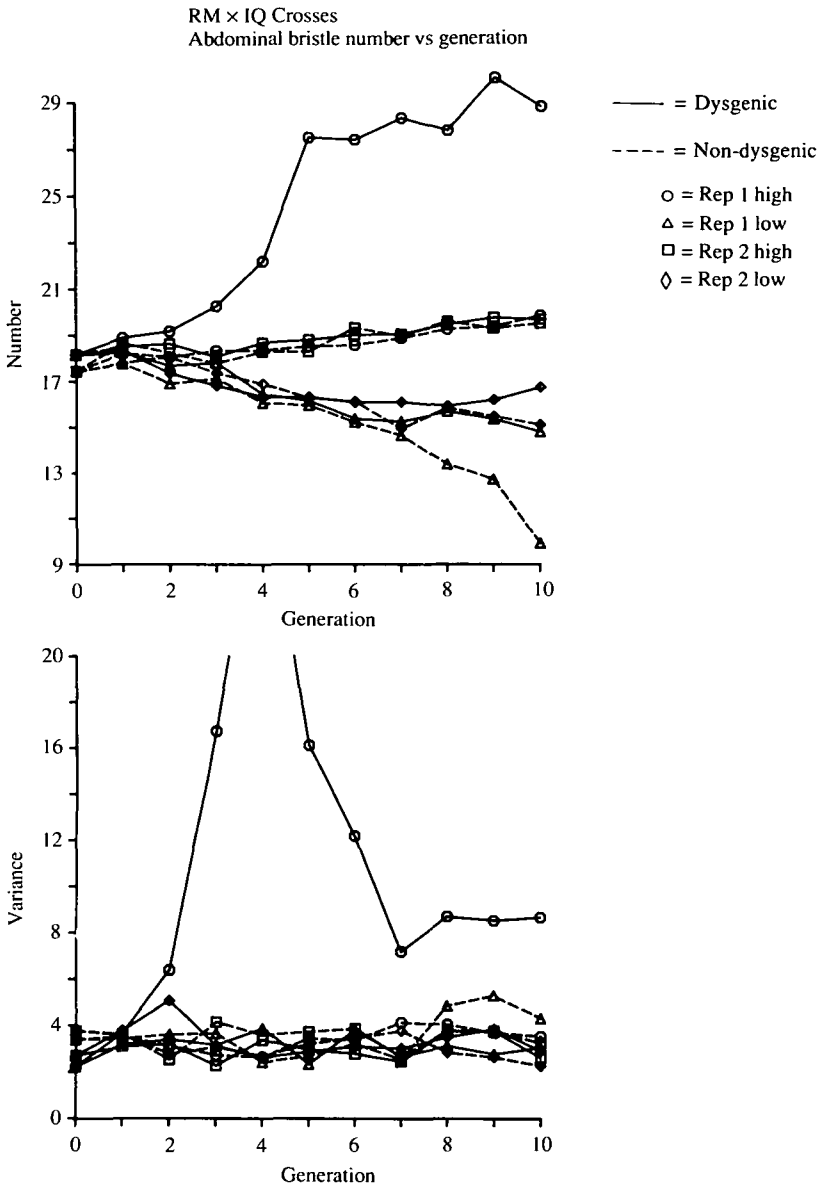

Figure 4. *RM* × *IQ* crosses, selection for abdominal bristle number.

is in agreement with that from Mackay (1985) (5/16 = 31%). However, the instances of increased response, phenotypic variance, and heritability were specifically associated with lines founded from dysgenic hybrids in the experiment of Mackay (1985), but this is clearly not always the case. Of the 14 lines which showed increased response in this experiment, 6 were from dysgenic hybrids, and 8 from nondysgenic hybrids. The two bristle traits appear to be equally susceptible to TE mutagenesis, as judged by the frequency of lines derived from interstrain crosses selected for each which gave increased responses to selection. Similarly, transposition of *I* elements seems as effective as transposition of *P* elements in generating bristle mutations which contribute to selection response.

