Genetic analysis of the \( t^{w3} \) haplotype of the mouse using deletion mutations: evidence for a parasitic lethal mutation

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(Received 23 March 1981 and in revised form 4 September 1981)

SUMMARY

Matings between mice bearing the dominant deletion \( T^{hp} \) and mice segregating for the \( t^{w3} \) haplotype failed to produce the expected viable tailless \( (T^{hp}/t^{w3}) \) progeny. Histological analysis of litters from \( T^{hp}/+ \times +/+t^{w3} \) matings revealed an abnormal class of embryos which failed to implant normally between days 6.5 and 7.5 of gestation, and were indistinguishable from \( t^{w3}/t^{w3} \) homozygotes. \( T^{hp} \) homozygotes displayed a different lethal phenotype, failing to successfully make the transition from morula to blastocyst at day 3.5. These studies indicate that the mutation responsible for the \( t^{w3} \) implantation defect maps within the \( T^{hp} \) deletion. Since \( t^{w3} \) is viable with another deletion, \( T^{OrI} \), the \( t^{w3} \) defect must occur in the region of non-overlap between \( T^{hp} \) and \( T^{OrI} \). The possibility that the \( t^{w3} \)-associated implantation defect is a parasitic lethal mutation \( (p) \), mapping to the proximal part of the \( t^{w3} \) chromosome, is discussed.

1. INTRODUCTION

The \( T/t \)-complex is a region of mouse chromosome 17 that affects embryonic development, sperm production, and local genetic recombination. The region was originally identified (Dobrovolskaia-Zavadskaiia, 1927) by the dominant mutation Brachyury \( (T) \) which produces a short-tailed phenotype when heterozygous \( (T/+ \) ), and embryonic death when homozygous \( (T/T) \) (Chesley, 1935). A number of recessive \( t \)-mutations have been characterized at the \( T/t \)-complex in both wild and laboratory mice. These mutations are typified by their interaction with \( T \) to produce a tailless phenotype \( (T/t) \) (Bennett, 1975).

Recessive lethal \( t \)-haplotypes exist as polymorphisms in wild populations where they are presumably maintained by their unique non-mendelian high transmission through males. Another unusual feature of such haplotypes is that, when heterozygous with wild type chromosomes, they almost completely suppress genetic recombination between the locus of \( T \) and the H-2 complex (Hammerberg & Klein, 1975). Thus the naturally occurring recessive \( t \)-haplotypes contain a 15 centimorgan

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segment of chromosome which is effectively locked in place and isolated from exchange with normal genetic material.

Occasional \((1\,\text{to}\,2 \times 10^{-3})\) recombinants are produced by \(t/\+)
heterozygotes, apparently always by crossing over that occurs in the region between the loci of \(T\) and \(tf\). In all cases so far studied, these recombinants clearly map the tail interaction factor \(tT\) to the locus of \(T\), and a single factor responsible for lethality close to another marker, \(tf\), about 7 cM distal to \(T\) (Lyon & Meredith, 1964).

More than 50 \(t\)-haplotypes have been independently isolated from wild populations of Mus musculus musculus and Mus musculus domesticus around the world, and their study has revealed some interesting and unexpected features. First of all, genetic complementation tests show that all \(t\)-haplotypes fall into no more than eight complementation groups (Bennett, 1980). Second, members of the same \(t\)-complementation group usually are associated with the same \(H-2\) haplotype, although a few \(t\)-haplotypes have the \(H-2\) type typical of some other \(t\)-complementation group (Hammerberg & Klein, 1975). These data can be interpreted to mean that wild \(t\)-haplotypes are ancient anomalies that originated very early in the phylogenetic history of Mus, and that they contain a highly conserved segment of chromosome 17 locked in by recombination suppression. This being in all likelihood the case, it is surprising that the \(t\)-haplotypes that have so far been studied have not accumulated other lethal factors or in fact other viable mutations, since these chromosomes, lethal in any case when homozygous but protected against natural selection by their male transmission distortion, should act as sinks for other mutations.

