Genet. Res., Camb. (1970), 15, *pp.* 43–53
Printed in Great Britain

Parental influence on *X*-autosome translocation-induced variegation in the mouse

BY B. M. CATTANACH AND J. N. PEREZ
City of Hope Medical Center, Department of Biology, Duarte, California, U.S.A.

(*Received* 3 *July* 1969)

SUMMARY

Females heterozygous for the *T(1; X)Ct* *X*-autosome translocation tend to have lower levels of *c*-variegation when their rearranged *X* is inherited from the father rather than from the mother. The difference is not due to a maternal effect. It is postulated that a paternal or parental-source effect, such as that found to modify position effect variegation in *Drosophila*, is operating but the possibility that a bias in the inactivation of the maternal and paternal *X* chromosomes is responsible cannot be ruled out.

1. INTRODUCTION

The variegation associated with the mouse *X*-autosome translocations (Cattanach, 1961*a*; Russell & Bangham, 1959, 1961) appears to be dependent upon the *X*-inactivation process (Lyon, 1961), for it is not found in the hemizygous male (X^TY) or single-X female (X^TO) but only in the heterozygous female (X^TX) or the exceptional male (X^TXY) (Cattanach, 1961*a*, *b*). Two mechanisms are considered to be responsible. It is thought that most of the variegation is due to the inactivation of the rearranged autosomal genes in those cells in which the rearranged *X* (X^T) is in its inactive, heterochromatic condition. The random inactivation of one or the other *X* thus gives rise to a variegated phenotype for the rearranged autosomal genes. A second source of variegation also exists, however. This is thought to be analogous to the *V*-type position effects described in *Drosophila* (see reviews by Baker, 1968; Lewis, 1950). Suppression of activity of the rearranged autosomal genes does not always follow X^T inactivation, and the more remote the autosomal locus from the break point the less susceptible it is to the inactivating influence of the heterochromatic *X*, i.e. there is a 'spreading effect' (Cattanach, 1961; Russell, 1963).

Although *X*-inactivation appears to be a random process, the mechanism causing the *Drosophila*-type position effect variegation is under genetic control (Cattanach & Isaacson, 1965, 1967). Located in the *X* chromosome is a controlling element which is closely linked to the *T(1; X)Ct* break point and alternative 'states' of the element have been found which permit different levels of *T(1; X)Ct* position effect variegation. The influence of the 'states' is not limited to the position effect variegation, however. The heterozygous phenotypes of at least two *X*-linked genes are similary modified and it would therefore seem probable that the

primary effect is upon the inactivation of the *X* itself (Cattanach, Pollard & Perez, 1969).

The present communication reports a second factor which modifies the variegation associated with the *T(1; X)Ct X*-autosome translocation. A small but consistent difference has been found between the levels of variegation of females derived from reciprocal crosses and the data indicate that this is not due to some effect of the mother's genotype or cytoplasm but to whether the source of the X^T was maternal or paternal. It is not clear whether the responsible mechanism operates upon the randomness of the *X*-inactivation process or upon the position effect variegation.

2. METHODS AND MATERIALS

The translocation, *T(1; X)Ct*, is one in which a piece of linkage group I bearing the wild type alleles of *pink-eye* (*p*) and *albino* (*c*) has been inserted into the *X*-chromosome (Cattanach, 1961*a*; Ohno & Cattanach, 1962). In the experiments to be described all the translocation-bearing animals carry the chromosomally unbalanced duplication form, *Dp(1; X)Ct*, of the rearrangement and *albino* (*c*) is present on both normal linkage group I chromosomes. The heterozygous female thus exhibits a *c*-variegated or *flecked* phenotype and this is normally observed on a *non-agouti* (*a*), *black* (b^+) background coat colour. In the present communication the term Dp will be applied to both *Dp(1; X)Ct* heterozygotes and hemizygotes.