4. Discussion

The results presented above extend the observations of Mackay (1985) on selection response for abdominal bristle score from P × M and M × P strain hybrids to another bristle trait, sternopleural bristle count, and to selection from hybrids established by I × R and R × I interstrain crosses. Lines established by selection from such crosses frequently show sudden 'jumps' in response and increases in heritability and phenotypic variance over a period of only 10 generations. From the data avaiable to date, roughly 1 in 3 replicate selection lines initiated from P × M, M × P, I × R and R × I interstrain crosses behave in this way (Mackay, 1985; Torkamanzehi, Moran & Nicholas, 1988; this report), regardless of the direction of the original interstrain cross. Consequently, there is greater variation in response to selection of such replicated

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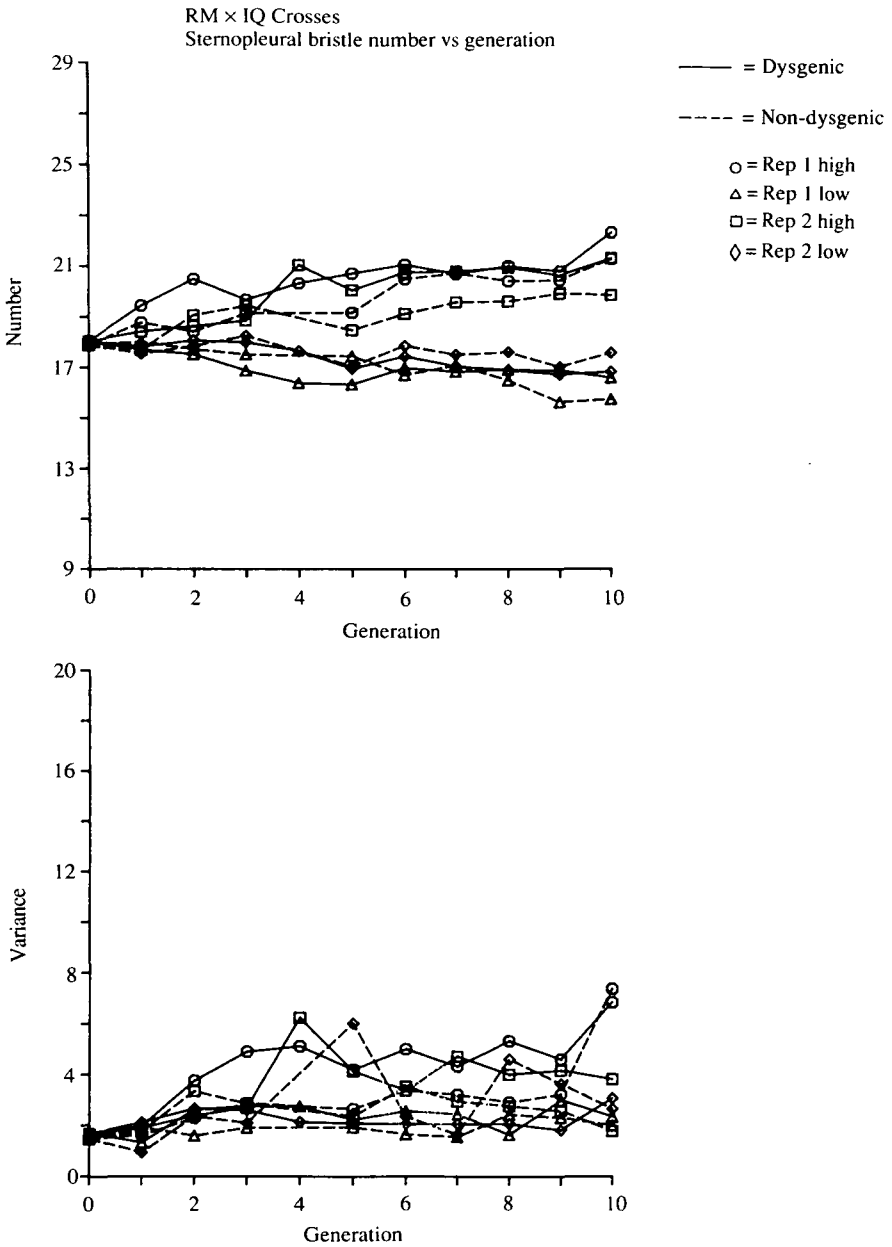