We report here the finding for the first time of a ‘parasitic’ lethal factor associated with a typical \(t\)-haplotype, \(t\)\(^{w3}\). Since this is clearly a rare situation, the implication may be that informational DNA is relatively sparse in the region of chromosome 17 covered by the recombination suppression associated with \(t\)-haplotypes.

2. MATERIALS AND METHODS

(A) Mice

Mapping of the \(t\)\(^{w3}\) haplotype was carried out with the deletions \(T^{hp}\) (Johnson, 1974; Alton et al. 1980) and \(T^{Orl}\) (Moutier, 1973a, b). Both deletions have the properties of \(T\) mutations, and both elicit pseudodominance of quaking (qk), a recessive mutation 3 cM distal to locus of \(T\), but they must differ in their extent since \(T^{hp}\) has a maternal effect not associated with \(T^{Orl}\) (Johnson, 1974; Erickson, Lewis & Slusser, 1978). Crosses were made between short-tailed males \((T^x/+)\) and normal tailed \((+/t\)\(^y\)) or tailless \((T/t\)\(^y\)) females, to detect tailless \((T^x/t\)\(^y\)) offspring. These crosses included matings between \(T^{hp}\) heterozygotes and heterozygous females segregating for members of seven different complementation groups \((t^0, t^0, t^{12}, t^{w1}, t^{w3}, t^{wP}, t^{wPA})\). Similar matings between male \(T^{Orl}\) heterozygotes and females segregating for members of six different complementation groups \((t^0, t^0, t^{12}, t^{w1}, t^{w2}, t^{w3})\) were also studied.
Genetic analysis of the $t^{w73}$ haplotype

For histological observation, crosses between $T^{hp}$ heterozygotes ($T^{hp}/+ \times T^{hp}/+$) and $t^{w73}$ heterozygotes (+/$t^{w73} \times +/t^{w73}$) were made, in addition to the $T^{hp}/+ \times +/t^{w73}$ matings.

Complementation data were compiled from crosses between tailless $T/t^{w73}$ heterozygotes and tailless ($T/t^k$) mice segregating for $t$-haplotypes in 6 different complementation groups: $t^3$, $t^2$, $t^{12}$, $t^{w1}$, $t^{w5}$, $t^{wPA}$. In such crosses complementation is revealed by the production of normal tailed $t^x/t^y$ progeny. Recombination between $T$ and $t^f$ was tested by crossing $T/tf/t^{w73} \times T/tf/t^{w73}$, and the transmission ratio of the $t^{w73}$ haplotype was determined by mating wild type (+/+ ) females with $T/t^{w73}$ males.

(B) Embryos

Embryos on the appropriate day of gestation were examined histologically. Embryos, still in the uterine decidua, were fixed in Bouin's fluid for 24 h, embedded in paraffin, sectioned serially at 7 µm, and stained with hematoxylin and eosin. The presence of a vaginal plug was considered day 0 of gestation; more precise staging of embryos was determined by comparison of the histological sections with Sobotta's figures (Sobotta, 1911). Specimens were viewed and photographed with a Zeiss photomicroscope.

3. RESULTS

The results of complementation tests between $T/t^{w73}$ mice and tailless ($T/t^y$) members of six other complementation groups appear in Table 1. Since normal tailed offspring appeared in each case, $t^{w73}$ represents a complementation group of its own.

In tests for exceptional recombination between $T$ and $t^f$ in $T/tf/t^{w73}$ heterozygotes (see Fig. 1), no normal tailed offspring were observed in 3282 births, whereas 3-6 would have been expected (Table 2). Of the tailless progeny, 1178 were scored for tufting, and three tailless tufted exceptional recombinants were detected (Table 2). The transmission frequency of the $t^{w73}$ mutation in males was 83.9% (Table 3).

When heterozygotes for $t^{w73}$ were crossed to mice bearing the dominant deletion mutation $T^{hp}$, no tailless animals were born (Table 4), although $T^{hp}$ heterozygotes produced tailless offspring when crossed with lethal $t$-haplotypes of the other six other complementation groups tested (Table 4). This suggested that the $T^{hp}$ deletion covers a lethal factor associated with $t^{w73}$ haplotypes, resulting in the embryonic death of the $T^{hp}/t^{w73}$ progeny.