All the Dp animals carried one or the other of the two alternative 'states' of the controlling element in their X^T chromosome. The 'state' designated high permits a near-50 % level of *c*-variegation, that designated low, a near-30 % level. The difference is attributed to the frequency of X^T-inactive cells in which the rearranged c^+ gene is inactivated (Cattanach & Isaacson, 1965, 1967).

An indication that the levels of variegation of females derived from reciprocal crosses might differ was present in some earlier data on the controlling elements (Cattanach & Isaacson, 1967), but since the difference was small and therefore an inconsistent feature of the few data in which other possible factors could be considered reasonably controlled, the validity of the observation was not recognized.

The first clear evidence of a reciprocal cross difference was obtained when the 'two' states of the controlling element were isolated and established in two sublines of an inbred stock (JU/Fa). The sublines were routinely maintained by repeatedly backcrossing the Dp females of each generation to JU males. These crosses provided the maternal X^T females; the paternal X^T females were produced in progeny tests that were carried out on all Dp males. The tests involved crossing the males to a series of JU females and deducing their genotypes with respect to the 'state' of their controlling element from the mean level of variegation of their daughters. The paternal X^T and maternal X^T females to be compared were thus derived from reciprocal crosses. This type of data was only available in the third generation of each subline; after the second generation of inbreeding the Dp male which normally exhibits a low viability (Cattanach, 1961) became a lethal class.

A second set of data indicating a reciprocal cross difference was obtained with

crossbred derivatives of the two sublines. Progeny tests on Dp males, produced by outcrossing the increasingly inbred females of each generation, yielded large groups of paternal X^T females. In the absence of reciprocal cross data, the scores on these females were compared with those of the F_1 outcross maternal X^T females of the preceding generation. The justification for this comparison will become apparent when the data are presented. A more detailed description of the sublines and crosses is described elsewhere (Cattanach *et al.* 1969).

When the reciprocal cross difference was first observed it was thought that selection might be operating differentially on the viabilities of the *Dp* females produced in the two types of cross. The rationale was as follows. (*a*) It is known that the viability of the hemizygous Dp male is very low and that that of the heterozygous Dp female is somewhat reduced (Cattanach, 1961*a*; Cattanach & Isaacson, 1965), (*b*) it is reasonable to suppose (in the absence of evidence) that the degree of reduction in Dp female viability will be proportional to the number of cells with the autosomal duplication (or X^T) genetically active, (*c*) it is then likely that any factor which enhances viability will allow the survival of those Dp females possessing greater number of cells with the duplication genetically active. It should be noted that the argument rests on the assumption that the proportion of cells with the duplication active will tend to be the same in all cell types. There would then be a correlation between reduction in viability and extent of pigmented areas in the coat.

On this basis, there are at least two mechanisms by which Dp female viability might differ in reciprocal crosses. The first and most likely is that Dp females, being less viable and somewhat less healthy, would provide a poorer pre-natal and post-natal environment for their progeny than the chromosomally normal *c* females of the reciprocal cross. The second possibility is that some autoincompatibility between the *c* mothers and their *c* progeny might exist such as has been demonstrated by Hull (1964, 1968) in his studies with the *agouti* and *histocompatibility-3* loci. A histocompatibility locus (*H-4*) may be carried in the piece of linkage group I translocated to the *X* and, if the allele differes from that of the inbred stock, might favour the survival of Dp progeny of *c* females over their *c* sibs.

In order to test for an inviability/pigmentation correlation the viabilities of the Dp females produced in all crosses were calculated. Pre-natal viability was estimated from the ratio of Dp (dark-eyed) females to *c* males at birth and the post-natal viability from the ratio of Dp females at birth to that at 3 weeks of age. The estimate of the pre-natal viability is reduced by the sex ratio but allows comparison of equivalent data in reciprocal crosses.