Figure 5. *RM* × *IQ* crosses, selection for sternopleural bristle number.

selection lines than would be expected from drift and sampling variance, given the genetic and phenotypic parameters of the base population, which is often apparent as a marked asymmetry in response to divergent selection. These features are not typical of early response to artificial selection (see examples in Falconer, 1981), but are what would be expected from the segregation of initially rare alleles with major effects on the selected traits (Frankham & Nurthen, 1981). Since the transposition rate of *P* (or *I*) elements is known to be markedly accelerated in such interstrain crosses (Bingham, Kidwell & Rubin, 1982), the irregular selection responses have been interpreted therefore to be caused by increases in frequency of TE-induced mutations with major effects on the selected traits. Such mutations may arise from the novel insertion of an element at or near a locus which affects bristle production, from the imprecise excision of an element already residing near a bristle locus, or from chromosomal rearrangements involving bristle loci, the breakpoints of which are the sites of residence of elements. Mutations arising from the excision of elements may be expected to be strain-specific, as the chromosomal location of elements is highly variable between (and within) strains.

The interpretation of aberrant selection responses from reciprocal interstrain crosses in terms of transposable element-induced mutational variation affecting the selected quantitative trait requires enhanced transposition rates of *P* (or *I*) elements in the progeny of nondysgenic hybrids. It is clear that *P* (or *I*) elements are active in the germline of dysgenic hybrids. The estimated transposition rate of *P* elements following a dysgenic cross is 15 elements/haploid

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Table 2. *Response (R) to selection at Generation 10, realized heritability (h^2) and phenotypic (V_p) and additive genetic (V_a) variance of selection lines established from inter-Harwich (IP) and Canton-S (IM) hybrids. Those responses marked with an asterisk (*) were found to be significantly increased over the average response on the basis of the test described in the text. Those marked with a cross (x) only show increased phenotypic variance over that observed in the base population.*

	IM♀♀ × *IP*♂♂		*IP*♀♀ × *IM*♂♂	
Bristles	High	Low	High	Low
		Replicate 1		
Abdominal[a]				
R	12·81*	−11·87*	3·40	−4·01
h^2	0·33	0·24	0·13	0·20
V_p	12·74	14·84	4·14	3·50
V_a	4·20	3·56	0·54	0·70
		Replicate 2		
R	6·67[x]	−9·44*	3·90	−5·15
h^2	0·21	0·22	0·16	0·22
V_p	7·70	13·97	4·02	4·17
V_a	1·62	3·08	0·64	0·92
		Replicate 3		
R	8·00*	−6·90[x]	3·59	−4·34
h^2	0·25	0·19	0·14	0·17
V_p	6·65	9·98	3·99	3·53
V_a	1·66	1·90	0·56	0·60
		Replicate 4		
R	5·74	−10·75*	3·22	−4·20
h^2	0·18	0·35	0·14	0·15
V_p	5·52	8·13	4·07	3·86
V_a	0·99	2·84	0·57	0·58
		Replicate 1		
Sternopleural				
R	8·96*	−2·02	2·87	−4·47
h^2	0·38	0·12	0·13	0·26
V_p	7·11	2·80	2·82	2·46
V_a	2·70	0·34	0·37	0·64
		Replicate 2		
R	5·88[x]	−7·41*	5·26	−3·44
h^2	0·21	0·35	0·24	0·18
V_p	5·52	3·23	4·07	2·13
V_a	1·16	1·13	0·98	0·38

[a] Data of Mackay (1985).