To define the lethal $T^{hp}/t^{w73}$ embryos, litters were examined histologically on days 6-0-8-0 of development (Table 5). An abnormal class of embryos was first recognized on day 6-5 of development, when the normal littermates are elongate egg cylinders (Plate 1a). The putative $T^{hp}/t^{w73}$ embryos are stunted and poorly implanted. The ectoplacental cone is, at best, rudimentary in these embryos, giant
Table 1. Summary of complementation tests of $t^{w73}$ with other groups ($T/t^{w73} \times T/t^2$), presented as normal tailed/tailless offspring

<table>
<thead>
<tr>
<th>Cross</th>
<th>At birth</th>
<th>Scored for tufting at 28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tailless</td>
<td>Normal tailed</td>
</tr>
<tr>
<td>$T/t^9$</td>
<td>2/7</td>
<td>1/9</td>
</tr>
<tr>
<td>$T/t^{w73}$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Tests of recombination between $T$ and $tf$ when heterozygous with a $t^{w73}$ chromosome

<table>
<thead>
<tr>
<th>Cross</th>
<th>Progeny</th>
<th>At birth</th>
<th>Scored for tufting at 28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T tf_{tw73} \times T tf_{tw73}$</td>
<td></td>
<td>3282</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 3. Transmission of the $t^{w73}$ chromosome in matings of tailless ($T/t^{w73}$) males with wild-type (+/+ ) females

<table>
<thead>
<tr>
<th>Cross</th>
<th>Progeny</th>
<th>Transmission ratio of $t^{w73}$ chromosome</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T/t^{w73} +/+$</td>
<td>Normal tailed</td>
<td>Short tailed</td>
</tr>
<tr>
<td></td>
<td>1466</td>
<td>283</td>
</tr>
</tbody>
</table>

Table 4. Cross tests of male $T^{hp}$ and $T^{ori}$ heterozygotes with females carrying recessive t-haplotypes

<table>
<thead>
<tr>
<th>Crosses</th>
<th>Normal tailed (+/+ or $+/t^2$)</th>
<th>Short tailed ($T^y/+)$</th>
<th>Tailless ($T^y/t^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T^{hp} + \times t^0$</td>
<td>64</td>
<td>43</td>
<td>29</td>
</tr>
<tr>
<td>$T^{hp} + \times t^9$</td>
<td>38</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>$T^{hp} + \times t^{12}$</td>
<td>16</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>$T^{hp} + \times t^{w73}$</td>
<td>25</td>
<td>25</td>
<td>12</td>
</tr>
<tr>
<td>$T^{hp} + \times t^{wPA}$</td>
<td>109</td>
<td>63</td>
<td>0</td>
</tr>
<tr>
<td>$T^{ori} + \times t^0$</td>
<td>20</td>
<td>37</td>
<td>28</td>
</tr>
<tr>
<td>$T^{ori} + \times t^9$</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>$T^{ori} + \times t^{12}$</td>
<td>7</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>$T^{ori} + \times t^{w73}$</td>
<td>39</td>
<td>39</td>
<td>44</td>
</tr>
<tr>
<td>$T^{ori} + \times t^{wPA}$</td>
<td>35</td>
<td>31</td>
<td>22</td>
</tr>
<tr>
<td>$T^{w73} + \times t^{w73}$</td>
<td>28</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>$T^{w73} + \times t^{wPA}$</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>
cells are rarely seen, and the trophectoderm is poorly adherent to the uterine decidua (Plate 2a). By day 7.5 of development, the normal littermates have reached the primitive streak stage (Plate 1b). In contrast, the Thp/tw73 embryos are arrested at the egg cylinder stage, and although they appear to be fully viable, have not formed mesoderm (Plate 2b). Most obvious is the failure of the implantation process in these embryos. Little association remains between the trophectoderm and uterine decidua, the ectoplacental cone has neither increased in size nor penetrated the decidua, and the space between the embryo and uterine tissue has become filled with maternal lymphocytes and polymorphonuclear leukocytes.