In the absence of any selective effect on the viabilities of Dp females, it is difficult to imagine how the maternal environment or maternal cytoplasm could influence the level of pigmentation of the Dp progeny. The observation that *more* pigmentation is found in the variegated daughters of females that do *not* carry the X^T seems to be a variance with any simple maternal effect interpretation. However, in order to determine whether the observed reciprocal cross difference was due to any such effect, a comparison was made of the levels of variegation exhibited by paternal

X^T daughters of Dp and chromosomally normal mothers. These were produced by crossing Dp females and their *c* sibs with Dp males of their own line. The homozygous Dp female is inviable and hence the Dp daughters of both crosses possess a paternal X^T and a normal X from the mother. Only if a maternal effect were operating would the scores of the daughters of Dp and *c* mothers be expected to differ. All the animals employed in these crosses were derived from the third generation of outcrossing of the two sublines. The crossbred animals were heterozygous for the coat colour gene, *brown* (*b*) and hence *brown* offspring were produced among the intercross progeny.

The lines carrying the high and low 'states' of the controlling element are designated H and L, respectively, and their outcross derivatives HX and LX. Numbers associated with these symbols, e.g. L_2, indicate the generation of inbreeding of the animals or, in the case of the outcross animals, e.g. L_2X, the generation of inbreeding of the mother.

The levels of *c*-variegation in the coats were determined in the standard manner (Cattanach & Isaacson, 1967; Cattanach *et al.* 1969); the amount of white areas in the coats of individual females was estimated to the nearest 5 % and the scoring was carried out on groups of at least 50 animals and without knowledge of their identity. This practice was found to reduce the errors liable to occur with this admittedly subjective scoring procedure. It should be stressed that the method overestimates the true levels of variegation by about 10–15 %; the levels, determined by counts on hair samples, are near-50 % for lines carrying the high 'state' and near-30 % for lines carrying the 'low' state. The data to be presented here have not been corrected for the scoring bias.

3. RESULTS

The first data indicating a difference between the mean scores of reciprocally derived females are shown in Tables 1 and 2. Since each 'state' of the controlling element was introduced into the inbred line by way of Dp males, all the females of the first generation possessed a paternally derived X^T. In the second generation both Dp males and females were produced and the progeny tests on the former and the standard backcross of the latter produced third generation reciprocal cross animals of identical genetic backgrounds. It can be seen that with both 'states' the mean score of the paternal X^T females is lower than that of the equivalent maternal X^T females and the difference in each case is statistically significant. The consistency of the observation becomes more apparent when the scores of the individual progeny tests are considered. Although the maternal X^T/paternal X^T female difference is small, almost all the individual progeny test scores were lower than the maternal X^T female scores. It should also be noted that the maternal X^T female scores varied little from generation to generation; none of the differences were statistically significant. This was also true for the difference between the paternal X^T female scores of the first and third generations. Since the genetic background changed in each generation of backcrossing this factor cannot be considered to play any significant part in modifying the level of variegation.

Table 1. *Levels of* c*-variegation observed in* H *line Dp females derived from reciprocal crosses*

(The score in parentheses is the mean of several incomplete progeny tests.)

	Maternal X^T ♀♀		Paternal X^T ♀♀	
Generation	No. ♀♀	Mean amount of *c*	No. ♀♀	Mean amount of *c*
1	—	—	61	58·44 ± 1·25 %
2	227	61·54 ± 0·66 %	—	—
3	144	61·56 ± 0·82 %*	22	57·27 ± 1·89 %
			20	62·50 ± 1·87 %
			20	56·25 ± 2·59 %
			27	56·48 ± 2·40 %
			20	57·25 ± 2·45 %
			15	55·67 ± 2·92 %
			15	57·67 ± 2·28 %
			10	57·00 ± 3·18 %
			(21)	(58·81 ± 2·74 %)
			Total 170	57·71 ± 0·82 %*
4	60	59·17 ± 1·40 %	—	—

* Significantly different: $t_{313} = 3{\cdot}32$; $P < 0{\cdot}001$.