Table 3. *Response (R) to selection at Generation 10, realized heritability (h^2) and phenotypic (V_p) and additive genetic (V_a) variance of selection lines established from inter-Canton-S (IM) and se F_8 (RM) hybrids. Those responses marked with an asterisk (*) were found to be significantly increased over the average response on the basis of the test described in the text.*

	RM♀♀ × *IM*♂♂		*IM*♀♀ × *RM*♂♂	
Bristles	High	Low	High	Low
		Replicate 1		
Abdominal				
R	0·57	−1·57*	1·86*	−0·48
h^2	0·05	0·09	0·07	0·03
V_p	2·53	2·71	2·73	2·52
V_a	0·13	0·24	0·19	0·08
		Replicate 2		
R	−0·15	0·08	1·66*	−1·45*
h^2	0·00	0·04	0·10	0·07
V_p	2·65	2·59	3·08	2·22
V_a	0·00	0·10	0·31	0·16
		Replicate 1		
Sternopleural				
R	5·67*	−1·88	6·25*	−1·55
h^2	0·22	0·13	0·34	0·04
V_p	5·87	2·14	4·70	2·08
V_a	1·29	0·28	1·60	0·08
		Replicate 2		
R	2·97	−1·80	6·66*	−2·43
h^2	0·13	0·16	0·30	0·17
V_p	3·56	2·25	7·30	2·13
V_a	0·46	0·36	2·19	0·36

genome/generation, (averaging the male and female X chromosome transposition rates observed by Bingham, Kidwell & Rubin (1982) and multiplying by five as the X chromosome is roughly 20% of the haploid genome). *P* (or *I*) elements are repressed in the germline of reciprocal, nondysgenic hybrids (reviewed by Bregliano & Kidwell, 1983). Engels (1979) proposed the cytotype model of *P* element regulation to account for the observations of genetic segregation of hybrid dysgenesis determinants coupled with the reciprocal cross effect. In this model *P* elements are quiescent in the *P* cytotype and active in the *M* cytotype, so transposition is under the short-term control of the maternal cytoplasm and the longer term control of the chromosomal complement of *P* elements. The regulation of transposition of *I* elements has similar properties (Picard 1976; Bucheton & Picard, 1978).

Engels (1979) has shown that while F_1 females of a dysgenic cross are themselves *M* cytotype, their progeny obtained by crossing to *P* strain males are a mixture of *M* and *P* cytotypes. Hybrids of nondysgenic crosses are not themselves uniformly *P* cytotype, and their progeny obtained by a further cross to *P* males are again a mixture of *P* and *M* cytotypes. These observations were made on backcrosses of dysgenic and nondysgenic hybrid females to *P* males, but would be expected to be qualitatively similar for random mating within lines started from initial dysgenic and nondysgenic crosses, as practiced in the selection experiments. Inasmuch as *P* element transposition occurs when *M* cytotype females are crossed to *P* cytotype males, these results indicate the potential for appreciable transposition in the progeny of nondysgenic females.

How can Engels' (1979) observations on the segregation of cytotype, and our proposal that dysgenic crosses and hence *P* element transposition occur in selection lines started from nondysgenic

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Table 4. *Response (R) to selection at Generation 10, realized heritability (h^2) and phenotypic (V_p) and additive genetic (V_a) variance of selection lines established from inter-Luminy (IQ) and se F_8 (RM) hybrids. Those responses marked with an asterisk (*) were found to be significantly increased over the average response on the basis of the test described in the text.*

	$RM♀♀ + IQ♂♂$		$IQ♀♀ + RM♂♂$	
Bristles	High	Low	High	Low
		Replicate 1		
Abdominal				
R	10·01*	−3·47	1·63	−7·84*
h^2	0·30	0·20	0·08	0·32
V_p	11·65	3·10	3·38	3·56
V_a	3·50	0·62	0·27	1·14
		Replicate 2		
R	1·16	−1·61	0·87	−2·76
h^2	0·07	0·08	0·07	0·17
V_p	2·99	3·35	3·45	2·99
V_a	0·21	0·27	0·24	0·51
		Replicate 1		
Sternopleural				
R	3·90*	−1·12	3·68*	−2·66
h^2	0·11	0·03	0·14	0·15
V_p	4·59	2·35	3·26	1·90
V_a	0·50	0·07	0·46	0·29
		Replicate 2		
R	2·91	−1·00	3·21*	−0·30
h^2	0·15	0·07	0·17	0·02
V_p	3·73	2·25	2·64	2·90
V_a	0·56	0·16	0·45	0·06