The same syndrome of abnormal development is found in litters segregating for tw73 previousl reported (Spiegelman, Artzt & Bennett, 1976) and confirmed in our observations (Table 5 and Plate 3a and b), the trophectoderm of tw73 homozygotes does not form normal numbers of giant cells nor does it become the invasive and adhesive tissue necessary for normal implantation. Histologically, the two classes of abnormal embryos, tw73/tw73 and Thp/Thp, are indistinguishable. Therefore, the mutation in the tw73 haplotype affecting the implantation process must reside in the region of chromosome 17 deleted by the Thp mutation.

Thp homozygotes show a different syndrome of developmental failure. Between days 3.5 and 4.5 of development, when the normal littermates are expanded blastocysts (Plate 4a), the homozygous Thp embryos are stunted at the morula stage (Plate 4b). In litters analysed on days 5–5.5, the putative Thp homozygotes were never observed to develop past the morula stage and by day 6.5 are totally resorbed (Table 5).

In an attempt to map the tw73 defect more precisely, matings were made between male heterozygotes for the Torl deletion, and tailless females heterozygous for members of six different complementation groups. These matings produced viable

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Table 5. Classification of embryos in litters segregating for tw73/tw73 and Thp/Thp phenotypes

<table>
<thead>
<tr>
<th>Crosses</th>
<th>Gestational age</th>
<th>No. of litters</th>
<th>No. of embryos</th>
<th>Observed abnormal</th>
<th>Abnormal (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T^hp/+ x +/tw73</td>
<td>Day 6-5</td>
<td>2</td>
<td>20</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Day 7-5</td>
<td>4</td>
<td>36</td>
<td>11</td>
<td>31</td>
</tr>
<tr>
<td>T^hp/+ x T^hp/+</td>
<td>Day 3-5</td>
<td>4</td>
<td>46</td>
<td>12</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Day 4-5</td>
<td>4</td>
<td>42</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Day 6-5</td>
<td>7</td>
<td>68</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>T/tw73 x T/tw73</td>
<td>Day 6-5</td>
<td>13²</td>
<td>108</td>
<td>34</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>Day 7-5</td>
<td>5²</td>
<td>40</td>
<td>11</td>
<td>28</td>
</tr>
</tbody>
</table>

1 – includes typical abnormals and resorbed embryos.
2 – includes results from Spiegelman et al. 1976.
3 – abnormal embryos completely resorbed.

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tailless heterozygotes ($T^{Orl}/t^2$) for all $t$-haplotypes tested, including $t^{w73}$ (Table 4). Since $T^{Orl}/t^{w73}$ is viable, the lethal factor common to $T^{hp}$ and $t^{w73}$ must reside in a segment of $T^{hp}$ that is non-overlapping with $T^{Orl}$. Since both deletions cover only the proximal region of the $T/t$-complex, that is from some point proximal to $T$ to somewhere between $qk$ and $if$, it is clear that the $t^{w73}$ lethal factor is not found in the same region of the $T/t$-complex as all other known $t$-lethal factors, which map closer to tufted.

4. DISCUSSION

The results presented here show that the $t^{w73}$ haplotype contains a lethal factor that maps within the $T^{hp}$ deletion. This was detected when crosses of $T^{hp}/+ \times +/t^{w73}$ failed to produce viable tailless progeny. Subsequent histological analysis of embryos from such crosses revealed a lethal class of embryos which failed during implantation in a way indistinguishable from $t^{w73}$ homozygotes.

The $T^{hp}$ homozygotes showed a different embryological defect, the failure to make the transition from morula to blastocyst. This indicates that the deleted portion of chromosome 17 contains at least two factors which result in embryonic lethality. It is not surprising that a deletion of more than 3 cM should contain more than one gene important in early development.