Table 2. *Levels of* c*-variegation observed in* L *line Dp females derived from reciprocal crosses*

	Maternal X^T ♀♀		Paternal X^T ♀♀	
Generation	No. ♀♀	Mean amount of *c*	No. ♀♀	Mean amount of *c*
1	—	—	42	45·36 ± 1·85 %
2	105	50·71 ± 1·29 %	—	—
3	35	53·00 ± 1·81 %	25	43·60 ± 2·44 %
			26	46·35 ± 2·90 %
			19	43·68 ± 3·50 %
			22	47·27 ± 2·43 %
			26	51·54 ± 2·40 %
			9	46·66 ± 3·12 %
			8	46·25 ± 4·51 %
			Total 135	46·63 ± 1·12 %*
4	34	51·91 ± 1·76 %	—	—

* Significantly different: $t_{189} = 3{\cdot}08$; $P < 0{\cdot}01$.

The second set of data indicating a reciprocally-derived female difference is shown in Table 3. The comparison here is between animals of different generations and slightly different backgrounds; however, this seemed justifiable in view of the findings made in the two sublines and also in view of the consistency of scores obtained on all genetic backgrounds (Tables 1–3). If this argument is accepted, then the results presented again demonstrate a small but consistent difference in the scores of maternal X^T and paternal X^T females. The paternal X^T female data

https://doi.org/10.1017/S0016672300001361 Published online by Cambridge University Press

are too extensive to permit the presentation of the individual progeny test scores, but with certain notable exceptions all fell within the range of scores obtained with *L* and *H* line Dp males. All the exceptions were found in tests of *HX* males; these Dp males bred as though they possessed the low 'state' of the controlling element, an indication that a change in the 'state' of the element had occurred (Cattanach & Isaacson, 1967; Cattanach *et al.* 1969). The data from these 'changed' males have not been included in the Table.

Table 3. *Levels of* c*-variegation observed in crossbred Dp females derived from the reciprocal types of crosses*

(*T* (as in L_2XT, L_3XT, etc.) indicates progeny test data.)

Line and generation	Maternal X^T ♀♀		Paternal X^T ♀♀	
	No. ♀♀	Mean amount of *c*	No. ♀♀	Mean amount of *c*
L_2X	25	54·00 ± 2·22 %	—	—
L_2XT	—	—	144	43·54 ± 1·03 %
L_3X	10	48·50 ± 3·00 %	—	—
L_3XT	—	—	226	45·29 ± 0·69 %
L_4X	66	51·29 ± 1·47 %	—	—
L_4XT	—	—	469	44·03 ± 0·55 %
H_2X	25	61·60 ± 1·99 %	—	—
H_2XT	—	—	205	58·66 ± 0·78 %
H_3X	74	62·16 ± 1·29 %	—	—
H_3XT	—	—	584	57·78 ± 0·60 %
H_4X	59	59·15 ± 1·54 %	—	—
H_4XT	—	—	200	57·30 ± 0·82 %

Table 4. *Viabilities of Dp females derived from* L *and* H *line reciprocal crosses*

Line and generation	Viability of maternal X^T ♀♀			Viability of paternal X^T ♀♀		
	Pre-natal	Post-natal	Total	Pre-natal	Post-natal	Total
L_1	—	—	—	0·90	0·94	0·85
L_2	0·49	0·91	0·45	—	—	—
L_3	0·56	0·92	0·52	0·78	0·69	0·54
L_4	0·83	0·80	0·66	—	—	—
H_1	—	—	—	0·80	0·94	0·75
H_2	0·74	0·96	0·71	—	—	—
H_3	0·69	0·91	0·63	0·88	0·88	0·77
H_4	0·72	0·83	0·60	—	—	—

The viabilities of the Dp females produced in the various crosses are summarized in Tables 4 and 5 and it can be seen that the survival of Dp females is consistently higher in litters of *c* mothers than in those of Dp mothers. This evidence would tend to support the hypothesis that the lower mean scores of the paternal X^T females are due to the survival of Dp females possessing greater numbers of cells with the duplication genetically active. However, a search for a viability/variegation score correlation within each type of cross did not provide any sup-

porting evidence. The viabilities varied widely in different generations and on different genetic backgrounds (see Tables 4 and 5), but no accompanying change in the variegation scores could be found (see Tables 1, 2 and 3). In fact, more often than not, minor variations in the scores tended to lie in the opposite direction from that predicted by the hypothesis. It can thus be concluded that although viability may be influenced by a number of genetic and environmental factors, this is not true of the variegation score. There is no evidence of an interaction between the two characters.