hybrids, be explained given our current understanding of the regulation of *P*-element transpostion? It is known that: (1) Strong *P* strains contain 30–50 *P*-element copies. Although the sites of residence of *P* elements vary among strong *P* strains, and among individuals within strains, their copy number per individual is relatively constant (Shrimpton, Mackay & Leigh Brown, unpublished data), which implies regulation of individual copy number. (2) The population of *P* elements within a strong *P* strain are homologous in sequence but heterogenous in structure, comprising full-sized 2·9 kb elements (O'Hare & Rubin, 1983) and various sizes of nonautonomous deletion-derivatives (O'Hare & Rubin, 1983; Karess & Rubin, 1984). The actual relative proportions of full-sized to incomplete elements probably varies from strain to strain, but data on this are scarce. Data of O'Hare & Rubin, (1983) and Daniels *et al.* (1987) indicated approximately one-third of the elements of the strong *P* strains studied were potentially complete. (3) Only complete elements encode transposase (Karess & Rubin, 1984; Rio, Laski & Rubin, 1986); they are required to produce *P* activity, but alone are insufficient to confer *P* cytotype (Karess & Rubin, 1984; Daniels *et al.* 1987; W. Engels & C. Preston, unpublished data, quoted in Engels, 1988). (4) Nonautonomous elements are implicated in the regulation of *P* activity. Strains vary in their phenotypic properties as judged by ability to induce *P* activity and ability to regulate *P* activity, depending on their absolute numbers of complete and nonautonomous elements, their ratio of nonautonomous to autonomous elements, and the structure of their nonautonomous elements (Todo *et al.* 1984; Sakoyama *et al.* 1985; Black *et al.* 1987; Boussy *et al.* 1988). Regulation by nonautonomous elements may be general, by 'transposase titration' (Simmons & Bucholz, 1985). In addition, several specific deletion derivatives which presumably produce repressor molecules have been identified (Nitasaka, Mukai & Yamazaki, 1987; Black *et al.* 1987; H. Robertson & W. Engels, unpublished data, reported in Engels, 1988). (5) The position of both autonomous and nonautonomous *P* elements in the host genome affects their ability to transpose (Robertson *et al.* 1988) and to regulate transposition (H. Robertson & W. Engels, unpublished data, reported in Engels, 1988). There appear to be therefore several separate mechanisms through which the regulation of *P* activity can be achieved.

When strong *P* and *M* strains are crossed, the autosomal copy number is immediately reduced by half and the *X* copy number by one or two thirds, depending on the direction of the cross. There will be segregation in the F_2 (and the F_1 if the parent *P* strain is not inbred) and subsequent generations for the absolute numbers of autonomous and nonautonomous *P* elements and their ratio. The system(s) of regulation adopted by the parental *P* strain are disrupted, and must be re-established. For the case of a dysgenic cross, it is clear that the *M* cytotype can be maternally transmitted through at least 4 generations, and that the *P* cytotype may be reached by 10 generations (Engels, 1979; Kidwell, Novy & Feeley, 1981; Kiyasu & Kidwell, 1984). One aspect of the cytotype switch from *M* to *P* must therefore involve an increase in *P* copy number through replicative transposition, and perhaps the generation of specific regulatory deletion derivatives as well. Transposition rates will continue to be high until regulation of *P* activity is reestablished.