Since $T^{Orl}/t^{w73}$ animals are viable, the lethal factor shared by $t^{w73}$ and $T^{hp}$ must map to the area of non-overlap of the $T^{hp}$ and $T^{Orl}$ deletions. Unfortunately, almost nothing is known about the relative extent of these deletions proximal to $T$ and distal to $qk$. However, some inferences can be made from the interactions that they show with the factor Low, which is located one cM distal to $qk$. In the heterozygous state, Low reduces its own transmission through males to approximately 14% (Dunn & Bennett, 1968, 1971, and Table 6). In Low/Low homozygotes, no effect is observed (Dunn & Bennett, 1971). As seen in Table 6, $T^{hp}$ and $T^{Orl}$ interact differently with Low. $T^{hp}$/Low heterozygotes show the characteristic decrease in the transmission of the Low bearing chromosome, producing only 140 normal tailed progeny in 822 births (17%). Therefore, the $T^{hp}$ chromosome might be visualized as $T^{hp} + Low$. In contrast, as reported by Hammerberg (1981) and also here, heterozygotes for the $T^{Orl}$ deletion and Low show anomalous segregation, with Low transmitted at 30%. The difference between the transmission ratios of the two kinds of heterozygotes is highly statistically significant ($\chi^2 = 33.3$, $p < 0.001$).

The compound $T^{Orl}$/Low is thus intermediate between conventional Low heterozygotes and Low homozygotes; this information raises the possibility that the $T^{Orl}$ deletion may extend part way through the locus of Low, or influence Low through some sort of position effect. If this assumption is correct, then the $T^{Orl}$ deletion must extend further to the right than $T^{hp}$, and conversely, the $T^{hp}$ deletion must cover a longer part of the area to the left of $T$ than $T^{Orl}$. It is in this area of non-overlap that the $t^{w73}$ lethal factor must map.

Another interpretation is possible if one considers the Tcp-1 genes which code for a 63,000 dalton protein (Silver, White & Artzt, 1980). The wild type gene which
Light micrographs of normal (+/+ ) embryos. (a) 6.5 day embryo, at the egg cylinder stage (× 640). (b) 7.5 day embryo, at the early primitive streak stage (× 400).

B. BABIARZ, G. J. GARRISI AND D. BENNETT  
(Facing p. 116)
Light micrographs of $T^{hp}/u^{73}$ embryos. (a) At 6.5 days, exhibiting an implantation defect ($\times 640$). (b) At 7.5 days, development was arrested prior to mesoderm formation ($\times 640$).

B. BABIARZ, G. J. GARRISI AND D. BENNETT
Light micrographs of $tw^{73}$ homozygotes. (a) An oblique section after 6.5 days of development ($\times 640$). (b) At 7.5 days, these embryos are indistinguishable from $T^{BP}/tw^{73}$ compounds ($\times 640$).

B. BABIARZ, G. J. GARRISI AND D. BENNETT
Light micrographs from litters segregating for $T^{hp}$. (a) A normal expanded blastocyst at day 4.0 (x 640). (b) A putative $T^{hp}/T^{hp}$ embryo stunted at the morula stage at day 4.0 (x 640).

B. BABIARZ, G. J. GARRISI AND D. BENNETT
maps just to the right of \(qk\) produces one form of this protein (p63b), whereas all \(t\)-haplotypes that contain \(t^T\) express a variant form (p63a), detectable by two-dimensional gel electrophoresis (Silver, Artzt & Bennett, 1979). The \(T^{hp}\) deletion acts as a null allele of \(Tcp-1\), suggesting that the deletion extends past \(qk\) to delete \(Tcp-1\)-b (Alton et al. 1980). The \(T^{Or}\) deletion, in contrast, does not delete \(Tcp-1\) since animals bearing this deletion surprisingly express both p63a and b (Alton et al. 1980). This complexity of the region coding for \(Tcp-1\) in \(T^{Or}\) animals has not yet been resolved, and it is therefore difficult to assess the deletion length or any other genetic abnormalities located to the right of \(qk\) on the \(T^{Or}\) chromosome. The possibility does exist, however, that the \(Thp\) deletion extends further to the right of \(qk\) than does \(T^{Or}\), which would thus map the \(t^{w73}\) defect between \(qk\) and \(Tcp-1\)-b.