Table 5. *Viabilities of crossbred Dp females derived from the reciprocal type of crosses*

(T (as in L_2XT, L_3XT, etc.) indicates progeny test data.)

Line and generation	Viability of maternal X^T ♀♀			Viability of paternal X^T ♀♀		
	Pre-natal	Post-natal	Total	Pre-natal	Post-natal	Total
L_2X	0·81	1·00	0·81	—	—	—
L_2XT	—	—	—	0·95	0·88	0·84
L_3X	0·50	0·91	0·46	—	—	—
L_3XT	—	—	—	0·81	0·83	0·67
L_4X	0·66	0·87	0·58	—	—	—
L_4XT	—	—	—	0·85	0·82	0·70
H_2X	0·78	1·00	0·78	—	—	—
H_2XT	—	—	—	0·88	0·87	0·77
H_3X	0·74	0·92	0·68	—	—	—
H_3XT	—	—	—	0·82	0·84	0·69
H_4X	0·61	0·92	0·56	—	—	—
H_4XT	—	—	—	0·74	0·90	0·66

Table 6. *Levels of* c*-variegation observed in Dp daughters of Dp and chromosomally normal* (c) *females*

Line	Cross	Background coat colour	No. ♀♀ scored	Mean amount of *c*
H_3X	Dp ♀♀ × Dp ♂♂	b^+	65	55·62 ± 1·39 %
	c ♀♀ × Dp ♂♂	b^+	83	57·05 ± 1·26 %
	Dp ♀♀ × Dp ♂♂	*b*	17	62·65 ± 2·42 %*
	c ♀♀ × Dp ♂♂	*b*	34	58·68 ± 1·90 %*
L_3X	Dp ♀♀ × Dp ♂♂	b^+	21	43·10 ± 2·45 %
	c ♀♀ × Dp ♂♂	b^+	24	44·38 ± 2·54 %
	Dp ♀♀ × Dp ♂♂	*b*	9	44·44 %
	c ♀♀ × Dp ♂♂	*b*	14	49·64 %

* Not significantly different: $t_{52} = 1{\cdot}20$; $P > 0{\cdot}2$.

The results of the experiment designed to determine whether the reciprocal cross difference was due to a maternal effect is shown in Table 6. The collection of large numbers of Dp females from the Dp × Dp cross was made a long and tedious process by the low fertility and high incidence of sterile matings typical of the cross. Nevertheless, sufficient data were accumulated to demonstrate any difference in the scores between the two crosses were one to exist. It can be seen that with

both 'states' of the controlling element the scores of the b^+ Dp daughters of c mothers was actually higher, rather than lower, than those of the equivalent daughters of Dp mothers. The same observation was made with the b animals carrying the low state but the data here were too few to be meaningful. Only with the b females carrying the high 'state' was the difference between the scores in the two crosses in the right direction to indicate a maternal effect and here the difference was not statistically significant. The results of the experiment do not therefore support the concept that a maternal effect is responsible for the difference observed in the sublines and their crossbred derivatives.

It should be added that the viability of the Dp daughters of the Dp females in these crosses was higher than that generally observed in the earlier crosses (Tables 4, 5) and it might be argued that this was the cause of the lower variegation scores, i.e. it would support a viability/variegation score correlation. However, the viabilities tended to be high in both sets of crosses, this no doubt being due to the fact that the parents were F_1 outcross animals and that in the Dp × Dp crosses the viability estimate would be further enhanced by the early loss of the homozygous Dp progeny (Cattanach, 1961*a*; Lyon, 1967). Despite these elevated viabilities there remained a difference between the estimates obtained for the Dp females derived from the Dp × Dp and c × Dp crosses, e.g. in the H_3X groups the pre-natal viabilities were 0·85 and 0·92 respectively and both post-natal viabilities were 0·87, and yet the variegation scores differed little from each other or from the scores obtained in the earlier crosses (Tables 1–3). The apparent association between viability and variegation score in between-cross comparisons seems to be a fortuitous one; it cannot be demonstrated within crosses.