The situation for populations descending from nondysgenic inter-*P* and -*M* strain crosses is less clear. The populations of Kidwell, Novy & Feeley (1981) and Kiyasu & Kidwell (1984) retained their *P* cytotype. However, Engels (1979) found that although *P* activity was repressed in the germline of most nondysgenic females from an interstrain cross, about 40% were themselves *M* cytotype. Sved (1987) has shown that there is no maternal inheritance of *P* cytotype (in contrast to the strong maternal inheritance of *M* cytotype); *P* cytotype depends on the presence of *P* elements in the genome. Therefore the cytotype of F_2 individuals from a nondysgenic cross will depend on

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their chromosomal complement of autonomous and nonautonomous *P* elements. Because of the segregation of numbers of complete and defective elements and the reduction in *P* copy number caused by crossing to an *M* strain, some F_2 individuals may be unable to repress *P* activity (*M* cytotype) while others may retain the ability to induce *P* activity (which only requires autonomous *P* elements). This creates the potential for dysgenic crosses and associated high transposition rates in the randomly mating F_2 and later generations following a nondysgenic interstrain cross. Because the *M* cytotype does show true maternal inheritance and the switch from *M* to *P* cytotype requires several generations, dysgenesis and transposition rates could remain high for several generations until *P* regulation is established. The regulation of *I*-element activity is apparently equally complex (Bucheton & Picard, 1978).

There has been indirect evidence for enhanced transposition rates following nondysgenic interstrain crosses, based on inferred high polygenic mutation rates. These observations can be readily accounted for by the above proposal. Mackay (1985) found high frequencies of lethal and deleterious second and third chromosomes segregating in selection lines started from both dysgenic and nondysgenic *P–M* crosses that were not present in the parental *P* and *M* strains, although only the lines founded from dysgenic crosses exhibited obvious accelerated responses to selection. When the experimental design of Mackay (1984, 1985) was repeated by Torkamanzehi, Moran & Nicholas (1988), only one of four replicate selection lines showed features which could be attributed to *P*-element-induced mutations affecting the selected trait, and this was a 'nondysgenic' selection line. This report further extends observations on selection lines started from initially dysgenic and nondysgenic crosses, and finds that lines showing larger than expected responses to selection are as likely to come from a nondysgenic as a dysgenic replicate. Mackay (1986, 1987) showed that *M*-strain second chromosomes passed through one dysgenic and one nondysgenic interstrain cross, followed by eight nondysgenic backcross generations to a strong *P* strain, differed very little for *P*-induced mutational variation for six quantitative traits, as judged relative to control *M* second chromosomes that had not been contaminated with *P* elements. Direct evidence that transposition occurs following nondysgenic as well as dysgenic interstrain croses is from *in situ* hybridization analysis of the selection lines of Mackay (1985) (Shrimpton, Mackay & Leigh Brown, unpublished data). Over 1300 independent transposition events wre observed among the lines, and new *P*-element sites were equally common in dysgenic and nondysgenic replicates. Given the high transposition rates in all lines it was clearly coincidental that the selection responses described by Mackay (1984, 1985) were consistently larger among the dysgenic lines than the nondysgenic lines, and just as clearly this was an atypical result.

P- and *I*-transposable elements in Drosophila are potent inducers of polygenic mutations, as judged by the magnitude of their mutational effects and the high frequency with which they are generated. It is feasible therefore to use transposable element mutagenesis in this species to identify quantitative trait loci and study them at the molecular level, and to determine the spectra of direct and pleiotropic TE-induced mutant effects for quantitative traits (Mackay, 1988). However, the method of generating mutations through dysgenic interstrain crosses and selecting the progeny for extreme expression of a quantitative trait is limited to detecting polygenic mutations which have large effects on the selected trait, because TE-induced mutations have to be detected against the segregating genetic background caused by crossing different strains. Control selection lines with the same segregating background but without enhanced transposition rates cannot be constructed using reciprocal, nondysgenic interstrain crosses because transposition is apparently only repressed for one generation. More elaborate mutagenesis procedures designed to introduce a small number of stable *P* insertions into an originally *P*-free isogenic genome promise to be rather more informative (Mackay, 1988).

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