For all naturally occurring \(t\)-haplotypes, two separable factors have been mapped: \(t^T\) (tail interaction factor) which interacts with \(T\) to produce the tailless phenotype and \(t^l\) (lethal factor) which when homozygous leads to a stage specific death of the embryo (Lyon & Meredith, 1964). Their relative positions on chromosome 17 are shown in Fig. 1. The \(t^T\) factor maps at the locus \(oi\), and the \(t^l\) factors distal to \(qk\). The mapping of the \(t^{w73}\) lethal factor in the proximal portion of the \(T/t\)-complex (to the left of \(T\) or very close to the locus of \(qk\)) suggests that it is a 'parasitic' mutation trapped in the region of recombination suppression. It is an interesting point that no other \(t\)-haplotypes contain parasitic lethal genes in the region covered by the \(Thp\) and \(T^{Or}\) deletions. This is unexpected since wild \(t\)-haplotypes appear to be ancient chromosomes, lethal in any case when homozygous, that should, because of the transmission distortion and recombination suppression associated with them, act as 'sinks' for new lethal mutations. Since \(t^{w73}\) displays all of the properties of \(t\)-haplotypes, it is assumed that there is a conventional \(t^{w73}\) lethal or semilethal factor mapping in the \(t\) region of the chromosome. If this is the case, the parasitic lethal affecting the implantation process must mask the true phenotype of the \(t^{w73}\)-haplotype.

The idea of a 'parasitic mutation' (\(p\)) mapping in the proximal portion of the \(T/t\)-complex in mice carrying the \(t^{w73}\)-haplotype is also supported by the following
observation. When carried in 'balanced lethal' tailless stocks marked with tf (T tf/tf+), all of the naturally occurring t-haplotypes produce recombinant mice by exceptional cross-over events at the rate of approximately 1 in every 500–1000 births, as shown in Fig. 1. The recombinant phenotypes from such crosses include tailless tufted and normal-tailed non-tufted animals. However, in a total of 3282 progeny from T tf/tf+ x T tf/tf+ matings, no normal tailed non-tufted exceptions were found. This suggests that in chromosomes generated by recombination that separates the T tf/tf+ segments retain an additional lethal factor, as diagrammatically presented in Fig. 2. In this case the combination

\[
(p) \ t^T + \ t^w_{73} + \ (p) \ t^T + + \ tf
\]

would be lethal because of homozygosity for the putative parasitic (p) mutation.

It is likely that a separate, later acting Methal or <-semilethal factor is present in the distal region of the T/t-complex of the twlz chromosome. Only after the histological analysis of exceptional recombinants from the twlz haplotype can an assessment of the second or 'true' t^w_{73} phenotype be made. Experiments have been initiated to separate the t^l region of the t^w_{73}-haplotype from the (p) t^T segment.

![Diagram of exceptional recombination](image-url)
Genetic analysis of the $t^{w73}$ haplotype

Brachyury chromosome $T_{qk} + tf$

$t^{w73}$ chromosome $(p)t^T + t^{w73} +$

Exceptional recombination

Recombinant chromosomes Parental gametes

$T_{qk} t^{w73} + (p)t^T + + tf$

$T_{qk} + tf (p) + +$

Progeny genotypes

$T_{qk} + tf T_{qk} + tf (p) + +$

$T_{qk} + tf (p)+ +$

$T_{qk} + tf (p)+ +$

$T_{qk} + tf (p)+ +$

lethal
tailless
lethal

Fig. 2. Exceptional recombination in $T tf/t^{w73} \times T tf/t^{w73}$ matings.

This work was supported by NSF Grant PCM 77-17835, NCI Core Grant CA-08748, NIH Grant HD-10668, and DOE Contract DE-AC02-77EV04159. Dr Bruce Babiarz was supported by National Research Service Award 1 F32 HD-09647.

REFERENCES


SILVER, L. M. (1981). A structural gene ($Tcp-1$) within the mouse t complex is separable from effects on tail length and lethality but may be associated with effects on spermatogenesis. *Genetical Research* (in the Press).