4. DISCUSSION

The data presented clearly demonstrate that Dp females inheriting their X^T from the father tend to have lower levels of c-variegation, i.e. more pigmented hair in the coats, than Dp females inheriting their X^T from the mother. This was observed in the two sublines in which the high and low 'states' of the controlling element were being introduced into an inbred background and also in the crossbred derivatives of the two sublines. The difference in the phenotype between maternal and paternal X^T females must therefore be a real phenomenon and one that is not dependent upon any one genetic background.

Although it seemed possible that there might be a correlation between viability and variegation score, this was only evident in reciprocal crosses. The variations in viability within each type of cross was equally as high as that between reciprocal crosses, and yet in all crosses of each type the variegation score remained constant. Viability differences, whether resulting from differences in the maternal environment or from autoincompatibility between c mothers and c progeny, cannot therefore be the cause of the reciprocal cross differences in variegation score. This conclusion could also be drawn from the comparison of the Dp female × Dp male and c female × Dp male crosses, and in these crosses it was also clear that mother's

genotype or cytoplasm was not responsible for the maternal X^T/paternal X^T female difference; some other parental effect must be involved.

Before seeking an interpretation of the reciprocal cross difference, the mechanisms responsible for the variegation should be considered. The *c*-variegation observed in the coats of *T(1; X)Ct* and other *X*-autosome translocation heterozygotes is thought to be due to the presence of two populations of melanocytes, one capable of producing pigment and the other not, and this conclusion has recently found support in the observation that $cc \parallel c^+c^+$ allophenic mice show similar variegated phenotypes (Mintz, 1967). In the case of the translocations, the two cell populations arise from the random *X*-inactivation process and the superimposed position effect variegation (Cattanach & Isaacson, 1965, 1967; Russell, 1963, 1964). Any parental influence upon the variegation would therefore be expected to operate upon one or both of these mechanisms or upon the two cell populations once established.

In the absence of a maternal effect, a paternal effect might be considered the most likely cause of difference between Dp daughters of Dp and *c* males and the fact that phenotypes tend towards those of the father appears to support this. However, it is difficult to imagine how cytoplasmic differences between the sperm of Dp and *c* fathers could bias the randomness of the *X*-inactivation process or modify the inactivating properties of the *X* and it is most improbable that a cytoplasmic influence could be transmitted through many cell generations to modify pigment production in the melanocytes or alter the proliferation rates or migration of one of the two cell populations. Nuclear differences resulting from the presence or absence of the rearrangement may, instead, be responsible.

'Residual' influences of the parental genotype have long been recognized in *Drosophila* (Noujdin, 1944) and have more recently been the subject of intensive study in both *D. melanogaster* (Baker & Spofford, 1959; Cohen, 1962; Hessler, 1961; Spofford, 1959, 1961, 1967) and *D. virilis* (Schneider, 1962). One of these influences, the parental source effect, may be applicable to the observations described here in the mouse. Differences in the level of variegation which could not be explained by a maternal effect were detected in reciprocal crosses. That the parental-source of the rearrangement was the responsible factor was best demonstrated by Baker (1963) using the $Dp(1:3)w^{m264\cdot58a}$ rearrangement of *D. melanogaster*. From crosses in which both parents carried the duplication he was able to recover offspring inheriting the duplication from either the father or the mother and these exhibited differing phenotypes.

Unfortunately, the equivalent test cannot be made with the mouse *X*-autosome translocation and hence a clear distinction between a paternal and parental-source effect cannot be made. However, in view of the parental nature of the effect and the mechanisms upon which it must operate, it seems most probable that the *X* chromosome, or perhaps the controlling element, is conditioned in some way during its passage through the male or female germ line such that its behaviour in the embryo is modified. By analogy with the V-type position effects described in *Drosophila*, the conditioning could be thought to modify the inactivating properties

of the heterochromatic X but it could equally well apply to the behaviour of the X at the time of inactivation; a bias in the randomness of X-inactivation may exist such that the paternal X is less likely to be inactivated. Whatever the mechanism affected, the same type of process may be working as that described in *Sciara* and the mealy bugs (Crouse, 1960; Hughes-Schrader, 1949; Metz, 1939; Nelson-Rees, 1962); the chromosomes are said to acquire an 'imprint' during their passage through the germ cells of either sex such that the behaviour of the maternal and paternal chromosomes may differ in the embryo (Crouse, 1960).

In concluding, it may be pointed out that if any such conditioning of the X occurs, reciprocal cross differences in the heterozygous phenotypes of X-linked genes might be expected. This would obviously follow if the conditioning biased the X-inactivation process; it would also follow if the conditioning modified the inactivating properties of the X, for modification of the inactivating properties by the mouse X-chromosome controlling element system has been found to influence the heterozygous phenotypes of two X-linked genes, *Tabby* (*Ta*) and *Viable-brindled* (*Vbr*) in the same manner as the position effect variegation (Cattanach *et al.* 1969). Such a reciprocal cross difference has in fact been observed with *Ta*. *Ta* reduces the vibrissa number and when this criterion is used as a measure of the level of phenotypic expression of the *Ta* allele in the heterozygote, it is found with complete regularity that *Ta*/+ progeny of *Ta*/+ females and + males have higher vibrissa scores (more nearly normal) than *Ta*/+ progeny of +/+ females and *Ta* males (Dun & Frazer, 1959; Frazer & Kindred, 1960). Unfortunately, the equivalence of the observations made on *Ta* and the *T(1; X)Ct* variegation is confused by the fact that a maternal effect is considered to be the cause of the *Ta* reciprocal cross difference (Kindred, 1961). This conclusion was based on a single set of data and the validity of the results perhaps should be reconsidered in light of the seemingly identical behaviour of the translocation-induced variegation. It would appear to be too much of a coincidence that two X-linked traits, operating in different cell types, should show reciprocal cross differences in the heterozygous females and that the phenotype in each case should be biased towards that of the father. Surely a common mechanism must be responsible, one that is in some way related to X-inactivation.

This work was supported by a grant (GM-15885) from the National Institutes of Health, U.S. Public Health Service.

REFERENCES

BAKER, W. K. (1963). Genetic control of pigment differentiation in somatic cells. *Am. Zool.* **3**, 57.

BAKER, W. K. (1968). Position effect variegation. *Adv. Genetic.* **14**, 133.

BAKER, W. K. & SPOFFORD, J. B. (1959). Heterochromatic control of position-effect variegation in *Drosophila*. Reprinted from Biological Contributions, University of Texas, Austin, Fall.

CATTANACH, B. M. (1961*a*). A chemically induced variegated-type position effect in the mouse. *Z. VererbLehre.* **92**, 165.

CATTANACH, B. M. (1961*b*). *XXY* mice. *Genet. Res., Camb.* **2**, 156.

CATTANACH, B. M. & ISAACSON, J. H. (1965). Genetic control over the inactivation of autosomal genes attached to the X-chromosome. *Z. VererbLehre.* **96**, 313.

CATTANACH, B. M. & ISAACSON, J. H. (1967). Controlling elements in the mouse *X* chromosome. *Genetics, Princeton* **57**, 331.

CATTANACH, B. M., POLLARD, C. E. & PEREZ, J. N. (1969). Controlling elements in the mouse *X*-chromosome. I. Interaction with the *X*-linked genes. *Genet. Res., Camb.* **14**, 223.

COHEN, J. (1962). Position-effect variegation at several closely linked loci in *Drosophila melanogaster*. *Genetics, Princeton* **47**, 647.

CROUSE, H. V. (1960). The controlling element in sex chromosome behavior in *Sciara*. *Genetics, Princeton* **45**, 1429.

DUN, R. B. & FRAZER, A. S. (1959). Selection for an invariant character, vibrissae number, in the house mouse. *Aust. J. biol. Sci.* **12**, 506.

FRAZER, A. S. & KINDRED, B. M. (1960). Selection for an invariant character, vibrissae number, in the house mouse. II. Limits to variability. *Aust. J. biol. Sci.* **13**, 45.

HESSLER, A. Y. (1961). A study of parental modification of variegated position effects. *Genetics, Princeton* **46**, 463.

HUGHES-SCHRADER, S. (1948). Cytology of coccids (*Coccoidea-Homoptera*) *Adv. Genetics, Princeton* **2**, 127.

HULL, P. (1964). Partial incompatibility not affecting total litter size in the mouse. *Genetics, Princeton* **50**, 563.

HULL, P. (1968). Maternal-foetal incompatibility associated with the H-3 locus in the mouse. *Heredity* **24**, 203.

KINDRED, B. M. (1961). A maternal effect on vibrissae score due to the Tabby gene. *Aust. J. biol. Sci.* **14**, 627.

LEWIS, E. B. (1950). The phenomenon of position effect variegation. *Adv. Genet.* **3**, 73.

LYON, M. F. (1961). Gene action in the *X*-chromosome of the mouse (*Mus musculus* L.). *Nature, Lond.* **190**, 372.

LYON, M. F. (1967). *Mouse News Letter* **36**, 36.

METZ, C. W. (1938). Chromosome behaviour, inheritance and sex determination. *Z. Zellforsch. mikrosk. Anat.* **19**, 595.

MINTZ, B. (1967). Gene control of mammalian pigmentary differentiation. I. Clonal origin of melanocytes. *Proc. Natn. Acad. Sci., U.S.A.* **58**, 344.

NELSON-REES, W. A. (1962). The effects of radiation damaged heterochromatic chromosomes on male fertility in the mealy bug, *Planococcus citri* (*Risso*). *Genetics, Princeton* **47**, 661.

NOUJDIN, N. I. (1944). The regularities of heterochromatin influence on mosaicism. *J. gen. Biol.* **5**, 357.

OHNO, S. & CATTANACH, B. M. (1962). Cytological study of an *X*-autosome translocation in *Mus musculus*. *Cytogenetics* **1**, 129.

RUSSELL, L. B. (1963). Mammalian *X*-chromosome action: Inactivation limited in spread and in region of origin. *Science, N.Y.* **140**, 976.

RUSSELL, L. B. (1964). Another look at the single-active-*X* hypothesis. *Trans. N.Y. Acad. Sci.* **26**, 726.

RUSSELL, L. B. & BANGHAM, J. W. (1959). Variegated-type position effects in the mouse. *Genetics, Princeton* **44**, 532.

RUSSELL, L. B. & BANGHAM, J. W. (1961). Variegated-type position effects in the mouse. *Genetics, Princeton* **46**, 509.

SCHNEIDER, I. (1962). Modification of *V*-type position effects in *Drosophila virilis*. *Genetics, Princeton* **47**, 25.

SPOFFORD, J. B. (1959). Parental control of position-effect variegation. I. Parental heterochromatin and expression of the white locus in compound X-*Drosophila melanogaster*. *Proc. natn. Acad. Sci. U.S.A.* **45**, 1003.

SPOFFORD, J. B. (1961). Parental control of position-effect variegation. II. Effect of sex of parent contributing white mottled rearrangement in *Drosophila melanogaster*. *Genetics, Princeton* **46**, 1151.

SPOFFORD, J. B. (1967). Single-locus modification of position-effect variegation in *Drosophila melanogaster*. *Genetics, Princeton* **57**, 751.